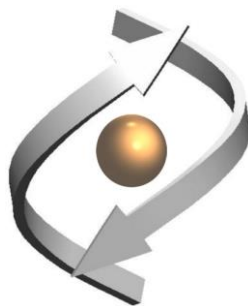


Multi-cage systems and dynamic transformations

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What is the most resilient parasite? Bacteria? A virus? An intestinal worm? An idea. Resilient... highly contagious. Once an idea has taken hold of the brain it's almost impossible to eradicate. An idea that is fully formed - fully understood - that sticks; right in there somewhere.

Cobb, Inception

Abstract

Biological systems use multi-component low-symmetry receptors with dynamic structures operating in networks far from equilibrium to perform complex functions. While coordination cages have taken great inspiration from the structure of these receptors by harnessing their cavities, the use of their dynamic nature and function is still in its infancy. The introduction of heteroleptic cages has brought the possibility of forming low-symmetry assemblies but also of going towards multi-functional species. However, several of the previously described features are missing to this day in order to get closer to biological complexity and function.

Hence, this thesis aims to introduce a new concept in the field: multi-cage systems. The complexity does not only arise anymore from the number of components in a single assembly but from the number of discernable assemblies and their structure within a population of cages. A new type of self-sorting namely *heteromeric complete self-sorting* is coined and defines cage populations where multiple heteroleptic structures coexist orthogonally. This is further extended to the creation of cage systems in which heteroleptic and homoleptic hosts coexist. This concept allows a further step towards mimicking biological systems as it enables the possibility of both *intramolecular* and *intermolecular* transmission of information. Multiple coexisting assemblies can in theory perform orthogonal, cooperative or antagonist functions opening new avenues for the applications of cages in systems chemistry.

The proof of concept of multi-cage systems is introduced by taking advantage of a singular diketopyrrolopyrrole (DPP) ligand, which can adopt distinct conformations and thus offers the possibility of forming coexisting cages with different topologies. One of these topologies is the *trans*-figure-of-eight Pd₂A₂B₂ heteroleptic structure and is central to most of the results of the thesis. The two DPP ligands form the eight by adopting an *S* shape conformation and interlacing in the middle of the assemblies, occupying the cavity. It allows a precise arrangement of ligands, giving also robust heteroleptic cages, and owns an inherent chirality as the “8” can adopt *P* or *M* chirality. Not only this ligand is fostered for its structure and variability of conformation but it is also a well-known dye with strong luminescence. Therefore, we demonstrate its use for the emergence of a new multi-cage self-sorting as well as its utilization for the formation of single multi-chromophore assemblies with outstanding photophysical properties thanks to *intramolecular* energy transfer.

A second system presenting the premises of functionality is then introduced. Taking advantage of guest affinity, we show that an increase in the number of components of a system results in the simplification of its self-sorting outcome. This can be seen as a case of “simplicity”. A heteroleptic cage can eventually coexist with a homoleptic host-guest complex and subsequently uptake another anionic guest orthogonally to the first binding event. This is defined as *guest segregation* in a multi-cage system and differs from the classical narcissistic self-sorting. Further harnessing the slight guest affinity for one of the homoleptic species finally allows the creation of a system where three host-guest complexes coexist orthogonally without shuffling their components or guests.

Eventually, the concept of cage population is extended to dynamic mixtures in which competition for resources between components allows the emergence of chiral memory and out-of-equilibrium phenomenon. We use a chiral ligand derived from the Tröger base structure to both induce chirality on pristine fullerene C₆₀ and C₇₀ and drive the formation of a unique chiral diastereoisomer of the figure-of-eight species. Because of the high affinity of this ligand to form a host-guest complex with fullerene, it is then possible to create a transformable multi-cage system in which the chiral figure-eight ‘releases’ its outer ligands and exchanges them for non-chiral ones. However, we still observe a chiral answer in circular dichroism witnessing the (partial) retention of chirality of the central “8” created by the DPP ligands. We then take advantage of the differences in both thermodynamic and kinetic behaviors to drive the transformative system out of equilibrium and demonstrate the transient formation of the chiral figure-eight before its decay to reform the thermodynamically preferred complex with fullerene.

This thesis introduces the concept of populations, networks, segregated functions, and transformative out-of-equilibrium behavior in the field of cages.

Zusammenfassung

Biologische Systeme nutzen Multikomponenten-Rezeptoren mit geringer Symmetrie und dynamischen Strukturen, die in Netzwerken fernab des Gleichgewichts arbeiten, um komplexe Funktionen zu erfüllen. Koordinationskäfige sind durch die Nutzung ihrer Kavitäten von der Struktur dieser Rezeptoren sehr inspiriert sind, allerdings steckt die Verwendung ihrer dynamischen Natur und Funktion noch in den Kinderschuhen. Die Einführung heteroleptischer Käfige hat die Möglichkeit eröffnet, Assemblierungen mit geringer Symmetrie zu bilden, aber auch multifunktionale Spezies zu entwickeln. Allerdings fehlen bis heute mehrere der zuvor beschriebenen Merkmale, um der biologischen Komplexität und Funktionalität näher zu kommen.

Daher zielt diese Arbeit darauf ab, ein neues Konzept auf diesem Gebiet einzuführen: Multikäfigsysteme. Die Komplexität ergibt sich nicht mehr nur aus der Anzahl der Komponenten in einer einzelnen Assemblierung, sondern aus der Anzahl der unterscheidbaren Assemblierungen und ihrer Struktur innerhalb einer Population von Käfigen. Es wird eine neue Art der Selbstsortierung, nämlich die heteromere komplementäre Selbstsortierung, definiert. Hierbei handelt es sich um Käfigpopulationen, in denen mehrere heteroleptische Strukturen orthogonal koexistieren. Dies wird weiter ausgedehnt auf die Schaffung von Käfigsystemen mit heteroleptischen und homoleptischen Wirten. Dieses Konzept stellt einen weiteren Schritt zur Nachahmung biologischer Systeme dar, da es die Möglichkeit einer intramolekularen und intermolekularen Informationsübertragung bietet. Theoretisch können mehrere koexistierende Assemblierungen orthogonale, kooperative oder antagonistische Funktionen ausüben, was neue Wege für die Anwendung von Käfigen in der Systemchemie eröffnet.

In den hier vorgestellten Multikäfigsysteme wird ein einzelner Diketopyrrolopyrrol (DPP)-Ligand genutzt, welcher verschiedene Konformationen einnehmen kann und somit die Möglichkeit bietet, nebeneinander existierende Käfige mit unterschiedlichen Topologien zu bilden. Eine dieser Topologien ist die *trans*-Figur Acht heteroleptische Pd2A2B2-Struktur und steht im Mittelpunkt der meisten Ergebnisse dieser Arbeit. Die beiden DPP-Liganden bilden die Acht, indem sie eine S-förmige Konformation annehmen und sich in der Mitte der Anordnungen verschränken, wodurch der Hohlraum besetzt ist. Das ermöglicht eine präzise Anordnung der Liganden, wodurch auch robuste heteroleptische Käfige entstehen, und führt zu einer inhärente Chiralität, da die Acht eine P- oder M-Chiralität annehmen kann. Dieser Ligand ist nicht nur wegen seiner Struktur und Variabilität in der Konformation interessant, sondern ist auch ein bekannter Farbstoff mit intensiver Lumineszenz. Daher demonstrieren wir seine Verwendung für die Entstehung einer neuen Selbstsortierung mit mehreren Käfigen sowie seine Nutzung für die Synthese einzelner Multi-Chromophor-Assemblierungen mit hervorragenden photophysikalischen Eigenschaften, welche auf intramolekularem Energietransfer beruhen.

Anschließend wird ein zweites System mit den Prämissen der Funktionalität vorgestellt. Unter Ausnutzung der Gastaffinität zeigen wir, dass eine Erhöhung der Anzahl der Komponenten eines Systems zu einer Vereinfachung seiner Selbstsortierung führt. Ein heteroleptischer Käfig kann mit einem homoleptischen Wirt-Gast-Komplex koexistieren und anschließend einen weiteren anionischen Gast orthogonal zum ersten Bindungsereignis aufnehmen. Dies wird als Gastsegregation in einem Mehrkäfigsystem definiert und unterscheidet sich von der klassischen narzisstischen Selbstsortierung. Wenn man sich die geringe Affinität der Gäste zu einer der homoleptischen Spezies der Systeme zunutze macht, kann man schließlich ein System schaffen, in dem drei Wirt-Gast-Komplexe orthogonal koexistieren, ohne ihre Komponenten oder Gäste zu vertauschen.

Schließlich wird das Konzept der Käfigpopulation auf dynamische Mischungen erweitert, in denen die Konkurrenz um Ressourcen zwischen den Komponenten das Entstehen eines chiralen Gedächtnisses und ein Phänomen fernab des Gleichgewichts ermöglicht. Wir verwenden einen chiralen Liganden, der von der Struktur der Trägerschen Base abgeleitet ist, um sowohl die Chiralität von unmodifiziertem Fulleren C60 und C70 zu induzieren

als auch die Bildung eines einzigen chiralen Diastereomers der Figur Acht zu begünstigen. Aufgrund der hohen Affinität dieses Liganden zur Bildung eines Wirt-Gast-Komplexes mit Fulleren ist es dann möglich, ein transformierbares Multikäfigsystem zu schaffen, in dem die chirale Acht ihren äußeren Liganden "freisetzt" und gegen nicht-chirale Liganden austauscht. Wir beobachten jedoch weiterhin eine chirale Antwort im Zirkulardichroismus, welche die (partielle) Retention der Chiralität der durch die DPP-Liganden gebildeten zentralen Acht bezeugt. Anschließend nutzen wir die Unterschiede im thermodynamischen und kinetischen Verhalten, um das transformative System aus dem Gleichgewicht zu bringen und die vorübergehende Bildung der chiralen Figur Acht zu demonstrieren, bevor sie zerfällt und den thermodynamisch bevorzugten Komplex mit Fulleren bildet.

In dieser Arbeit wird das Konzept der Populationen, Netzwerke, segregierten Funktionen und des transformativen Verhaltens fernab des Gleichgewichts auf dem Gebiet der Käfige eingeführt.

Awards

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- SupraChem Mainz 2022, *Thieme Chemistry* Poster Prize, July 5, 2022
- RSC Twitter 2022, *RSC Inorganic* Poster Prize, March 1, 2022
- ISMSC 2021, *Dalton Transaction* Poster Prize, July 12, 2021

Conferences and Contributions

Poster presentation

May 2024	SupraParis
February 2024	SupraChem Ulm
June 2023	ISMSC Iceland
Sept.2022	GRK symposium
August 2022	ICCC Rimini
July 2022	SupraChem Mainz
March 2022	RSC Twitter Conference
Dec. 2021	MASC 2021
July 2021	ISMSC 2021
July 2021	Systems Chemistry Symposium

Oral presentation

May 2024	Girona Seminar
Dec. 2023	Ph.D Seminars TU Dortmund
Sept. 2023	GRK 2376 retreat
June 2022	Tag der Chemie, TU Dortmund

Publications

Published works

- (1) Kristina E. Ebbert†, **Elie Benchimol**†, André Platzek, Christoph Drechsler, Joseph Openy, Shota Hasegawa, Julian J. Holstein and Guido H. Clever, “Ring-Size Control and Guest-Induced Circularly Polarized Luminescence in Heteroleptic Pd₃A₃B₃ and Pd₄A₄B₄ Assemblies” , **Angew. Chem. Int. Ed.**, 2024, DOI:10.1002/anie.202413323.
- (2) **Elie Benchimol**, Kristina. Ebbert, Alexandre Walther, Julian. Holstein, Guido Clever, “Ligand Conformation Controls Assembly of a Helicate/Mesocate, Heteroleptic [Pd₂L₂L'₂] Cages and a Six-Jagged [Pd₆L₁₂] Ring” **Chem. Eur. J.** 2024, DOI: 10.1002/chem.202401850.
- (3) **Elie Benchimol**†, Irene Regeni†, Bo Zhang, Michele Kabiri, Julian J. Holstein, Guido H. Clever*, “Heteromeric Complete Self-Sorting in Coordination Cage Systems”, **J. Am. Chem. Soc.** 2024, 146, 10, 6905–6911.
- (4) Kai Wu, **Elie Benchimol**, Ananya Baksi, Guido H. Clever*, “Non-statistical assembly of multicomponent [Pd₂ABCD] cages”, **Nat. Chem.** 2024, 16, 584–591.
- (5) **Elie Benchimol**, Jacopo Tessarolo*, Guido H. Clever*, “Photoswitchable coordination cages”, **Nat. Chem.** 2024, 16, 13–21. (Perspective article)
- (6) Lukas V Hoff, Simon D Schnell, **Elie Benchimol**, Fabio Pereira Foutinho, Andrea Tomio, Michel Rickhaus*, Karl Gademann*, “Preparation of 3-Bromo-1, 2, 4, 5-tetrazine”, **Helv. Chim. Acta** 2023, 106, e2022001.
- (7) Jacopo Tessarolo†, **Elie Benchimol**†, Abdelaziz Jouaiti, Mir Wais Hosseini, Guido H. Clever*, “Modular enhancement of circularly polarized luminescence in Pd₂A₂B₂ heteroleptic cages”, **Chem. Commun.** 2023, 59, 3467-3470.
- (8) Kevin Artmann, Ru-Jin Li, Selina Juber, **Elie Benchimol**, Lars V. Schäfer, Guido H. Clever*, Patrick Nuernberger*, “Steering the ultrafast opening and closure dynamics of a photochromic coordination cage by guest molecules”, **Angew. Chem. Int. Ed.**, 2022, 61, e20221211.
- (9) **Elie Benchimol**, Bao-Nguyen T Nguyen, Tanya K Ronson, Jonathan R. Nitschke*, “Transformation networks of metal–organic cages controlled by chemical stimuli”, **Chem. Soc. Rev.**, 2022, 51, 5101-5135. (Review article)
- (10) Katerina Duskova, Pauline Lejault, **Elie Benchimol**, Régis Guillot, Sébastien Britton, Anton Granzhan*, David Monchaud*, “DNA junction ligands trigger DNA damage and are synthetic lethal with DNA repair inhibitors in cancer cells”, **J. Am. Chem. Soc.** 2020, 142, 1, 424–435.

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Submitted and in preparation

- (1) Weichao Xue,* **Elie Benchimol**, Alexandre Walther, Nianfeng Ouyang, Julian J. Holstein, Tanya K. Ronson, Yujuan Zhou, Kai Wu, Rituparno Chowdhury, Guido H. Clever,* and Jonathan R. Nitschke*, “Interplay of Stereochemistry and Charge Governs Guest Binding in Flexible $Zn^{II}_4L_4$ Cages”, **submitted**
- (2) Mateusz Pawlak, Adam Pierzchała, **Elie Benchimol**, Jacopo Tessarolo, Lukas Rebholz, Marjan Krstić, Benedikt Zerulla, Ivan Fernandez-Corbaton, Tamás Jávorf, Giuliano Siligardi, Guido Clever, Carsten Rockstuhl,* and Wiktor Lewandowski*, “Highly Dissymmetric Circularly Polarized Luminescence via Multimode Chirality Induction in Liquid Crystal Templated Films”, **submitted**
- (3) **Elie Benchimol**†, Helen M. O’Connor†, Björn Schmidt, Julian J. Holstein, June I. Lovitt, Sankarasekaran Shanmugaraju, Guido H. Clever,* and Thorfinnur Gunnlaugsson*, “Circular Dichroism of Fullerenes C_{60} and C_{70} Encapsulated in an Enantiopure Pd_2L_4 Capsule”, **in preparation**
- (4) **Elie Benchimol**, Andrea Rivoli, Michele Khabiri, Bo Zhang, Julian J. Holstien, Pablo Ballester and Guido H. Clever*, “Guests segregation in heteromeric multi-cage system”, **in preparation**
- (5) **Elie Benchimol**, Rituparno Chowdhury, Irene Regeni, Nicola Bogo, Laura Neukirch, Alexandre Walther, Christopher Stein, Sascha Feldman and Guido H. Clever*, “Fine-tuning of Förster energy transfer efficiency in $Pd(II)$ heteroleptic cages”, **in preparation**
- (6) **Elie Benchimol**, Jacopo Tessarolo,* Haeri Lee, Abdelaziz Jouaiti, Mir W. Hosseini and Guido H. Clever*, “Ligand bulk controls the formation and chiral induction of heteroleptic $Pd_4A_4B_4$ tetrahedron and unconventional $Pd_2A_2B_4$ rings”, **in preparation**
- (7) **Elie Benchimol**, Laura Neukirch, Alexandre Walther and Guido H. Clever, “Chromophore embedded coordination cages and applications”, **in preparation** (Review article)
- (8) **Elie Benchimol**, Björn Schmidt, Helen M. O’Connor, Irene Regeni, Thorfinnur Gunnlaugsson,* and Guido H. Clever*, “Out of equilibrium $Pd(II)$ cage population with emerging chiral memory”, **in preparation**
- (9) Alvaro Polo†, **Elie Benchimol**†, Bastian Grabe, Yiming Yang, Alexandre Walther, Weichao Xue, Konstantin Jahn, Wolf Hiller and Guido H. Clever*, “Deciphering the thermodynamic and kinetic of Pd_4L_8 double and Pd_2L_4 single cage equilibrium by using pressure and temperature responsiveness”, **in preparation**
- (10) Björn Schmidt, **Elie Benchimol**, Helen M. O’Connor, Thorfinnur Gunnlaugsson,* and Guido H. Clever*, “Multi-stimuli responsive interconversion between chiral Pd_2L_4 cage and $Pd_4L_6X_4$ box”, **in preparation**
- (11) Christoph Drechsler, **Elie Benchimol**, and Guido H. Clever*, “Dissipative guest binding based on slow double cage formation”, **in preparation**
- (12) Laura Neukirch, Elie Benchimol, Jennifer Bou Zeid, Alexandre Walther, Marc Sallé, Sébastien Goeb,* and Guido H. Clever*, “Redox-responsive tetranuclear $Pd_4A_2B_4$ cages”, **in preparation**
- (13) Jennifer Bou Zeid, Laura Neukirch, Elie Benchimol, Marc Sallé, Sébastien Goeb,* and Guido H. Clever*, “Redox-stimulus allows switching between narcissistic and integrative self-sorting”, **in preparation**

Tentative working titles and author lists for the manuscript in preparation

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Table of content

General Introduction.....	15
1. A brief history of coordination cages.....	16
2. Complex self-sorting in coordination cage systems.....	19
2.1. Pd(II)-based heteroleptic assemblies.....	20
2.2. Protected metal-ions	23
2.3. Heteroleptic species based on other metals	24
3. Complex transformation networks.....	26
4. Complex system behaviors	30
5. Multi-cage systems	37
6. References.....	41
Scope of the thesis	46
Chapter I.....	49
Introduction	50
1. <i>Trans</i> heteroleptic Pd ₂ A ₂ B ₂ figure-of-eight assemblies and pseudo statistical mixture	51
2. From statistical mixture to heteromeric complete self-sorting of Pd ₂ A ₂ B ₂ figure-of-eight	53
3. From integrative to heteromeric complete self-sorting of Pd ₂ A ₂ B ₂ cages	54
4. Stoichiometry controlled self-sorting outcome: integrative vs heteromeric	59
5. <i>Trans</i> -heteroleptic figure-of-eight cages as a platform for intra-assembly energy transfer	62
Conclusion and outlook.....	69
6. Experimental section	70
7. References.....	125
Chapter II.....	127
Introduction	128
1. Assembly characterization	129
2. Guest-induced multi-cage system	130
3. Guests segregation I in multi-cage system.....	134
4. Guest segregation II in multi-cage system	138
Conclusion and outlook.....	139
5. Experimental section	140
6. References.....	168
Chapter III.....	171
Introduction	172
1. Tröger base ligand for chiral fullerene receptors	173
2. Homochiral figure-of-eight cage.....	182
3. Self-sorting and first steps into dynamic cage populations.....	185
4. Emergence of chiral memory	190
5. Dissipative nature of the transformation.....	193
6. Signal transduction and complex population control	197
Conclusion and Outlook	203
7. Experimental section	204
8. References.....	271
Conclusion and Personal Perspectives	273
Other Scientific Contributions	274

General Introduction

A world of cages

1. A brief history of coordination cages

When Saalfrank and coworkers published their first report on a self-assembled tetrahedral structure in 1988 (Figure 1),^[1] it is difficult to think they imagined how broad the realm of architectures that would derive from the same principles could be. Yet, further pioneered by giants like Makoto Fujita,^[2] Kenneth Raymond^[3] or Peter Stang,^[4] these self-assembled nano-objects have known an exponential growth in the last decades. One can find on a weekly basis new reports of coordination-driven supramolecular entities, flourishing in the literature greatly helped by the variety of metal cations or organic bridges that can be employed for their formation.

Saalfrank's initial report

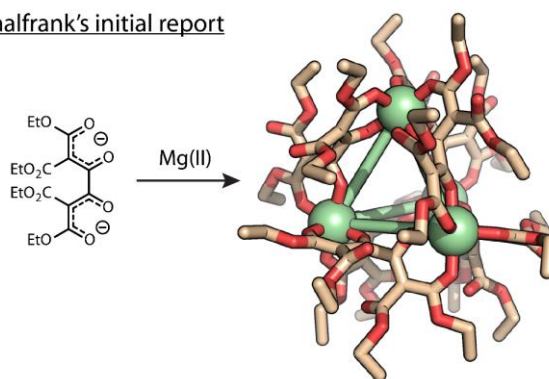


Figure 1: The first example of a ‘coordination cage’ reported by Saalfrank featuring Mg(II) cations bridged by anionic organic linkers.

In an interesting way, the three aforementioned pioneers of the field all adopted a different approach nearly simultaneously, to obtain similar yet very distinct, three-dimensional metal-organic architectures. On the one hand, Fujita and his group turned towards square-planar coordinated Pd(II) cations equipped with *cis*-protecting groups in combination with triangular panels with tris-pyridyl donors, yielding the now iconic “Fujita cage” or more scientifically correct a Pd₆L₄ octahedron (Figure 2). On the other hand, Raymond and his group focused on another type of organic moieties, namely catecholates, offering a different horizon in terms of coordination (Figure 2). They employed metals possessing an octahedral coordination geometry which enabled the formation of M₄L₆ tetrahedral assemblies, closer to Saalfrank’s initial report. It was very fast that they realized how versatile their approach was and diversified the metals as well as core organic moieties employed, but we will come to this discussion a bit further in this dissertation. Eventually, Stang also opted for square planar metals Pd(II) and Pt(II) but mastered the use of the latter one taking advantage of its more kinetically inert nature as well as easier access to (*cis*- and) *trans*-protected derivatives. Through this approach, and with a careful choice of bridges, they were able to create bigger objects such as cuboctahedra.

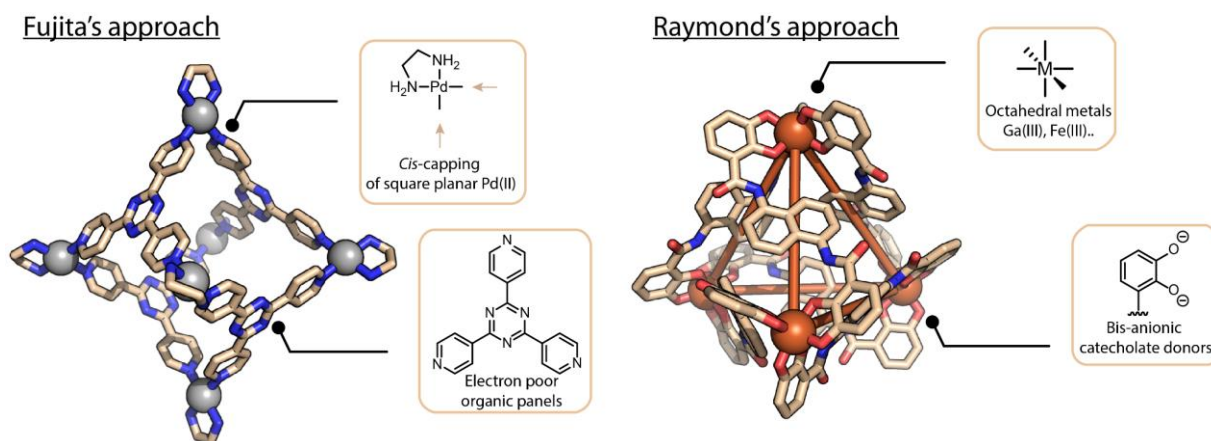


Figure 2: (Left) Pd₆L₄ octahedral cage reported in 1995 with triazine electron-poor organic panels covering half of the faces of an octahedron in which the vertexes are occupied by *cis*-protected Pd(II) cations. (Right) Raymond-type coordination cage: Tetrahedral assemblies with octahedral metals at the vertexes and aromatic bis-anionic catecholates along the edges of the polyhedron.

These initial studies have set the floor for the field and strongly influenced how the next generation, concomitantly to these groups, thought about the design principles for the creation of coordination-driven cages. The seeds quickly took off and a plethora of architectures started blooming in rather high journals, witnessing the newly discovered interest of a broader community towards these beautiful and soon more functional three-dimensional objects.^[5–9] However, a new wave of ideas was already emerging and will soon take over the world of metal-organic cages. In the background, Raymond focused on diversifying the tetrahedral cages and employed them to make the first “functional” assemblies with a strong interest in developing nanovessels with enzyme-like behavior and catalytic applications.^[10–12] This will later be taken over by Toste, initially an expert in catalysis.^[13,14] Stang turned even more towards Pt(II), also to develop photophysical applications.^[15–17] But, Steel and McMorran opened a new route when they employed “naked” Pd(II) cations with bis-monodentate ligands and reported the hexafluorophosphate templated formation of a quadruple-stranded Pd₂L₄ helicate or later coined “lantern-shaped” cage (Figure 3).^[18] This report, sometimes forgotten, sets the tone for some crucial parameters that need to be considered when creating new coordination-driven objects (not only with Pd(II)). As also observed by Raymond,^[19] templation can play a role in the formation of an assembly. But solvation effects are not to be disregarded, they are central. It also shows that employing more flexible organic moieties can yield distinct outcomes depending on the assembly conditions, an effect already observed prior to this report, and based on the rigid but dynamic nature of the metal-ligand bond. The second wave that will shake the field would arguably be the introduction of subcomponent self-assembly (Figure 3)^[20,21] which has played a pivotal role, led by the effort of the Nitschke group, in developing robust, yet very dynamic, and functional nano-hosts presenting very often outstanding host-guest properties.

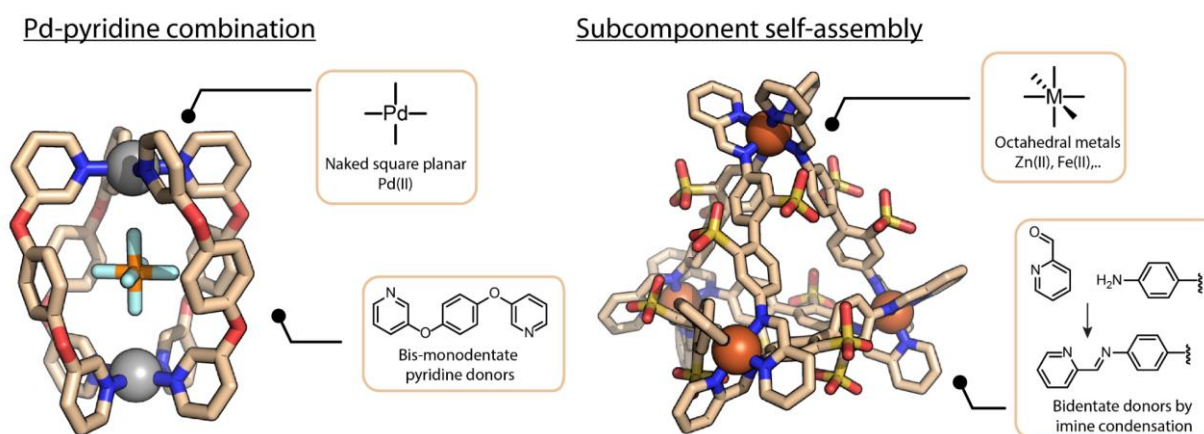


Figure 3: (Left) Steel's and McMorran's first instance of Pd₂L₄ cage with bis-pyridyl donors. (Right) Subcomponent self-assembly strategy in which the condensation of an imine creates a bidentate donor moiety coordinating (most often) an octahedral metal. Both dynamic covalent bonds and coordination bonds are implicated in this process.

If we look from a larger perspective, the lability of some of the metal-ligand bonds is the central feature of the field of coordination cages (Figure 4). One could disagree and tell that the cavity is occupying this place, but I would argue that the creation of cavities, functional or not, symmetrical or not, small or big, occupied or not, is fully conditioned by the metal-ligand bond lability offering the possibility of accessing such a wide (wild?) range of architectures. The control over this lability by a subtle balance between stiffness and error correction will be fully exploited by Makoto Fujita in the quest for Pd_nL_{2n} giant assemblies which has given rise to virus capsid-like assemblies,^[22–24] new polyhedral species,^[25] and nowadays entangled links based on other metals^[26,27] as well as endo-functionalized hollow spheres.^[28,29] It is also one of the factors at the origin of the formation of heteroleptic assemblies bearing multiple distinct building blocks,^[30] or guest-driven transformation by induced-fit phenomena (Figure 4).^[31] Eventually, it is greatly exploited in subcomponent self-assembly where the dynamic nature of the metal-ligand bond is intricately linked with the dynamic formation/destruction of imine bonds.^[21] This is an

ingenious way to ensure very stable, owing to the chelating effect offered by bidentate donors, but also tunable and adaptable assemblies, because of the large possible pool of subcomponents accessible.

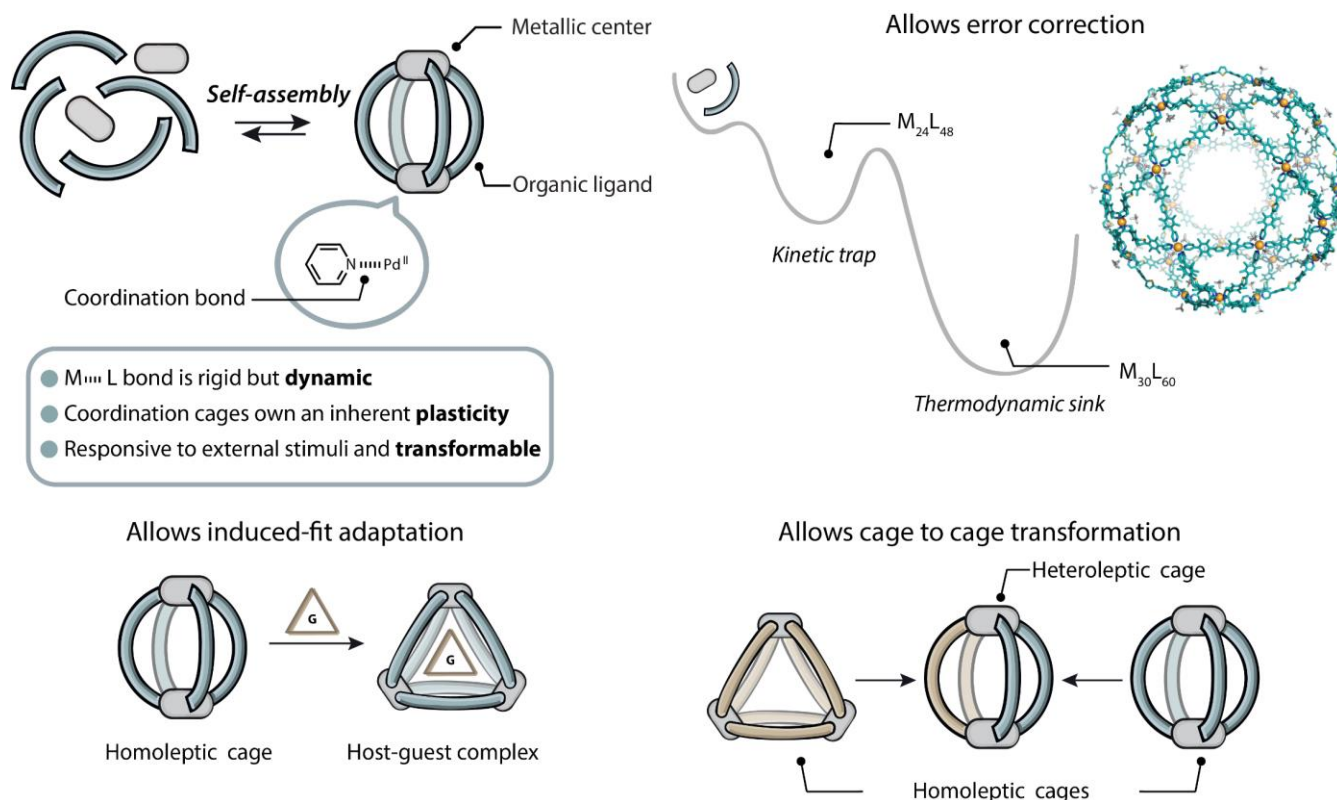


Figure 4: Schematic representation of the formation of coordination cages, depicted as a Pd_2L_4 . The dynamic nature of the coordination bond allows error correction and the formation of the most stable species, induced-fit adaption and cage transformation into, for example, heteroleptic cages.

From focusing on simple stiff building blocks to assemble rigid and fixed Archimedean or Platonic solids the field has slowly driven away to more complex and dynamic structures. The aim, however, is practically unchanged. Supramolecular cage chemists want to mimic bioreceptors or in a more general term “bio-systems” and their functions. Coordination cages present numerous of the necessary parameters allowing such mimicry. Deciphering the targeted features of their bio-analogs is therefore the first step for the design of innovative and novel assemblies or systems.

This first introduction chapter is an attempt to look back at already crafted “complex coordination cage systems” and envision the challenges ahead. Three axes, obviously strongly correlated, can be identified as emerging now in the literature and getting closer to the biological level. (1) Complex self-sorting processes (2) Complex transformation networks (3) Complex system behaviors. The following chapters of this dissertation will then add their humble contributions to each of these categories.

2. Complex self-sorting in coordination cage systems

Molecular receptors such as enzymes are not highly symmetrical entities.^[32–35] The selectivity of such molecules is actually often related to the specific size, shape and decoration of their substrate-binding pocket. As nature has engineered its workers through billions of years of evolution to tune the multiple amino acids, organic moieties and/or metal complexes used for a defined function, we, chemists, can get a glimpse into such manipulation. The question of selective multicomponent self-assembly (and thus self-sorting) was identified in 2005 in a special issue of *Science Magazine*^[36] as one of the central questions to be answered by scientists. For pushing this, multiple components with precise structural and/or functional abilities should be assembled concomitantly. Thus, we must comply with intrinsic physical/chemical rules that have been identified through serendipity and design.^[37,38]

Transitioning from homoleptic to heteroleptic self-assembled objects is nonetheless a more delicate process than it seems.^[37,39] Three distinct outcomes can arise namely statistical distribution, narcissistic self-sorting and so-called integrative self-sorting (Figure 5). While the first mentioned process is somewhat undesirable because not selective, the two others must be explained because they mean that the system undergoes “sorting”, so the creation of a certain level of order. Enthalpic factors must overcome the tendency to create mixtures driven by entropy. Narcissistic sorting occurs when different building blocks, let’s take **A** and **B**, can not recognize each other. They will then associate only with the alike molecules. **A** will recognize only **A** and form **AA** pairs, the same phenomenon happening for **B**. Herein, no **AB** pairs are formed. This end result is mostly disregarded when considering an increase in the complexity of in terms of the composition of single assemblies; however, we will see later that it might find its revival in a different type of cage system where several assemblies should coexist in an orthogonal fashion. But, for increasing structural complexity and functionality of single cages, the outcome of choice lies in integrative self-sorting: **A** and **B** recognize each other and associate into an **AB** couple. So, how is this translated into cage systems? This has been the central focus of the Clever Lab for the past years but it has also emerged as a more global target of choice for the field and many groups are now tackling the question (see later for proper referencing). For the sake of clarity, we will divide this into two parts depending on the metal cation of choice. While Pd(II) has really stood out as the favored alternative, thanks to its rather easily controllable square planar coordination, octahedral metals have, as well, shown their potential for holding heteroleptic assemblies together. It is interesting to note that the topic of heteroleptic cages has literally exploded in the span of seven to eight years. Even more to realize how the first examples (for “naked” metal ions) emerged simultaneously within a year between 2015 and 2016^[40–44] but also how the most complex ones were realized during the exact same year in 2023.^[45–50] While one might see this as a fierce competition, I find it rather fascinating and thriving for more beautiful accomplishments, in collaboration, or not, between the different groups tackling the field.

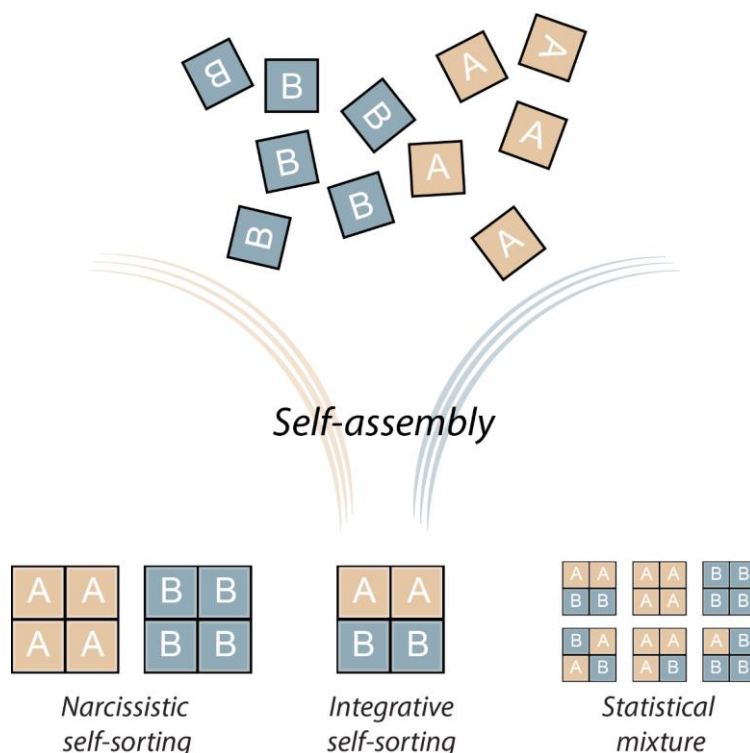


Figure 5: Schematic representation of the self-sorting outcomes between two distinct building blocks A and B in the case of Pd_2L_4 cages.

2.1. Pd(II)-based heteroleptic assemblies

Palladium is by far the most employed metal for the design of coordination cages. This is with no doubt owing to its ease of use in terms of structural control as well as its suitable exchange kinetics and diamagnetism. Mostly combined with bis-pyridyl donor ligands, and taking a look back at Steel and McMorran work,^[18] the more simple assemblies have a Pd_2L_4 structure. It is therefore rather easy to understand how one can increase the structural complexity and functionality of such architectures.^[30] Four different ligands can in principle be combined in a sole species. If these four components happen to be all distinct, a total of 55 species can be obtained without proper integrative self-sorting. But, before going too fast forward, the community has attempted the association of two different components together.

The first reports directly highlighted that there seem to be design rules allowing the formation of $\text{Pd}_2\text{A}_2\text{B}_2$ -type assemblies (Figure 6). These examples set the stage for further development. Herein, it is important to underline again that the metal-ligand bond lability is a key factor allowing (most often) to obtain the thermodynamic minimum of the system. In 2011, Hooley and co-workers introduced a heteroleptic assembly based on **ligand interaction** where bulky substituents positioned on a ligand B in *endo* of the cage cavity biased the stoichiometry and led to the formation of, although not selectively, a $\text{Pd}_2\text{A}_3\text{B}$ cage type.^[51] In 2015, Yoshizawa and his group showed that **guest templation** is another strategy to enable heteroleptic cage formation.^[41] Two structurally related ligands, one with a benzene and another with a naphthalene core, although capable of forming separate homoleptic assemblies, do not undergo integrative self-sorting when combined together. However, further introduction of fullerene C_{60} drives the selective formation of a $\text{C}_{60}@\text{Pd}_2\text{A}_2\text{B}_2$ host-guest complex, thanks to an induced-fit phenomenon leading to optimal host-guest interactions. In 2017, Crowley showed that installing amino groups in the ortho outer position of the pyridine donor moieties could also yield selectively a $\text{Pd}_2\text{A}_2\text{B}_2$ cage by another type of ligand interaction namely hydrogen bonding.^[44] Interesting to note that further calculation showed that this cage was, in fact, a kinetic trap and not the thermodynamic product of the system. This could also be classified as **coordination sphere engineering** (CSE), a term coined a year later by Clever when the group

used methyl substituents on both outer and inner ortho positions of the four pyridines around a naked Pd(II) cation to control the steric hindrance at the metal center and lead to Pd₂A₂B₂ cages as well.^[52] A similar technique was employed earlier by Fujita and coworkers but using their usual *cis*-protected Pd(II).^[53] This was further extended to the use of quinolines to introduce a “slight” hindrance at the metal center and allow the formation of various heteroleptic assemblies.^[54–56] Eventually, Clever also introduced the **shape complementary assembly** (SCA) principle in 2016.^[40,57] Worth noting that the same idea was used in other reports of bigger heteroleptic Pd(II) assemblies by Fujita^[43] (although the ligands present the same binding angles) or Chand^[58] (not really a cage) but was not properly rationalized and further exploited. Ligands with matching size and vectors associate with each other driven by the directionality of the Pd(II)-ligand bond. It is also helped by entropic factors leading to the single smallest possible assembly. This often results in a release of strain at the Pd(II) center and for the ligands as compared to what can be observed in several homoleptic structures. These approaches have resulted in an abundance of reports about Pd₂A₂B₂ cages showing the versatility of the methods and reachability of structures. Some of these principles are translated into the formation of higher nuclearity heteroleptic assemblies, but these species won't be discussed in the present subsection.

Following these successful first attempts, increasing further the complexity of Pd₂L₄ stood as a major challenge to achieve in terms of controlled self-assembly. As mentioned earlier, augmenting the number of components comes in pairs with the possibility of forming more isomers. Therefore, the possibility of bridging three or even four distinct organic linkers together in a single cage is a delicate task. In a remarkable synergy, in the span of a year, four reports have been attesting to the formation of heteroleptic cages Pd₂A₂BC or Pd₂ABCD, one being discussed as a chapter of this thesis.^[45,48,49,59] By a combination of the Hooley strategy of ligand bulk interaction and coordination sphere engineering, Zhang and coworkers reported the formation of a Pd₂A₂BC cage.^[48] In this study, the stoichiometry is therefore controlled solely by steric hindrance parameters and all ligands possess the same basic structure, being a benzene core with alkynyl spacers and equipped with pyridines as donor moieties. Diverging from conventional approaches, Hiraoka and colleagues demonstrated that heteroleptic cage formation can proceed under kinetic control^[46]. This actually allows the formation of otherwise non-stable species, because high in energy. This approach is poised to drive further developments in terms of complex behaviors and transformations, although detailed discussions will be deferred to subsequent sections. Nonetheless, they isolated architectures bearing three as well as four different ligands in a stepwise controlled assembly. These cages rely primarily on shape complementary assembly as the formation of a homoleptic or heteroleptic initial Pd₂L₂Cl₂ *trans*-ring is the key structural step. Through this method, the self-assembly is biased and only one isomer is possibly formed at every step. In most cases, prolonged heating resulted in the decomposition or scrambling of the assemblies although several show remarkable time stability.

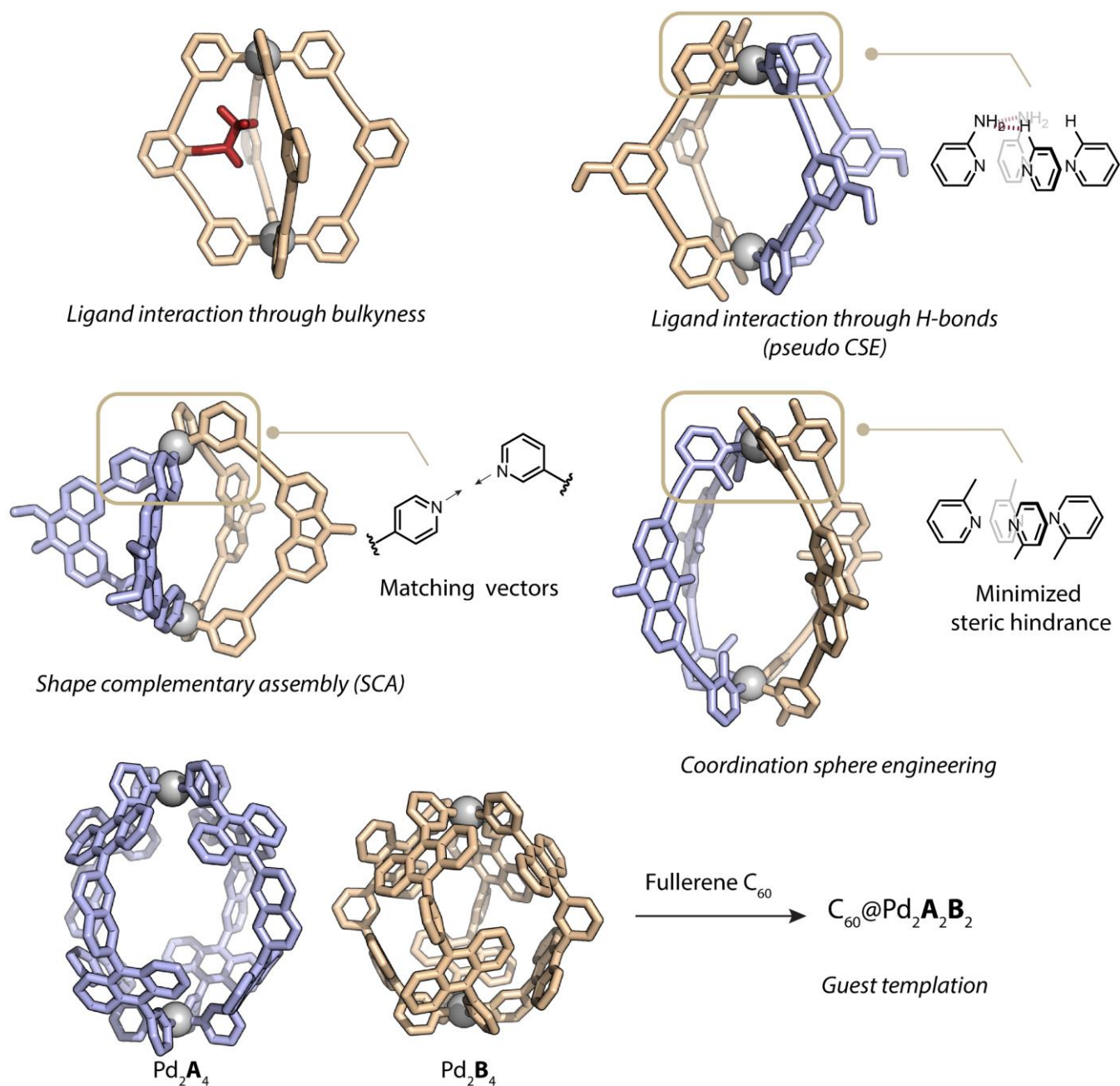


Figure 6: Representation of the strategies developed to create heteroleptic coordination cages based on naked Pd(II) cations.

Eventually, our group tackled the formation of a Pd_2ABCD cage under full thermodynamic control (Figure 7).^[45] By a careful ligand choice, accompanied by a subtle balance between shape complementarity and ligand-ligand C-H $\cdots\pi$ interaction, we demonstrated the formation of a unique species out of the possible 55 isomers. Interestingly, we also showed that the process can be conducted in an incremental fashion, starting with the 4 primary assemblies and forming consecutively by cage to cage transformations the binary, ternary and eventually quaternary species. An in-depth thermodynamic analysis allowed us to decipher the enthalpic and entropic parameters for each step and highlighted the thermodynamic control over the system. So far this constitutes the climax in terms of self-assembly complexity for single heteroleptic metal-organic cages.

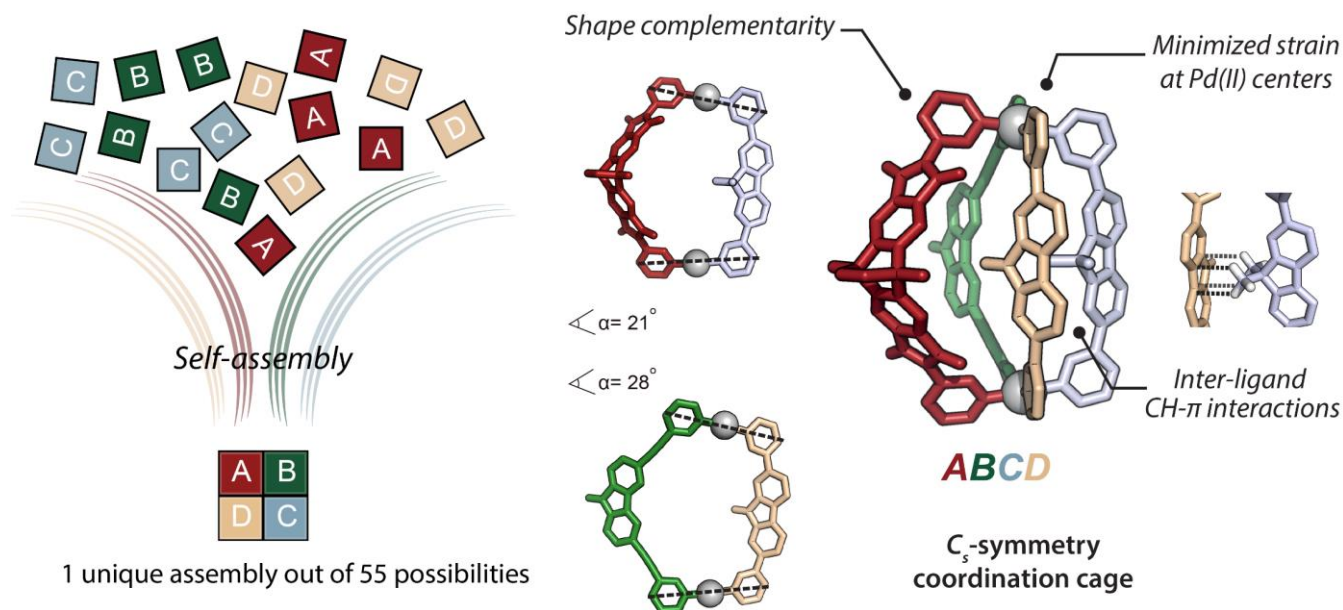


Figure 7: (Left) Schematic representation of the unique outcome, out of 55 possible, obtained from self-assembly of four different building blocks. (Right) X-ray structure of the Pd_2ABCD cage displaying some of the driving forces of its formation.

2.2. Protected metal-ions

While the focus of this introduction is set on homometallic assemblies based on “naked” metal ions, some major contributions to multicomponent self-assembled architecture have been made using protected metal cations. This approach allows the reduction of coordination sites available to undergo the self-sorting process (Figure 8). Herein, strategies have also been established in order to control integrative self-sorting. **Charge separation** or the use of different donor types,^[60,61] one being charged, is one of the aforementioned approaches that is commonly used. Pyridine and carboxylate assembled with Pt(II) has been a combination of choice and several reports, mainly by the Stang and Mukherjee groups, demonstrate the formation of prismatic structures based on this principle.^[62–65] Stang and his group showed by calculations that the heteroleptic coordination mode is drastically favored energetically.^[63] This was further employed in more recent studies to exploit the photophysical properties of Pt(II) assemblies.^[66–68] Ribas and coworkers have also used a similar approach employing a macrocycle with two anchor sites containing, each, three nitrogen donors coordinated to a Pd(II).^[69] The coordination sphere of the metals is completed by combination with a tetracarboxylate porphyrin affording a box-like cage made with two porphyrin moieties and four of the Pd_2 -macrocycles. However, the combination of two neutral donors can also be accomplished for obtaining similar structures, driven by entropic factors favoring the formation of smaller heteroleptic assemblies^[70–72] in a similar manner to **shape complementary assembly**. This approach is greatly inspired by initial work from the Fujita group taking also advantage of **coordination sphere engineering** where two types of pyridine donors, one bearing bulky methyl groups, associate in a heteroleptic fashion^[53,73–75] in order to minimize steric hindrance at the metal center.

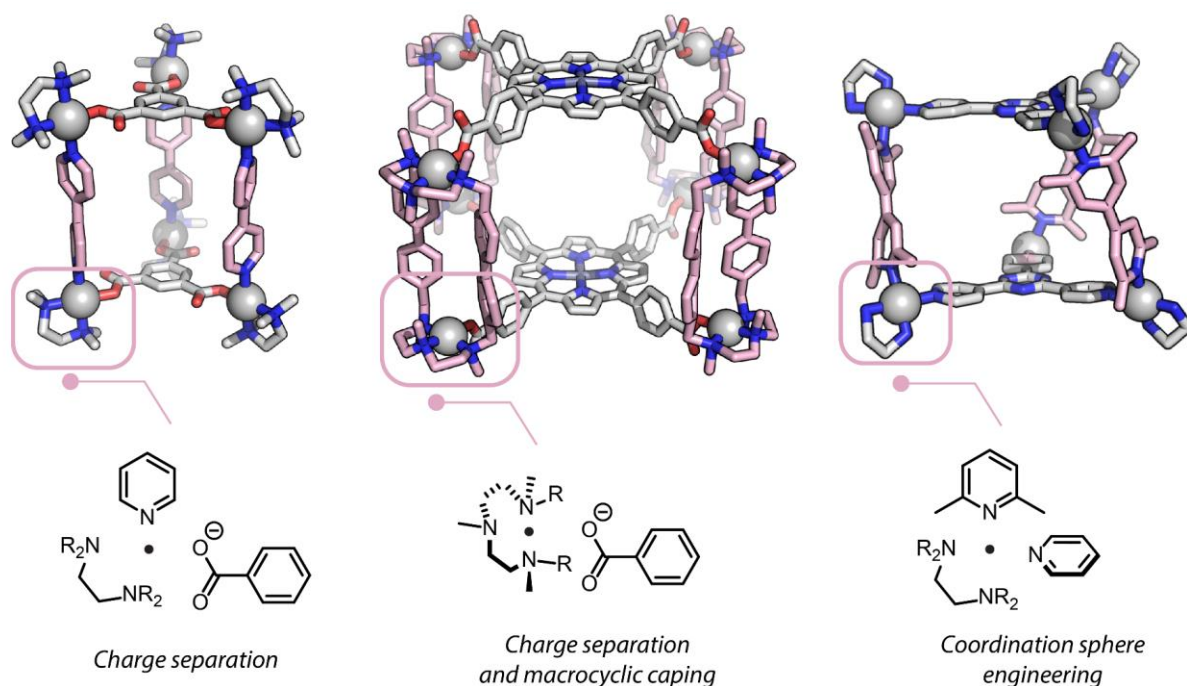


Figure 8: Representation of the different strategies for the formation of heteroleptic cages based on protected square planar metals.

2.3. Heteroleptic species based on other metals

Several examples of heteroleptic cages with other metals have been reported to date.^[76–80] In this case, different strategies can also be identified and exploited for controlling assembly formation. **Coordination sphere engineering** is among the choices when employing metals with a broader coordination geometry. Introducing bulky donor groups or a combination of ligands with different denticity can yield heteroleptic assemblies as shown in very early examples from Lehn.^[81,82] This was largely reintroduced by Schmittl and coworkers^[83] with considerable contributions in designing heteroleptic coordination environments to construct highly complex supramolecular entities.^[84–87]

A second strategy, recently employed by the Nitschke group relies on forming **entropically-driven** self-assembled heteroleptic prisms (Figure 9). This approach takes great advantage of subcomponent self-assembly and octahedral metals with a good lability such as Zn(II). Looking from a further perspective this also takes advantage of a sort of *shape complementarity* between the different types of ligands assembled together. The matching of forms, for example square-shaped and triangular-shaped ligands, yields a trigonal prism if mixed in a 3:2 ratio.^[88–90] The number of single trigonal prisms possibly formed outnumbers the one for cubes and tetrahedrons separately, therefore, the former is favored from an entropic perspective. It also necessitates a matching number of edges at the vertexes of the targeted polyhedron or, in some other cases, the use of adequate subcomponents. This was more recently extended to a rectangular prism by matching two rectangular ligands with fitting edges in a 3:2 ratio.^[91]

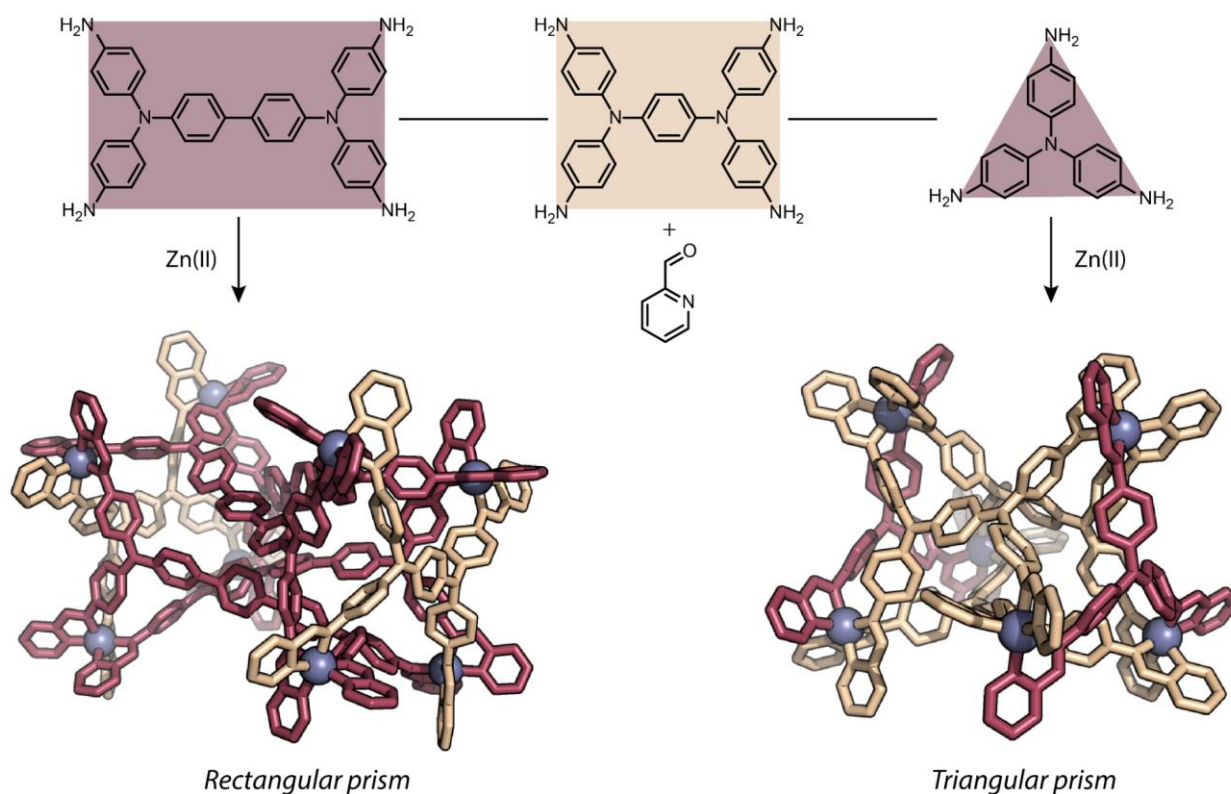


Figure 9: Formation of heteroleptic cages based on octahedral Zn(II) driven by entropy and size matching between the different building blocks.

While not deliberately overlooked, it's worth noting that certain assemblies have the capacity for "complex self-sorting", even if they ultimately result in homoleptic structures. This phenomenon can be observed in various ways, such as a single ligand occupying different positions within an assembly,^[25,92–94] metal vertices adopting different conformations (e.g., *fac* vs. *mer* isomerism),^[95–98] or through the utilization of unsymmetrical ligands,^[99–102] a concept predominantly advanced by Lewis and colleagues^[103–106] as well as Severin^[107–109] in recent studies. Eventually, multi-metallic species also fall into this category and have been reviewed over the years.^[110–112]

3. Complex transformation networks

Another intriguing feature, reminiscent of biological systems, involves the potential for transforming cages through stimuli responsiveness,^[113] which hinges on the dynamic nature of metal-ligand bonds. The concept of creating transformation networks^[114] is captivating as it underlines the prospect of reconfigurable assemblies capable of altering their shapes, sizes, and properties to execute targeted functions. Moreover, it delivers insights into how information can propagate within chemical systems. While most reports to date describe systems under equilibrium conditions, recent studies have ventured into behaviors more akin to the out-of-equilibrium essence of biological transformations (see later). Numerous high-quality reviews have detailed the ability of certain architectures to transform upon exposure to stimuli such as light,^[115,116] guest molecules,^[31] and redox agents^[117] to name a few. Noteworthy examples demonstrating multi-stimuli responsiveness highlight the emergence of more complex, multi-signal-driven processes poised to find diverse applications across a broader chemistry landscape.

Multi-chemically responsive assemblies are the most common in the literature because the rules that govern them are rather well understood while staying under thermodynamic control.^[114] Although switching between two different assemblies upon application of a unique stimulus has been extensively studied, Shionoya and coworkers have shown that it is possible to use a library of triggers for the same aim (Figure 10).^[118] Therefore, solvents, anions, pH and a guest could be utilized to convert a Zn(II) based tetrahedron into its bowl analog.

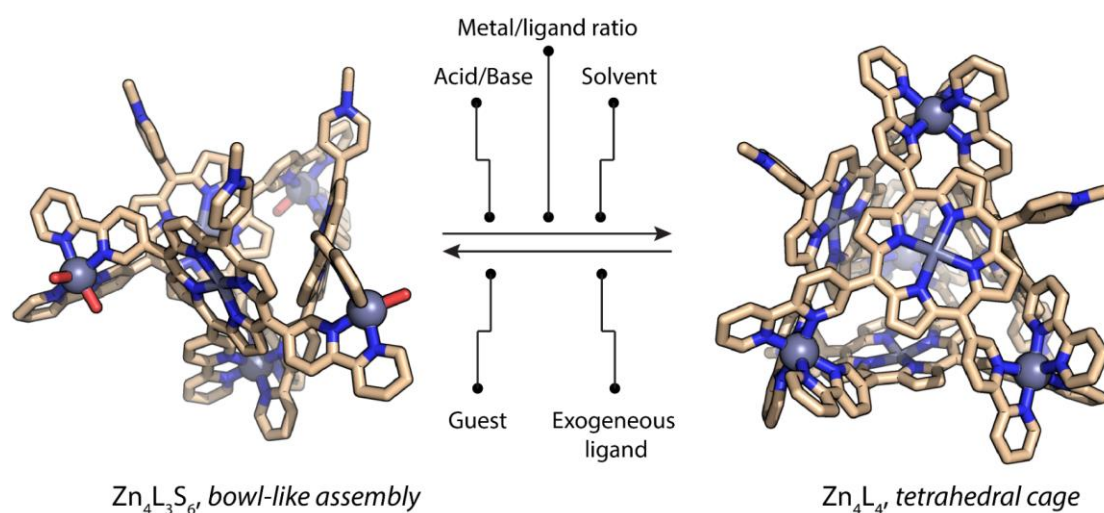


Figure 10: Multi-stimuli responsive reversible cage to cage transformation between a bowl-like assembly and a tetrahedron.

Nitschke and colleagues have shown impressive results in developing networks of cage to cage transformations greatly supported by their subcomponent approach that offers ease in tunability. For example, in 2020 they described a system of eight different Cd(II) assemblies that could be converted upon imine exchanges (Figure 11).^[119] As highlighted by the formation of an unexpected heteroleptic $\text{Cd}_6\text{L}_3\text{L}''_2$ prism, such network creation can lead to the emergence of unpredictable architectures but also behaviors, herein specific guest binding. Such multi-responsiveness extends with chiral ligands where the incorporation of racemic or enantiopure components did drive another system into distinct defined states (chiral social self-sorting vs. formation of *meso*-cage for example).^[120] In this further study, they could also show that some sorting processes presented a solvent dependency. Subcomponent exchange can be coupled, as well, with covalent post-assembly modifications to create intricate transformations with up to seven interconvertible supramolecular structures.^[121] Eventually, guests can be employed, in general driving the formation of smaller assemblies promoting host-guest interactions, either in solution or in the crystalline solid state.^[122] However, some instances have demonstrated that the use of an appropriate template can also drive the formation of higher nuclearity species as reported by

Sun and his group.^[123] Using a flexible bis imidazole ligand they could demonstrate interconversion between several Pd_nL_{2n} ($n=4-7$) homoleptic rings depending on the anions introduced.

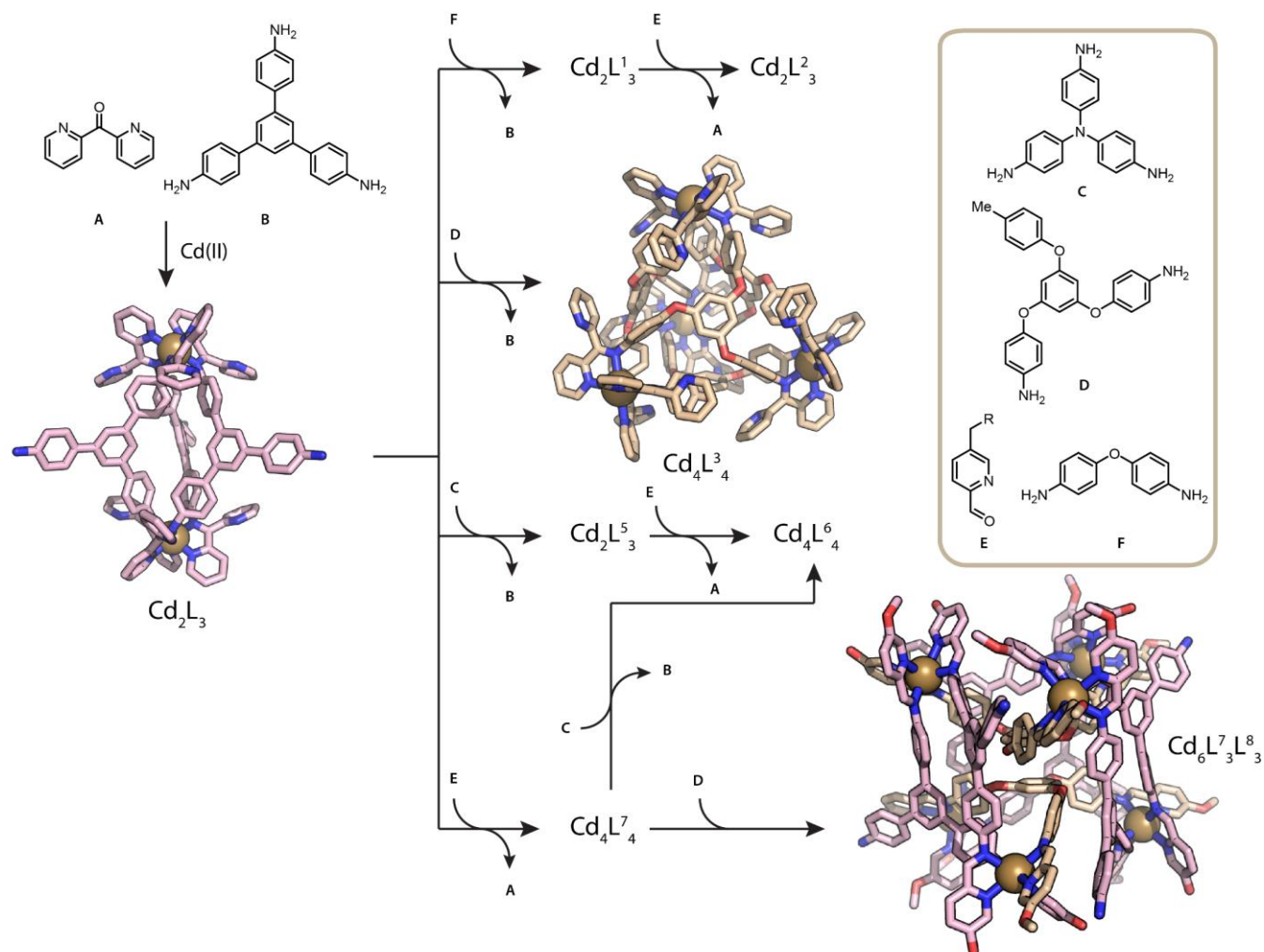


Figure 11: Complex transformation network of coordination cages based on labile Cd(II) cation and the use of subcomponent self-assembly.

Pd(II) cages do serve as an ideal platform for stimuli-responsive systems, given their inherent plasticity as discussed in the preceding section. Another remarkable study from the Sun group showcased the interconversion between three distinct assemblies, two of which are isomeric (*twisted vs. interlaced*).^[124] A variety of stimuli can be applied to switch between these two Pd_3L_6 diastereoisomers and a higher nuclearity Pd_6L_{12} architectures. Termed "twin-cages" or conjoined cages by the authors, these Pd(II) structures, despite their structural differences, consistently feature double cavities (Figure 12). Such systems offer promises for allosteric guest binding or the creation of intricate supramolecular catalytic setups. Additionally, Chand and colleagues have developed other interconvertible conjoined cages, marking a gradual advancement in leveraging heteroleptic assemblies for similar processes.^[125] The use of several extended ligands in association with Pd(II) ensured the formation of distinguishable cavities in homoleptic and heteroleptic cages, but their use for the emergence of complex behaviors will be discussed later.

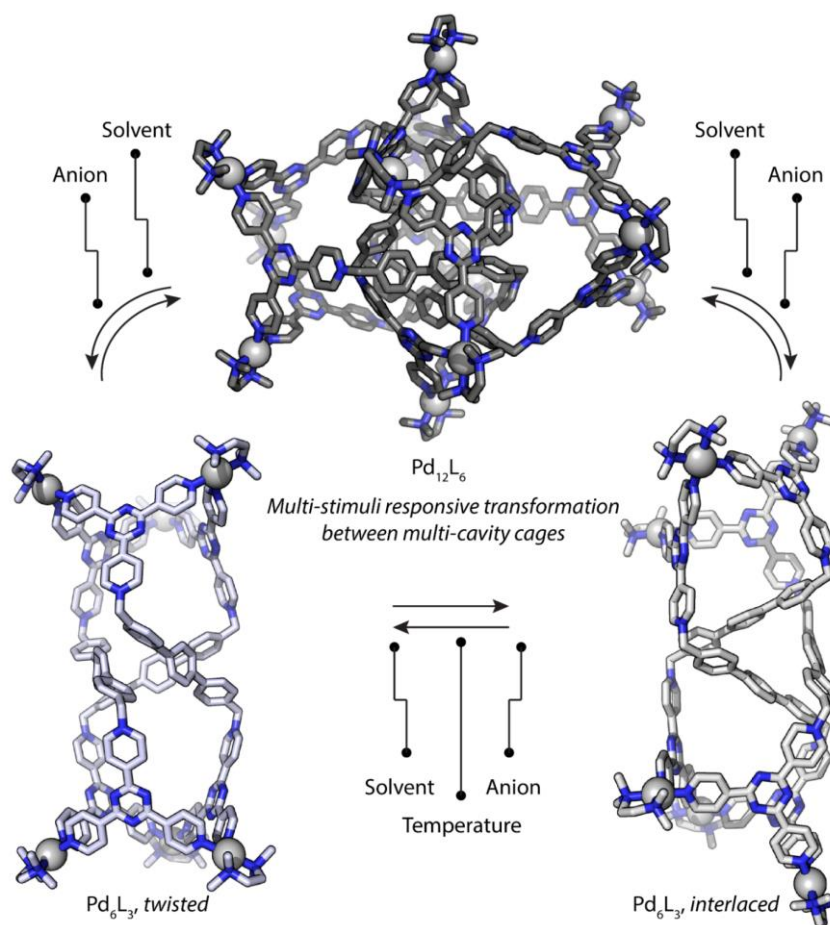


Figure 12: Multi-stimuli responsive Pd(II) cage system. The two lower assemblies are diastereoisomers of the same molecule. All the structures possess multiple cavities capable of segregating guests.

Heteroleptic assemblies prove to be excellent entities for crafting sophisticated transformation systems. This is not only due to the enhanced potential for diverse transformations afforded by incorporating multiple blocks into single assemblies but also because they enable the inclusion of more than one stimuli-responsive organic moiety. The combination of heteroleptic structures with switchable moieties is a pivotal choice for shaping the future landscape of this field. The study on the non-statistical assembly of Pd_2ABCD cages paved the way through their cage to cage transformations (Figure 13)^[45] but another report from our group highlights even more the potential of heteroleptic cages.

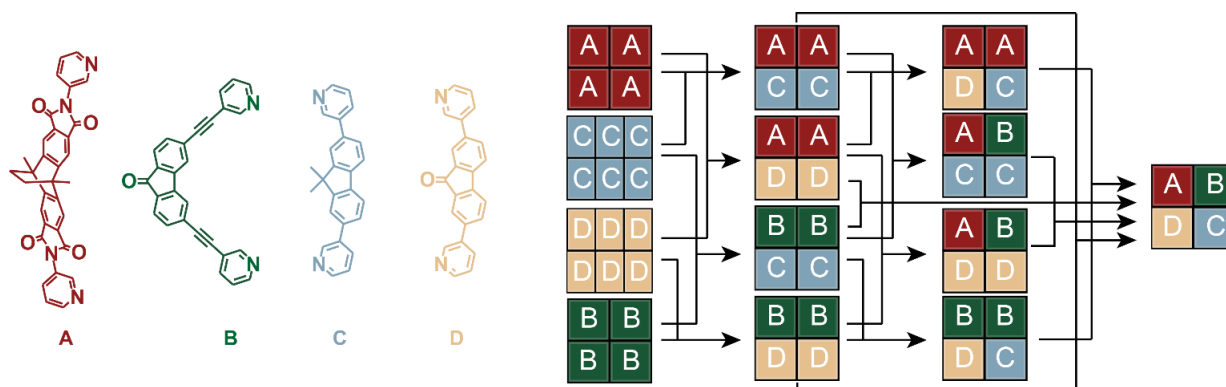


Figure 13: Cage to cage transformation networks of Pd(II) species. The stepwise increase in complexity passed through binary and ternary heteroleptic structures culminating in the formation of a unique Pd_2ABCD cage under full thermodynamic control.

In 2021, our research group merged our dithienylethene photoswitch^[126] with a coordination sphere engineering approach, resulting in the creation of photoswitchable $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ bowl structures (Figure 14, *o* stands for “open” and *c* for “closed” referring to the state of the photoswitch in which a C-C bond can be created or destroyed resulting in a six-membered ring opening/closing. See reference 126 for a more detailed account of the incorporation of this moiety into ligand and coordination cage).^[56] Introducing a quinoline donor induces steric hindrance at the palladium centers, favoring bowl formation and providing a free coordination site for further derivatization. Light irradiation at the appropriate wavelength interconverted the open and closed bowl isomers, each exhibiting distinct host-guest properties. The flexibility disparity between the two dithienylethene isomers controlled the cavity size, also allowing the open form to afford a Pd_2A_4 cage. Complementing ligands with near-linear coordination vectors completed the $\text{Pd}(\text{II})$ ligand sphere, resulting in $\text{Pd}_2\text{A}_3\text{B}$ assemblies. Various organic bridges with different shapes enabled fine-tuning of cavity size and further modification of host-guest capabilities. Eventually, the addition of chloride acted as a chemical stimulus, displacing the previously introduced neutral ligand, reducing the bowl's charge, and enhancing its stability. This triggered response was reversible using $\text{Ag}(\text{I})$ to recollect chloride anions, enabling the reuptake of the previously released guest molecule. As a broader take, and as elaborated in a recent perspective by our team,^[115] light is poised to play a central role in advancing multi-responsive complex systems. Though the integration of photoswitches into the framework of coordination cages remains somewhat restricted, more reports have recently emerged in the literature.^[115] Light serves as a precise and controllable stimulus, with the added benefit of generating minimal or no waste. The ability to finely tune responsiveness and the ease of application will foster the systematic integration of these responsive elements into cages, leading to the emergence of novel properties.

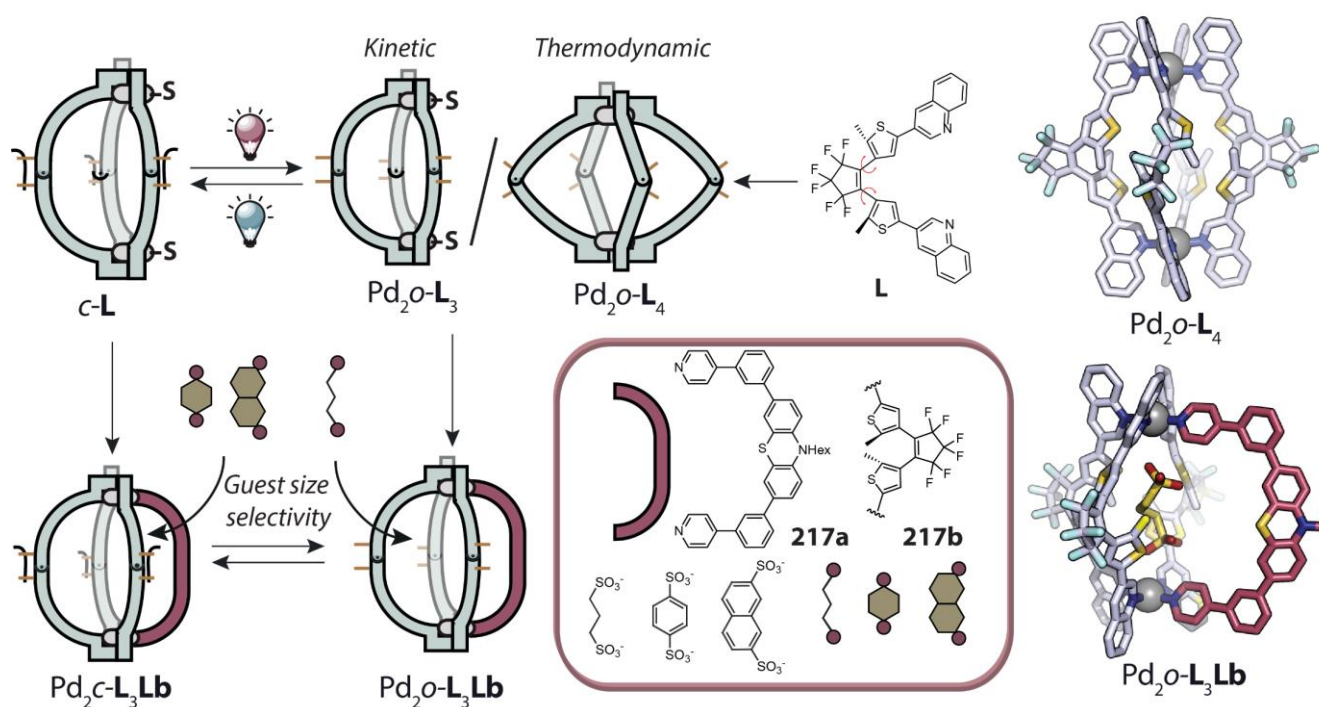


Figure 14: Transformation system based on photoswitchable DTE ligands which allow reversible conversions between bowls and cages.

4. Complex system behaviors

Eventually, the focus lies on achieving complex system behavior, or what can be termed as "bio-like" behavior, which represents one of the primary objectives of supramolecular chemists. The preceding sections have essentially laid down the groundwork by emphasizing two different tools necessary for the emergence of such behavior. While nature offers numerous patterns such as specific binding, structural adaptation, out-of-equilibrium processes, and efficient catalytic activity, many of these remain unparalleled in laboratory settings. The upcoming section seeks to highlight recent instances of coordination cage systems where such highly complex functions or properties are slowly beginning to manifest. The intention here is not to provide an exhaustive overview but rather to decipher how these processes are reshaping a new landscape of possibilities for the field, following nearly three decades of establishing the foundations and principles for understanding the design of more static systems.

If we were to delve into static systems exhibiting complex system behavior, a prominent feature would be the selective encapsulation of guests within host molecules. While host-guest chemistry is one of the peculiar abilities of coordination cages, not all guests are necessarily relevant or underlying a complex process. However, cages have shown the capacity of entrapping highly reactive species otherwise unstable in bulk conditions (Figure 15).^[127] Raymond and coworkers have pioneered this area by showing the encapsulation and stabilization of several cationic molecules within the cavity of their anionic tetrahedral cages. Examples include the trapping of multiple phosphine-acetone adducts^[128] or iminium salts in aqueous solution,^[129] aromatic tropylium or diazonium cations,^[130] and ruthenium organometallic species.^[131] In the same vein, Fujita also demonstrated the encapsulation of dinuclear ruthenium as well as manganese transition-metal complexes inside an octahedral cationic coordination cage.^[132,133] In these instances, the cavity's shielded character plays a crucial role in guest stabilization. A robust hydrophobic effect, facilitated by large aromatic panels, ensures the exclusion of water molecules from the inner space, safeguarding the guest from potential reactivity. A similar behavior was observed in several well-known examples including the encapsulation of white phosphorus by Nitschke,^[134] AIBN and AMBN stabilization by Yoshizawa^[135] as well as a recent report from Clever demonstrating the encapsulation of a long-lived fullerene C₆₀ radical anion within the cavity of a Pd₂L₄ capsule.^[136]

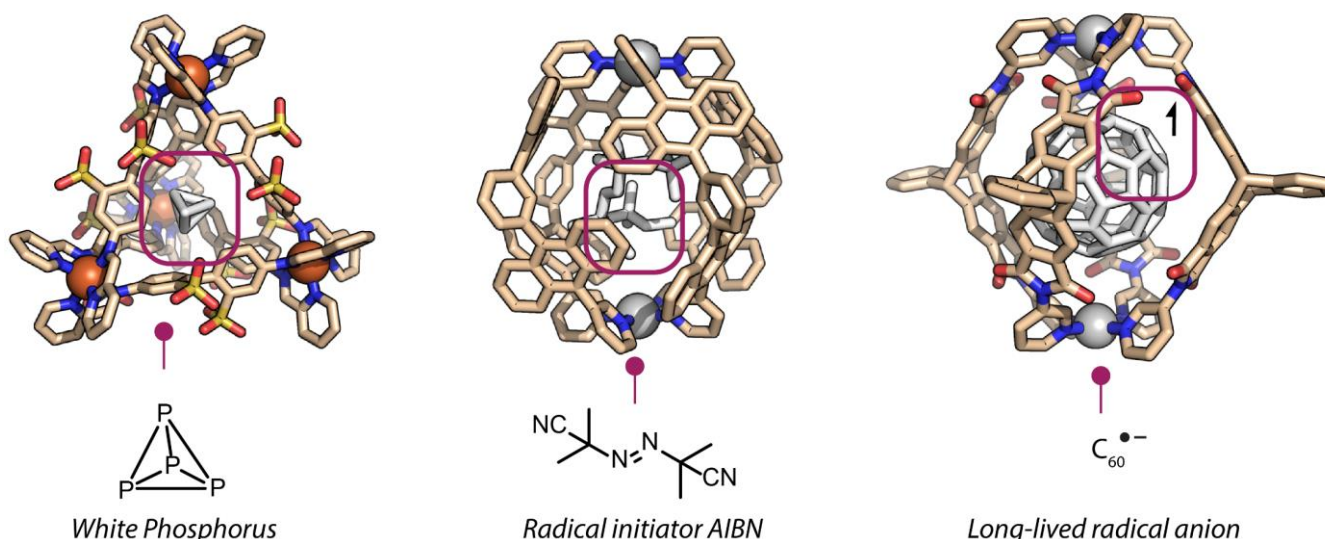


Figure 15: Stabilization of reactive species within the cavity of coordination cages enabled by the shielding from bulk solution by the cavity.

However, Fujita and coworkers have demonstrated another intriguing behavior emerging from the encapsulation of reactive species in the cavity of metal-organic assemblies. In a series of papers, they investigated the stabilization of polysilanol in several coordination assemblies.^[137–139] Initially, they demonstrated for the first time the isolation of trisilanol, a highly reactive compound, when encapsulated in an inert Pt(II) octahedron in

water.^[137] The cage accommodates the cyclic trimer and avoids its further condensation. Following this, they explored the possibility of cavity-directed synthesis of silanol oligomers in a controlled fashion inside cage or bowl Pd(II) assemblies witnessing the first real use of stabilizing a reactive species in a confined environment.^[138] Eventually, the most complex behavior was observed through host recombination following a tetrasiloxane formation. Using an unsymmetrical ligand, they induced the formation of a Pd₂₀L₈ fully walled octahedral capsule in water. In a remarkable fashion, when an excess of trimethoxysilane was added to water the authors observed a host recombination into a Pd₈L₄ bowl-shaped structure containing a tetra-condensated cyclic polysiloxane (Figure 16).^[139] This transformation, accompanied by the release of Pd(II), led to the entrapment of a unique all-*cis* stereoisomer of the tetrasiloxane, which templated the formation of the bowl via an induced-fit effect. This process of host recombination among substrate stabilization and stereo-selective transformation is reminiscent of behavior observed in biological media with enzyme activity. While architecture recombination upon guest binding has been observed more broadly, only one more recent example from Sun and coworkers has witnessed a similar adaptative behavior (Figure 16).^[140] In their system, another octahedral cage was capable of uptaking four guest molecules of 1-hydroxymethyl-2-naphthol. Upon strong heating and subsequent analysis aided by crystal structure determination, the authors could show that the substrate had undergone a transformation into 2,2'-dihydroxy-1,1'-dinaphthylmethane. The initial guest therefore self-coupled within the cavity of the octahedron, and its conversion triggered a host reorganization into "twin-cage" Pd₆L₃. This process allowed the creation of two separate cavities, bridged by a central ligand adopting a *trans* configuration, wherein for each cavity, one molecule of newly created guest resided. The possible reconfiguration of the host supported by the labile metal-ligand bond is therefore again at the center of emerging complex behavior.

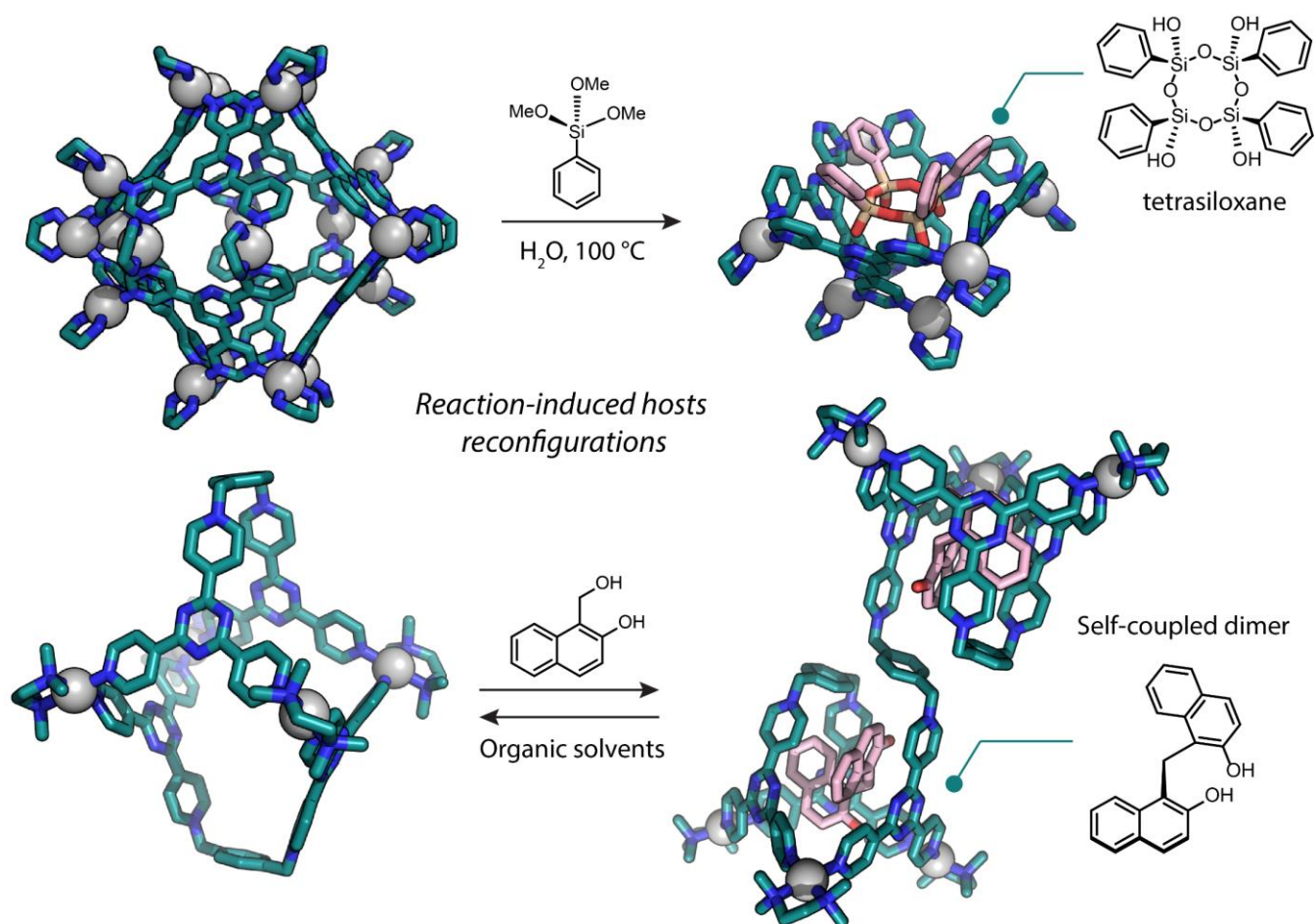


Figure 16: Structural rearrangement of coordination host upon guest transformation within the cavity. This process is reminiscent of an induced-fit phenomenon in biological systems.

Other intricate processes on static systems involving host-guest chemistry are found in the impressive array of studies on phase transfer and separation by the Nitschke group,^[141–145] as well as the diverse examples of unconventional substrate modification within the cavity of the “Fujita-cage”.^[146–148] Recently, they demonstrated the enhancement of amide reactivity through simple conformational twisting within octahedral coordination cages.^[146] It is important to notice that significant contributions to analogous substrate transformation processes have also been made by Yoshizawa,^[149] Mukherjee,^[150] Delius and Ribas,^[151–153] Raymond and Toste,^[10,154] Ward,^[155,156] Lusby^[157,158] and Su.^[159,160] In these instances, cages serve to either promote or catalyze transformations, alter stereo- and/or regioselectivity, and function as photosensitizers or protective shells around reaction substrates or products. Integrating this type of functionalities with dynamic reconfiguration processes could aid in addressing issues such as product inhibition, a common challenge in molecular reactions within supramolecular hosts. Additionally, one can envisage that successive transformations to create varying shapes and/or sizes of host structures could facilitate stepwise catalytic activity therefore developing further the concept of “smart/switchable supramolecular catalyst”.

The cavity of cages can serve as a platform to encapsulate guests with intriguing photophysical properties, altering or quenching their behavior. While numerous examples of dyes integrated into cage cavities have been reported,^[161–165] some instances, particularly involving photoswitchable guests, stand out for their resemblance to biological processes or their unusual selectivity, hinting in my opinion at promising applications. The group of Rafal Klajn has been delving into the study of photoswitchable guests and how confinement affects their properties.^[166–171] They make use of a cage reported by Mukherjee with a barrel shape,^[172] and presenting an interesting flexibility. Their investigations have focused on molecules like spiropyran,^[171] dihydropyrene,^[168] and, notably, azobenzenes and their derivatives.^[166,169,173] They demonstrated that two *trans*-azobenzene molecules could be encapsulated by the cavity of the barrel, whereupon irradiation and a size mismatch led to the expulsion of one, leaving a single *cis* azobenzene inside.^[169] Furthermore, they could also report the formation of a ternary host-guest complex under kinetic control.^[174] Two different dyes such as anthracene and BODIPY could therefore coexist within the cavity of the cage and trigger the previously quenched luminescence of the BODIPY. Eventually combining these two approaches, they introduced the concept of disequilibrium by sensitization under confinement (DESC) (Figure 17).^[167] Several azobenzene derivatives can be co-encapsulated with dyes such as BODIPY or resorufin which act as sensitizers. The sensitizer can absorb a photon and undergo intersystem-crossing (ISC) followed by a key step of triplet energy transfer (TET) to the azobenzene. The final relaxation results in the switching of the azobenzene and subsequent expulsion from the cavity due to steric hindrance. This strategy enables a drastic improvement (up to 98%!) of the azobenzene switching efficiency using long wavelengths that would not typically allow this process. From a thermodynamic standpoint, the aforementioned system functions in a similar way to a light-driven molecular machine which enables the conversion of light into chemical energy creating an out-of-equilibrium photostationary state requiring only a catalytic amount of cage. In another fashion, Yoshizawa and coworkers have demonstrated the use of a Pt(II)-based capsule to enforce azobenzene, but also stilbenes and imines, in their normally unstable *cis* configuration.^[175] Surprisingly when an equilibrated solution of these guests was mixed with the cage, the authors observed the uptake of one equivalent, but only in the *cis* form, and this, without irradiation of the sample. Furthermore, heating the sample or irradiating it did not result in back-switching, the cage acts as a shield. In the case of the imine, the cage also prevented the hydrolysis of the C=N bond although the system was fully in aqueous solution. This shielding and suppressing effect could be further employed for dynamic behavior in which a transformation of the cage or a guest replacement would allow the recovery of the initial switching or hydrolysis function *via* a secondary event, in a signal transduction way.

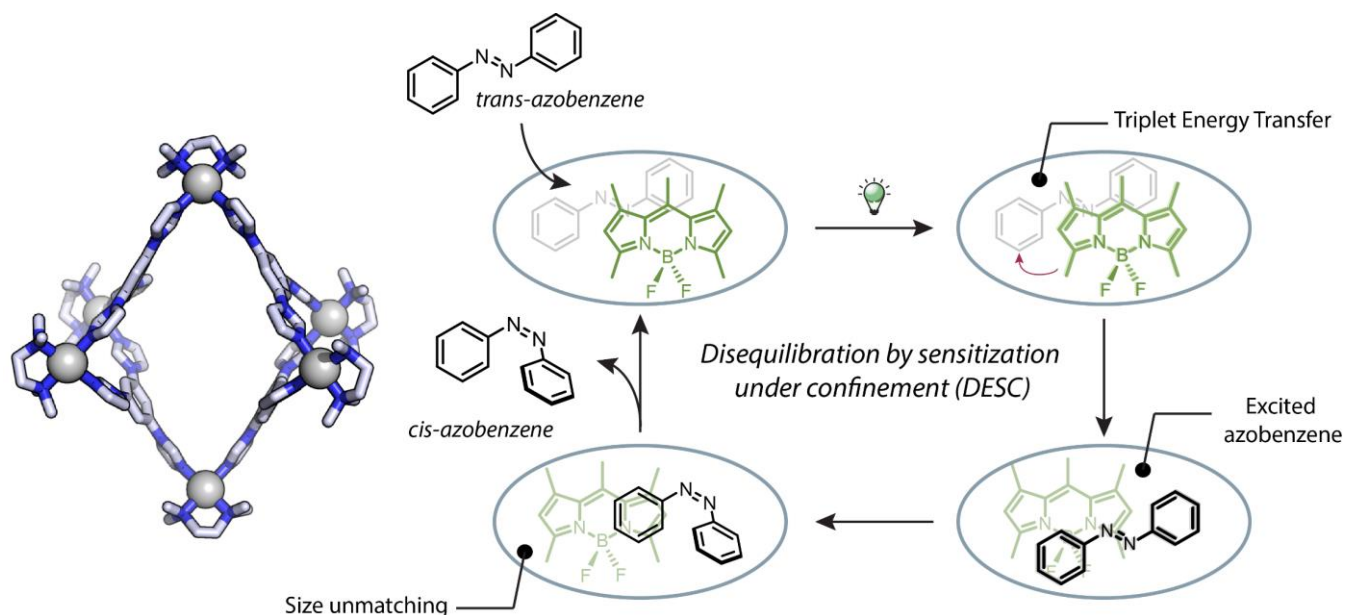


Figure 17: Confinement-controlled isomerization of azobenzene in the cavity of coordination cage by use of sensitization with a second co-encapsulated dye.

While we have discussed various phenomena of increasing complexity thus far, one main characteristic of the presented systems makes them drastically different than those observed in biology, namely that they are all under thermodynamic equilibrium. This constitutes a turning point in the discussion. The next step for the field entails venturing into the realm of far-from-equilibrium behaviors, with promises to bring it closer to the complexity and functionality inherent to biological systems. Only a handful of reports have taken the risks of delving into this fundamentally distinct chemistry (or even physical chemistry) area. The criteria defining a system as dissipative, meta-stable, out of equilibrium or merely a switch remain sometimes an ongoing debate. Considerable progress has been made in understanding the physical principles governing this domain, but the development of purely synthetic systems (as not found in nature or not using bio-like or bio-extracted components) is still in a nascent stage. Unlike the case of thermodynamic equilibrium or meta-stable state, a system far from equilibrium requires a constant influx of so-called fuel in order to maintain itself. Such a system is therefore in a constant transition between states. However, this continuous input and consumption of energy may lead to the accumulation of waste within the system. Thus, using light as a source of energy emerges as a compelling alternative to chemical fuel given its waste-free nature. Although comparable in the outcome, we will see that light and chemical fueling proceed through two different physical pathways to bring a system to a higher energy state.^[176] Additionally, the comparison with nature is also less straightforward as in biological systems the only process properly driven by light is photosynthesis.

The main difference between these processes lies in the way the system goes out of equilibrium or in the high-energy state.^[176] For light-powered systems, the initial inactive molecule interacts with a photon and an excited state is populated. Through the conical intersection, there are two possible pathways resulting in either a return to the initial inactive (ground) state or access to another state which will then be qualified as out of equilibrium as it will require a constant influx of photons to be maintained. The thermal kinetic barrier between this state and the thermodynamic one is very small or inexistent meaning that without the fuel the system simply always relaxes to its most stable state. As aforementioned, no waste is produced during such process, however, the components must be relatively resistant to prolonged irradiation (UV light is especially problematic) otherwise they will undergo degradation over time. This might also explain why these systems are only scarcely present in nature. On the other hand, a plethora of biological systems rely on chemical fueling with the most famous ATP hydrolysis. In this scenario, a chemical reaction serves as an activation step in which the initial molecule will then be transformed (or assembled) into its functional (high energy) “analog”.^[177] The chemical energy is transformed

into work (or function) and waste is created as a byproduct of the chemical fueling reaction. Of course, the “activated” state can be deactivated by an opposite reaction (sometimes being even the same, only the kinetics being differentiable: see kinetic asymmetry and micro-reversibility principles in pumps, molecular machines and other biological systems^[178–181]). The functions performed by the “activated” state are diverse in biological systems ranging from directional movement of molecules, catalytic activity, self-organization or compartmentalization just to name a few.^[182]

Using chemical fuel is also a more intricate process for coordination compounds as it can, purposely or not, interfere with or impede the coordination process. Nitschke and coworkers have demonstrated the first instance of fuel-controlled formation of a triangular Cu(I) host capable of encapsulating fullerene C₆₀.^[183] Self-assembly of porphyrin diamine with 2-formylpyridine in the presence of Cu(I) yields a Cu₃L₃ pseudo cage or barrel-like assembly. The large aromatic panels of the porphyrins facilitate the encapsulation of fullerene within the host cavity. Introduction of PPh₃ into the host-guest solution prompts the decomposition of the host by coordination to the Cu(I) cation. In addition, if a Rhenium catalyst and pyridine N-oxide are present, the PPh₃ fuel is gradually consumed, forming the corresponding phosphine oxide incapable of copper coordination. Consequently, this fuel consumption results in the reformation of the Cu₃L₃ cage and the reuptake of fullerene reverting the system into its thermodynamic state. One drawback of this system, potentially explaining the absence of follow-up application of this process, is the accumulation of pyridine as additional waste in the system. This could be further responsible for interferences with the coordination assemblies. In another chemically fueled system, Ayme and coworkers harnessed transient trichloroacetic acid to drive the rearrangement of imine-based metal-organic architectures (Figure 18).^[184] Playing with the length of two diamines they showed the fueled and transient assembly of Ag₂L₂ helical species and Ag₂L'₂ catenane. Upon addition of the longer diamine to the preformed helicate, no exchange was observed between the imines indicating thermodynamic equilibrium. However, as the two diamines possess different pK_a the addition of trichloroacetic acid triggers the sole protonation of the smaller one which is then gradually replaced leading to the formation of the catenane. The transient character of the acid prompts its slow decomposition into chloroform and carbon dioxide (wastes) over time. Remarkably, it leads to the deprotonation of the smaller diamine enabling it to reform the helicate. The catenane is uniquely obtained under fueling of the acid representing a dissipative state of the system that can relax into its thermodynamic sink upon fuel consumption. Other systems using similar processes and cage-like molecular hosts have been reported by Schmittl and his group, but it is pretty clear that “everything” is still to be done and that the landscape of exploration is vast.

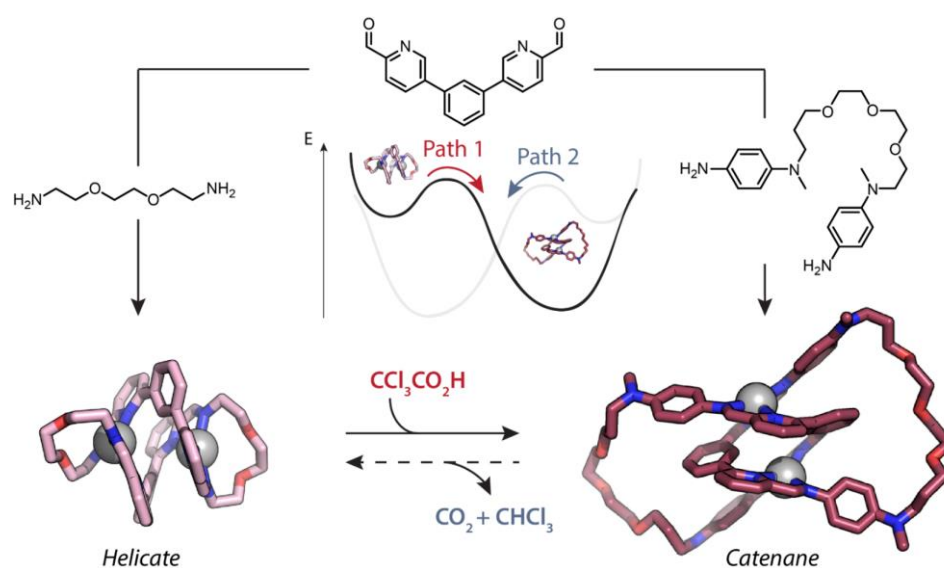


Figure 18: Dissipative system between Ag(I) helicate and catenane taking advantage of the unstable CCl₃CO₂H acid for creating a high energy state.

On the other hand, I have explained that light represents an intriguing tool to push systems out of equilibrium. However, implementation of photoswitchable moieties into coordination cages remains scarce. As of today, only one proper dissipative system based on a diazocine photoswitch has been developed by our group (Figure 19).^[185] In this energetic scenario, light serves as the driving force for the assembly of a host-guest system based on a Pd(II) coordination cage. This light-powered assembly maintains the host-guest species in an out-of-equilibrium state, wherein the high-energy state persists as long as the light stimulus is present. As typical for dissipative systems, thermal rearrangement takes over once the light stimulus is removed, bringing the system back to its thermodynamic sink. The described Pd(II)-based cage, established from a ligand featuring a diazocine core, exhibits photoswitching behavior akin to azobenzenes, albeit with an ethyl bridge between the aromatic rings. In this specific case, the *cis*-isomer is thermodynamically favored, while UV irradiation induces the formation of the metastable *trans*-isomeric form. Assembly of *cis*-L with Pd(II) cations results in a mixture of species, predominantly $\text{Pd}_2\text{cis-L}_4$ and traces of $\text{Pd}_3\text{cis-L}_6$, suggesting nonideal geometry for clean cage formation. Upon photoswitching, the system forms a defined but unstable cage $\text{Pd}_2\text{trans-L}_4$. Interestingly, the photoswitching properties of the diazocine switches remain largely unaffected by coordination with nearly the same PSS and kinetics of switching. While addition of a bis-sulfonate guest (G) to $\text{Pd}_n\text{cis-L}_{2n}$ leads to an external association, the same addition to the $\text{Pd}_2\text{trans-L}_4$ affords a clean host-guest complex, which exists only under continuous irradiation at 385 nm. Thermal relaxation leads to back-switching and guest release, with reassembly and guest binding being reversible upon reapplication of the light stimulus. Comparable light-fueled transformations of non-Pd(II)-based supramolecular organic macrocycles and cages have also been reported by the groups of Schmidt^[186] and Feringa^[187]. This highlights a growing interest in this type of receptors with new behaviors and there is no doubt that many more instances will soon flourish in the literature.^[188]

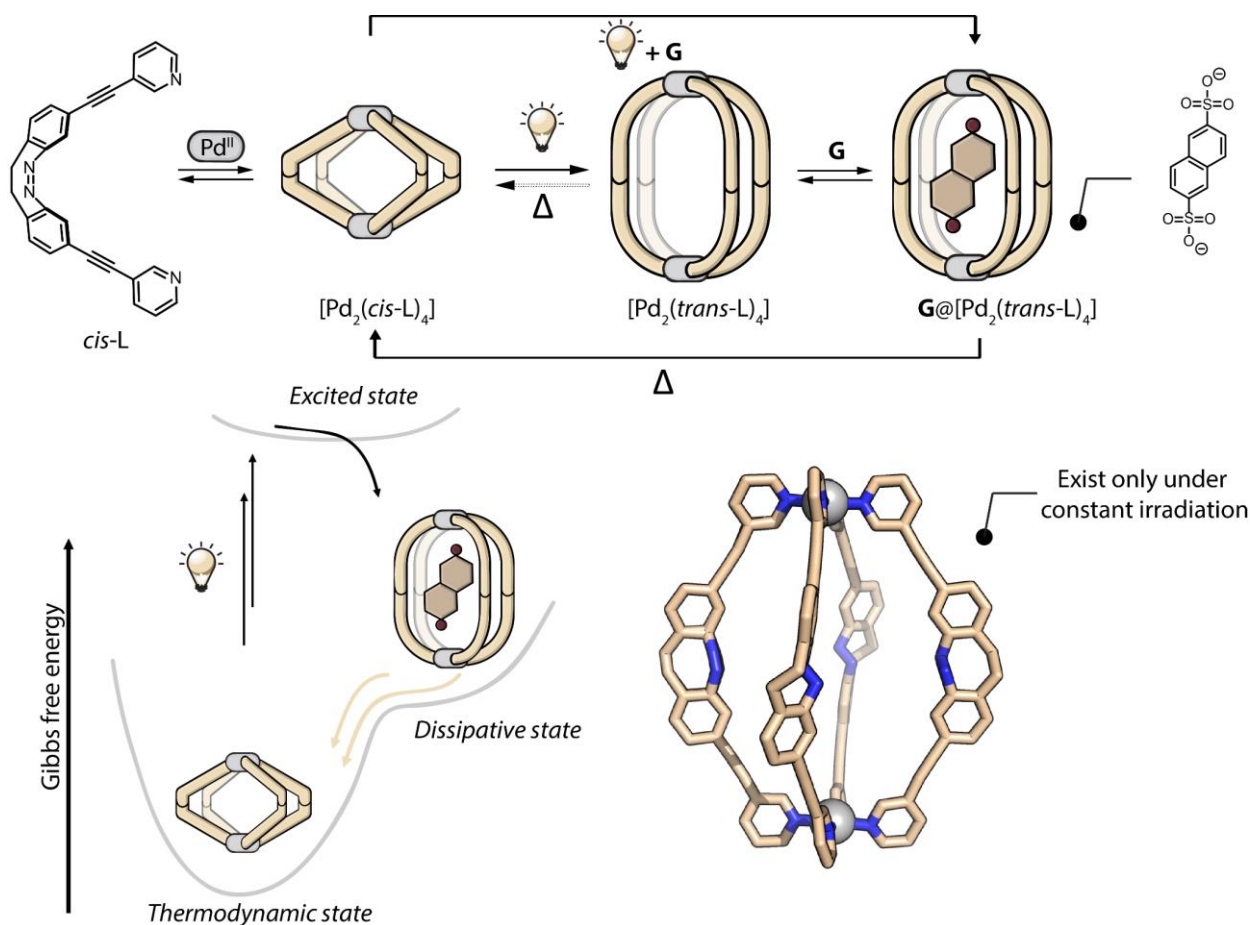


Figure 19: Diazocine-based coordination cage allows the formation of a dissipative host-guest system in which the species persists only under constant irradiation and otherwise relaxes in its stable state for which the guest is not bound within the cavity.

In another study on photoswitching, featuring a fluoro-azobenzene ligand equipped with pyridine, Beves and colleagues reported the generation of a cage system in a high-energy state, considered metastable (Figure 20).^[189] The authors described the formation of a mixture of a Pd_3L_6 ring and Pd_4L_8 tetrahedron from the *trans*-ligand. Interestingly, the *trans* leads to discrete assemblies, while the *cis*-analog obtained upon prolonged irradiation at 530 nm results in undefined, likely oligomeric species. The process was reversible, with the photoisomerization of the ligand requiring dissociation from the Pd(II) sites. Although the conversion of the *trans* to the *cis* caused disassembly of the discrete species, the partial conversion could be utilized to transition the system into a higher energy metastable state, altering the relative “population” of Pd_3L_6 and Pd_4L_8 species. Irradiation at 410 nm for a short period of time yielded a photostationary state of 15% of the ligand in the *cis* form. While this change was relatively small, it was sufficient to enrich the Pd_3L_6 ring from 44% to 82%, and thermal relaxation restored the initial thermodynamic state. This phenomenon arises due to the different assembly kinetics for the Pd_3L_6 ring and the Pd_4L_8 tetrahedron (unrelated to the kinetics of photoswitching!). By pumping the overall population of assemblies out of equilibrium for a certain period, this approach demonstrates the potential for developing a dissipative (host-guest) system but is also of interest for the control over cage populations in a systems chemistry approach.

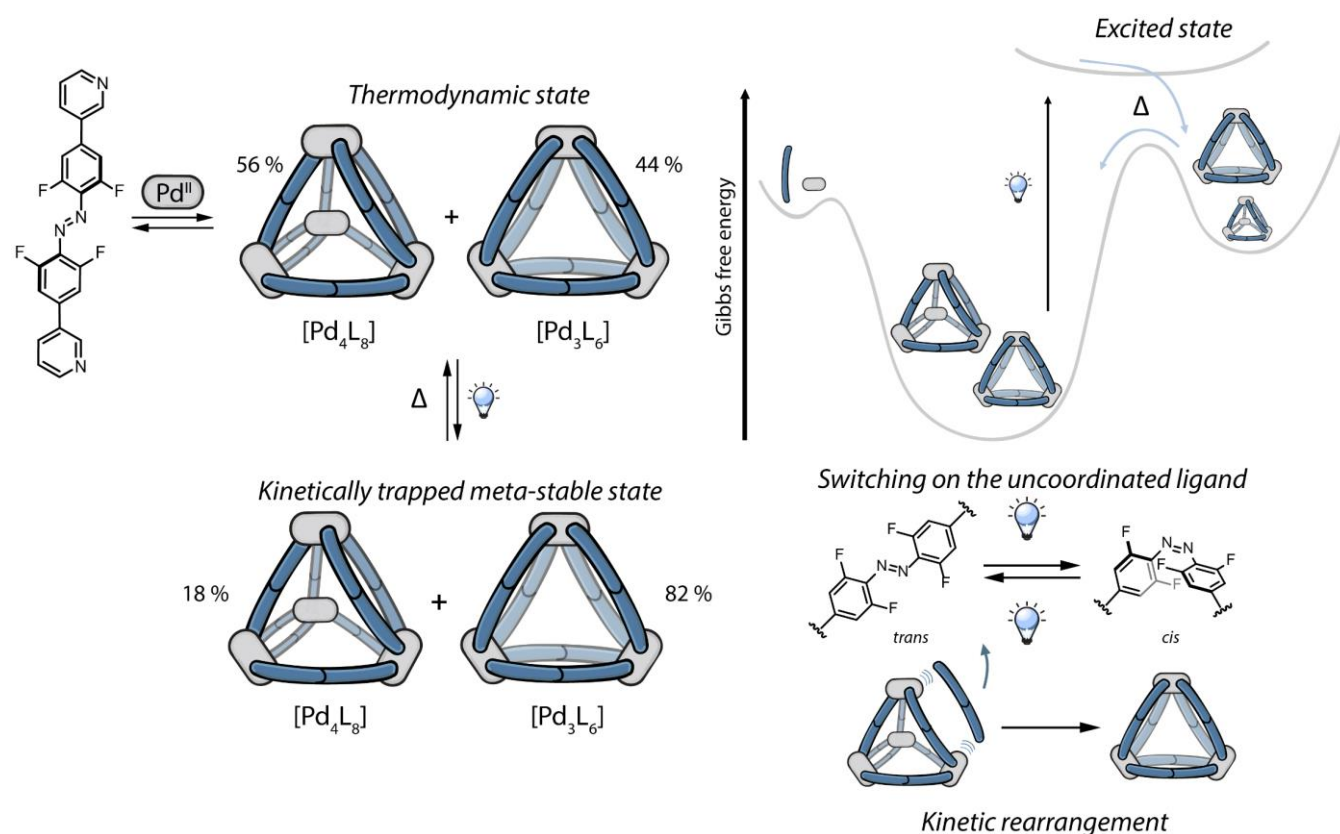


Figure 20: Light allows the formation of a kinetically trapped system in which the ratio between two architectures is modified because of a kinetic rearrangement between tetrahedron and ring. The meta-stable state relaxes to the initial ratio through irradiation or temperature increase.

5. Multi-cage systems

Finally, one last area has begun to enable and will further facilitate the emergence of complex behaviors: multi-cage systems. Despite the current equilibrium state of most reported multi-cage systems (except perhaps the one presented just above), I intentionally chose to address this topic at the end of this introduction. This decision was made deliberately because the subject is central to the subsequent dissertation, and it is therefore, crucial to have it fresh in mind when delving into the following chapters. There is no need to emphasize that the numerous components of natural biological systems do not function as separate individual entities like a cage or a catalyst in a flask. Rather, they comprise multiple assemblies and molecules, coexisting orthogonally (mostly) within the same set of conditions, and capable of communication, cooperation, inhibition as well as the simultaneous performance of several functions. As hinted in the transformation section, responsive and transformable cages are therefore a prerequisite for complex systems, but it becomes apparent that the coexistence of multiple cages will then also be a major advancement towards a biological type of complexity. The creation of populations of cages can rely on phenomena such as narcissistic self-sorting, allowing the components to assemble into orthogonal structures. Eventually, all the features mentioned earlier necessitate signal transduction between different assemblies. While only a few instances of signal transduction in cage systems have been reported so far, they lay the groundwork for further exploration. The Nitschke group has leveraged strategies for narcissistic self-sorting to develop different complex cage systems where more than one architecture is present in solution.^[190,191] A Fe(II) cube composed of tetrazine-based ligands and an edge-directed Fe(II) tetrahedron with pending dienophile units could be mixed in organic solvent without a shuffling of their components (Figure 21).^[192] When norboradiene was introduced into the system, it rapidly underwent an Inverse-Electron demand Diels-Alder (IEDA) reaction with the tetrazine, transforming the cube through so-called post-assembly modifications. However, this reaction resulted in the formation of cyclopentadiene which, in presence of the dienophile on the tetrahedral cage, proceeded to a Diels-Alder (DA) reaction thereby modifying also the second cage. This is a remarkable example of a cascade post-assembly modification. The transduction phenomenon arises from the necessity of having the first cage react with norboradiene in order to trigger the following reaction on the second cage. This was cleverly demonstrated with a control experiment in which a competitive cyclooctyne is introduced and reacts faster with the tetrazine, preventing the formation of cyclopentadiene and therefore inhibiting the cascade. It is worth noticing that it still led to the coexistence of a new population of cages where only one had been transformed.

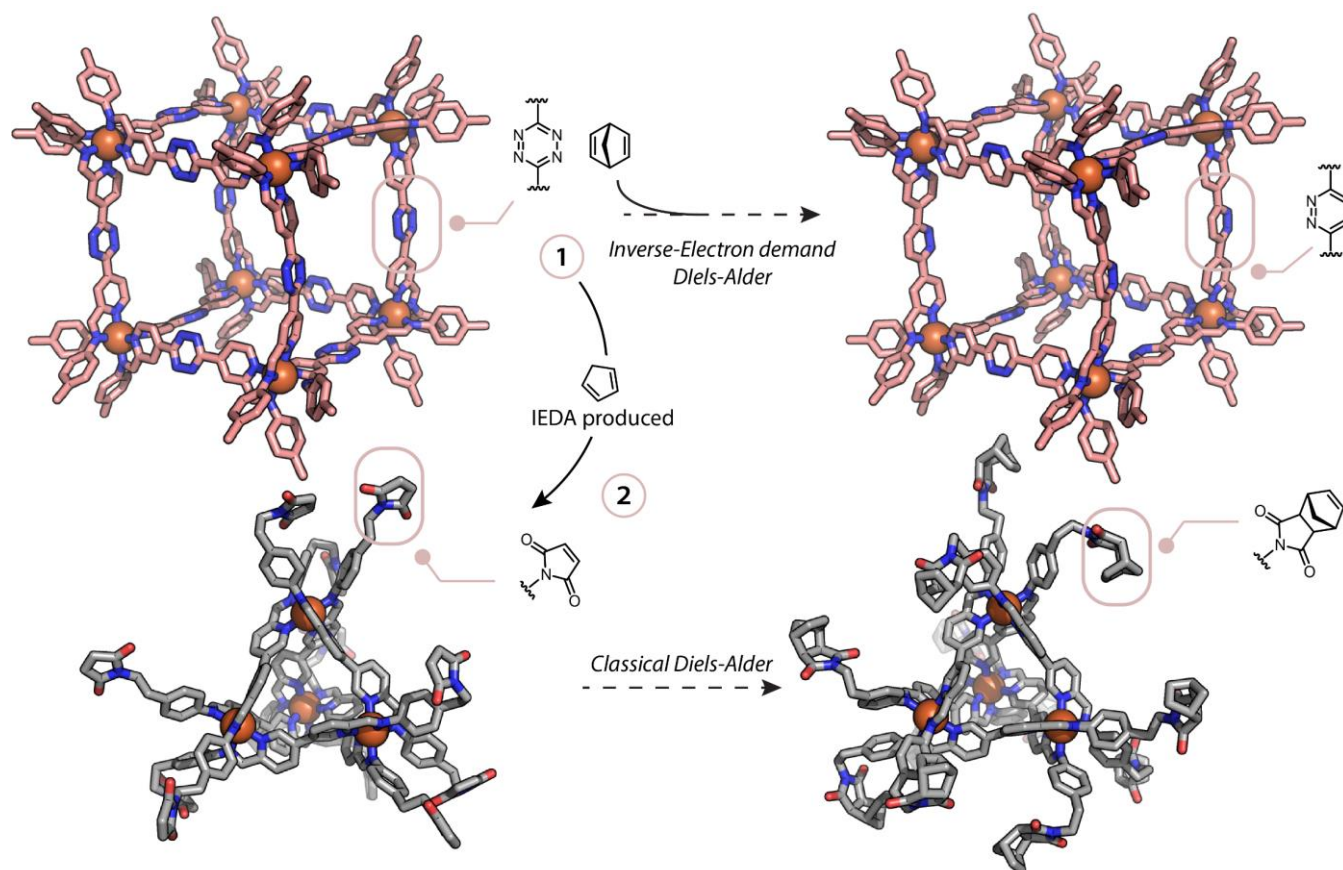


Figure 21: Cascade of transformations in a multi-cage system. The tetrazine moieties of the cubic cage react through IEDA generating cyclopentadiene which can further proceed to a DA reaction with the maleimide moieties of the tetrahedral assembly. Eventually, the two cages are modified by covalent post-assembly modification in a transductional fashion.

Alternatively, anion affinity can be harnessed to induce cascade exchange and construct networks. Two tetrahedral cages with only slight disparities in the size of their edges can coexist in solution without interfering.^[193] This is also the result of the observation of a template effect exerted by triflimide anions (Figure 22) for the larger assembly. In solution, upon introduction of perchlorate anions, encapsulation occurs within the smaller cage driven by its stronger association with these anions compared to the larger analog. However, guided by the same affinity process in a cascade manner, the introduction of hexafluoro phosphate triggers the displacement of perchlorate from the small cage followed by the subsequent displacement of triflimide, from the larger one, by the perchlorate. While the system is not perfectly selective, the sequential process is rather complex and offers valuable insights into information transmission. In a following study, the Nitschke group advanced a step further this concept by realizing a similar system in which the cargoes were, this time, neutral molecules.^[194] For this aim, they employed face-capped architectures, which are known to have better host-guest capabilities thanks to better shielded cavities. By thoroughly studying the kinetics and thermodynamics of guest binding, as well as the stability of cages upon the introduction of TREN they established a network with two different pathways (Figure 22). Starting from chloroform and cyclohexane contained in separate assemblies respectively, the two distinct routes enable the two neutral guests to be sequentially replaced by perrhenate or released upon chemical transformation or destruction of the cages in the network. Other studies using pH^[195] or fluorine^[196] as a stimulus and implicating two cages exchanging their cargoes were also reported by the same group more recently. Eventually, these principles were also beautifully applied to phase transfer systems.^[141–143,192,197]

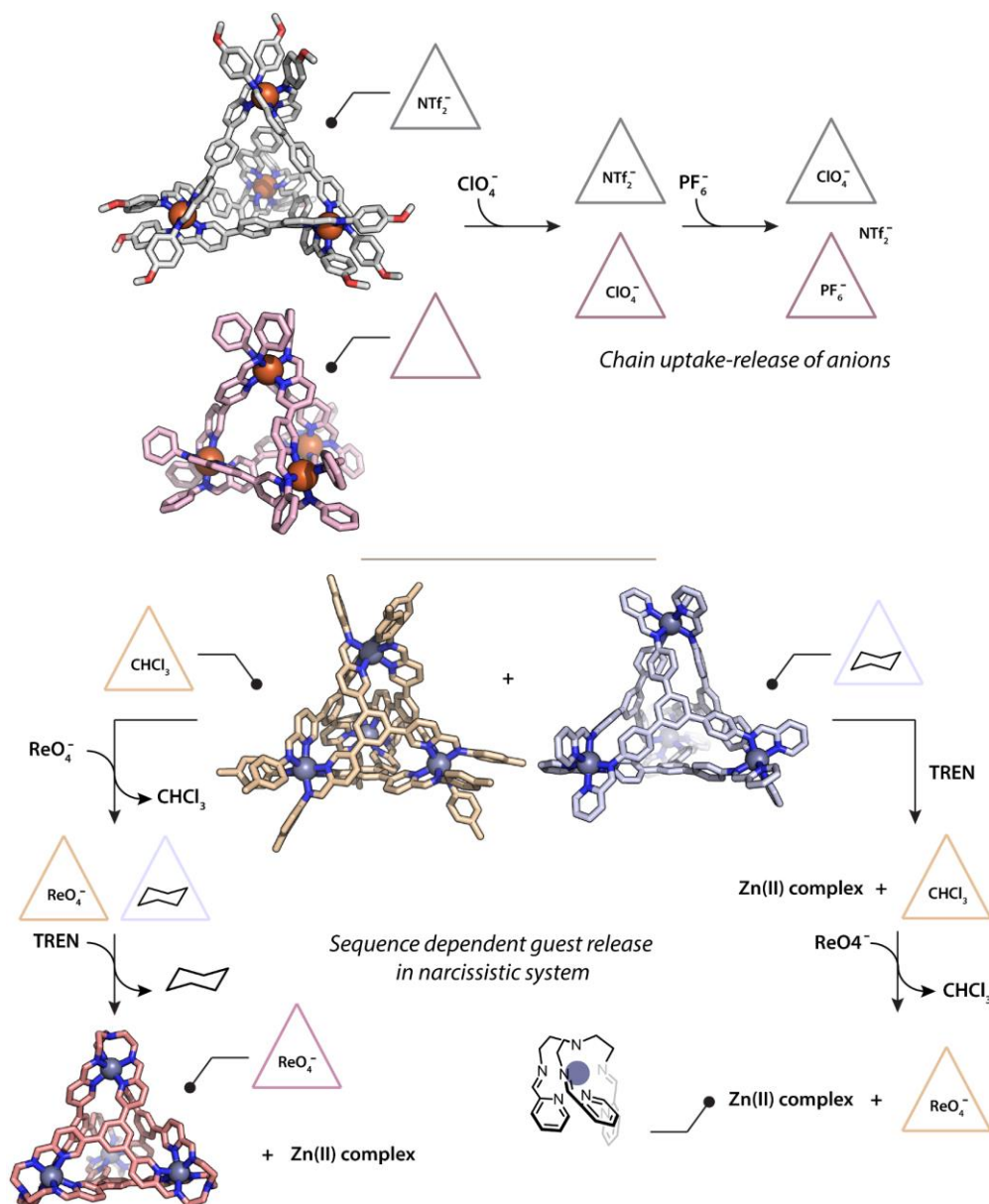


Figure 22: Narcissistic sorting between cages allows them to exist in an orthogonal fashion and to encapsulate distinct guests within their inner cavities respectively. Two separate transformation networks with guest exchanges can be implemented depending on the order of stimuli.

Our group has reported that cages can dynamically interact even in the context of narcissistic self-sorting.^[198] Indeed, in a recent study, we observed an azulene-based lantern-shaped cage undergoing transformation into a tetrahedron, templated by two bis-sulfonate guests (Figure 23). Subsequently, utilizing another cage bearing Methylene Blue (MB) charged moieties, the tetrahedron reverted back to the lantern assembly, the guest being "captured" by the MB cage^[199] due to the greater electrostatic interactions. Eventually, the two assemblies coexist in an orthogonal fashion once reaching the thermodynamic minimum.

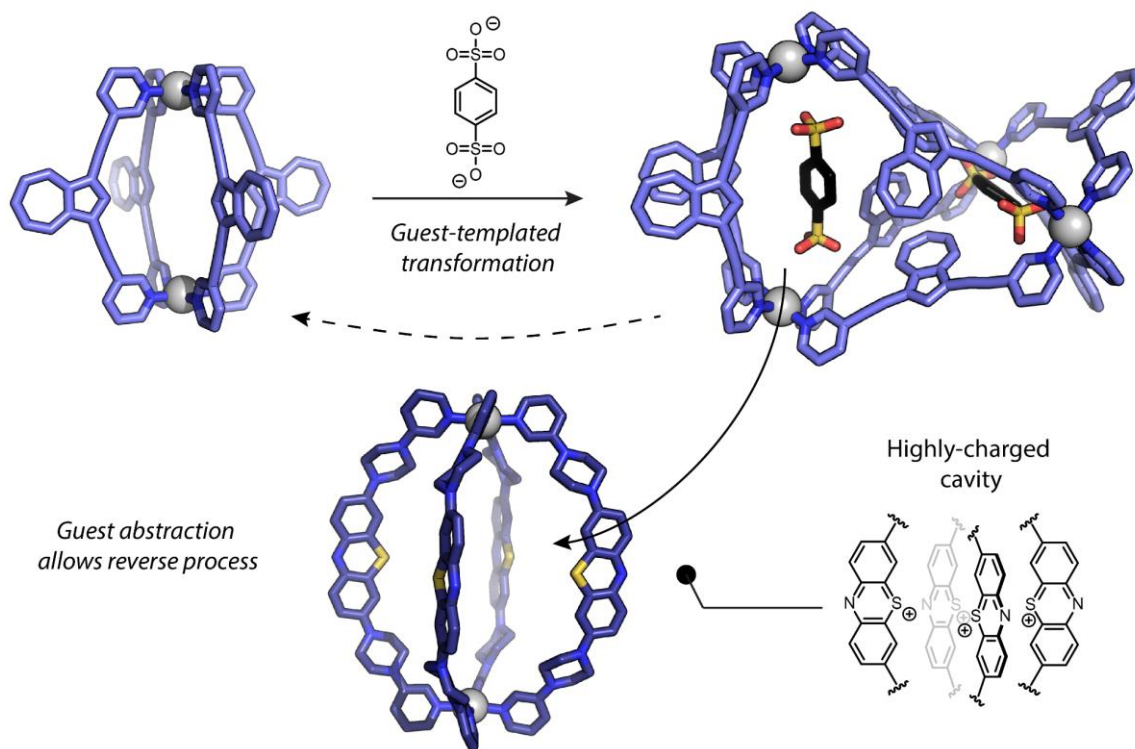


Figure 23: Reversible transformation of an azulene-based Pd_2L_4 cage into a guest-templated tetrahedron. The back conversion is allowed by the introduction of a second cage with a higher affinity for the guest owing to a highly charged cavity.

Despite advancements, examples of dynamic processes and system behaviors in cages remain scarce, particularly in the realm of more complex self-sorting beyond narcissistic phenomenon, where multiple heteroleptic and multicomponent assemblies coexist. This area warrants further exploration to unlock new avenues in supramolecular chemistry. Let's then dive into this.

6. References

- [1] R. W. Saalfrank, A. Stark, K. Peters, H. G. von Schnering, *Angew. Chem. Int. Ed.* **1988**, *27*, 851–853.
- [2] M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi, K. Ogura, *Nature* **1995**, *378*, 469–471.
- [3] D. L. Caulder, R. E. Powers, T. N. Parac, K. N. Raymond, *Angew. Chem. Int. Ed.* **1998**, *37*, 1840–1843.
- [4] B. Olenyuk, J. A. Whiteford, A. Fechtenkötter, P. J. Stang, *Nature* **1999**, *398*, 796.
- [5] J. D. Crowley, A. J. Goshe, B. Bosnich, *Chem. Commun.* **2003**, *0*, 2824–2825.
- [6] N. Kishi, Z. Li, K. Yoza, M. Akita, M. Yoshizawa, *J. Am. Chem. Soc.* **2011**, *133*, 11438–11441.
- [7] G. H. Clever, S. Tashiro, M. Shionoya, *Angew. Chem. Int. Ed.* **2009**, *48*, 7010–7012.
- [8] S. Mirtschin, A. Slabon-Turski, R. Scopelliti, A. H. Velders, K. Severin, *J. Am. Chem. Soc.* **2010**, *132*, 14004–14005.
- [9] P. Mal, B. Breiner, K. Rissanen, J. R. Nitschke, *Science* **2009**, *324*, 1697–1699.
- [10] D. Fiedler, R. G. Bergman, K. N. Raymond, *Angew. Chem. Int. Ed.* **2004**, *43*, 6748–6751.
- [11] R. M. Yeh, J. Xu, G. Seeber, K. N. Raymond, *Inorg. Chem.* **2005**, *44*, 6228–6239.
- [12] D. Fiedler, D. H. Leung, R. G. Bergman, K. N. Raymond, *Acc. Chem. Res.* **2005**, *38*, 349–358.
- [13] S. M. Bierschenk, J. Y. Pan, N. S. Settineri, U. Warzok, R. G. Bergman, K. N. Raymond, F. D. Toste, *J. Am. Chem. Soc.* **2022**, *144*, 11425–11433.
- [14] T. A. Bender, R. G. Bergman, K. N. Raymond, F. D. Toste, *J. Am. Chem. Soc.* **2019**, *141*, 11806–11810.
- [15] X. Yan, T. R. Cook, P. Wang, F. Huang, P. J. Stang, *Nat. Chem.* **2015**, *7*, 342–348.
- [16] M. L. Saha, X. Yan, P. J. Stang, *Acc. Chem. Res.* **2016**, *49*, 2527–2539.
- [17] Y. Sun, C. Chen, J. Liu, P. J. Stang, *Chem. Soc. Rev.* **2020**, *49*, 3889–3919.
- [18] D. A. McMorran, P. J. Steel, *Angew. Chem. Int. Ed.* **1998**, *37*, 3295–3297.
- [19] M. Scherer, D. L. Caulder, D. W. Johnson, K. N. Raymond, *Angew. Chem. Int. Ed.* **1999**, *38*, 1587–1592.
- [20] D. Zhang, T. K. Ronson, J. R. Nitschke, *Acc. Chem. Res.* **2018**, *51*, 2423–2436.
- [21] T. K. Ronson, S. Zarra, S. P. Black, J. R. Nitschke, *Chem. Commun.* **2012**, *49*, 2476–2490.
- [22] M. Tominaga, K. Suzuki, M. Kawano, T. Kusakawa, T. Ozeki, S. Sakamoto, K. Yamaguchi, M. Fujita, *Angew. Chem. Int. Ed.* **2004**, *43*, 5621–5625.
- [23] D. Fujita, Y. Ueda, S. Sato, H. Yokoyama, N. Mizuno, T. Kumasaka, M. Fujita, *Chem* **2016**, *1*, 91–101.
- [24] Q.-F. Sun, J. Iwasa, D. Ogawa, Y. Ishido, S. Sato, T. Ozeki, Y. Sei, K. Yamaguchi, M. Fujita, *Science* **2010**, *328*, 1144–1147.
- [25] D. Fujita, Y. Ueda, S. Sato, N. Mizuno, T. Kumasaka, M. Fujita, *Nature* **2016**, *540*, 563.
- [26] Y. Domoto, M. Abe, M. Fujita, *J. Am. Chem. Soc.* **2021**, *143*, 8578–8582.
- [27] Y. Domoto, M. Abe, T. Kikuchi, M. Fujita, *Angew. Chem. Int. Ed.* **2020**, *59*, 3450–3454.
- [28] K. Harris, D. Fujita, M. Fujita, *Chem. Commun.* **2013**, *49*, 6703–6712.
- [29] M. Tominaga, K. Suzuki, T. Murase, M. Fujita, *J. Am. Chem. Soc.* **2005**, *127*, 11950–11951.
- [30] S. Pullen, J. Tessarolo, G. H. Clever, *Chem. Sci.* **2021**, *12*, 7269–7293.
- [31] E. G. Percástegui, *Eur. J. Inorg. Chem.* **2021**, *2021*, 4425–4438.
- [32] M. Miciaccia, B. D. Belviso, M. Iaselli, G. Cingolani, S. Ferorelli, M. Cappellari, P. L. Polosa, M. G. Perrone, R. Calandro, A. Scilimati, *Sci. Rep.* **2021**, *11*, 4312.
- [33] S. Mazurkewich, R. Helland, A. Mackenzie, V. G. H. Eijssink, P. B. Pope, G. Brändén, J. Larsbrink, *Sci. Rep.* **2020**, *10*, 13775.
- [34] B. T. Wimberly, D. E. Brodersen, W. M. Clemons, R. J. Morgan-Warren, A. P. Carter, C. Vonrhein, T. Hartsch, V. Ramakrishnan, *Nature* **2000**, *407*, 327–339.
- [35] U. Uhlin, H. Eklund, *Nature* **1994**, *370*, 533–539.
- [36] R. F. Service, *Science* **2005**, *309*, 95–95.
- [37] Z. He, W. Jiang, C. A. Schalley, *Chem. Soc. Rev.* **2014**, *44*, 779–789.
- [38] M. M. Safont-Sempere, G. Fernández, F. Würthner, *Chem. Rev.* **2011**, *111*, 5784–5814.
- [39] W. M. Bloch, G. H. Clever, *Chem. Commun.* **2017**, *53*, 8506–8516.
- [40] W. M. Bloch, Y. Abe, J. J. Holstein, C. M. Wandtke, B. Dittrich, G. H. Clever, *J. Am. Chem. Soc.* **2016**, *138*, 13750–13755.
- [41] M. Yamashina, T. Yuki, Y. Sei, M. Akita, M. Yoshizawa, *Chem. Eur. J.* **2015**, *21*, 4200–4204.

- [42] T. K. Ronson, D. A. Roberts, S. P. Black, J. R. Nitschke, *J. Am. Chem. Soc.* **2015**, *137*, 14502–14512.
- [43] Q. Sun, S. Sato, M. Fujita, *Angew. Chem. Int. Ed.* **2014**, *53*, 13510–13513.
- [44] D. Preston, J. E. Barnsley, K. C. Gordon, J. D. Crowley, *J. Am. Chem. Soc.* **2016**, *138*, 10578–85.
- [45] K. Wu, E. Benchimol, A. Baksi, G. H. Clever, *Nat. Chem.* **2024**, 1–8.
- [46] T. Abe, N. Sanada, K. Takeuchi, A. Okazawa, S. Hiraoka, *J. Am. Chem. Soc.* **2023**, *145*, 28061–28074.
- [47] D. Preston, J. D. Evans, *Angew. Chem. Int. Ed.* **2023**, e202314378.
- [48] Y. Liu, S. Liao, W. Dai, Q. Bai, S. Lu, H. Wang, X. Li, Z. Zhang, P. Wang, W. Lu, Q. Zhang, *Angew. Chem. Int. Ed.* **2023**, *62*, e202217215.
- [49] E. Benchimol, I. Regeni, B. Zhang, M. Kabiri, J. J. Holstein, G. H. Clever, *J. Am. Chem. Soc.* **2024**, *146*, 6905–6911.
- [50] R.-J. Li, J. de Montmollin, F. Fadaei-Tirani, R. Scopelliti, K. Severin, *Dalton. Trans.* **2023**, *52*, 6451–6456.
- [51] A. M. Johnson, R. J. Hooley, *Inorg. Chem.* **2011**, *50*, 4671–3.
- [52] R. Zhu, W. M. Bloch, J. J. Holstein, S. Mandal, L. V. Schäfer, G. H. Clever, *Chem. Eur. J.* **2018**, *24*, 12976–12982.
- [53] M. Yoshizawa, J. Nakagawa, K. Kumazawa, M. Nagao, M. Kawano, T. Ozeki, M. Fujita, *Angew. Chem. Int. Ed.* **2005**, *44*, 1810–1813.
- [54] B. Chen, J. J. Holstein, S. Horiuchi, W. G. Hiller, G. H. Clever, *J. Am. Chem. Soc.* **2019**, *141*, 8907–8913.
- [55] B. Chen, J. J. Holstein, A. Platzek, L. Schneider, K. Wu, G. H. Clever, *Chem. Sci.* **2022**, *13*, 1829–1834.
- [56] R.-J. Li, J. Tessarolo, H. Lee, G. H. Clever, *J. Am. Chem. Soc.* **2021**, *143*, 3865–3873.
- [57] W. M. Bloch, J. J. Holstein, W. Hiller, G. H. Clever, *Angew. Chem. Int. Ed.* **2017**, *56*, 8285–8289.
- [58] S. Prusty, K. Yazaki, M. Yoshizawa, D. K. Chand, *Chem. Eur. J.* **2017**, *23*, 12456–12461.
- [59] T. Abe, N. Sanada, K. Takeuchi, A. Okazawa, S. Hiraoka, *J. Am. Chem. Soc.* **2023**, *145*, 51, 28061–28074.
- [60] M. Yamanaka, Y. Yamada, Y. Sei, K. Yamaguchi, K. Kobayashi, *J. Am. Chem. Soc.* **2006**, *128*, 1531–1539.
- [61] K. Kobayashi, Y. Yamada, M. Yamanaka, Y. Sei, K. Yamaguchi, *J. Am. Chem. Soc.* **2004**, *126*, 13896–13897.
- [62] Z. Zhao, Y.-R. Zheng, M. Wang, J. B. Pollock, P. J. Stang, *Inorg. Chem.* **2010**, *49*, 8653–8655.
- [63] Y.-R. Zheng, Z. Zhao, M. Wang, K. Ghosh, J. B. Pollock, T. R. Cook, P. J. Stang, *J. Am. Chem. Soc.* **2010**, *132*, 16873–82.
- [64] A. K. Bar, G. Mostafa, P. S. Mukherjee, *Inorg. Chem.* **2010**, *49*, 7647–7649.
- [65] A. K. Bar, S. Raghothama, D. Moon, P. S. Mukherjee, *Chem. Eur. J.* **2012**, *18*, 3199–3209.
- [66] H. Liu, C. Guo, Z. Zhang, C. Mu, Q. Feng, M. Zhang, *Chem. Eur. J.* **2023**, *29*, e202203926.
- [67] Z. Zhang, Z. Zhao, L. Wu, S. Lu, S. Ling, G. Li, L. Xu, L. Ma, Y. Hou, X. Wang, X. Li, G. He, K. Wang, B. Zou, M. Zhang, *J. Am. Chem. Soc.* **2020**, *142*, 2592–2600.
- [68] P.-P. Jia, Y.-X. Hu, Z.-Y. Peng, B. Song, Z.-Y. Zeng, Q.-H. Ling, X. Zhao, L. Xu, H.-B. Yang, *Inorg. Chem.* **2022**, *62*, 1950–1957.
- [69] C. García-Simón, M. Garcia-Borràs, L. Gómez, T. Parella, S. Osuna, J. Juanhuix, I. Imaz, D. Maspoch, M. Costas, X. Ribas, *Nat. Commun.* **2014**, *5*, 5557.
- [70] M. Wang, Y.-R. Zheng, K. Ghosh, P. J. Stang, *J. Am. Chem. Soc.* **2010**, *132*, 6282–6283.
- [71] D. Samanta, P. S. Mukherjee, *Chem. Commun.* **2013**, *50*, 1595–1598.
- [72] D. Samanta, S. Shanmugaraju, S. A. Joshi, Y. P. Patil, M. Nethaji, P. S. Mukherjee, *Chem. Commun.* **2012**, *48*, 2298–2300.
- [73] M. Yoshizawa, M. Nagao, K. Kumazawa, M. Fujita, *J Organomet Chem* **2005**, *690*, 5383–5388.
- [74] K. Kumazawa, K. Biradha, T. Kusukawa, T. Okano, M. Fujita, *Angew. Chem. Int. Ed.* **2003**, *42*, 3909–3913.
- [75] M. Yoshizawa, K. Ono, K. Kumazawa, T. Kato, M. Fujita, *J. Am. Chem. Soc.* **2005**, *127*, 10800–10801.
- [76] S. P. Black, D. M. Wood, F. B. Schwarz, T. K. Ronson, J. J. Holstein, A. R. Stefankiewicz, C. A. Schalley, Jeremy. K. M. Sanders, J. R. Nitschke, *Chem. Sci.* **2016**, *7*, 2614–2620.
- [77] J.-R. Li, H.-C. Zhou, *Nat. Chem.* **2010**, *2*, 893.
- [78] C. T. McTernan, J. A. Davies, J. R. Nitschke, *Chem. Rev.* **2022**, *122*, 10393–10437.
- [79] Y.-M. Guan, Q. Bai, Z. Zhang, T. Wu, T.-Z. Xie, P. Wang, *Dalton. Trans.* **2023**, *53*, 45–49.
- [80] S. Prusty, Y.-T. Chan, *Chem. Lett.* **2021**, *50*, 1202–1212.
- [81] P. Baxter, J. Lehn, A. DeCian, J. Fischer, *Angew. Chem. Int. Ed.* **1993**, *32*, 69–72.
- [82] P. N. W. Baxter, J. Lehn, G. Baum, D. Fenske, *Chem. Eur. J.* **1999**, *5*, 102–112.
- [83] S. De, K. Mahata, M. Schmittel, *Chem. Soc. Rev.* **2010**, *39*, 1555–1575.
- [84] K. Mahata, M. L. Saha, M. Schmittel, *J. Am. Chem. Soc.* **2010**, *132*, 15933–15935.

- [85] M. Schmittel, V. Kalsani, R. S. K. Kishore, H. Cölfen, J. W. Bats, *J. Am. Chem. Soc.* **2005**, *127*, 11544–11545.
- [86] M. L. Saha, M. Schmittel, *J. Am. Chem. Soc.* **2013**, *135*, 17743–17746.
- [87] K. Mahata, M. Schmittel, *J. Am. Chem. Soc.* **2009**, *131*, 16544–16554.
- [88] F. J. Rizzuto, J. P. Carpenter, J. R. Nitschke, *J. Am. Chem. Soc.* **2019**, *141*, 9087–9095.
- [89] T. K. Ronson, J. P. Carpenter, J. R. Nitschke, *Chem* **2022**, *8*, 557–568.
- [90] Y. Yang, T. K. Ronson, D. Hou, J. Zheng, I. Jahović, K. H. Luo, J. R. Nitschke, *J. Am. Chem. Soc.* **2023**, *145*, 19164–19170.
- [91] J. A. Davies, T. K. Ronson, J. R. Nitschke, *J. Am. Chem. Soc.* **2024**, *146*, 5215–5223.
- [92] S. Sudan, F. Fadaei-Tirani, R. Scopelliti, K. E. Ebbert, G. H. Clever, K. Severin, *Angew. Chem. Int. Ed.* **2022**, *61*, e202201823.
- [93] M. Käseborn, J. J. Holstein, G. H. Clever, A. Lützen, *Angew. Chem. Int. Ed.* **2018**, *57*, 12171–12175.
- [94] H. Zhu, T. K. Ronson, K. Wu, J. R. Nitschke, *J. Am. Chem. Soc.* **2024**, *146*, 2370–2378.
- [95] J. A. Davies, T. K. Ronson, J. R. Nitschke, *Chem* **2022**, *8*, 1099–1106.
- [96] A. Stephenson, S. P. Argent, T. Riis-Johannessen, I. S. Tidmarsh, M. D. Ward, *J. Am. Chem. Soc.* **2011**, *133*, 858–870.
- [97] M. Kieffer, B. S. Pilgrim, T. K. Ronson, D. A. Roberts, M. Aleksanyan, J. R. Nitschke, *J. Am. Chem. Soc.* **2016**, *138*, 6813–6821.
- [98] Z. R. Bell, L. P. Harding, M. D. Ward, *Chem. Commun.* **2003**, *0*, 2432–2433.
- [99] Y. Wang, P. Cheng, Y. Song, D. Liao, S. Yan, *Chem. Eur. J.* **2007**, *13*, 8131–8138.
- [100] Y. Liu, V. Ch. Kravtsov, D. A. Beauchamp, J. F. Eubank, M. Eddaoudi, *J. Am. Chem. Soc.* **2005**, *127*, 7266–7267.
- [101] D. Ogata, J. Yuasa, *Angew. Chem. Int. Ed.* **2019**, *58*, 18424–18428.
- [102] S. Hiraoka, Y. Sakata, M. Shionoya, *J. Am. Chem. Soc.* **2008**, *130*, 10058–10059.
- [103] J. E. M. Lewis, A. Tarzia, A. J. P. White, K. E. Jelfs, *Chem. Sci.* **2020**, *11*, 677–683.
- [104] P. Molinska, A. Tarzia, L. Male, K. E. Jelfs, J. E. M. Lewis, *Angew. Chem. Int. Ed.* **2023**, *62*, e202315451.
- [105] A. Tarzia, J. E. M. Lewis, K. E. Jelfs, *Angew. Chem. Int. Ed.* **2021**, *60*, 20879–20887.
- [106] J. E. M. Lewis, *Angew. Chem. Int. Ed.* **2022**, *61*, e202212392.
- [107] J. de Montmollin, A. B. Solea, D. W. Chen, F. Fadaei-Tirani, K. Severin, *Inorg. Chem.* **2024**, *63*, 4583–4588.
- [108] R.-J. Li, A. Tarzia, V. Posligua, K. E. Jelfs, N. Sanchez, A. Marcus, A. Baksi, G. H. Clever, F. Fadaei-Tirani, K. Severin, *Chem. Sci.* **2022**, *13*, 11912–11917.
- [109] R.-J. Li, A. Marcus, F. Fadaei-Tirani, K. Severin, *Chem. Commun.* **2021**, *57*, 10023–10026.
- [110] H. Li, Z.-J. Yao, D. Liu, G.-X. Jin, *Coordin. Chem. Rev.* **2015**, *293*, 139–157.
- [111] Y.-Y. Zhang, W.-X. Gao, L. Lin, G.-X. Jin, *Coordin. Chem. Rev.* **2017**, *344*, 323–344.
- [112] L. K. Moree, L. A. V. Faulkner, J. D. Crowley, *Chem. Soc. Rev.* **2023**, *53*, 25–46.
- [113] H.-Y. Lin, Y.-T. Wang, X. Shi, H.-B. Yang, L. Xu, *Chem. Soc. Rev.* **2023**, *52*, 1129–1154.
- [114] E. Benchimol, B.-N. T. Nguyen, T. K. Ronson, J. R. Nitschke, *Chem. Soc. Rev.* **2022**, *51*, 5101–5135.
- [115] E. Benchimol, J. Tessarolo, G. H. Clever, *Nat. Chem.* **2024**, *16*, 13–21.
- [116] S. J. Wezenberg, *Chem. Lett.* **2020**, *49*, 609–615.
- [117] S. Goeb, M. Sallé, *Acc. Chem. Res.* **2021**, *54*, 1043–1055.
- [118] K. Endo, H. Ube, M. Shionoya, *J. Am. Chem. Soc.* **2019**, *142*, 407–416.
- [119] D. Zhang, T. K. Ronson, L. Xu, J. R. Nitschke, *J. Am. Chem. Soc.* **2020**, *142*, 9152–9157.
- [120] Felix J. Rizzuto, P. Pröhm, A. J. Plajer, J. L. Greenfield, J. R. Nitschke, *J. Am. Chem. Soc.* **2019**, *141*, 1707–1715.
- [121] D. A. Roberts, B. S. Pilgrim, G. Sirvinskaite, T. K. Ronson, J. R. Nitschke, *J. Am. Chem. Soc.* **2018**, *140*, 9616–9623.
- [122] K. Wu, T. K. Ronson, L. Goh, W. Xue, A. W. Heard, P. Su, X. Li, M. Vinković, J. R. Nitschke, *J. Am. Chem. Soc.* **2023**, *145*, 11356–11363.
- [123] T. Zhang, L.-P. Zhou, X.-Q. Guo, L.-X. Cai, Q.-F. Sun, *Nat. Commun.* **2017**, *8*, ncomms15898.
- [124] L.-X. Cai, D.-N. Yan, P.-M. Cheng, J.-J. Xuan, S.-C. Li, L.-P. Zhou, C.-B. Tian, Q.-F. Sun, *J. Am. Chem. Soc.* **2021**, *143*, 2016–2024.
- [125] S. Samantray, S. Krishnaswamy, D. K. Chand, *Nat. Commun.* **2020**, *11*, 880.
- [126] M. Han, R. Michel, B. He, Y. Chen, D. Stalke, M. John, G. H. Clever, *Angew. Chem. Int. Ed.* **2013**, *52*, 1319–1323.
- [127] A. Galan, P. Ballester, *Chem. Soc. Rev.* **2016**, *45*, 1720–1737.
- [128] J. L. Brumaghim, M. Michels, K. N. Raymond, *Eur. J. Org. Chem.* **2004**, *2004*, 4552–4559.

- [129] V. M. Dong, D. Fiedler, B. Carl, R. G. Bergman, K. N. Raymond, *J. Am. Chem. Soc.* **2006**, *128*, 14464–14465.
- [130] J. L. Brumaghim, M. Michels, D. Pagliero, K. N. Raymond, *Eur. J. Org. Chem.* **2004**, *2004*, 5115–5118.
- [131] D. Fiedler, R. G. Bergman, K. N. Raymond, *Angew. Chem. Int. Ed.* **2006**, *45*, 745–748.
- [132] S.-Y. Yu, T. Kusukawa, K. Biradha, M. Fujita, *J. Am. Chem. Soc.* **2000**, *122*, 2665–2666.
- [133] S. Horiuchi, T. Murase, M. Fujita, *J. Am. Chem. Soc.* **2011**, *133*, 12445–12447.
- [134] P. Mal, B. Breiner, K. Rissanen, J. R. Nitschke, *Science* **2009**, *324*, 1697–1699.
- [135] M. Yamashina, Y. Sei, M. Akita, M. Yoshizawa, *Nat. Commun.* **2014**, *5*, 4662.
- [136] S. Hasegawa, S. L. Meichsner, J. J. Holstein, A. Baksi, M. Kasanmascheff, G. H. Clever, *J. Am. Chem. Soc.* **2021**, *143*, 9718–9723.
- [137] M. Yoshizawa, T. Kusukawa, M. Fujita, K. Yamaguchi, *J. Am. Chem. Soc.* **2000**, *122*, 6311–6312.
- [138] M. Yoshizawa, T. Kusukawa, M. Fujita, S. Sakamoto, K. Yamaguchi, *J. Am. Chem. Soc.* **2001**, *123*, 10454–10459.
- [139] S. Wang, T. Sawada, M. Fujita, *Chem. Commun.* **2016**, *52*, 11653–11656.
- [140] P. Cheng, L. Cai, S. Li, S. Hu, D. Yan, L. Zhou, Q. Sun, *Angew. Chem. Int. Ed.* **2020**, *59*, 23569–23573.
- [141] B.-N. T. Nguyen, J. D. Thoburn, A. B. Grommet, D. J. Howe, T. K. Ronson, H. P. Ryan, J. L. Bolliger, J. R. Nitschke, *J. Am. Chem. Soc.* **2021**, *143*, 12175–12180.
- [142] A. J. McConnell, C. J. E. Haynes, A. B. Grommet, C. M. Aitchison, J. Guilleme, S. Mikutis, J. R. Nitschke, *J. Am. Chem. Soc.* **2018**, *140*, 16952–16956.
- [143] Angela B. Grommet, J. B. Hoffman, E. G. Percástegui, J. Mosquera, D. J. Howe, J. L. Bolliger, J. R. Nitschke, *J. Am. Chem. Soc.* **2018**, *140*, 14770–14776.
- [144] M. Kieffer, A. M. Garcia, C. J. E. Haynes, S. Kralj, D. Iglesias, J. R. Nitschke, S. Marchesan, *Angew. Chem. Int. Ed.* **2019**, *58*, 7982–7986.
- [145] N. Mihara, T. K. Ronson, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2019**, *58*, 12497–12501.
- [146] H. Takezawa, K. Shitozawa, M. Fujita, *Nat. Chem.* **2020**, *12*, 574–578.
- [147] H. Takezawa, K. Iizuka, M. Fujita, *Angew. Chem. Int. Ed.* **2024**, *63*, e202319140.
- [148] K. Iizuka, H. Takezawa, M. Fujita, *J. Am. Chem. Soc.* **2023**, *145*, 25971–25975.
- [149] M. Yoshizawa, J. K. Klosterman, M. Fujita, *Angew. Chem. Int. Ed.* **2009**, *48*, 3418–3438.
- [150] P. Howlader, P. Das, E. Zangrando, P. S. Mukherjee, *J. Am. Chem. Soc.* **2016**, *138*, 1668–1676.
- [151] V. Iannace, C. Sabrià, Y. Xu, M. von Delius, I. Imaz, D. MasPOCH, F. Feixas, X. Ribas, *J. Am. Chem. Soc.* **2024**, *146*, 5186–5194.
- [152] F. M. Steudel, E. Ubasart, L. Leanza, M. Pujals, T. Parella, G. M. Pavan, X. Ribas, M. von Delius, *Angew. Chem. Int. Ed.* **2023**, *62*, e202309393.
- [153] E. Ubasart, O. Borodin, C. Fuertes-Espinosa, Y. Xu, C. García-Simón, L. Gómez, J. Juanhuix, F. Gándara, I. Imaz, D. MasPOCH, M. von Delius, X. Ribas, *Nat. Chem.* **2021**, 1–8.
- [154] C. J. Hastings, M. D. Pluth, R. G. Bergman, K. N. Raymond, *J. Am. Chem. Soc.* **2010**, *132*, 6938–6940.
- [155] C. Mozaceanu, C. G. P. Taylor, J. R. Piper, S. P. Argent, M. D. Ward, *Chemistry* **2020**, *2*, 22–32.
- [156] M. D. Ludden, C. G. P. Taylor, M. B. Tipping, J. S. Train, N. H. Williams, J. C. Dorrat, K. L. Tuck, M. D. Ward, *Chem. Sci.* **2021**, *12*, 14781–14791.
- [157] R. L. Spicer, H. M. O’Connor, Y. Ben-Tal, H. Zhou, P. J. Boaler, F. C. Milne, E. K. Brechin, Guy. C. Lloyd-Jones, P. J. Lusby, *Chem. Sci.* **2023**, *14*, 14140–14145.
- [158] J. Wang, T. A. Young, F. Duarte, P. J. Lusby, *J. Am. Chem. Soc.* **2020**, *142*, 17743–17750.
- [159] J. Guo, Y. Fan, Y. Lu, S. Zheng, C. Su, *Angew. Chem. Int. Ed.* **2020**, *59*, 8661–8669.
- [160] J. Chen, X. Wu, S. Huang, J. Yang, Y.-L. Lu, Z. Jiao, C.-Y. Su, *ACS Catal.* **2024**, *14*, 3733–3741.
- [161] O. Yanshyna, M. J. Białek, O. V. Chashchikhin, R. Klajn, *Commun. Chem.* **2022**, *5*, 44.
- [162] M. Ueda, N. Kishida, L. Catti, M. Yoshizawa, *Chem. Sci.* **2022**, *13*, 8642–8648.
- [163] H. Wang, L. Li, X. Li, C. He, *Israel J. Chem.* **2018**, *59*, 273–279.
- [164] X. Tang, H. Jiang, Y. Si, N. Rampal, W. Gong, C. Cheng, X. Kang, D. Fairen-Jimenez, Y. Cui, Y. Liu, *Chem* **2021**, *7*, 2771–2786.
- [165] M. Yamashina, M. M. Sartin, Y. Sei, M. Akita, S. Takeuchi, T. Tahara, M. Yoshizawa, *J. Am. Chem. Soc.* **2015**, *137*, 9266–9269.
- [166] D. Samanta, J. Gemen, Z. Chu, Y. Diskin-Posner, L. J. W. Shimon, R. Klajn, *Proc. National Acad. Sci.* **2018**, *115*, 9379–9384.
- [167] J. Gemen, J. R. Church, T.-P. Ruoko, N. Durandin, M. J. Białek, M. Weißenfels, M. Feller, M. Kazes, M. Odaybat, V. A. Borin, R. Kalepu, Y. Diskin-Posner, D. Oron, M. J. Fuchter, A. Priimagi, I. Schapiro, R. Klajn, *Science* **2023**, *381*, 1357–1363.

- [168] M. Canton, A. B. Grommet, L. Pesce, J. Gemen, S. Li, Y. Diskin-Posner, A. Credi, G. M. Pavan, J. Andréasson, R. Klajn, *J. Am. Chem. Soc.* **2020**, *142*, 14557–1456.
- [169] L. Pesce, C. Perego, A. B. Grommet, R. Klajn, G. M. Pavan, *J. Am. Chem. Soc.* **2020**, *142*, 9792–9802.
- [170] A. B. Grommet, L. M. Lee, R. Klajn, *Acc. Chem. Res.* **2020**, *53*, 2600–2610.
- [171] D. Samanta, D. Galaktionova, J. Gemen, L. J. W. Shimon, Y. Diskin-Posner, L. Avram, P. Král, R. Klajn, *Nat. Commun.* **2018**, *9*, 641.
- [172] D. Samanta, S. Mukherjee, Y. P. Patil, P. S. Mukherjee, *Chem. Eur. J.* **2012**, *18*, 12322–12329.
- [173] A. I. Hanopolskyi, S. De, M. J. Białek, Y. Diskin-Posner, L. Avram, M. Feller, R. Klajn, *Beilstein J. Org. Chem.* **2019**, *15*, 2398–2407.
- [174] J. Gemen, M. J. Białek, M. Kazes, L. J. W. Shimon, M. Feller, S. N. Semenov, Y. Diskin-Posner, D. Oron, R. Klajn, *Chem* **2022**, *8*, 2362–2379.
- [175] M. Yuasa, R. Sumida, Y. Tanaka, M. Yoshizawa, *Chem. Eur. J.* **2022**, *28*, e202104101.
- [176] M. Weißenfels, J. Gemen, R. Klajn, *Chem* **2021**, *7*, 23–37.
- [177] G. Ragazzon, L. J. Prins, *Nat Nanotechnol* **2018**, *13*, 882–889.
- [178] R. D. Astumian, *Angew. Chem. Int. Ed.* **2024**, *63*, e202306569.
- [179] R. D. Astumian, *Nat. Nanotechnol.* **2012**, *7*, 684–688.
- [180] S. Borsley, D. Leigh, B. M. W. Roberts, *Angew. Chem. Int. Ed.* **2024**, e202400495.
- [181] S. Borsley, D. A. Leigh, B. M. W. Roberts, *Nat. Chem.* **2022**, *14*, 728–738.
- [182] K. Das, L. Gabrielli, L. J. Prins, *Angew. Chem. Int. Ed.* **2021**, *60*, 20120–20143.
- [183] C. S. Wood, C. Browne, D. M. Wood, J. R. Nitschke, *Acs Central. Sci.* **2015**, *1*, 504–509.
- [184] J.-F. Ayme, B. Bruchmann, L. Karmazin, N. Kyritsakas, *Chem. Sci.* **2023**, *14*, 1244–1251.
- [185] H. Lee, J. Tessarolo, D. Langbehn, A. Baksi, R. Herges, G. H. Clever, *J. Am. Chem. Soc.* **2022**, *7*, 3099–3105.
- [186] E. Nieland, J. Voss, A. Mix, B. M. Schmidt, *Angew. Chem. Int. Ed.* **2022**, *61*, e202212745.
- [187] M. Ovalle, M. Kathan, R. Toyoda, C. N. Stindt, S. Crespi, B. L. Feringa, *Angew. Chem. Int. Ed.* **2023**, *62*, e202214495.
- [188] A. Ghosh, L. Slappendel, B.-N. T. Nguyen, L. K. S. von Krbek, T. K. Ronson, A. M. Castilla, J. R. Nitschke, *J. Am. Chem. Soc.* **2023**, *145*, 3828–3832.
- [189] A. D. W. Kennedy, R. G. DiNardi, L. L. Fillbrook, W. A. Donald, J. E. Beves, *Chem. Eur. J.* **2022**, *28*, e202104461.
- [190] A. J. McConnell, C. M. Aitchison, A. B. Grommet, J. R. Nitschke, *J. Am. Chem. Soc.* **2017**, *139*, 6294–6297.
- [191] A. Jiménez, R. A. Bilbeisi, T. K. Ronson, S. Zarra, C. Woodhead, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2014**, *53*, 4556–4560.
- [192] B. S. Pilgrim, D. A. Roberts, T. G. Lohr, T. K. Ronson, J. R. Nitschke, *Nat. Chem.* **2017**, *9*, 1276–1281.
- [193] S. Ma, M. M. J. Smulders, Y. R. Hristova, J. K. Clegg, T. K. Ronson, S. Zarra, J. R. Nitschke, *J. Am. Chem. Soc.* **2013**, *135*, 5678–5684.
- [194] A. M. Castilla, T. K. Ronson, J. R. Nitschke, *J. Am. Chem. Soc.* **2016**, *138*, 2342–2351.
- [195] L. Xu, D. Zhang, T. K. Ronson, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2020**, *59*, 7435–7438.
- [196] Y. Yang, T. K. Ronson, J. Zheng, N. Mihara, J. R. Nitschke, *Chem* **2023**, *9*, 1972–1982.
- [197] A. B. Grommet, J. L. Bolliger, C. Browne, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2015**, *54*, 15100–15104.
- [198] A. Walther, I. Regeni, J. J. Holstein, G. H. Clever, *J. Am. Chem. Soc.* **2023**, *145*, 25365–25371.
- [199] I. Regeni, B. Chen, M. Frank, A. Baksi, J. J. Holstein, G. H. Clever, *Angew. Chem. Int. Ed.* **2021**, *60*, 5673–5678.

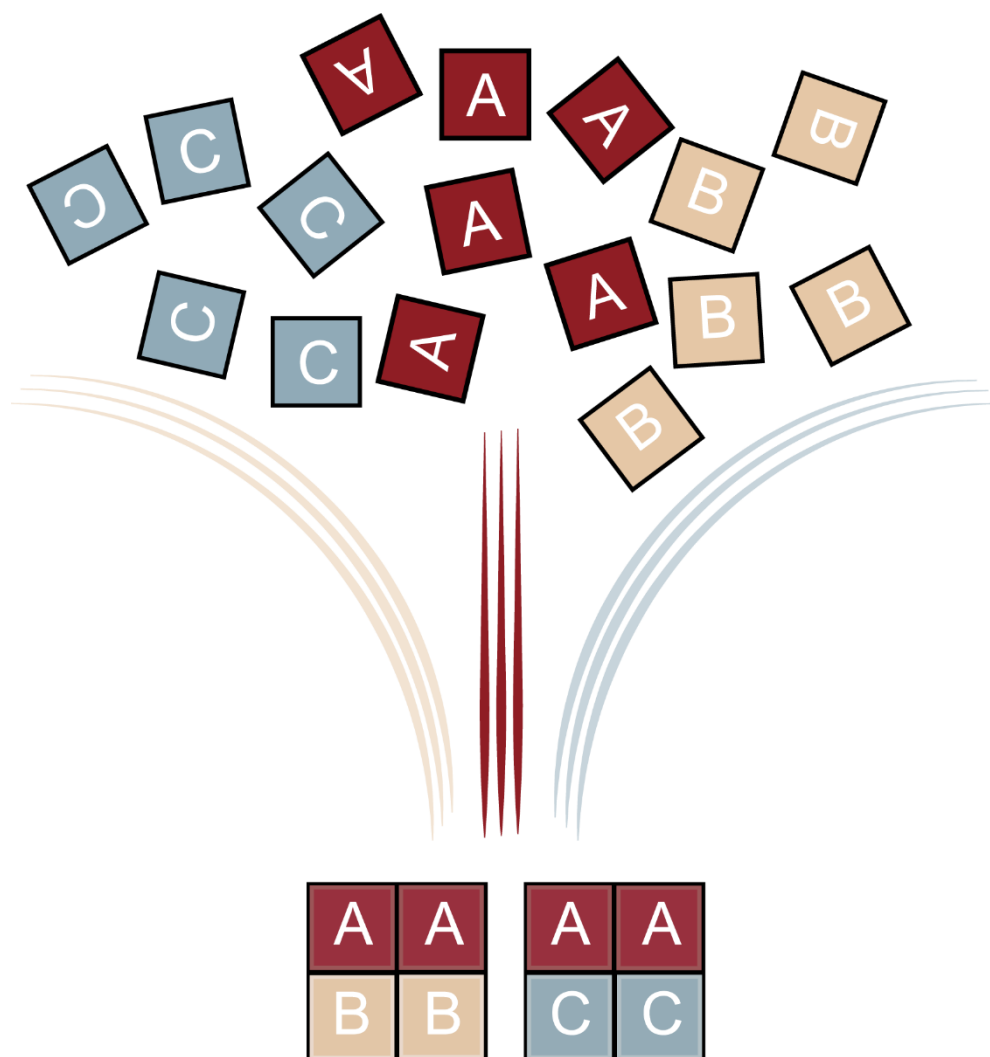
Scope of the thesis

The complexity and functionality of cages have rapidly developed over the past years, yet the focus has been set on making single assemblies. Heteroleptic and multifunctional species are now common in the literature and there is a general understanding of the rules that govern their assembly. However, systems in which more than one of these assemblies coexist in solution are yet to be reported. Their complexity is not only translated in the number of components but also the number of assemblies, giving it another layer. In light of this, I chose to investigate multi-cage systems where at least one heteroleptic species is present thus differing from the known narcissistic self-sorting. This dissertation describes the following topics:

- Introduction of *heteromeric complete self-sorting* and the formation of the first heteroleptic cage populations.
- Control in the self-sorting outcome between *heteromeric* and *integrative* through component's stoichiometry.
- Development of a cage population capable of guest segregation *e.g.* where each individual can encapsulate a specific guest within its cavity.
- Dynamic population of cages with emergent properties such as chiral memory.
- Out-of-equilibrium behavior of a cage population.

Chapter I

Making multiple heteroleptic assemblies coexist through heteromeric complete self-sorting



Heteromeric complete self-sorting

Part of this chapter is reported in the following paper:

Elie Benchimol (†), Irene Regeni (†), Bo Zhang, Michele Kabiri, Julian J. Holstein, and Guido H. Clever*

“Heteromeric Complete Self-Sorting in Coordination Cage Systems”

J. Am. Chem. Soc. **2024**, *146*, 10, 6905–6911, (†) These authors contributed equally to the work

Introduction

Self-sorting refers to the phenomenon wherein mixtures containing several different molecules that recognize and associate with each other lead to a defined assembly rather than a collection of all possible combinations of components. Therefore, organized systems possess a higher information content compared to statistical mixtures.^[1,2] In biological systems, self-sorting is an important phenomenon that enables the assembly of complex structures through the specific association of different subcomponents. Similarly, in the field of systems chemistry, self-sorting plays a pivotal role, especially when competing association processes lead to adaptive populations of assemblies, cross-talk between coexisting species, and the emergence of a broad range of functionalities.^[3–6]

With the aim of advancing the level of control over multicomponent systems, supramolecular chemists have focused on strategies for the exclusive formation of discrete self-sorted structures composed of a defined set of building blocks.^[7] We have seen in the introduction of this thesis that several strategies have been established for creating heteroleptic assemblies, yet making several of these coexist without any further shuffling of the components is a greater challenge. One intuitive approach involves using ligands with limited association possibilities, such that only specific combinations result in integrative self-sorting. For example, taking a ligand A capable of associating with both B (pair AB) and C (pair AC) while the two latter can't associate into a heteroleptic species together (no pair BC). Before delving deeper into this chapter and its experimental aspects, it is imperative to establish some nomenclature. Schmittl has been a pioneer in the development of complex self-sorting processes in which more than two building blocks are mixed.^[8–14] Several other key contributors must be evoked with among them monuments like Lehn,^[15–18] Sanders or Otto^[6,19,20] which have contributed to the development of dynamic covalent chemistry and to a deeper understanding of self-sorting phenomena. Dynamicity, error correction and the ability to rearrange are key features for successful sorting processes and for creating complex organized systems, making coordination cages an ideal platform for such phenomena. In a review paper, Schmittl has established a nomenclature defining the possible outcomes arising from the mixing of three components together (Figure 1).^[8] One is of particular interest as it corresponds to multiple heteroleptic species coexisting, namely **heteromeric complete self-sorting**. In the case presented, all the components can associate together in pairs and therefore once mixed in a 1:1:1 ratio, the three possible combinations are formed. However, by modifying the relative amount of components it is conceivable to envision a situation in which one might be able to selectively assemble two out of the three possible pairs. This scenario still results in unconventional self-sorting and the formation of a so-called “population”.

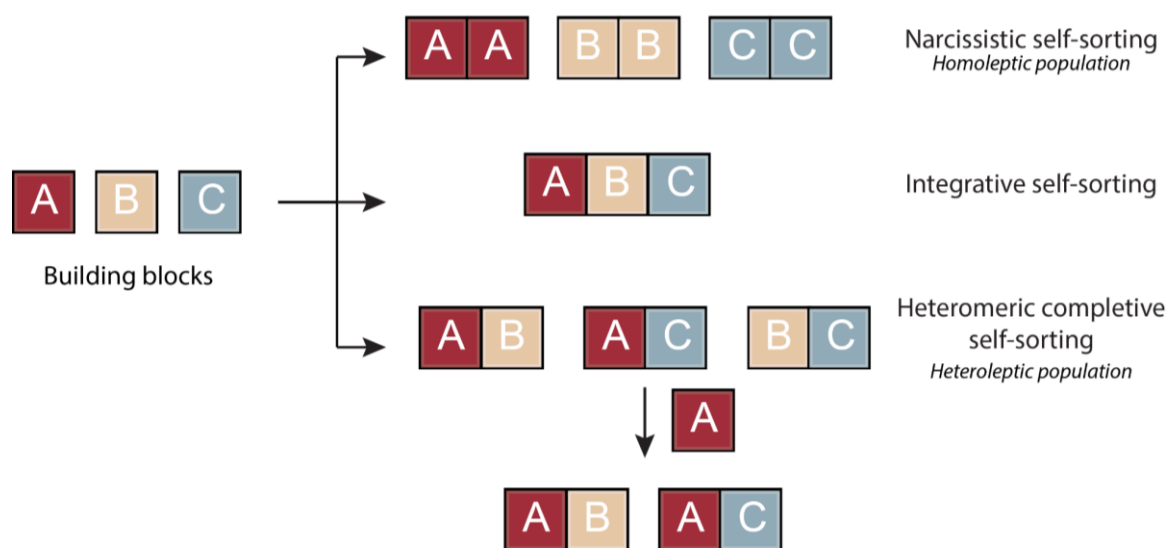


Figure 1: Schematic representation of the self-sorting outcomes possibly obtained from mixing three distinct building blocks.

While exploring the implementation of dyes in the backbone of coordination cages, Dr. Irene Regeni, from Clever Lab, realized that it was possible to use a specific diketopyrrolopyrrole (DPP) ligand **A** equipped with quinolines^[21] to associate separately with either a carbazole^[22] or a dimethyl fluorene ligands.^[23] The two heteroleptic assemblies could coexist without further shuffling when mixed in the proper ratio. The following results are based on her initial observations.

1. *Trans* heteroleptic Pd₂A₂B₂ figure-of-eight assemblies and pseudo statistical mixture

To extend this system and rationalize it, I started off by employing ligand **A** in combination with several other organic building blocks (Figure 2). When combined with a Pd(II) source in deuterated acetonitrile (CD₃CN), ligand **A** yields a Pd₂A₃(MeCN)₂ assembly (see structure in Figure 4), because its coordination vectors do not allow the accommodation of four of its own around the d⁸ square planar Pd(II) cation.^[21] All the ligands annotated **B_x** (x= 1-6) give rise to lantern shape Pd₂**B_x**₄ cages in CD₃CN^[22,24,25] while all ligands annotated **C_x** (x= 1,2,3) form Pd₃**C_x**₆ and/or Pd₄**B_x**₈ architectures.^[7,23,26]

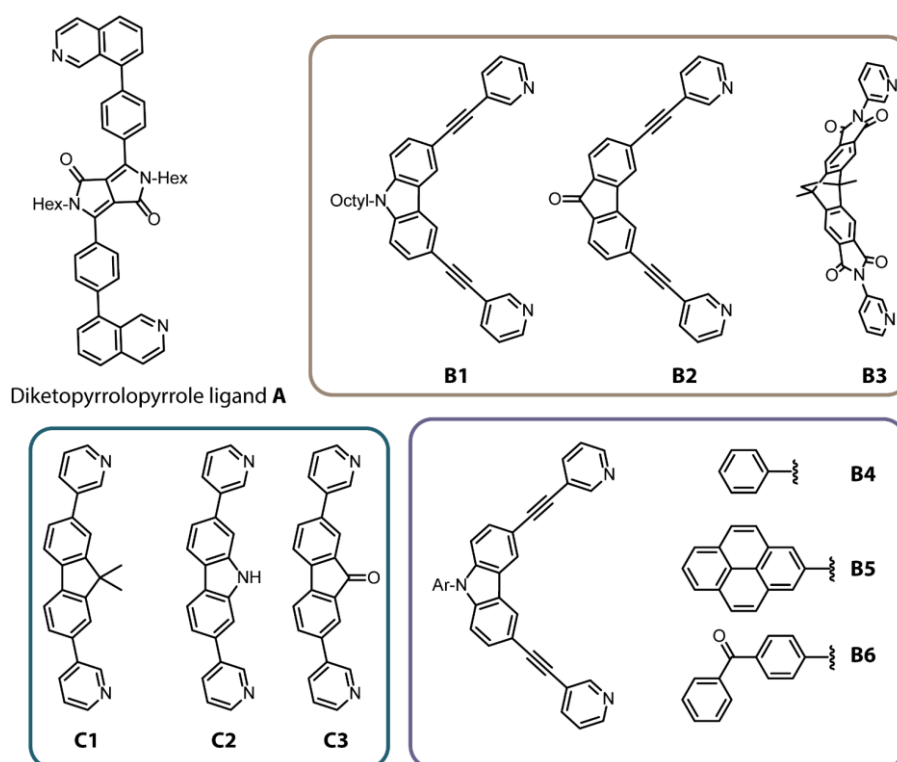


Figure 2: Ligands employed in this chapter. (brown box) These ligands form figure-of-eight *trans* architectures with **A** and were employed both for the population study as well as their photophysical properties. (blue box) These ligands form *cis* cages with **A** and were solely used for the population study. (purple box) These ligands form, as well, figure-of-eight, and were only employed for the photophysical study.

The combination of ligand **A** and **B1** with Pd(II) in an equimolar ratio affords a *trans*-Pd₂A₂B₂ type assembly with a *figure-of-eight* topology (Figure 3).^[21,27] The ligands **A** adopt an S conformation and intertwine through a stacking of chromophores in the middle of the cage leaving no inner cavity accessible and creating the **8**. This motif is crucial throughout this thesis and presents many advantages that will be discussed in this chapter and the last one of the dissertation. It is also important to notice that this motif is chiral and two enantiomers of the **8**, *P* or *M*, can be formed.

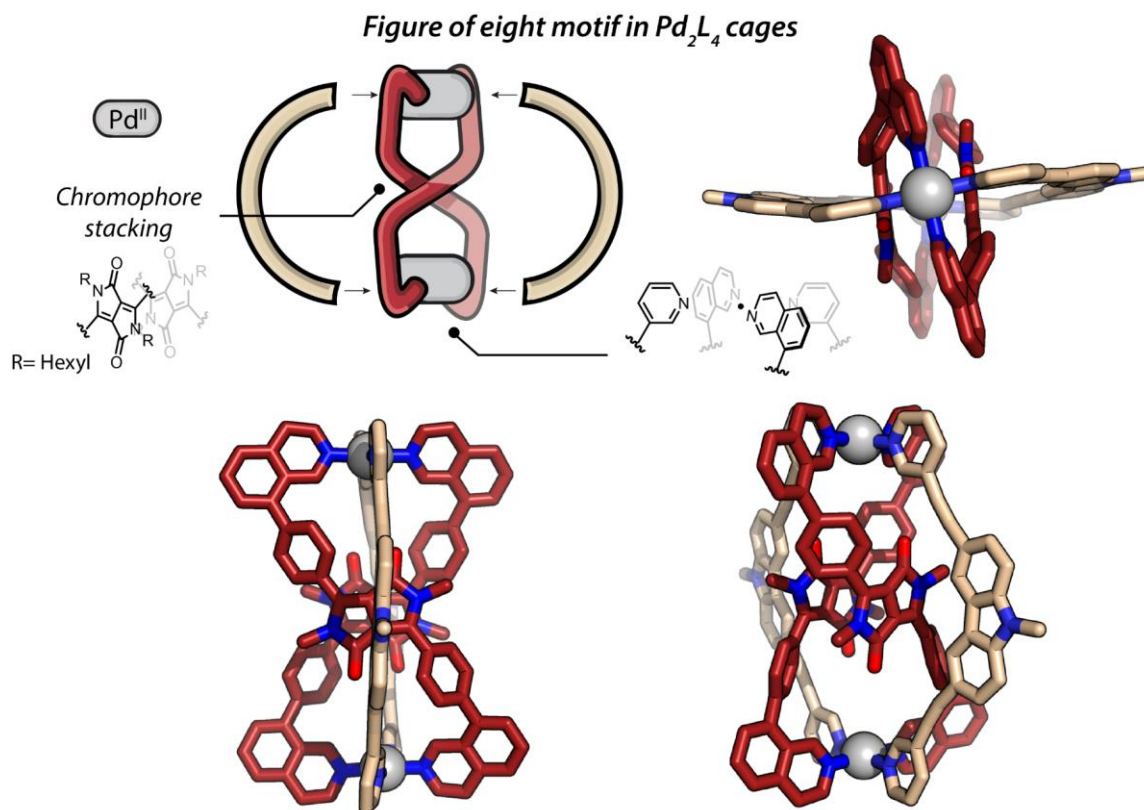


Figure 3: The figure-eight motif obtained from the use of ligand **A** and C-shaped ligands with (near) converging vectors. The two **A** interlace in the middle of the assembly resulting in a stacking of the chromophores. The outer ligands complete the Pd(II) square planar coordination environment creating a *trans*- $Pd_2A_2B_2$ type structure.

Because of the structural similarities between **B1** and **B2**, it was anticipated that combining them would result in a statistical mixture and that **B2** would also lead to the formation of the same type of heteroleptic structure when associated with **A**. As expected, we obtained the $Pd_2A_2B_2$ interpenetrated species in CD_3CN as confirmed by NMR and ESI-MS. DOSY-NMR gave access to the hydrodynamic radius of the cage, with $r_h=1.22$ nm, in accordance with the previously observed value for $Pd_2A_2B_1$.^[21] In the absence of suitable crystals for X-ray diffraction analysis, the structure was optimized in the gas phase on DFT level ($\omega B97X-D/def2-SVP$) in order to provide a better visualization. The two ligands **A** present one rotated quinoline moiety allowing binding vectors with opposite directions and capable of coordinating the Pd(II) in a *trans* manner, the square planar coordination sphere of the metal being fulfilled by the two outer fluorenone ligands. No cavity is found in the structure as ligand **A** must adopt such configuration crossing in the inner available space. I demonstrated that the two ligands **B1** and **B2** do not associate into a discrete species but that they respectively form heteroleptic assemblies with the same third ligand **A**. This matches the requirements established earlier to go a step further in complexity. Therefore, $Pd_2A_3(MeCN)_2$, the homoleptic assembly from ligand **A**, was added to a solution of the statistical mixture from **B1** and **B2** (Figure 4a). The resulting 1H NMR spectrum was highly complex, suggesting the presence of multiple species in solution. Further ESI-MS analysis allowed us to better understand the outcome of the reaction. The spectrum shows that $Pd_2A_2B_1$, $Pd_2B_1A_2B_2$, and $Pd_2A_2B_2$ form as a *pseudo*-statistical mixture (Figure 4b). The observed peaks correspond to $[cages + nBF_4](4-n)^+$ with $n=0-2$. The complexity of the NMR spectrum can, therefore, be attributed to the presence of three different heteroleptic assemblies in varying ratios. From this mixture, we obtained red crystalline plates suitable for X-ray diffraction analysis. It enabled unveiling the structure of $Pd_2B_1A_2B_2$, the first architecture presenting a ternary *trans*- Pd_2AB_2C figure-of-eight topology (Figure 4c, middle). In this crystal structure both ligands **A** adopt an S-shape conformation and **B1** and **B2** complete the square-planar coordination sphere of the Pd(II) cations in a *trans*-arrangement. In the present case, because of the strong structural similarity between the two ligands, a second level of integrative self-sorting does not occur

and the mixture yields a statistical arrangement of the two outer ligand alternatives around the central pair of ligands **A**. Thus, it seems that components with closely similar geometries may not be suitable for making heteroleptic assemblies coexist in a defined way.

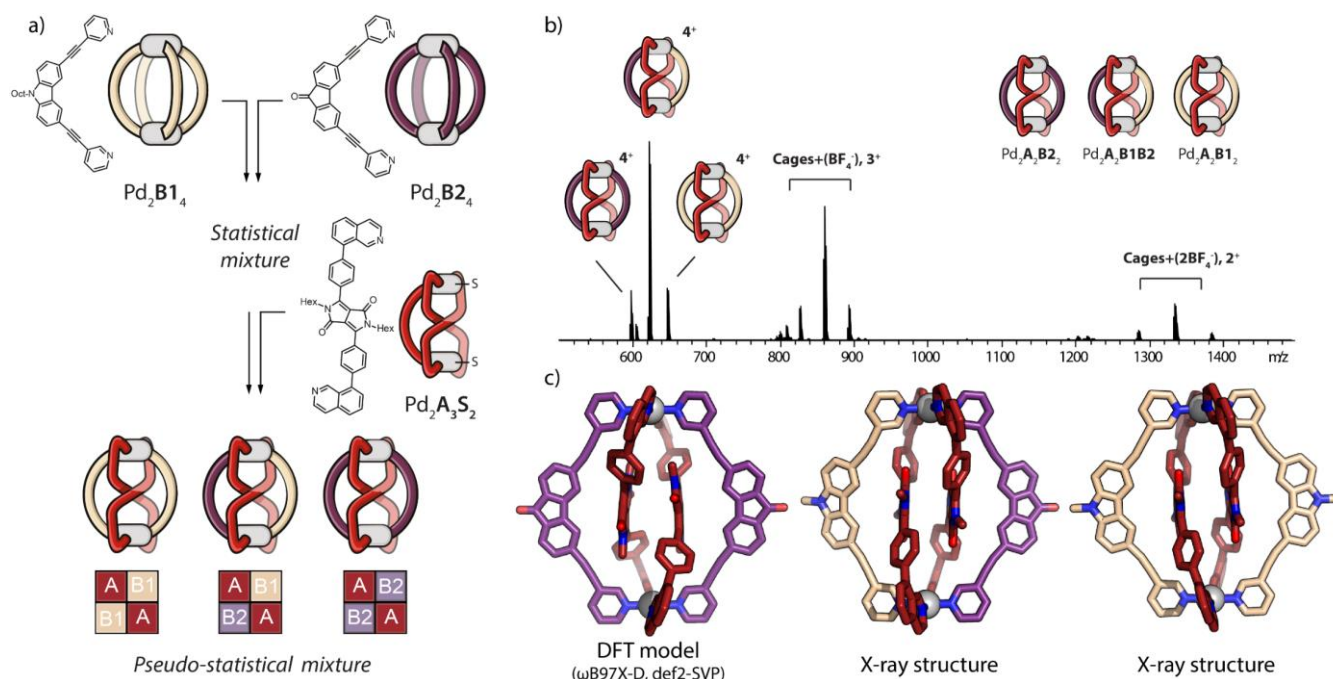


Figure 4: a) Schematic representation of the two-step process leading to pseudo-statistical mixture. b) HR-ESI MS of the final mixture. The observed peaks correspond to $[\text{cages} + n\text{BF}_4](4-n)^+$ with $n=0-2$. c) Comparison of the three figure-of-eight cages in the solid state or gas phase optimized geometry.

2. From statistical mixture to heteromeric complete self-sorting of $\text{Pd}_2\text{A}_2\text{B}_2$ figure-of-eight

We had previously observed that **B2** also leads to a statistical mixture when combined with a ribbon-shaped bis-monodentate organic donor **B3**.^[26] Ligand **B3** assembles into a Pd_2B_3 capsule when introduced with Pd(II) in CD_3CN .^[25] Building upon these observations, the homoleptic assembly $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ was added to the statistical mixture obtained from **B2** and **B3** and heated it at 70 °C for 24 h (Figure 5a). This time I could observe the emergence of two separate species, corresponding to the two coexisting heteroleptic cages $\text{Pd}_2\text{A}_2\text{B}_2$ and $\text{Pd}_2\text{A}_2\text{B}_3$. The ^1H NMR overlaps with the spectra obtained individually from the separate assemblies (Figure 5b). ESI-MS analysis could also further confirm the coexistence of the two cages (Figure 5c). $\text{Pd}_2\text{A}_2\text{B}_3$ also has the same topology as confirmed by the analysis of the NMR data and DFT modeling ($\omega\text{B97X-D/def2-SVP}$). Therefore, it represented the first instance of two heteroleptic assemblies coexisting in solution, or the so-called *heteromeric complete self-sorting* in coordination cage systems. But how to understand this sorting phenomenon? Herein, in the absence of **A**, the geometrical differences between **B2** and **B3** prevent them to narcissistically or integratively sort in their binary mixture, and instead, their combination affords a statistical mixture of assemblies. Despite this fact, the differences between the ligands are pronounced enough to further drive the heteromeric sorting process once **A** is introduced in the system. The outcome is two discrete heteroleptic assemblies in solution that do not interfere with each other. Important to note that the component stoichiometry is a central parameter (see again later) as it enables the sole formation of the pair. Ribbon ligand **B3**, exhibiting significant structural flexibility, rather self-associates narcissistically in $\text{Pd}_2\text{A}_2\text{B}_3$ (Pd–Pd distance = 15.0 Å) while **B2** then cleanly forms the more elongated $\text{Pd}_2\text{A}_2\text{B}_2$ structure (Pd–Pd distance = 15.6 Å). It was inferred that the energetic cost associated with bridging **B2** and **B3** together in a single assembly, which would necessitate either the stretching of **B3** to the length dictated by the more rigid **B2** or otherwise enforce the Pd(II) coordination sites

to tilt, is higher than the potential entropic gain of statistically shuffling both **B2** and **B3** at the outer positions within the assemblies. To ensure that it did not represent an isolated instance the same mixing experiment was also conducted with **A**, **B1** and **B3** and yielded the same results. In both cases, two figure-of-eight assemblies, lacking an accessible cavity, were formed orthogonally from outer ligands that initially cannot associate with each other. While this marks the first instance of *heteromeric self-sorting*, the underlying reasons behind this phenomenon can be considered intuitive. Indeed, as I had hypothesized, the preferential associations of building blocks, in the appropriate ratio, result in a narcissistic sorting of heteroleptic assemblies. This naturally leads to the question of whether this phenomenon occurs when **A** is introduced with two building blocks that are already capable of associating through integrative self-sorting.

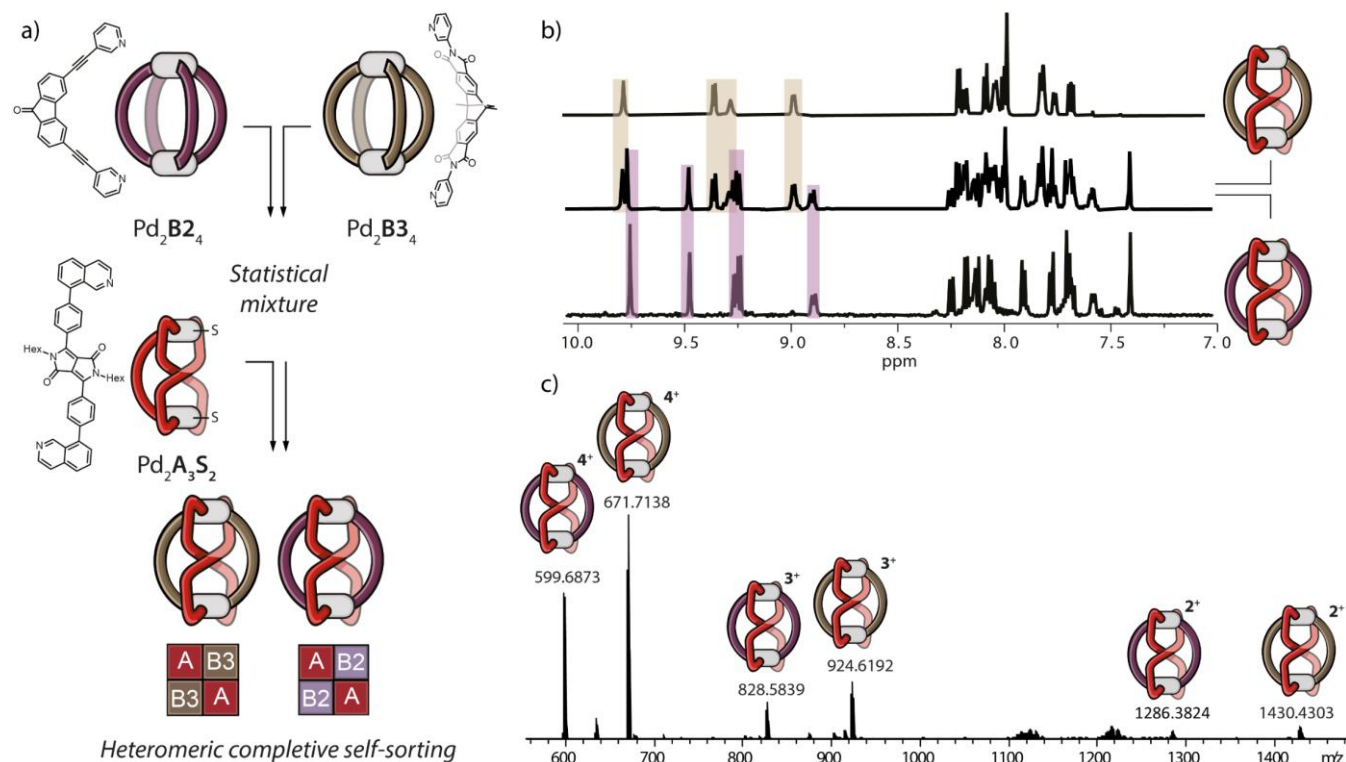


Figure 5: a) Schematic representation of the two-step process leading to heteromeric complete self-sorting. b) $^1\text{H-NMR}$ (CD_3CN , 500 MHz) stack of the two-separate figure-of-eight structures $\text{Pd}_2\text{A}_2\text{B}_2$ and $\text{Pd}_2\text{A}_2\text{B}_3$ and the heteromeric complete self-sorting result after mixing. c) HR-ESI-MS of the mixture of $\text{Pd}_2\text{A}_2\text{B}_2$ and $\text{Pd}_2\text{A}_2\text{B}_3$.

3. From integrative to heteromeric complete self-sorting of $\text{Pd}_2\text{A}_2\text{B}_2$ cages

Examining the structures of the ligands employed thus far, it became apparent that at least one of them needed to be altered to enable integrative self-sorting at the first level. It was already established that 2,7-fluorene, and derivatives, equipped with pyridine donors are capable of forming heteroleptic cages with ligands such as **B1**, **B2** or **B3**.^[23,26] Their diverging vectors match by shape complementarity those of the aforementioned ligands yielding *cis*- $\text{Pd}_2\text{A}_2\text{B}_2$ type cages. Subsequently, I sought to determine if these organic building blocks could also assemble into heteroleptic cages with ligand **A**. We tested the series **C1-C4** and realized that they all led to an unexpected pattern in their $^1\text{H-NMR}$ spectrum (Figure 6a). For example, when **C1** was mixed with **A** and Pd(II) in a 1:1:1 ratio in CD_3CN a new heteroleptic assembly was obtained. The stoichiometry leading to $\text{Pd}_2\text{A}_2\text{C1}_2$ was confirmed by mass spectrometry (Figure 6b).

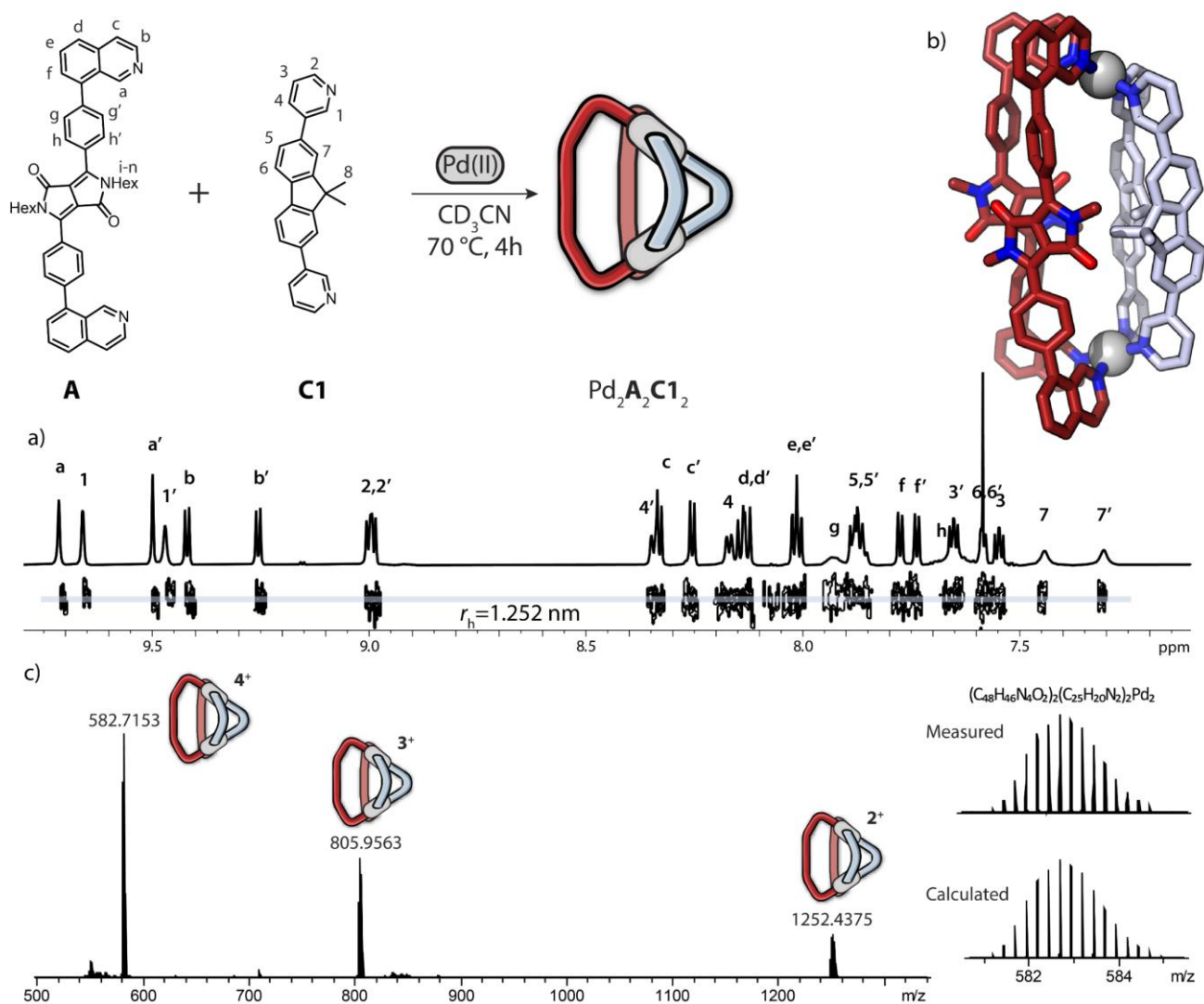


Figure 6: a) ^1H -NMR (CD_3CN , 500 MHz) of $\text{Pd}_2\text{A}_2\text{C1}_2$ with its DOSY trace showing that all the signals belong to a unique species ($D = 5.23 \cdot 10^{-10} \text{ m}^2 \cdot \text{s}^{-1}$, $R_h = 1.252 \text{ nm}$). b) Semi-empirical PM6 model of the *cis*-cage. c) HR-ESI MS where the observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{C1}_2 + n \text{BF}_4]^{(4-n)+}$ with $n=0-2$.

Due to the diverging binding vectors of the smaller ligand **C1**, the unfeasibility of forming a *trans*-figure-of-eight assembly when combined with **A** was anticipated (Figure 7). The calculated structure shows indeed a very high distortion of the ligand which seems unfavorable. I thus inferred this assembly to display a *cis*-heteroleptic cage topology with ligands positioned by shape complementarity between converging **A** and diverging **C1** coordination vectors. However, the previous observations on the formation of such a *cis*-cage point to a single set of signals for each ligand in the ^1H NMR spectrum as no further symmetry breaking would typically be expected. Surprisingly, analysis of this cage by NMR spectroscopy shows a 2-fold splitting of all proton signals for both **A** and **C1**. Further DOSY NMR spectroscopy confirmed that all signals belonged to a single unique assembly with a size-matching binuclear heteroleptic architecture (Figure 6a). Unfortunately, $\text{Pd}_2\text{A}_2\text{C1}_2$ never afforded crystals suitable for X-ray diffraction analysis. However, employing its carbazole analog **C2** proved to be successful for growing orange plate crystals of $\text{Pd}_2\text{A}_2\text{C2}_2$ by slow diffusion of diethyl ether into a solution of acetonitrile. It is important to note that the crystallization setup contained an excess amount of $(n\text{Bu})_4\text{NAsF}_6$ salt, relative to the cage, which enhanced the diffraction power of the crystals. As previously mentioned, the binding angles of the two ligands being nearly identical, they form the same type of *cis*-heteroleptic cage. Indeed, solving the crystal structure of $\text{Pd}_2\text{A}_2\text{C2}_2$ revealed the expected *cis*- $\text{Pd}_2\text{A}_2\text{B}_2$ arrangement of the two ligands (Figure 7). Accessing the energies of both *cis* and *trans* geometry optimized structures (gas phase semi-empirical PM6 level) showed that

$\Delta E(\text{trans vs. cis}) = +149.78 \text{ kJ/mol}$ (Figure 7). These calculations back up the preferential formation of the *cis* cage but the splitting remained a mystery until we compared more thoroughly the calculated structure with the X-ray data. In the solid-state structure, unlike the situation observed in other *cis*-heteroleptic architectures, displaying a unique signal set, the shape of ligand **A** created by the diketopyrrolopyrrole moieties leads to an overall loss of symmetry (Figure 7). This asymmetry could not have been anticipated from the calculations, as the hexyl chains of ligand **A** were omitted to avoid lengthy calculation time. However, a closer examination of the X-ray structure indicates that rotation of the cores is not possible due to the four hexyl chains hindering motion when positioned in *cis* in the cage. It could be hypothesized that this rotation occurs when more thermal energy is provided to the sample. To investigate this possibility, variable temperature (VT) NMR analysis was conducted in deuterated DMSO as it allows higher temperatures to be reached. At room temperature in DMSO, $\text{Pd}_2\text{A}_2\text{C1}_2$ and $\text{Pd}_2\text{A}_2\text{C2}_2$ both present the same pattern as in acetonitrile indicating the formation of the same assembly. The subsequent increase in temperature to 90 °C did not result in a merging of the two ^1H NMR signal sets. The *cis*-cage is therefore strongly locked in this symmetry-broken configuration.

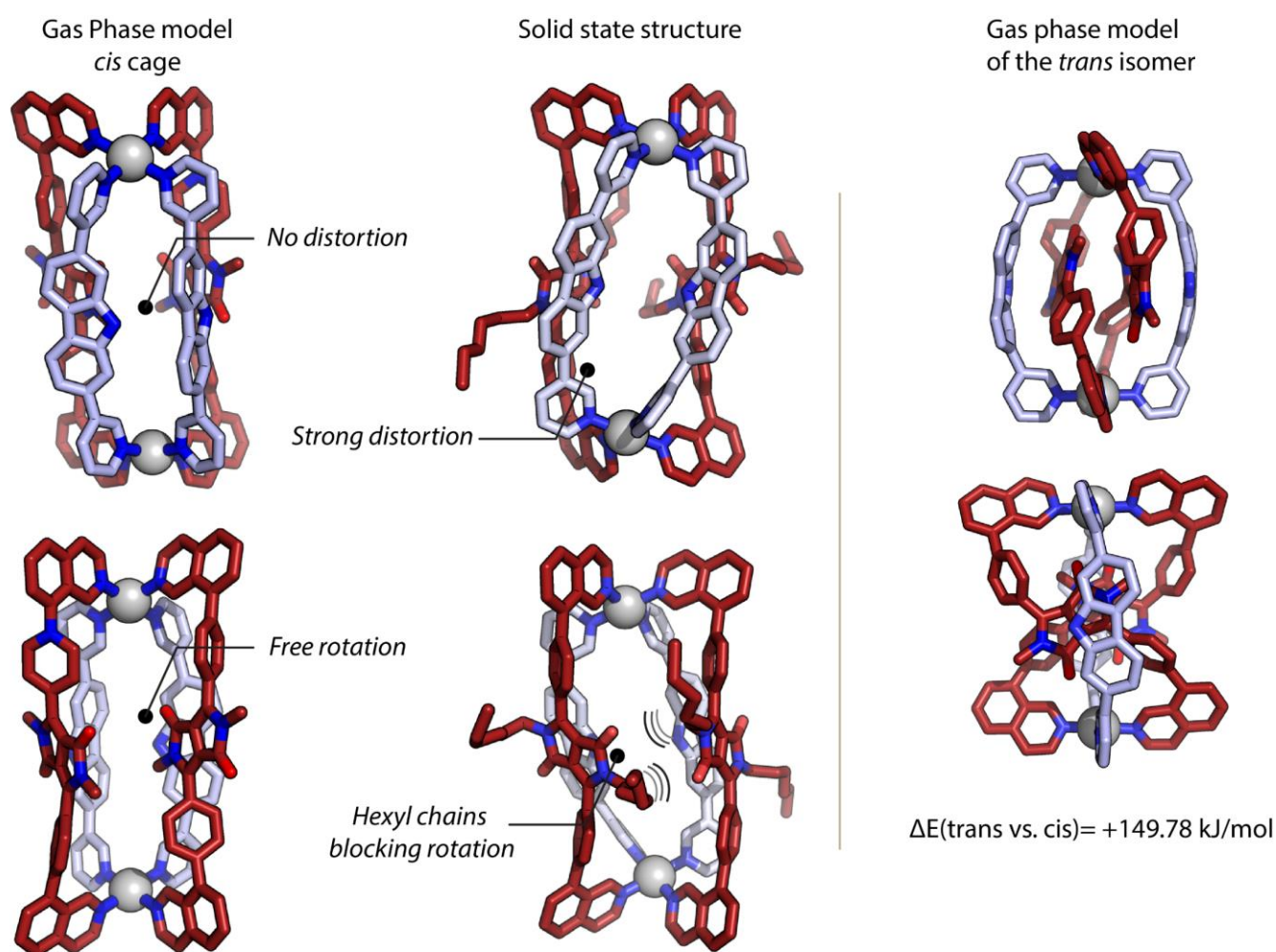


Figure 7: Structural analysis and comparison between the X-ray structure and the PM6 geometry optimized *cis*- $\text{Pd}_2\text{A}_2\text{C2}_2$. In the gas phase calculation, the hexyl chains of **A** were omitted to prevent lengthy calculations. The optimized structure of the *trans* isomer is also displayed showing a highly distorted structure translated in a higher energy as compared to the *cis* one.

Coming back to the mixing experiments, I then investigated what would happen when a preformed $\text{Pd}_2\text{B1}_2\text{C1}_2$ cage was mixed with $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ in an 8/3 ratio which ensures an overall ligand ratio **A**:**B1**:**C1** of 2:1:1. When the two cages were combined and heated at 70 °C overnight (Figure 8a), an overlap of the ^1H NMR traces of $\text{Pd}_2\text{A}_2\text{B1}_2$ and $\text{Pd}_2\text{A}_2\text{C1}_2$ was obtained. This is a synonym, once again, of two orthogonally coexisting coordination

cage and thus heteromeric complete self-sorting (Figure 8b). Prolonged heating over the course of a week did not change the outcome. Further analysis by ESI-MS also displayed perfect formation of both heteroleptic species, showing prominent peaks for the $[\text{Pd}_2\text{A}_2\text{B}_1\text{C}_1]^{4+}$ and $[\text{Pd}_2\text{A}_2\text{C}_1\text{C}_2]^{4+}$ species as well as corresponding 3+ and 2+ charged ones with one and two associated BF_4^- anions, respectively (Figure 8c). The same results were obtained by mixing directly the ligands in the right ratio in presence of $\text{Pd}(\text{II})$ or by combining the three homoleptic assemblies in a one-pot fashion. Interestingly, the sequential cage-to-cage transformation highlights the preferred formation of the pair $\text{Pd}_2\text{A}_2\text{B}_1\text{C}_2$ and $\text{Pd}_2\text{A}_2\text{C}_1\text{C}_2$ over assembly $\text{Pd}_2\text{B}_1\text{C}_1\text{C}_2$, with ligands exchanging between the cages. We initially had entitled this process *cannibalistic self-sorting* since it can be seen as ligand **A** disassembling ("devouring") the $\text{Pd}_2\text{B}_1\text{C}_1\text{C}_2$ cage to form the two coexisting heteroleptic cages. Another interesting feature of this system is that the cages exhibit different topologies. The versatility of ligand **A** can be underlined here. In $\text{Pd}_2\text{A}_2\text{B}_1\text{C}_2$ and $\text{Pd}_2\text{A}_2\text{C}_1\text{C}_2$, it sits in two distinct conformations (*transoid*, S shape and *cisoid*, C shape) and pairwise arrangements (*trans* and *cis*), enabling the creation of both a *trans* intertwined assembly and a classical nonentangled *cis*-cage (Figure 8d). In this example, all components can form homoleptic assemblies as well as discrete $\text{Pd}_2\text{A}_2\text{B}_2$ -type heteroleptic structures in opposition to the aforementioned cases. Therefore, it is clear that the second level of self-sorting does contain more information on the molecular level than before. By information, I am here referring to the preferential recognition and association of building blocks together affording a system with lower energy therefore thermodynamically more stable.

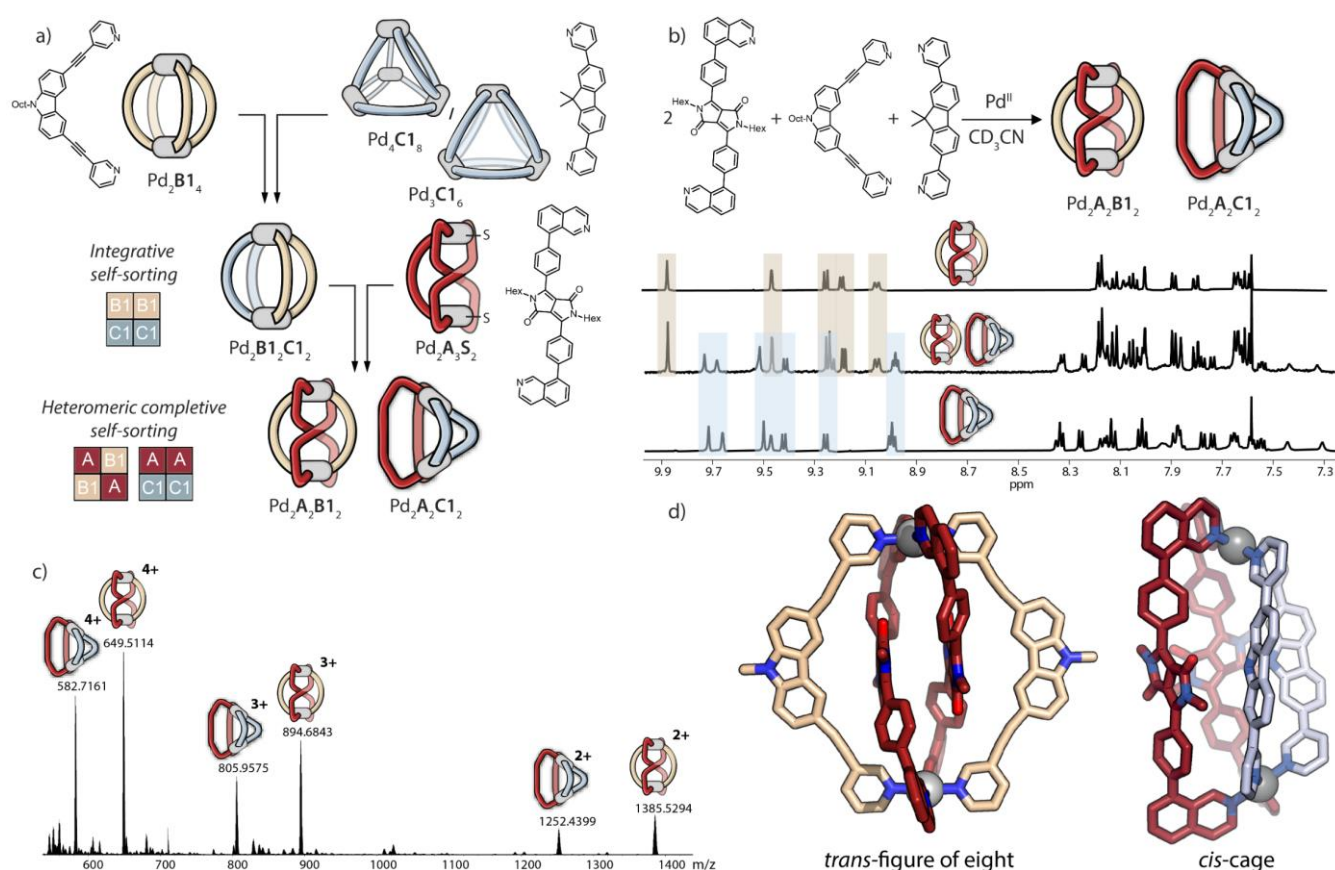


Figure 8: a) Schematic representation of the step-by-step formation of heteromeric self-sorting where two heteroleptic assemblies co-exist in a 1:1 manner. b) Stacked ^1H -NMR (CD_3CN , 500 MHz) spectra. From top to bottom: $\text{Pd}_2\text{A}_2\text{B}_1\text{C}_2$ only, mixture $\text{Pd}_2\text{A}_2\text{B}_1\text{C}_2$ and $\text{Pd}_2\text{A}_2\text{C}_1\text{C}_2$, $\text{Pd}_2\text{A}_2\text{C}_1\text{C}_2$ only. c) HR-ESI-MS of the mixture of $\text{Pd}_2\text{A}_2\text{B}_1\text{C}_2$ and $\text{Pd}_2\text{A}_2\text{C}_1\text{C}_2$. d) The two X-ray structures of the coexisting cages with distinct topologies.

Again, it is important to mention that stoichiometry is crucial and allows this precise self-sorting to occur. If one follows the nomenclature of Schmittl,^[8] this still represents a special case of heteromeric complete self-sorting. I conducted an experiment in which the ratio of the ligands was modified in order to probe the self-sorting

outcome (Figure 9). This experiment highlights the importance of stoichiometry but also the preferential formation of certain assemblies. When the relative amounts of organic building blocks are modified (conditions (i) and (ii)), no discrete self-sorting can be observed. Instead, different proportions of each of the heteroleptic assemblies can, mostly, be found in the mixtures. Therefore, only in the case described previously can the system reach heteromeric complete self-sorting in a selective manner. A sample in which the ligands are competing for Pd(II) was also prepared, meaning that not all possible assemblies can form. Interestingly, the outcome showed the preferential formation of the $\text{Pd}_2\text{A}_2\text{C1}_2$ (in blue) over $\text{Pd}_2\text{A}_2\text{B1}_2$ and $\text{Pd}_2\text{B1}_2\text{C1}_2$. Herein, it is assumed that this is the thermodynamic minimum of this system in those conditions (24 hours, 70 °C).

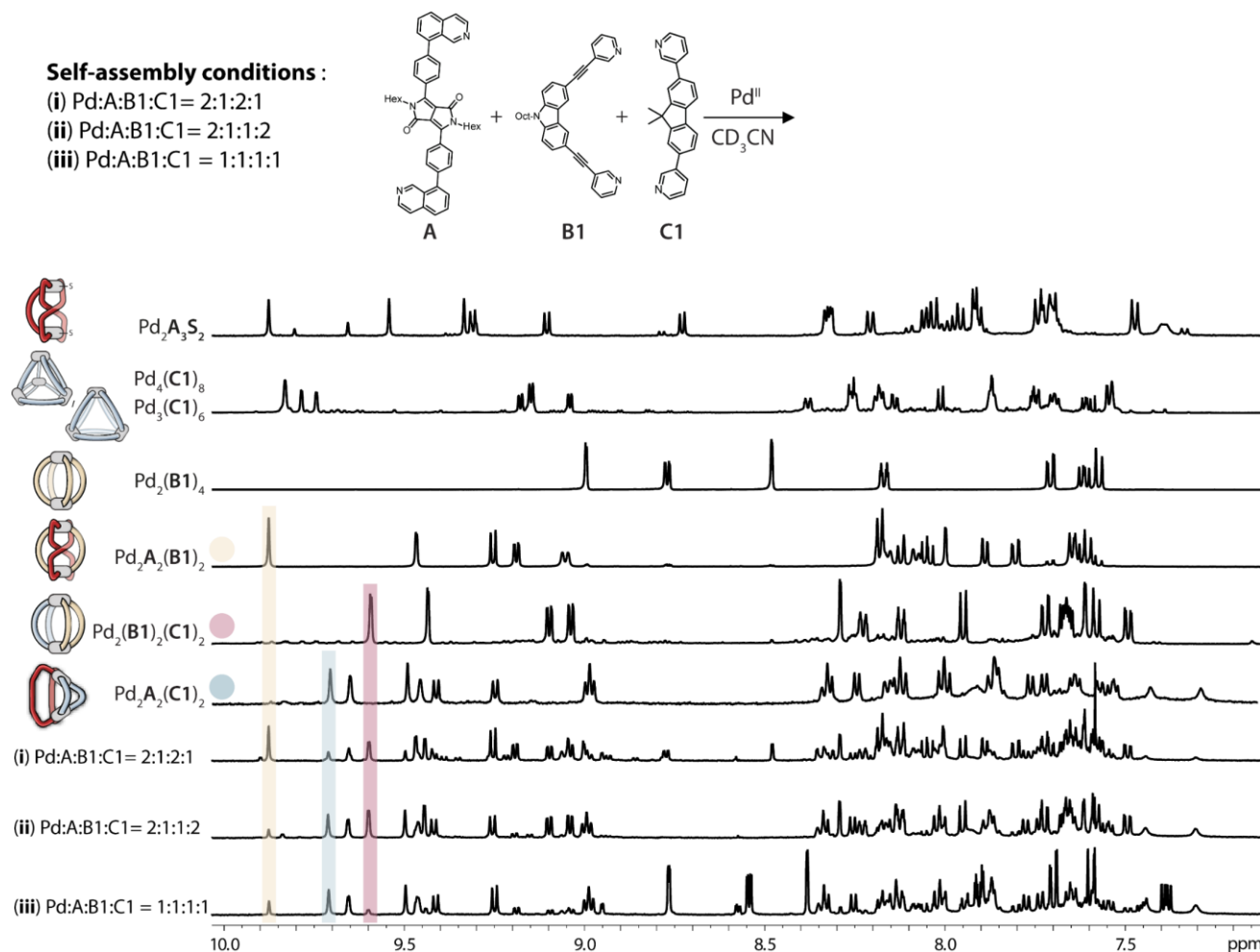


Figure 9: Stacked ^1H -NMR (CD_3CN , 500 MHz) spectra of the references for homoleptic and heteroleptic cages. The three lower spectra represent respectively the outcome of self-sorting when the conditions (i), (ii) or (iii) are applied. Highlighted in colors are the three possible heteroleptic cages showing that they are always present (although in different ratios) in the three cases. This highlights the importance of stoichiometry to obtain heteromeric complete self-sorting.

It was therefore possible to create the first “population” of heteroleptic cages as compared with narcissistic self-sorting which affords a defined population of homoleptic assemblies. Getting control over such systems, in the sense of a better manipulation of the self-sorting outcome depending on distinct output or the application of stimuli, was the logical next step to address. The possibility of population change within systems composed of the same building blocks is particularly interesting if one wants to control intra-and/or intermolecular functionalities. This brings us closer to a systems chemistry or network approach with the possible communication between individuals within the system. When analyzing the different combinations that could give rise to heteromeric self-sorting I realized that one particular set of ligands **A**, **B3** and **C1** could enable such control over population (Figure 10).

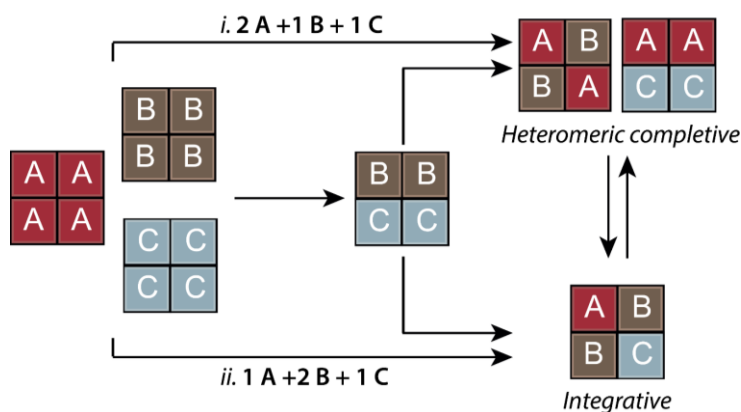


Figure 10: Schematic representation of a stoichiometry-dependent system in which it is possible to switch between integrative and heteromeric complete self-sorting with the same set of components.

4. Stoichiometry controlled self-sorting outcome: integrative vs heteromeric

It was previously reported that **B3** and **C1** could associate through integrative self-sorting and afforded a *cis*-cage $\text{Pd}_2\text{B}_3\text{C}_1$.^[26] Further addition of the homoleptic coordination assembly of **A** leads to heteromeric self-sorting (Figure 11a), in a similar manner to what we observed for the **A**, **B1-2**, and **C1** sets. Both NMR analysis and ESI-MS demonstrated the coexistence of a heteroleptic figure-of-eight $\text{Pd}_2\text{A}_2\text{B}_3$ and the *cis*-cage $\text{Pd}_2\text{A}_2\text{C}_1$ (Figure 11b-d).

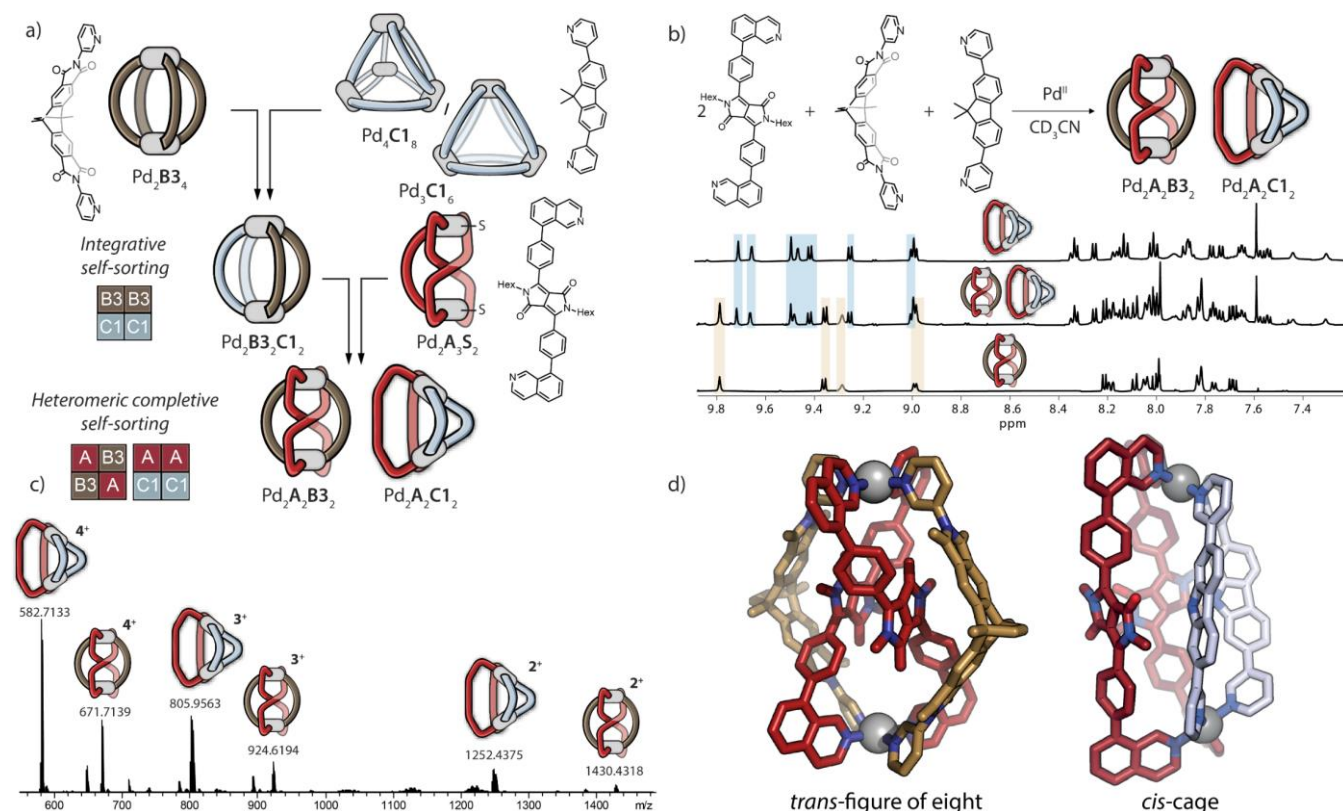


Figure 11: a) Schematic representation of the step-by-step formation of heteromeric self-sorting where two heteroleptic assemblies co-exist in a 1:1 manner. b) Stacked ^1H -NMR (CD_3CN , 500 MHz) spectra. From top to bottom: $\text{Pd}_2\text{A}_2\text{C}_1$ only, mixture of $\text{Pd}_2\text{A}_2\text{B}_3$ and $\text{Pd}_2\text{A}_2\text{C}_1$, $\text{Pd}_2\text{A}_2\text{B}_3$ only. c) HR-ESI-MS of the mixture of $\text{Pd}_2\text{A}_2\text{C}_1$ and $\text{Pd}_2\text{A}_2\text{B}_3$. d) The structures (left DFT optimized, right X-ray structure) of the coexisting cages with distinct topologies.

From a sample of this combination, I was able to obtain red needle crystals suitable for synchrotron diffraction analysis. Surprisingly, the crystal structure obtained was none of these cages, but a ternary *trans*-assembly $\text{Pd}_2\text{A}_1\text{B}_3\text{C}_1$ (Figure 12c). While we had already obtained *cis*-ternary cages when searching for Pd_2ABCD graal, this chapter, however, presents the group's first two *trans*-assemblies with the generic $\text{Pd}_2\text{AB}_2\text{C}$ formula. Meanwhile, Hiraoka^[28] and Zhang^[29] also reported similar assemblies using either kinetic control or coordination sphere engineering. In this architecture, **A** and **C1** sit facing each other and form a neat ring by shape complementary assembly. Ligand **A** adopts a third structural motif as it is present as a single unit in its *cisoid* form. The two remaining **B3** ligands complement the square planar geometry of the Pd(II) and are slightly twisted owing to their greater flexibility. It had to be verified that this species was not solely obtainable in the solid state and therefore mixed the ligands in the corresponding ratio in the presence of Pd(II). The emergence of a new set of signals was observed for each ligand (Figure 12a). However, while all the signals of **A** and **C1** were rather sharp at room temperature, the pyridyl protons corresponding to the chemical environment of ligand **B** underwent broadening. VT NMR analysis was employed and unveiled a complete set of sharp signals by increasing the temperature to 60 °C. Worth noting that the protons located on the sides of **B3** (marked as brown dots), did split into two sets since the left- and right lateral protons are coming close to a distinct ligand, i.e., **A** or **C1**, making them chemically nonequivalent. DOSY NMR confirmed that all protons belonged to the same assembly with a hydrodynamic radius fitting to a cage binuclear Pd(II) cage. Eventually, ESI-MS unambiguously depicts prominent peaks for the $\text{Pd}_2\text{A}_1\text{B}_3\text{C}_1$ with a 4+ charge as well as a 3+ charge with associated anions (Figure 12b).

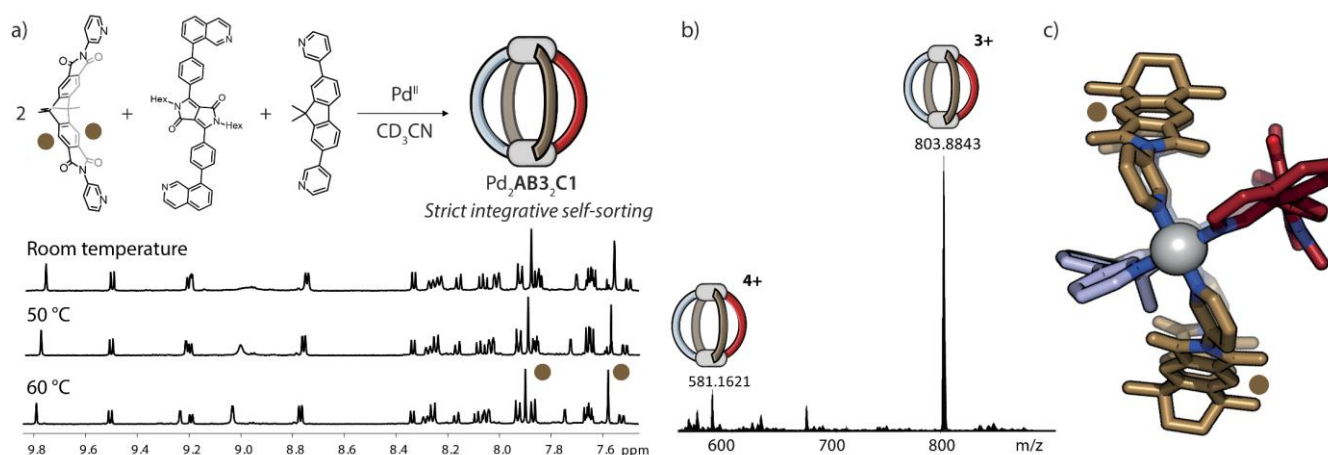


Figure 12: Stacked ¹H-NMR (CD₃CN, 500 MHz) spectra of the cage at RT, 50 °C and 60 °C showing the sharpening of signals. Highlighted in brown are the signals from **B3** undergoing a splitting because of the *trans* topology. b) HR-ESI-MS of $\text{Pd}_2\text{A}_1\text{B}_3\text{C}_1$. c) Top view of the X-ray structure in order to visualize the *trans* arrangement of the ligands **B3**.

Before diving again into the self-sorting process, let's have a look at this architecture as it presents many key parameters that could make it a tunable platform for a multi-functional cage (Figure 13). First, and I will return to this, **A** is a strong chromophore and luminophore that can be harnessed for developing guest sensing and multi-chromophore systems. Additionally, the two methyl groups of **C1** are oriented toward the inner space of the cage. One could envision replacing this moiety with the previously mentioned analog fluorenone **C3** (also a chromophore!), as well as with **C2** which presents an N-H functional group and could facilitate H-bond-driven guest binding. This H-bond driven recognition was already exploited by our group for the encapsulation of phosphate guests and holds great promise. Thus, installing precise inward-pointing moieties appears straightforward. Eventually, the two lateral ligands **B3** provide a shielded cavity, a factor well known to enhance the possibilities in terms of guest uptake as demonstrated numerous times by Yoshizawa and coworkers.^[30]

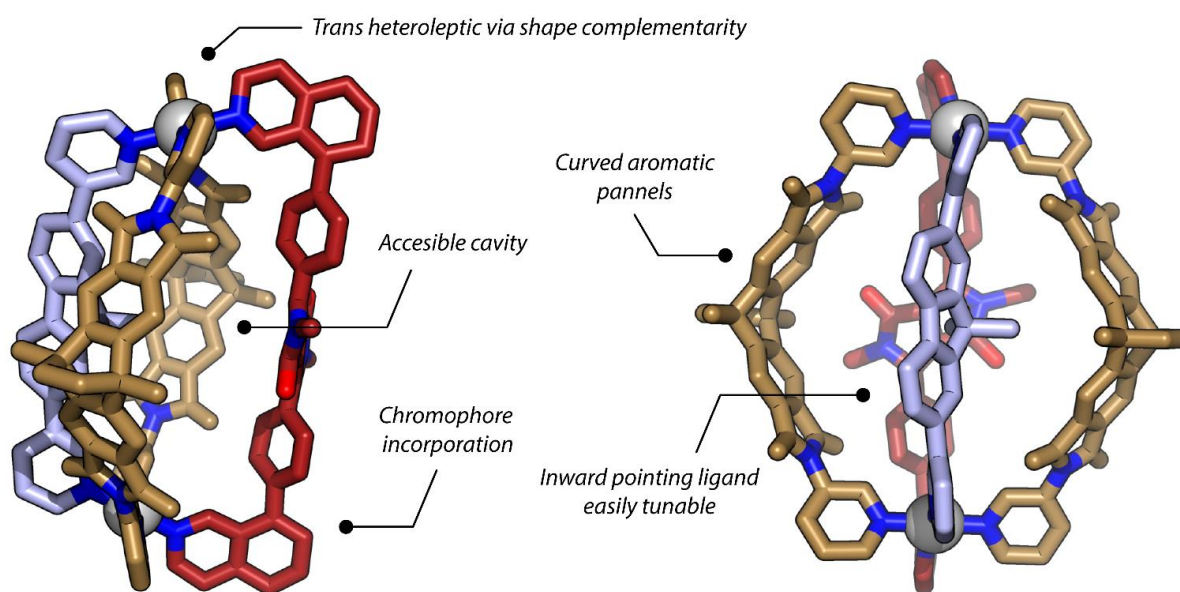


Figure 13: X-ray structure and analysis of the $\text{Pd}_2\text{A}_1\text{B}_3\text{C}_1$ cage which offers a unique platform for further development of multi-functional multicomponent coordination cages.

This assembly was achieved through integrative self-sorting, and unlike the previous experiments with different stoichiometries, the outcome could be modified by altering the relative ratios of each ligand in the system. Consequently, this combination of ligands offered a switchable system controlled by stoichiometry. It was further demonstrated that the addition of components enabled a transformation between a state containing a discrete mixture of binary assemblies (heteromeric complete self-sorting) and another one with a sole ternary species (integrative self-sorting) (Figure 14).

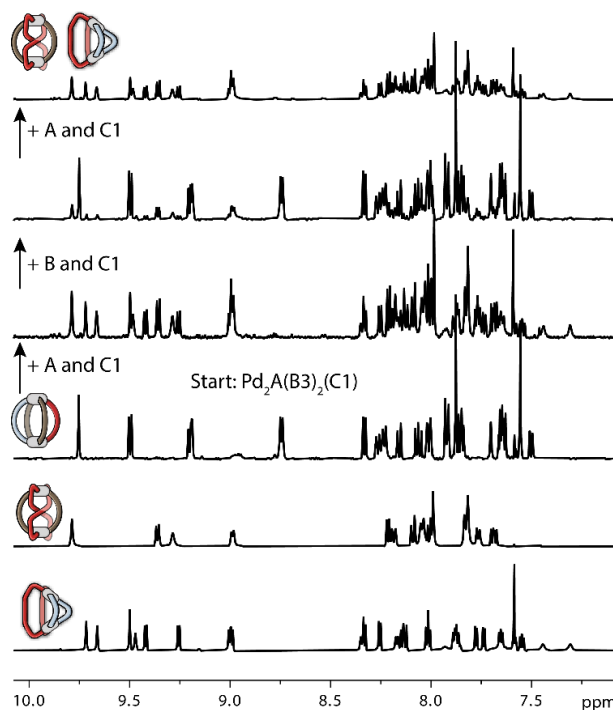


Figure 14: ^1H -NMR (CD_3CN , 500 MHz) spectra of at the bottom the references for the two binary heteroleptic cages. Starting from the ternary heteroleptic $\text{Pd}_2\text{A}_1\text{B}_3\text{C}_1$ cage, two cycles of switching between the self-sorting outcomes can be conducted by introducing the components to balance the desired ratio. This highlights the possibility of controlling cage populations.

5. *Trans*-heteroleptic figure-of-eight cages as a platform for intra-assembly energy transfer

Eventually, I would like to conclude this chapter by reflecting on heteroleptic *trans*-figure-of-eight binary species containing ligands **A** and **Bx**, which exhibit specific photophysical properties. As previously mentioned, ligand **A** contains a diketopyrrolopyrrole (DPP) core, a well-known dye initially used in the pigment for Ferrari cars and later brought into the fields of bioimaging^[31,32] and optoelectronics^[33,34] as it is also an excellent luminophore. It was then introduced to coordination cages by Dr. Irene Regeni. The base structure of DPP is inherently insoluble because of strong H-bonds between the N-H and carbonyl moieties and π - π interactions between the units. To increase solubility and prevent aggregation, alkyl chains are often installed on the nitrogen atoms. The aromatic moieties can be easily varied or further modified to tune the desired photophysical properties.^[34] The simple DPP moieties generally appear red or orange and possess a very bright and intense emission accompanied by an excellent high quantum yield. Dr. Regeni demonstrated that controlling the stacking of such organic building blocks in coordination cages allows tuning of these photophysical properties. Interestingly, Pd₂**A**₂**B1**₂ presents a remarkable quantum yield of 51%.^[21] Remarkable because it is well known that Pd(II) assemblies very often undergo (partial) quenching because of competitive pathways following photoexcitation.^[35] Furthermore, a combination of steady-state and time-resolved emission spectroscopy, in collaboration with Dr. Sascha Feldman, suggested an electronic communication between the two chromophores present in the structure and pointed to an intra-assembly, from **B1** to **A**, excitation transfer process.^[21] Additionally, in another related system in which similar chromophores (a DPP derivative and a carbazole/fluorenone) are positioned in a *cis* configuration (Figure 15a), an in-depth study of the photophysical properties unambiguously confirmed the occurrence of a FRET as well as “ping-pong” reverse FRET process depending on the respective use of either carbazole or fluorenone counter ligands.^[36] However, these systems present lower quantum yield of luminescence with respectively 29% and 24%. The connection between this study and the cages we have in our hands was then apparent. Can we therefore get a better understanding of what processes occur in the figure-of-eight cages and would it be possible to tune such properties?

In order to investigate these questions, I employed Pd₂**A**₂**B1**₂, Pd₂**A**₂**B2**₂ as well as another derivative Pd₂**A**₂**B4**₂ where the octyl chain of **B1** was replaced by a phenyl group creating a triarylamine-like moiety on the outer ligand of the figure-of-eight (Figure 15). This cage was fully characterized by NMR and ESI-MS as well as with a crystal structure leaving no doubts about the ligands' arrangement in the assembly (Figure 16a-c). Two other cages Pd₂**A**₂**B5**₂ and Pd₂**A**₂**B6**₂ with carbazole derivatives respectively bearing a pyrene or a benzophenone were also synthesized to show the potential versatility of this approach. This could open new avenues for the development of complex photophysical processes such as TADF/FRET, two photons absorptions as well as upconversion phenomenon. These two latest cages are not further discussed in this dissertation.

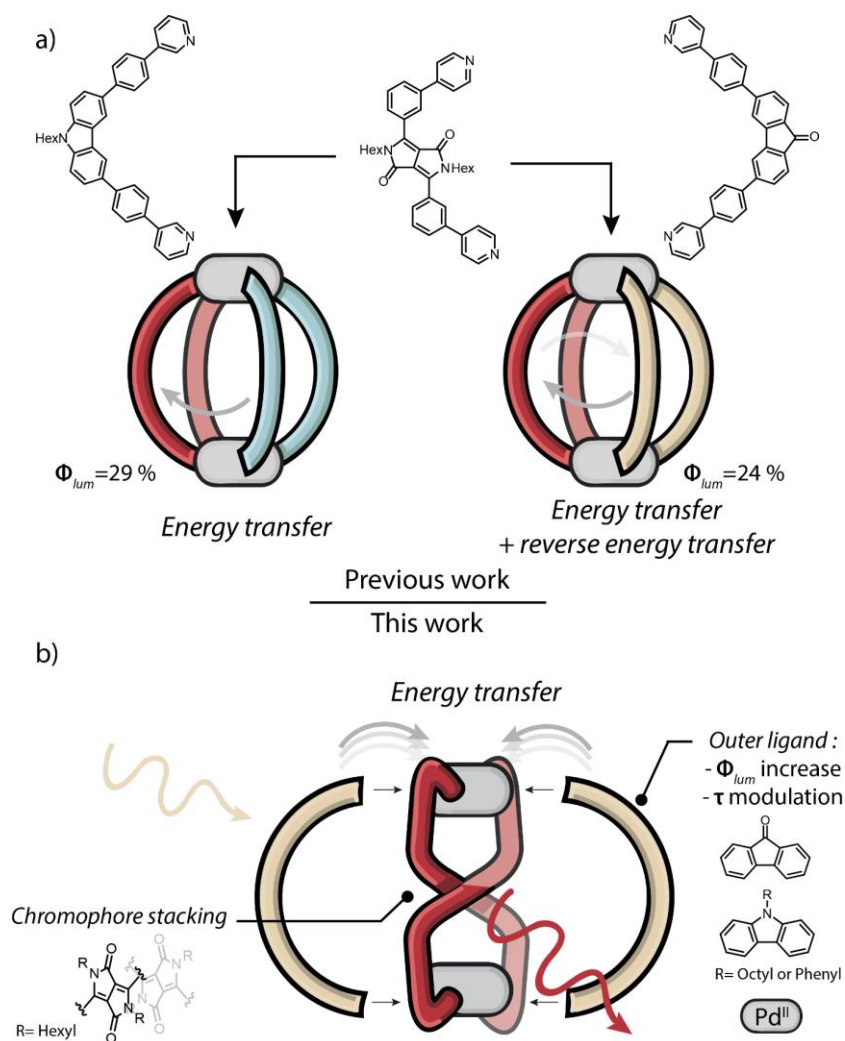


Figure 15: a) Previous system created to study energy transfer from fluorenone or carbazole chromophore to DPP in *cis*- Pd₂A₂B₂ cages. b) Schematic representation of the system employed for a systemic study of energy transfer in *trans*-Pd₂A₂B₂ structures.

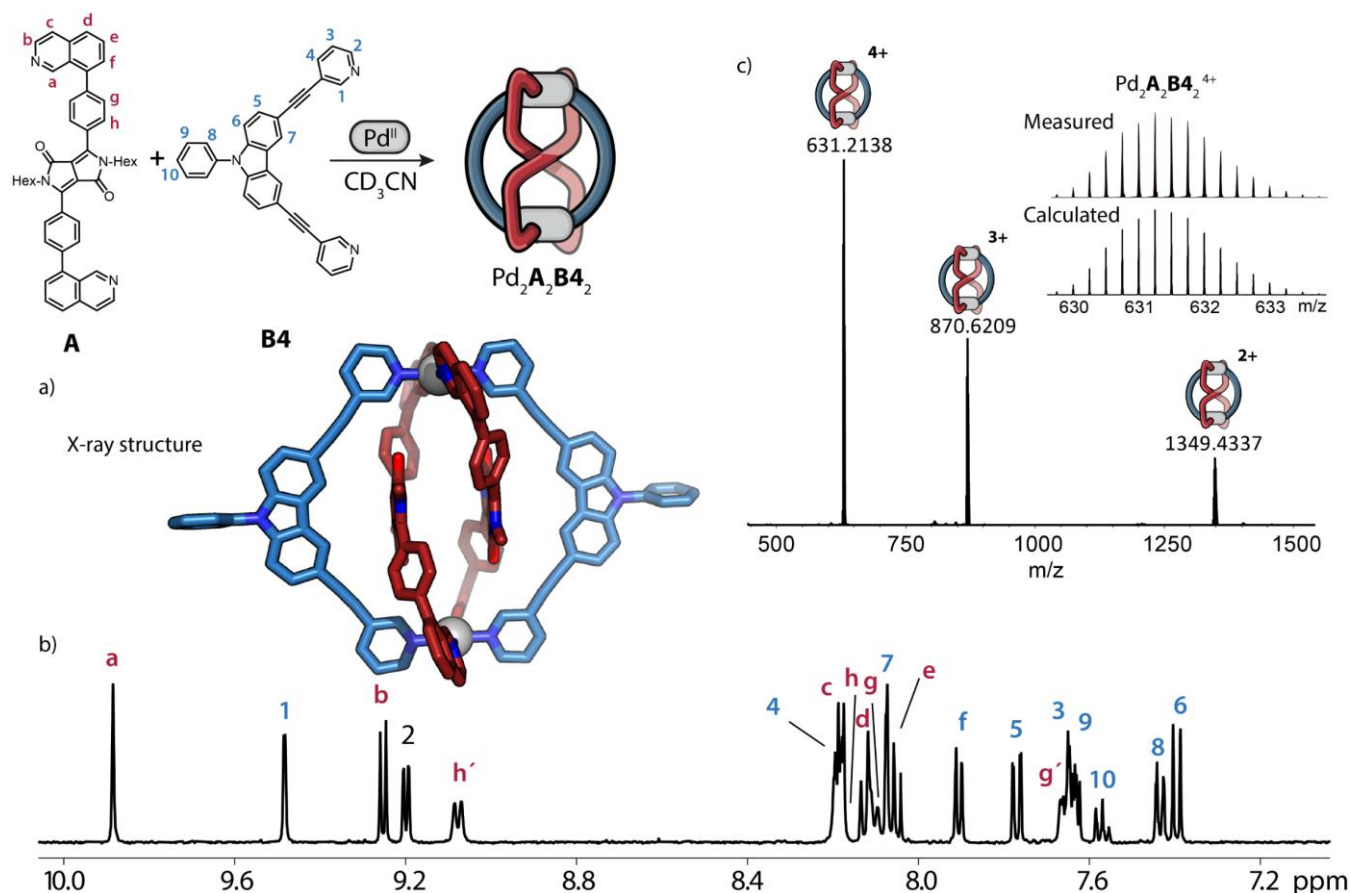


Figure 16: a) X-ray structure of $\text{Pd}_2\text{A}_2\text{B}_4$. Hexyl chains of **A** are omitted for clarity. b) $^1\text{H-NMR}$ (CD₃CN, 500 MHz) of the cage with the assignment of protons. c) HR-ESI-MS of $\text{Pd}_2\text{A}_2\text{B}_4$ with isotopic patterns of the 4+ species highlighted.

As depicted in Figure 15, during an energy transfer phenomenon within the assembly, the outer ligands **Bx** act as *donors* while the stack of ligands **A** are the *acceptors* subsequently emitting. Using electrochemistry (Table 1) we were able to measure the oxidation and reduction potential of ligands **A**, **B1**, **B2** and **B4** in the heteroleptic cages. This was used for calculating and accessing the energy levels of the HOMO and LUMO orbitals of the different homoleptic and heteroleptic cages. By comparing the HOMO energy levels we could therefore rank the ligands in terms of electron-donating ability as follow: **B4** > **B1** > **B2**. These results were compiled and discussed with Ph.D colleague Laura Neukirch, leveraging her expertise in electrochemistry.

	$\text{Pd}_2\text{A}_2\text{B1}_2$		$\text{Pd}_2\text{A}_2\text{B4}_2$		$\text{Pd}_2\text{A}_2\text{B2}_2$		$\text{Pd}_2\text{A}_3(\text{MeCN})_2$	$\text{Pd}_2\text{B1}_4$
	B1	A	B4	A	B2	A		
$E_{p/2}$ in V	1.06	-1.58	0.77	-1.51	-1.39	-1.58	-1.57	1.00
E_{HOMO} in eV ^[1]	-5.86		-5.57		-6.51 ^[2]			-5.80
E_{LUMO} in eV ^[1]	-3.22		-3.29		-3.22		-3.23	

Table 1: Summary of the electrochemical data for the heteroleptic species. $E_{p/2}$ is referenced to Fc/Fc^+ . [1] $E_{\text{HOMO}}/E_{\text{LUMO}} = -4.8 \text{ eV} - e \cdot E_{p/2}$. [2] $E_{\text{HOMO}} = E_{\text{LUMO}} - \Delta E$ with ΔE the HOMO-LUMO gap obtained by UV-Vis abs. spectroscopy.

I looked into the photophysical properties of the different homoleptic and heteroleptic species (Figure 17). As observable in the absorption spectrum of $\text{Pd}_2\text{A}_2\text{B}_4$, the heteroleptic contribution was similar to the combined ones of the two homoleptic cages, with the characteristic absorption band of the DPP **A** arising between 450 nm and 550 nm (Figure 17a,d). When excited at different wavelengths, the species displayed a broad emission between 500 nm and 700 nm with two distinct bands centered at 550 nm and 590 nm which are typical of the emission of **A** (Figure 17b). Exciting the sample at 350 nm, where both chromophores absorb, resulted in a higher relative emission intensity than an excitation at 470 nm, where only **A** absorbs. This could be the first indication of energy transfer within our heteroleptic structures, strengthened by the fact that the emission corresponding to **B4** could not be detected (Figure 17c). This emission occurred for the homoleptic Pd_2B_4 with a band centered at 400 nm and tailing until 500 nm, therefore overlapping with the absorption feature from **A** (Figure 17c). The three heteroleptic species depicted the same emission profile (Figure 17d) with the unique contribution of the DPP, emphasizing that the same process occurred in all of them.

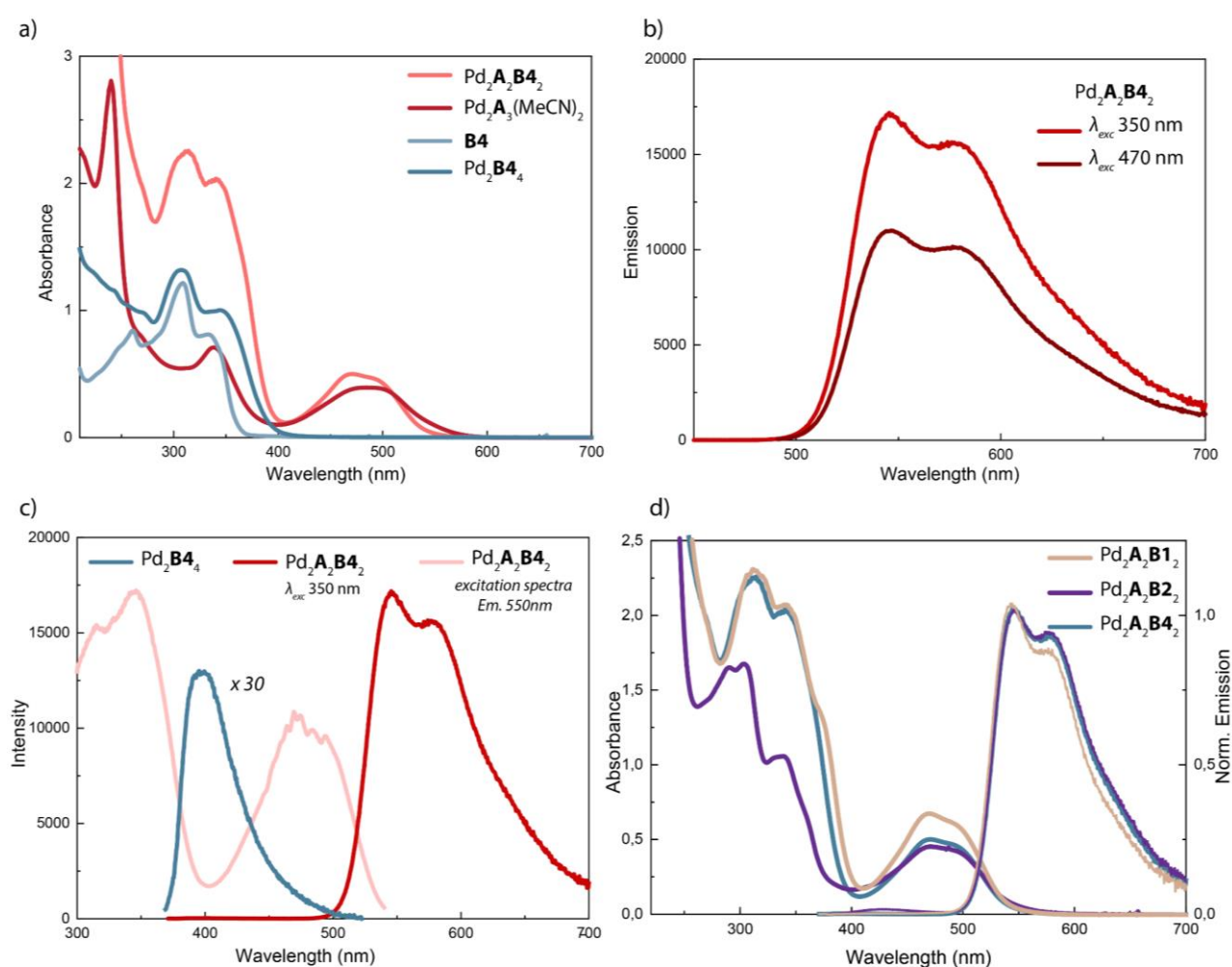


Figure 17: a) UV-Vis absorption spectra of $\text{Pd}_2\text{A}_2\text{B}_4$ and its different component homoleptics. b) relative emission intensity of $\text{Pd}_2\text{A}_2\text{B}_4$ when excited at 350 nm or 450 nm. c) Excitation spectra of $\text{Pd}_2\text{A}_2\text{B}_4$ for emission at 550 nm with corresponding emission spectra of $\text{Pd}_2\text{A}_2\text{B}_4$ and homoleptic Pd_2B_4 (increase 30 times). d) UV-Vis absorption and corresponding normalized emission (excitation 350 nm) of $\text{Pd}_2\text{A}_2\text{B}_1$, $\text{Pd}_2\text{A}_2\text{B}_2$, and $\text{Pd}_2\text{A}_2\text{B}_4$. Acetonitrile 2 mm cuvette, 0.15 mM chromophore concentration for absorption, 0.01 mM for emission.

We then teamed up with physicists and the team of Dr. Sascha Feldman in order to delve deeper into the optical properties of these systems. When examined independently of the cages, the free ligands demonstrated exceptional photoluminescence quantum efficiency (PLQE) of approximately 80-90% (Table 2). In stark contrast, all homoleptic cages exhibited near-complete quenching, with PLQE value below 1% for $\text{Pd}_2\text{A}_3(\text{MeCN})_2$. The

isolated ligands also displayed relatively short lifetimes ($\tau < 7$ ns), characteristic of highly efficient singlet emitters, indicating a radiative rate, k_{rad} about ten times higher than the non-radiative rate, $k_{\text{non-rad}}$. This rapid radiative rate is ideal because positioning the donor and acceptor fragments sufficiently close, as in heteroleptic cages, and maintaining parallel transition dipole moments, through ligand design, should allow us to engineer highly efficient, sub-nanosecond Förster Resonance Energy Transfer (FRET) with good emission for otherwise non-luminescent metal-organic cages. Indeed, luminescence measurements of the heteroleptic cages revealed two emission bands at 550 nm and 600 nm, exclusively from the acceptor ligand **A**, signifying successful energy transfer. The PLQEs of the heteroleptic species were drastically higher than those of homoleptic assemblies and they correlate with the previously established donor ability hierarchy. Specifically, $\text{Pd}_2\text{A}_2\text{B4}_2$ exhibited a 64 % quantum yield while those of $\text{Pd}_2\text{A}_2\text{B1}_2$ and $\text{Pd}_2\text{A}_2\text{B2}_2$ were respectively 52 % and 42% (Table 2). These values are among the highest for Pd(II) based coordination cages. To the best of our knowledge only two examples from Crowley^[37] (59%) and Casini^[38] (66%) present Pd(II) cages with comparable PLQE. However, both cases differ in nature to the cages presented here as they make use of pending organic or Ru(II)-based luminophores, decoupled from the cage structure. The examples presented herein are therefore the most potent Pd(II) cage luminophores with organic dyes directly integrated into the cage backbone.

	λ_{PL} (nm)	τ (ns)	Φ (%)
A	550, 600	6.5	95
B4	540	5.8	85
B1	490	4.8	83
B2	500	3.6	71
$\text{Pd}_2\text{A}_3(\text{MeCN})_2$	550, 600	2.1	0.5
$\text{Pd}_2\text{A}_2\text{B4}_2$	550, 600	7.0	64
$\text{Pd}_2\text{A}_2\text{B1}_2$	550, 600	11.2	52
$\text{Pd}_2\text{A}_2\text{B2}_2$	550, 600	5.7	42

Table 2: Summary of emission wavelengths, emission lifetime and quantum yield of the different ligands compared with the homoleptic assembly $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ as well as the three heteroleptic assemblies. $\lambda_{\text{exc}} = 350$ nm.

To get more insight into the emission process nanosecond transient photoluminescence (TRPL) of the cages was performed by selectively pumping the donor ligands via a 350 nm pump beam. This revealed that the two observable bands in the emission from $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ are emerging from states with different spin multiplicities as they decay at different rates (Figure 19). The 550 nm feature corresponds to the singlet $S_{1, \text{FRDQ}}$ state while the 600 nm feature could correspond to the $T_{1, \text{FRDQ}}$ state or another bright populated $T_{n, \text{FRDQ}}$ state. We found that the 600 nm contribution decayed faster than the 550 nm feature (Figure 18). This longer 550nm emission kinetics could attributed to a reverse intersystem crossing (rISC), by TADF, which is enhanced within the cage due to the presence of Pd as heavy atom accelerates ISC through spin-orbit coupling. Transient absorption spectroscopy and further time-resolved emission spectroscopy are ongoing and will help to further decipher the kinetics of FRET, ISC and rISC and give a full explanation of the phenomena taking place within those cages.

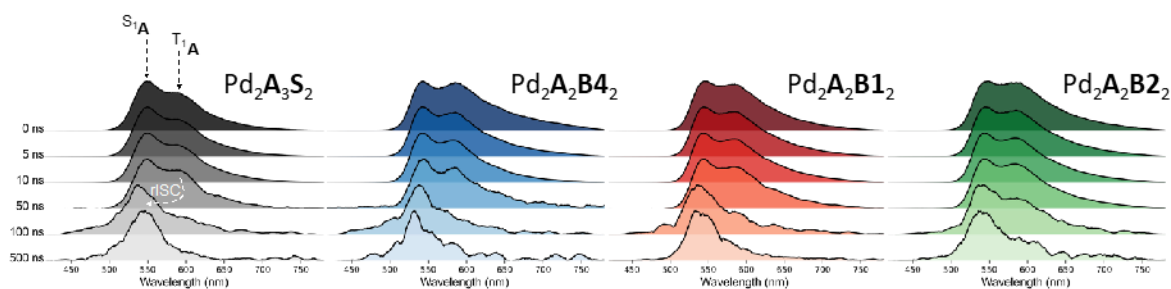


Figure 19: Transient photoluminescence spectral slices measured for (from left) $\text{Pd}_2\text{A}_3\text{S}_2$, $\text{Pd}_2\text{A}_2\text{B}_4_2$, $\text{Pd}_2\text{A}_2\text{B}_1_2$ and, $\text{Pd}_2\text{A}_2\text{B}_2_2$. All the heteroleptic cages show emission from ligand **A** though we excite the higher absorbing donor-ligand band, this is due to fast FRET from donor to the acceptor (**A**) ligand. The singlet, $S_{1,A}$ and triplet, $T_{1,A}$ bands are labeled for the spectral slices from $\text{Pd}_2\text{A}_3\text{S}_2$ and the probable $r\text{ISC}$ process which leads to long-lived emission in the blue 550 nm band is shown to occur between 50-100 ns. This behavior is consistent in all heteroleptic cages.

We performed DFT geometry optimizations (B3LYP/def2-SVP) and single point energy calculations (B3LYP and $\omega\text{B97X-D/def2-TZVP}$) for the three heteroleptic species to compare their structures and the differences in the orbital energy levels with the experimental data (see SI). From the optimized geometries we also cropped the ligands and computed (single point energy calculation B3LYP/def2-TZVP) them separately in order to access their respective HOMO-LUMO gap in those specific arrangements (Figure 18a-b). The trend did fit the data obtained in the previous system^[36] with the fluorenone chromophore presenting the smallest energy gap compared to its carbazole analogs. Despite a close HOMO-LUMO gap between the two carbazole ligands, they differed as expected with **B4** having the largest one. Overlaying the three obtained structures highlights their expected geometrical similarities and strengthens the assumption that the differences in properties emerge only from their respective electronic situation. While two chromophore-chromophore distances are still present in the cages, the chromophores are in very close proximity (see $d1$ and $d2$ in Figure 18c) with a precise orientation. The *trans*-figure-of-eight configuration restricts the distances between the chromophore but also the degrees of freedom of the overall structure which likely benefits the chromophore communication. TD-DFT should allow us to access the excited state geometries and energy levels for both singlet and triplet states and rationalize the experimental results.

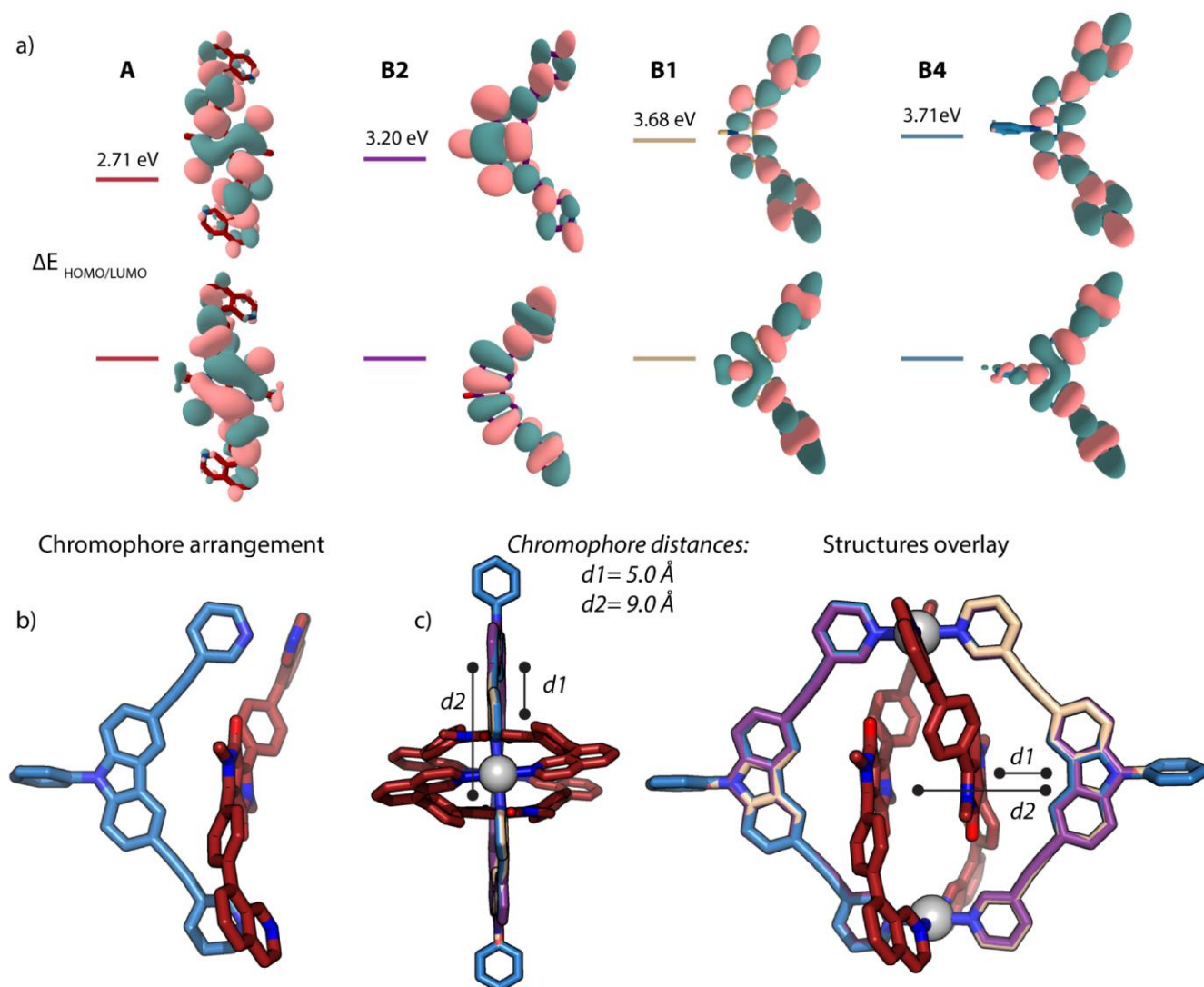


Figure 18: a) Frontier orbitals of the respective ligands **A**, **B1**, **B2** and **B4** in their conformation within the cages. b) General chromophore arrangement in the heteroleptic cages using $\text{Pd}_2\text{A}_2\text{B}_4$ as an example. c) Overlay of the three geometry-optimized structures displaying their high structural similarities. The two chromophore distances $d1$ and $d2$ are highlighted.

Conclusion and outlook

In **Chapter I**, I presented a novel type of self-sorting in coordination cages, namely *heteromeric complete self-sorting*. By using the distinct organic building blocks, it was demonstrated that we can now reach so-called “cage populations” where, upon stoichiometry control, several heteroleptic assemblies coexist orthogonally. We therefore stepped out of the nowadays more conventional target of *integrative self-sorting* which aim at developing single multicomponent assemblies. I showed that this self-sorting relied on a diketopyrrolopyrrole (DPP) ligand **A** with the peculiar ability to adopt *S* or *C* conformations which allowed either *cis*-Pd₂A₂B₂ cage or *trans*-Pd₂A₂B₂ figure-of-eight. The final populations could be obtained from ligands initially forming statistical mixtures and therefore resembled a second step of *narcissistic self-sorting* between heteroleptic structures. On the other hand, it was also possible to reach this sorting with an initial combination of ligands undergoing *integrative self-sorting*. This highlighted the higher degree of molecular information contained in this second step. Eventually, I could also study a case in which a variation in the stoichiometry of the ligands resulted in either *integrative self-sorting* or *heteromeric*, and where these outcomes were interchangeable. This paved the way for more dynamic systems potentially operating in synergy or through positive/negative feedback mechanisms.

It is also conceivable that only very specific ligand combinations will prove suitable for achieving such heteromeric self-sorting. Although this statement is already valid for integrative self-sorting alone, the information content required for these distinct processes is likely fundamentally different. Therefore, a deeper understanding of the strategies required to achieve such self-sorting will be necessary, akin to the efforts started around 10 years ago in crafting discrete heteroleptic cages. Furthermore, a retrospective examination of the competition experiment detailed earlier in this chapter unveils the potential for conducting additional insightful investigations. Monitoring the system's evolution under conditions where the Pd(II) concentration is substoichiometric could elucidate the pathways to cage populations. One might anticipate the formation of transient species, kinetically favored, gradually transitioning into thermodynamic sinks. Kinetic control is a crucial factor in systems chemistry. Thus, this type of experiment and investigation, even more on cage populations, is likely to open new doors for systems chemistry on Pd(II) cages. Making ligands compete for a “resource” (here Pd(II) in order to form the cages) could serve as a means of exerting “environmental pressure” (various stimuli/triggers/conditions) and possibly observing different “selections” (sorting outcomes) from a unique set of components. This is of course not a new concept as it stands as the basis for dynamic covalent chemistry (DCC) but it is surprisingly unexplored for coordination cages, although the parallel is easily drawn between these areas. Many exciting developments lie ahead for the field.

Eventually, taking advantage of the luminophore properties of **A**, we studied the possibilities of making highly emissive Pd(II)-based cages where the emitter was fully organic and comprised in the cage backbone. We demonstrated the occurrence of a FRET phenomenon from the outer ligand to the δ of multi-chromophore *trans*-Pd₂A₂B₂ figure-of-eight assemblies. While further calculations and measurements are needed to fully decipher the pathways and rationalize the efficiency and emission bands of the FRET process, this represents an exciting step further in the development of functional chromophore architectures.

6. Experimental section

General Method

NMR

NMR spectroscopic data was measured on the spectrometers Bruker AV 500 Avance NEO and AV 600 Avance III HD. For ^1H and ^{13}C NMR spectra, chemical shifts were calibrated to the solvent lock signal. Chemical shifts δ are given in ppm, coupling constants J in Hz. The following abbreviations are used to describe signal multiplicity for ^1H NMR spectra: s: singlet, d: doublet, t: triplet, dd: doublet of doublets; dt: doublet of triplets; m: multiplet, br: broad. All proton signals were assigned with the aid of 2D NMR spectra. All spectra were recorded in standard 5 mm NMR tubes at the indicated temperature.

Mass Spectrometry

Mass spectra were measured on Bruker ESI-timsTOF (electrospray ionization-trapped ion mobility-time of flight) and Bruker compact high-resolution LC mass spectrometers (positive mode). For calibration of the TIMS and TOF devices, Agilent ESI-Low Concentration Tuning Mix was used.

Computational analysis

Models of the structures $\text{Pd}_2\text{A}_2\text{C1}_2$, $\text{Pd}_2\text{A}_2\text{B1}_2$, $\text{Pd}_2\text{A}_2\text{B3}_2$, $\text{Pd}_2\text{A}_2\text{B2}_2$ and $\text{Pd}_2\text{A}_2\text{B4}_2$ were constructed using Wavefunction SPARTAN '18.1 The MMFF-optimized model was then optimized on semi-empirical PM6 level of theory without constraints. $\text{Pd}_2\text{A}_2\text{B3}_2$, $\text{Pd}_2\text{A}_2\text{B1}_2$, $\text{Pd}_2\text{A}_2\text{B2}_2$ and $\text{Pd}_2\text{A}_2\text{B4}_2$ were then further refined by DFT optimization on the $\omega\text{B97X-D/def2-SV(P)}$ level or B3LYP/def2-SVP. Energies were computed on the B3LYP/def2-TSVP level.

Cyclic voltammetry

The cyclic voltammograms were measured with a Metrohm potentiostat PGSTAT101. The data were recorded with the help of the NOVA electrochemistry software (Version 1.9) included in Metrohm Autolab. A homemade electrochemical cell with minimum 3 mL sample volume was used for the electrochemical measurements in a glove box. The sample and electrolyte salt were dissolved in dry and degassed MeCN. The electrochemical cell and degassed samples were arranged in the glove box. A glassy carbon electrode was used as working electrode and a Pt wire as counter electrode. After each measurement, the glassy carbon electrode and the Pt counter electrode were carefully polished with an appropriate polishing powder and rinsed with acetone and MeCN. The minimum sample volume is 3 mL. As reference electrode, the nonaqueous electrode Ag/AgNO_3 was utilized. A solution of 0.01 M AgNO_3 and 0.1 M tetrabutylammonium perchlorate of electrochemical purity grade was prepared in dry and degassed MeCN and filled inside the electrode. The reference electrode was kept in MeCN/0.1 M tetrabutylammonium hexafluorophosphate solution between the measurements and it was rinsed with MeCN prior to every measurement. All measurements have been performed at room temperature.

UV-Vis absorption and emission spectroscopy

UV-vis spectra were recorded on a DAD HP-8453 UV-Vis spectrometer; wavelength: 240 nm – 700 nm, step size: 1 nm. Emission spectra were recorded on a Jasco FP-8300 fluorimeter. Cuvette path length 0.2 cm in absorption and 1 cm in emission.

Experimental procedures

All the ligands of this study were previously reported and fully characterized by our group. Homoleptic assemblies for ligands **A**,¹ **B1-3**,¹⁻³ **C1**⁴ and **C2**⁵ and heteroleptic cages $\text{Pd}_2\text{A}_2(\text{B1})_2$, $\text{Pd}_2(\text{B1})_2(\text{C1})_2$, $\text{Pd}_2(\text{B3})_2(\text{C1})_2$ were also previously reported.

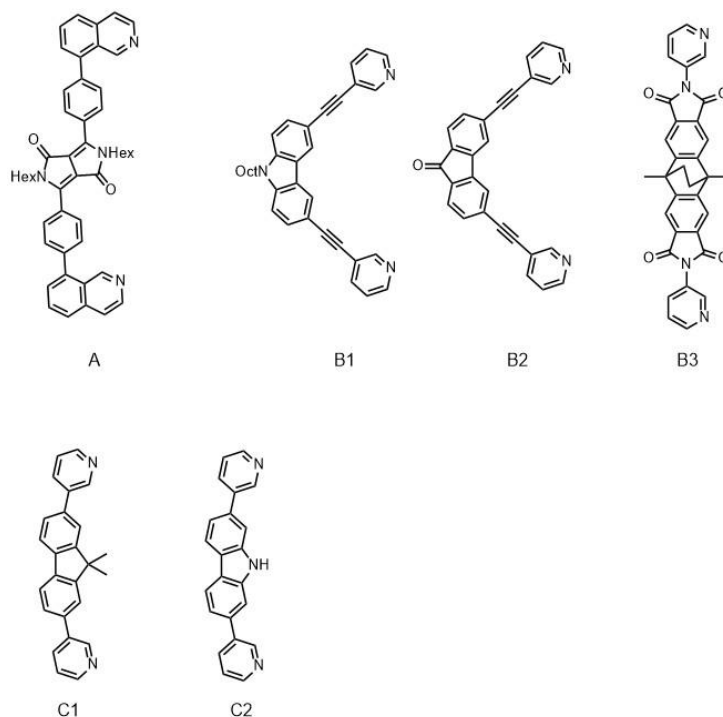


Figure S1: List of ligand structures employed in this study.

Synthesis of the single heteroleptic assemblies

Synthesis of $\text{Pd}_2\text{A}_2(\text{B2})_2$

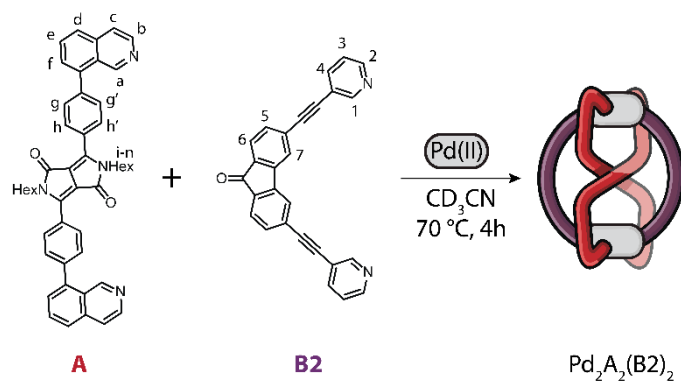


Figure S2: Formation of heteroleptic cage $\text{Pd}_2\text{A}_2(\text{B2})_2$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of both ligands.

225 μL of 3.11 mM solutions of each ligand in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{B2})_2$ as the main species in the equilibrated solution.

^1H NMR (500 MHz, CD_3CN), aromatic region, δ 9.76 (s, 1H), 9.48 (s, 1H), 9.26 (d, J = 6.4 Hz, 1H), 9.24 (d, J = 6.6 Hz, 1H), 8.89 (d, J = 8.0 Hz, 1H), 8.25 (d, J = 7.9 Hz, 1H), 8.18 (d, J = 6.6 Hz, 1H), 8.15 (d, J = 10.6 Hz, 1H), 8.08 (d, J = 7.3 Hz, 1H), 8.05 (d, J = 7.7 Hz, 1H), 7.91 (d, J = 6.8 Hz, 1H), 7.78 (dd, J = 7.6, 1.2 Hz, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.58 (d, J = 7.9 Hz, 1H), 7.41 (s, 1H).

HR ESI-MS (m/z): measured for $[\text{Pd}_2\text{A}_2(\text{B2})_2]^{4+}$: 599.6872

expected: 599.6890

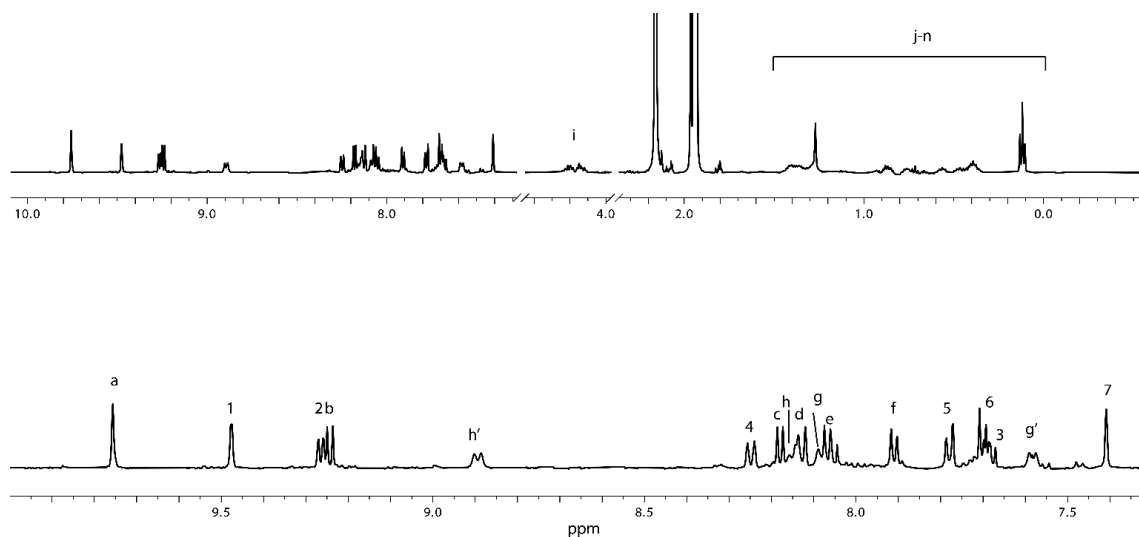


Figure S3: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B}_2)_2$ as the main species in solution.

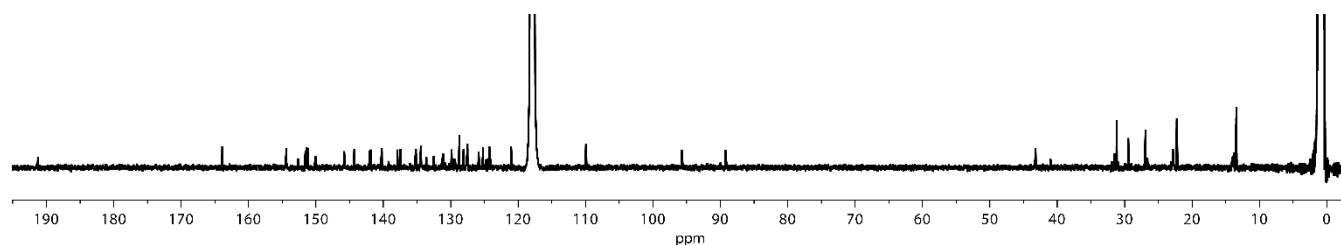


Figure S4: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B}_2)_2$.

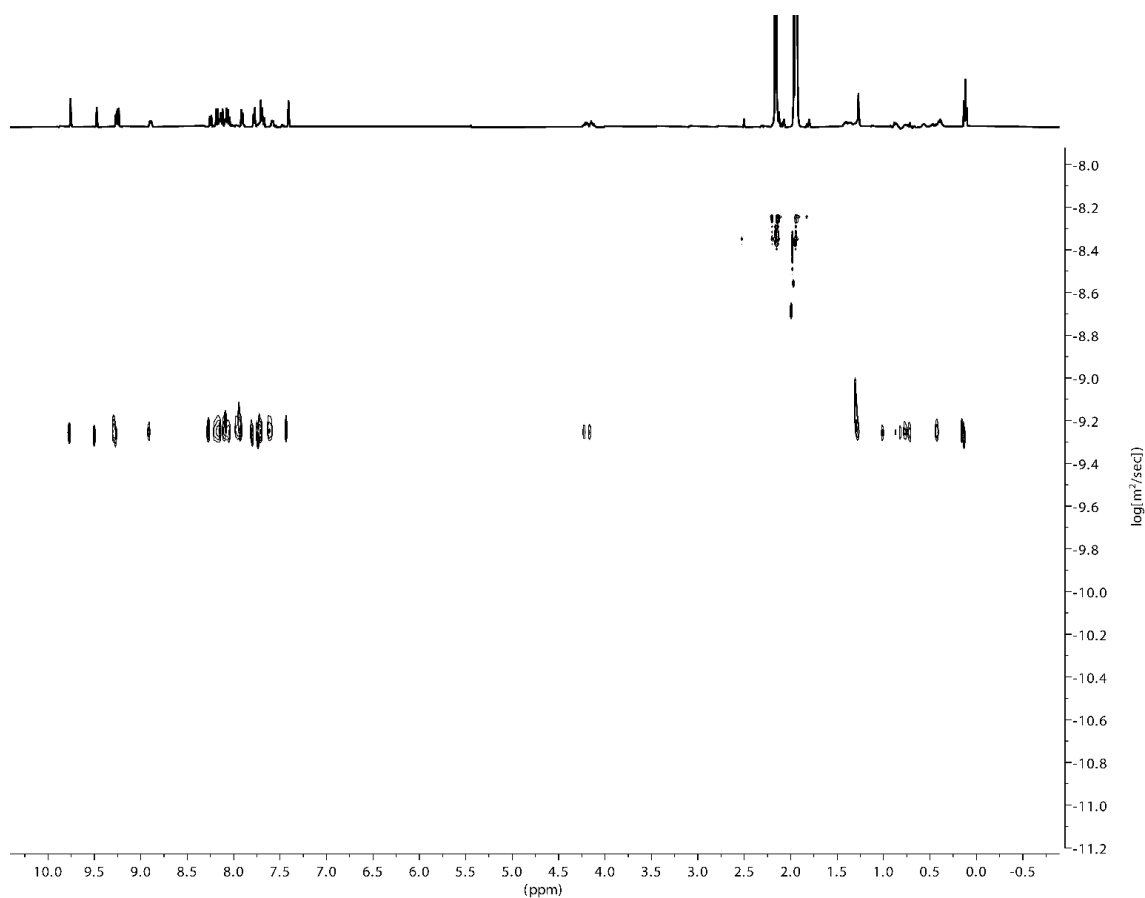


Figure S5: ^1H -DOSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B}_2)_2$. $D = 5.37 \times 10^{-10} \text{ m}^2\text{s}^{-1}$, $R_h = 1.215 \text{ nm}$.

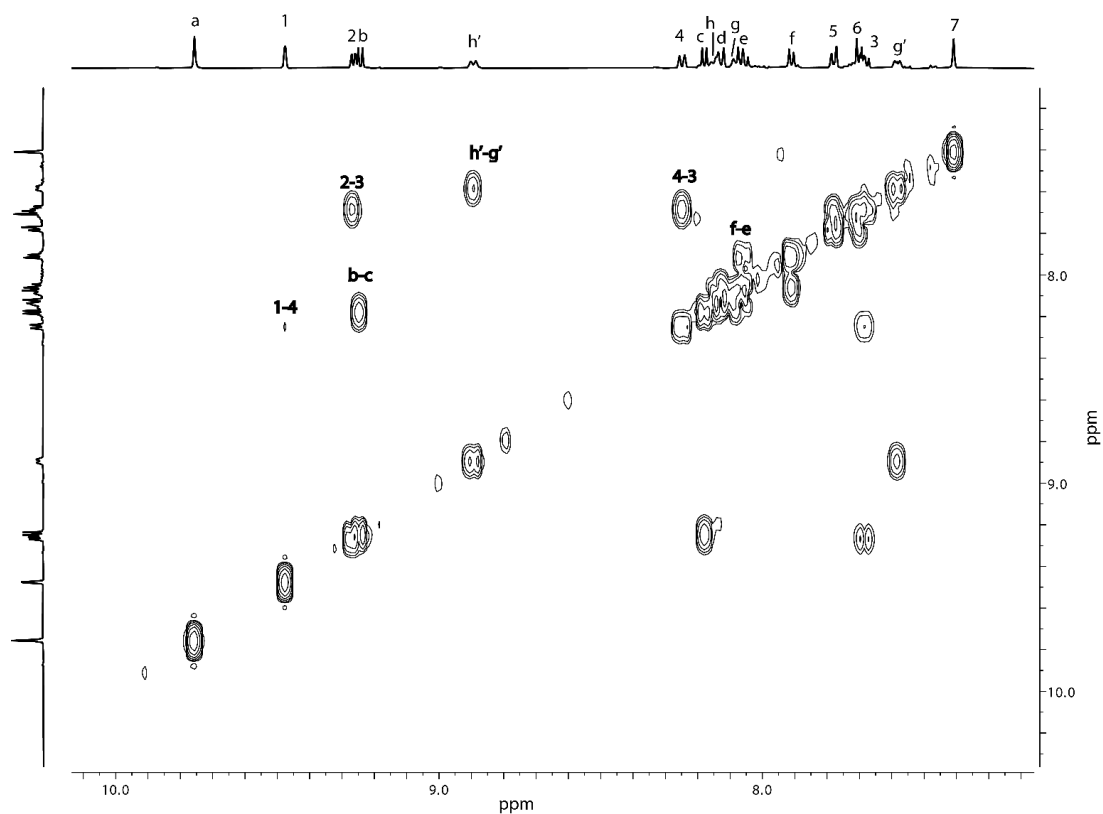


Figure S6: Enlargement of the aromatic region of the ^1H - ^1H COSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B2})_2$.

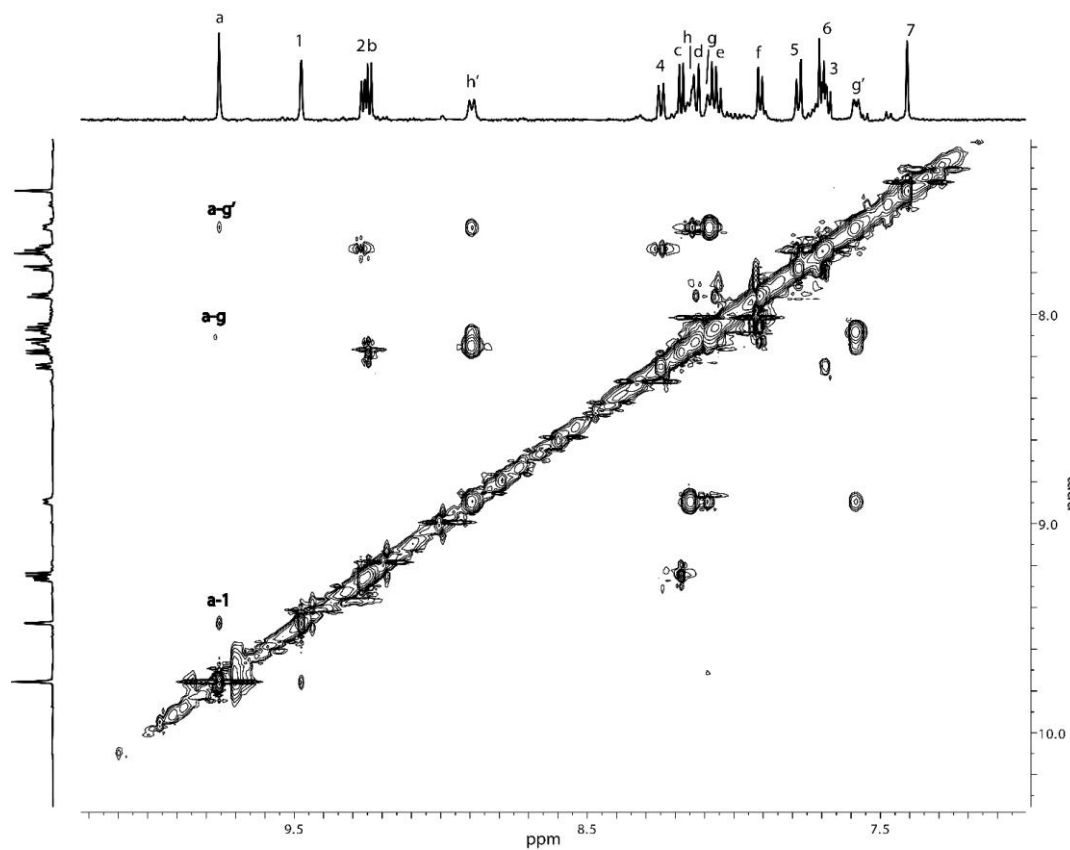


Figure S7: Enlargement of the aromatic region of the ^1H - ^1H NOESY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B2})_2$.

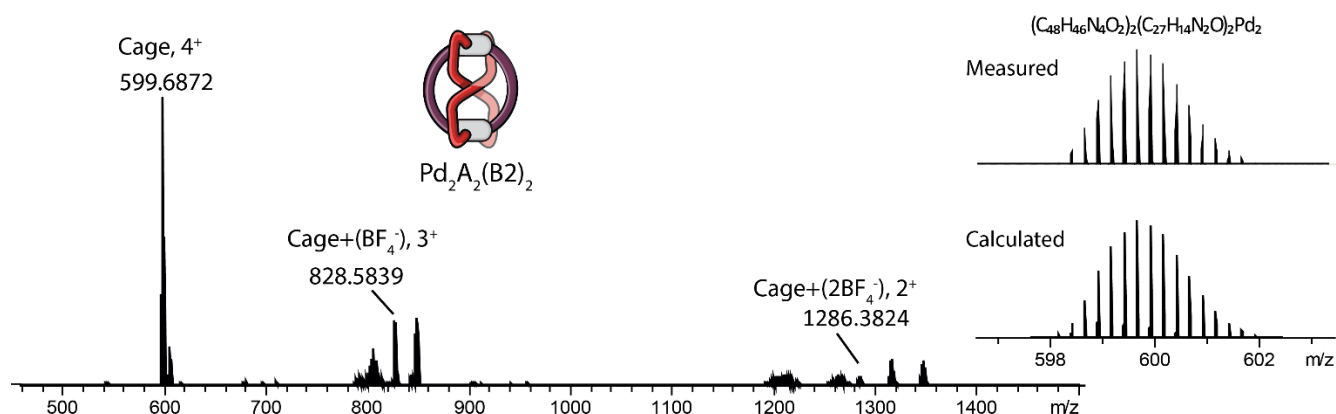


Figure S8: ESI-MS spectrum of an acetonitrile solution of **A** and **B2** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{A}_2(\text{B2})_2+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{A}_2(\text{B2})_2]^{4+}$ are shown in the inset.

Synthesis of $\text{Pd}_2\text{A}_2(\text{B3})_2$

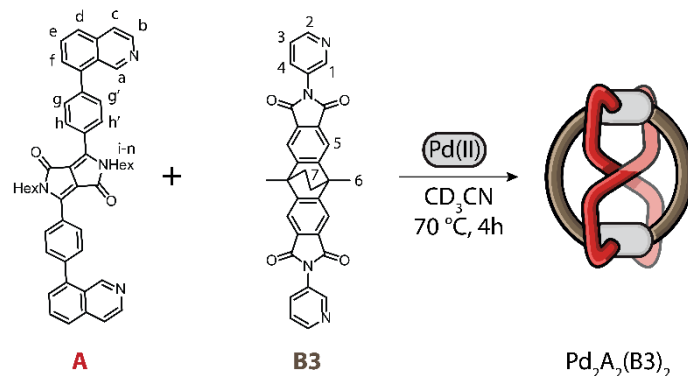


Figure S9: Formation of heteroleptic cage $\text{Pd}_2\text{A}_2(\text{B3})_2$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of both ligands.

225 μL of 3.11 mM solutions of each ligand in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{B3})_2$ in the equilibrated solution.

^1H NMR (600 MHz, CD_3CN), aromatic region δ 9.79 (s, 1H), 9.36 (d, $J = 6.7$ Hz, 1H), 9.29 (s, 1H), 8.99 (d, $J = 5.8$ Hz, 1H), 8.21 (d, $J = 6.6$ Hz, 1H), 8.18 (ddd, $J = 8.2, 2.3, 1.2$ Hz, 1H), 8.09 (d, $J = 8.3$ Hz, 1H), 8.04 (d, $J = 7.5$ Hz, 2H), 8.02 – 7.99 (m, 1H), 7.99 (s, 1H), 7.85 – 7.80 (m, 2H), 7.76 (d, $J = 6.9$ Hz, 1H), 7.69 (dd, $J = 8.3, 5.8$ Hz, 1H).

HR ESI-MS (m/z): measured for $[\text{Pd}_2\text{A}_2(\text{B3})_2]^{4+}$: 671.7135
 expected: 671.7159

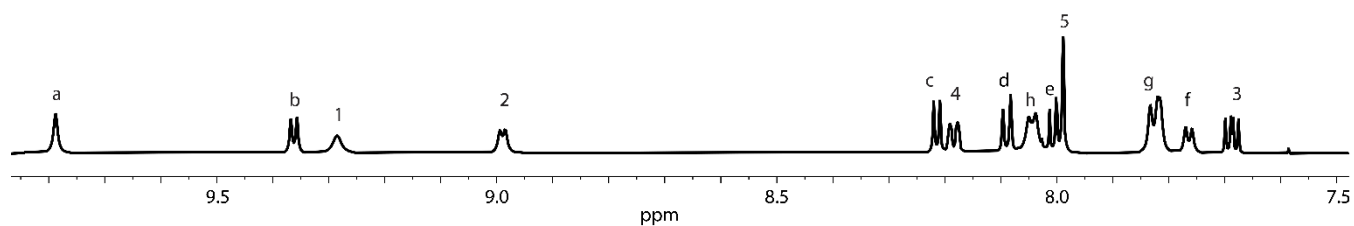
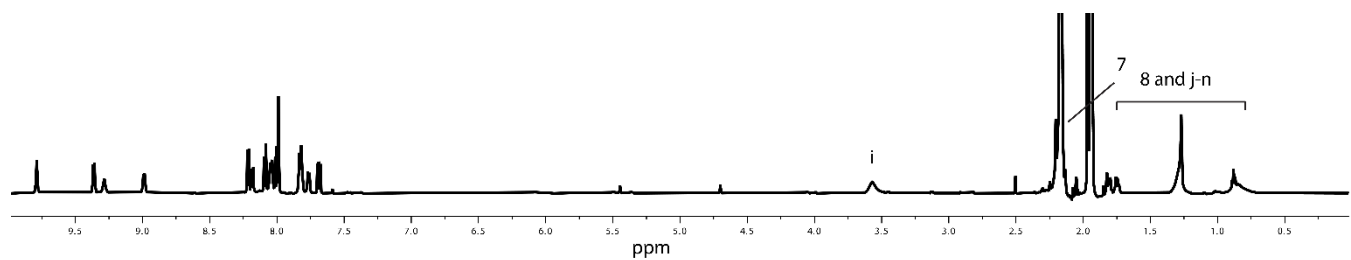


Figure S10: ^1H NMR spectrum (600 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B3})_2$.

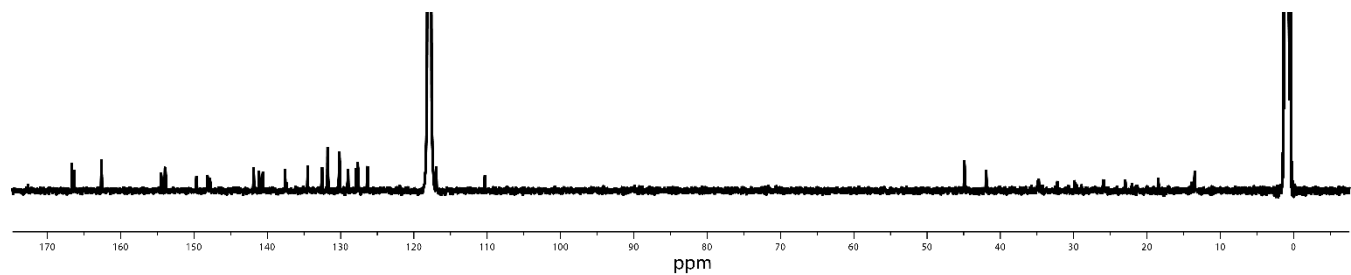


Figure S11: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B3})_2$.

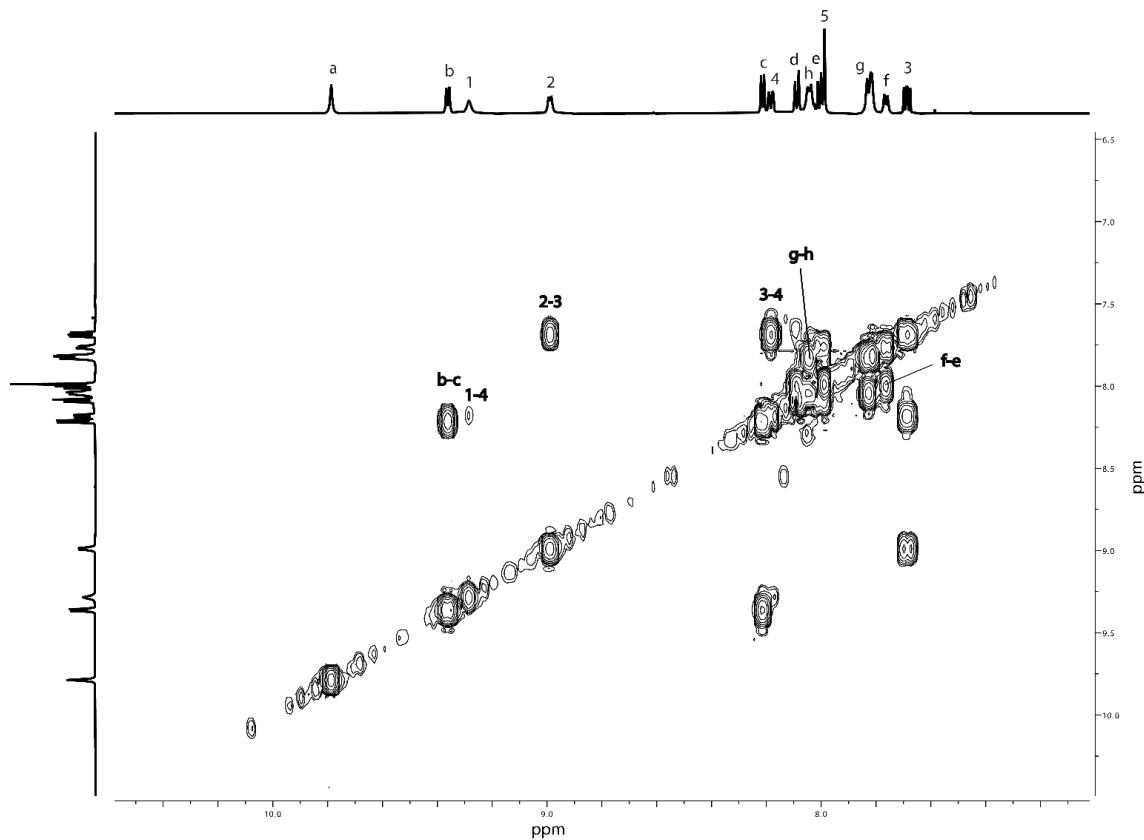


Figure S12: Enlargement of the aromatic region of the ^1H - ^1H COSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B3})_2$.

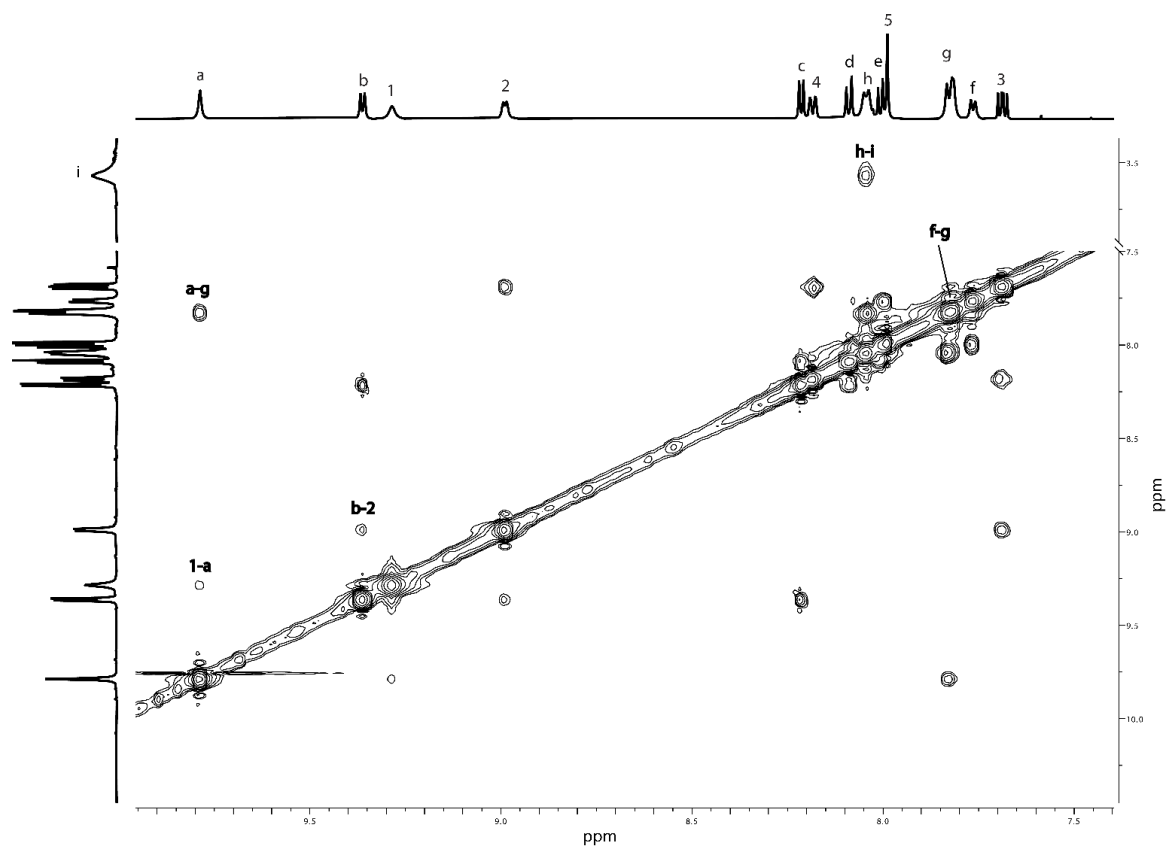


Figure S13: Enlargement of the aromatic region of the ^1H - ^1H NOESY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B3})_2$.

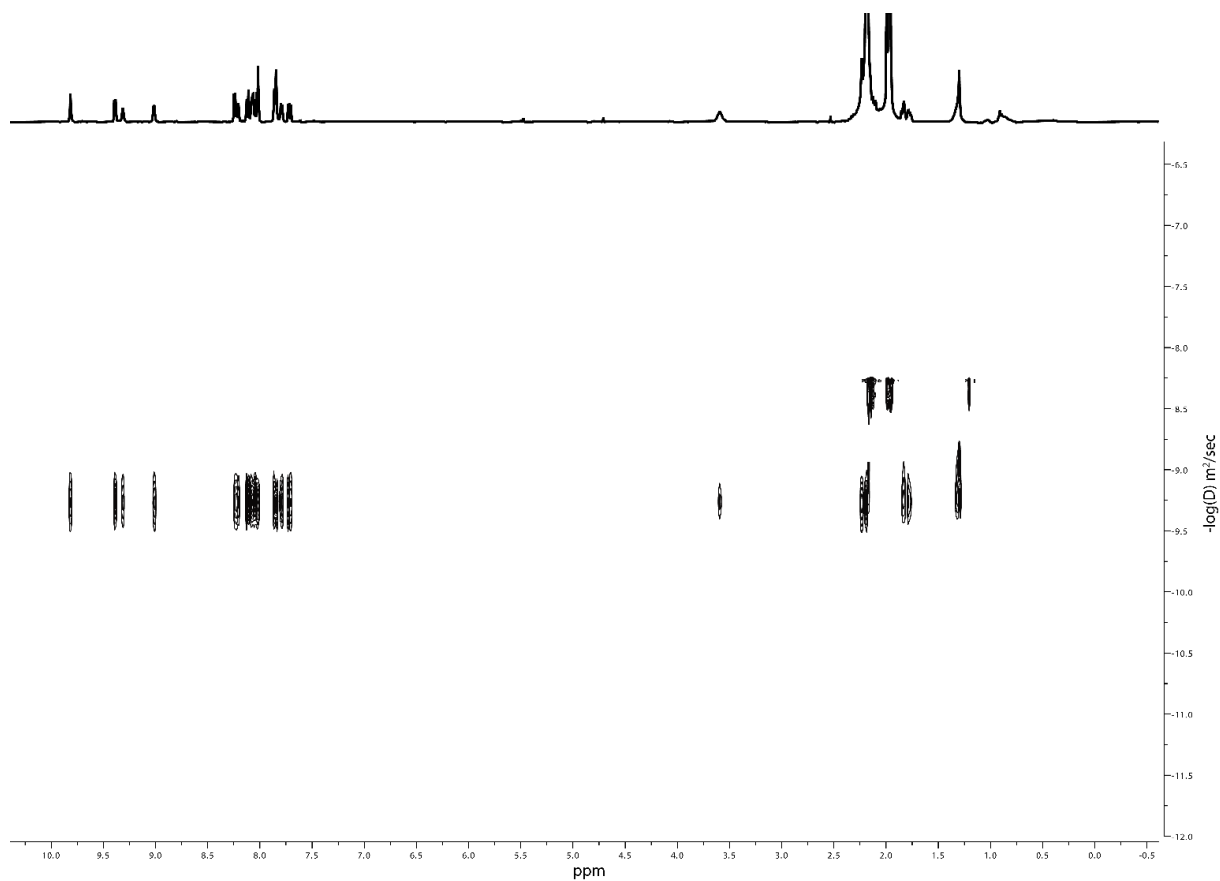


Figure S14: ^1H -DOSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B3})_2$. $D = 5.36 \times 10^{-10} \text{ m}^2\text{s}^{-1}$, $R_h = 1.219 \text{ nm}$.

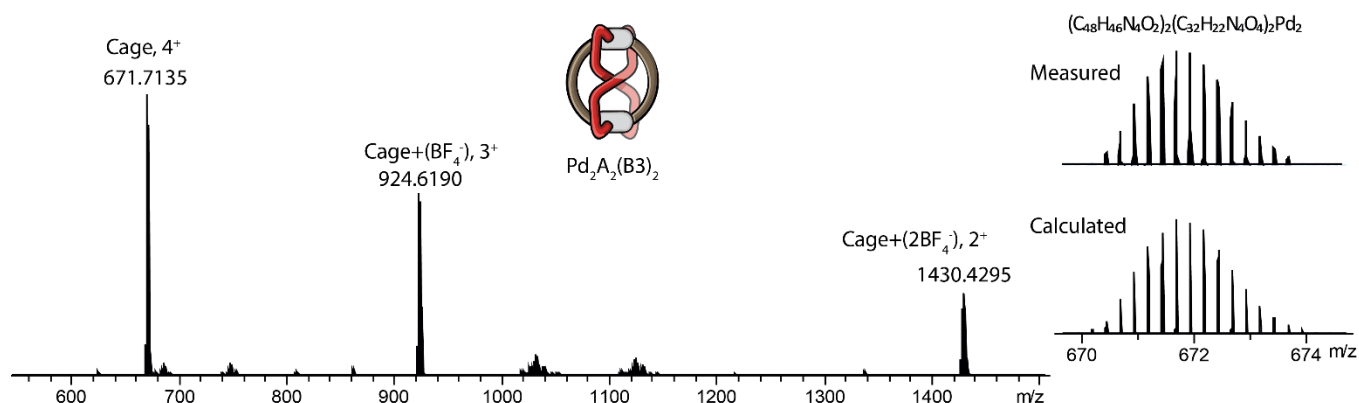


Figure S15: ESI-MS spectrum of an acetonitrile solution of **A** and **B3** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{A}_2(\text{B3})_2+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{A}_2(\text{B3})_2]^{4+}$ are shown in the inset.

Synthesis of $\text{Pd}_2\text{A}_2(\text{B4})_2$

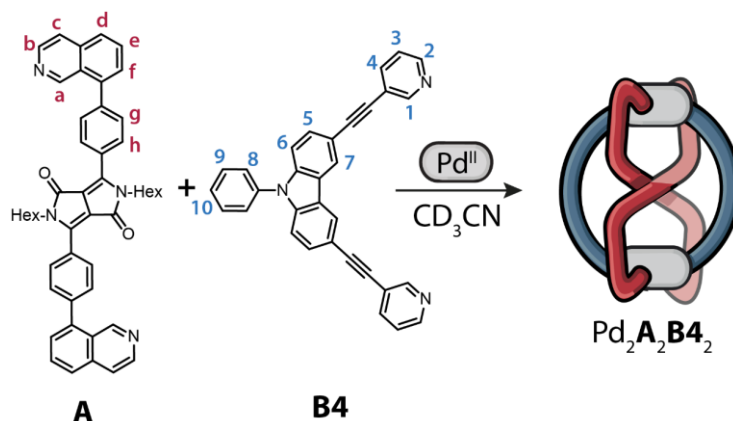


Figure S16: Formation of heteroleptic cage $\text{Pd}_2\text{A}_2(\text{B4})_2$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of both ligands.

225 μL of 3.11 mM solutions of each ligand in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{B4})_2$ in the equilibrated solution.

HR ESI-MS (m/z): measured for $[\text{Pd}_2\text{A}_2(\text{B3})_2]^{4+}$: 631.2138
 expected: 631.2159

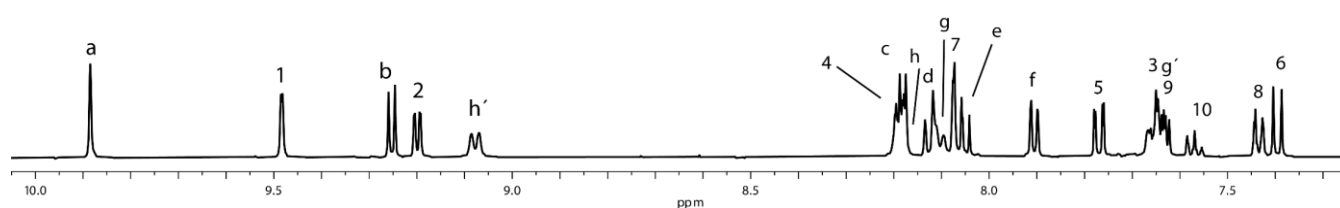
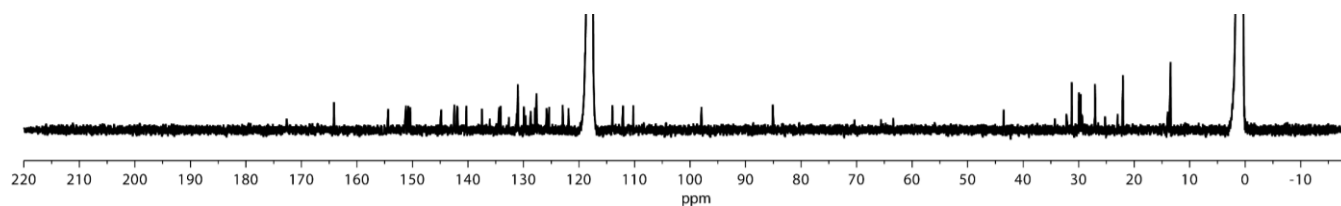
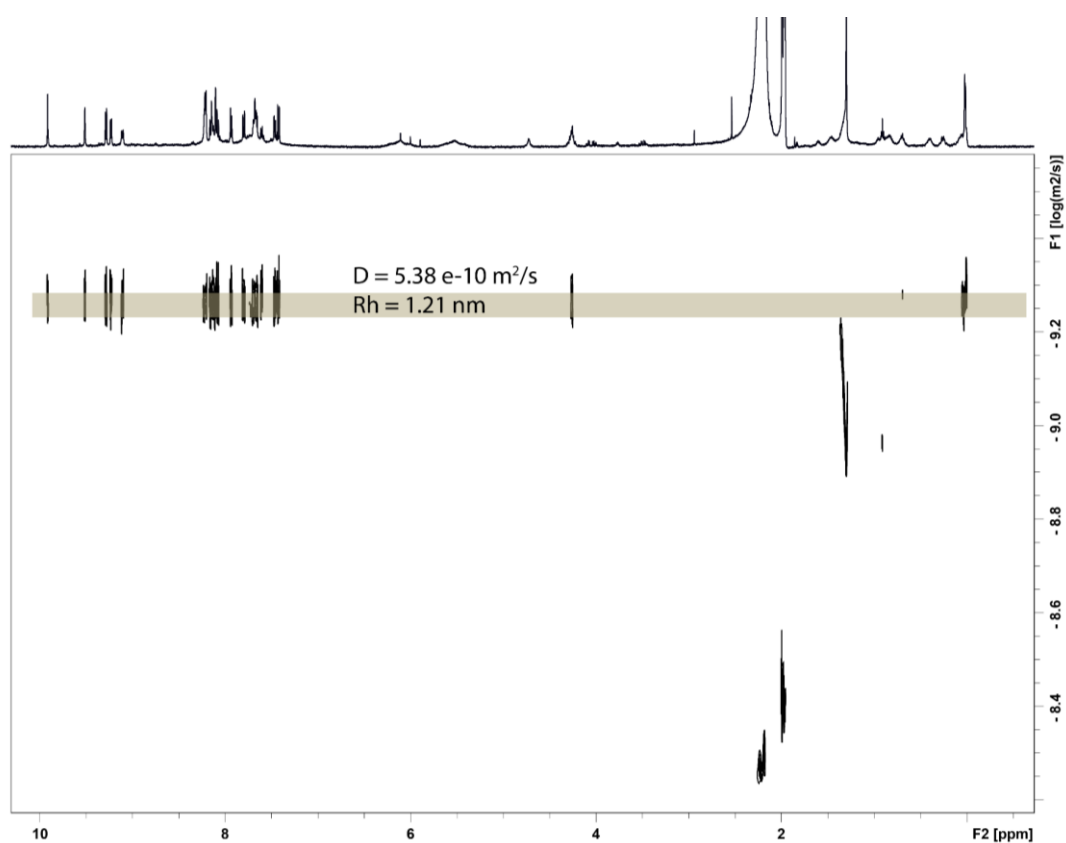


Figure S17: ^1H NMR spectrum (600 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B4})_2$.**Figure S18:** ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B4})_2$.**Figure S19:** ^1H -DOSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B4})_2$. $D = 5.38 \times 10^{-10} \text{ m}^2\text{s}^{-1}$, $R_h = 1.21 \text{ nm}$.

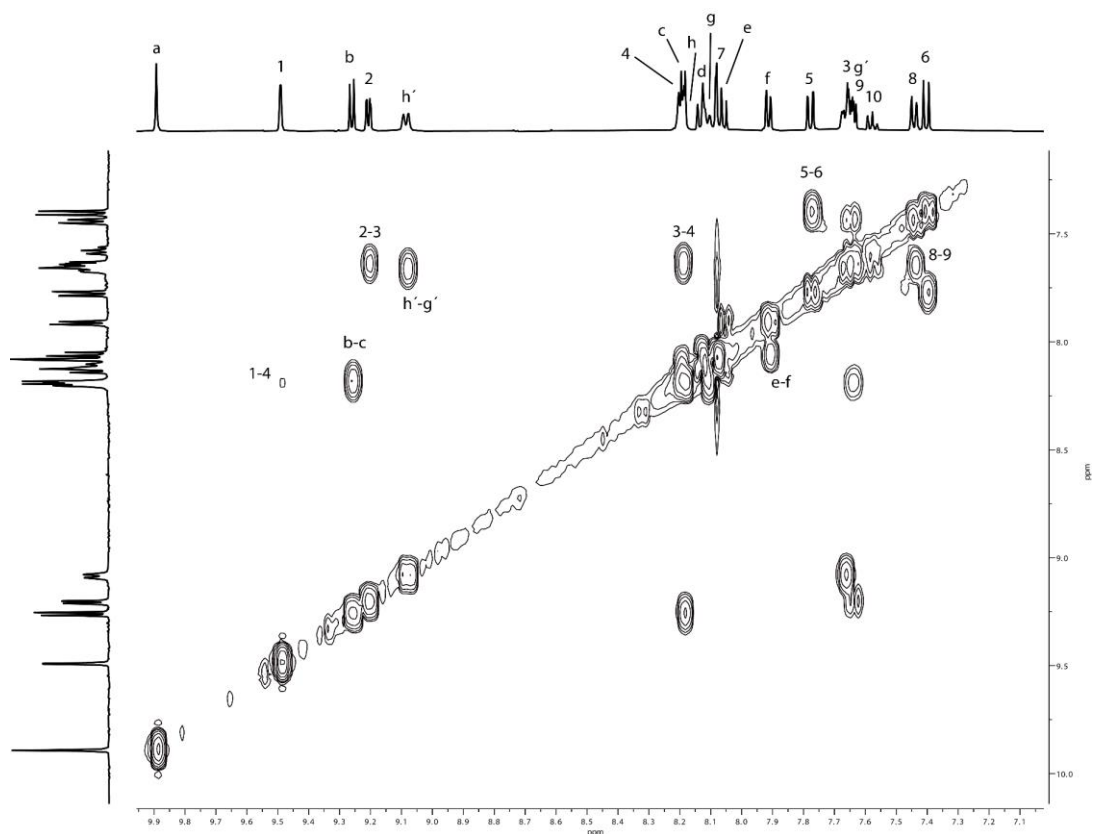


Figure S20: Enlargement of the aromatic region of the ^1H - ^1H COSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B4})_2$.

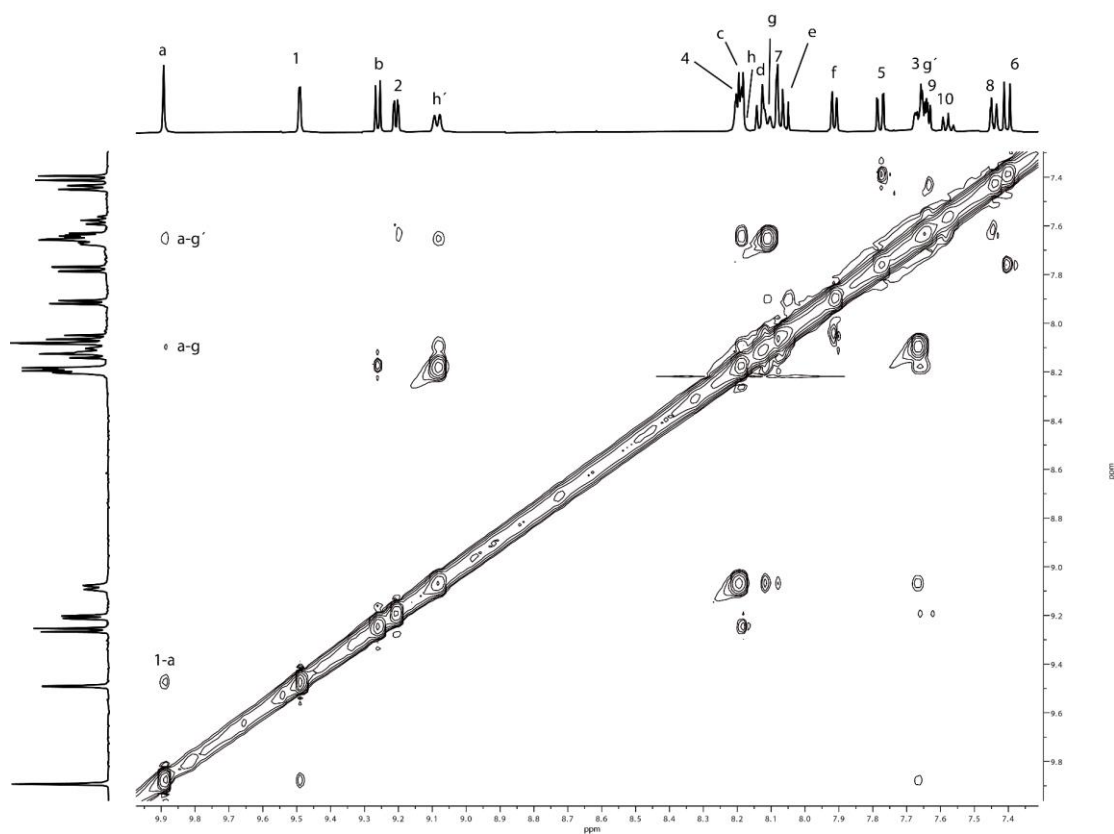


Figure S21: Enlargement of the aromatic region of the ^1H - ^1H NOESY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B4})_2$.

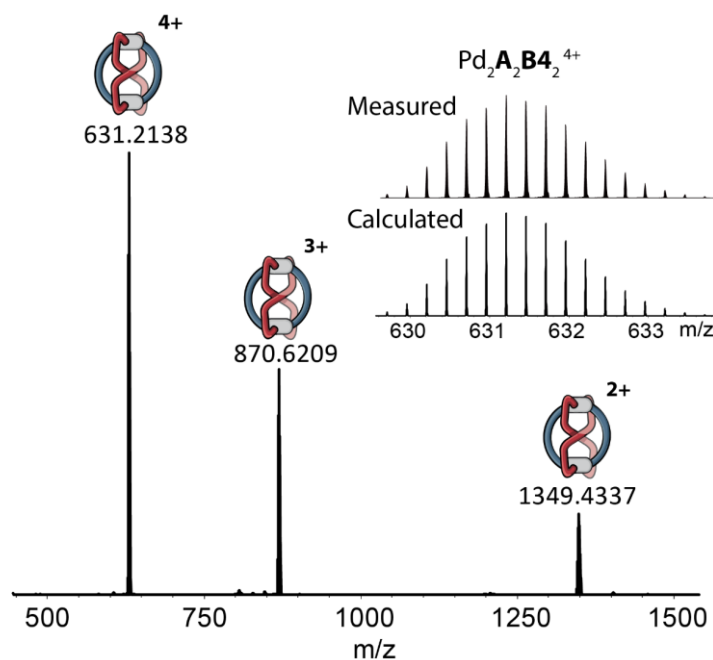


Figure S22: ESI-MS spectrum of an acetonitrile solution of **A** and **B4** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{A}_2(\text{B4})_2+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{A}_2(\text{B4})_2]^{4+}$ are shown in the inset.

Synthesis of $\text{Pd}_2\text{A}_2(\text{B5})_2$

225 μL of 3.11 mM solutions of each ligand in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{B5})_2$ in the equilibrated solution.

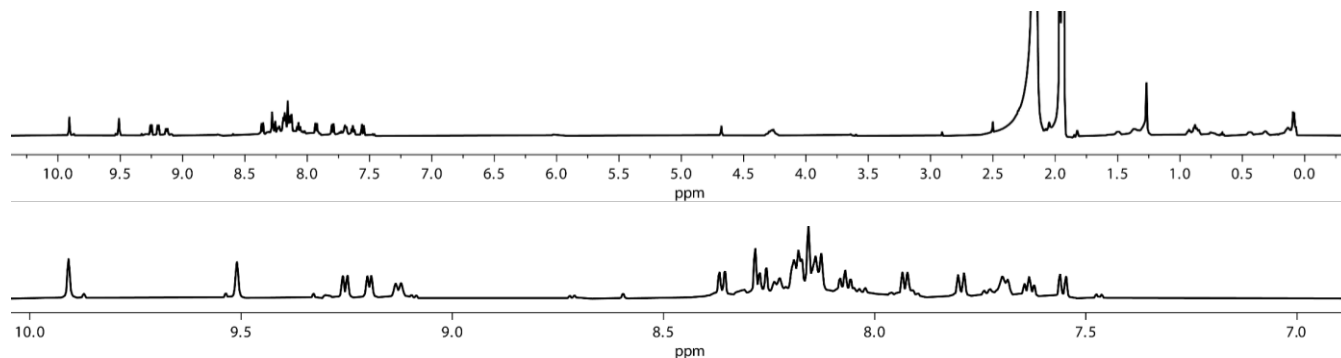


Figure S23: ^1H NMR spectrum (600 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B5})_2$.

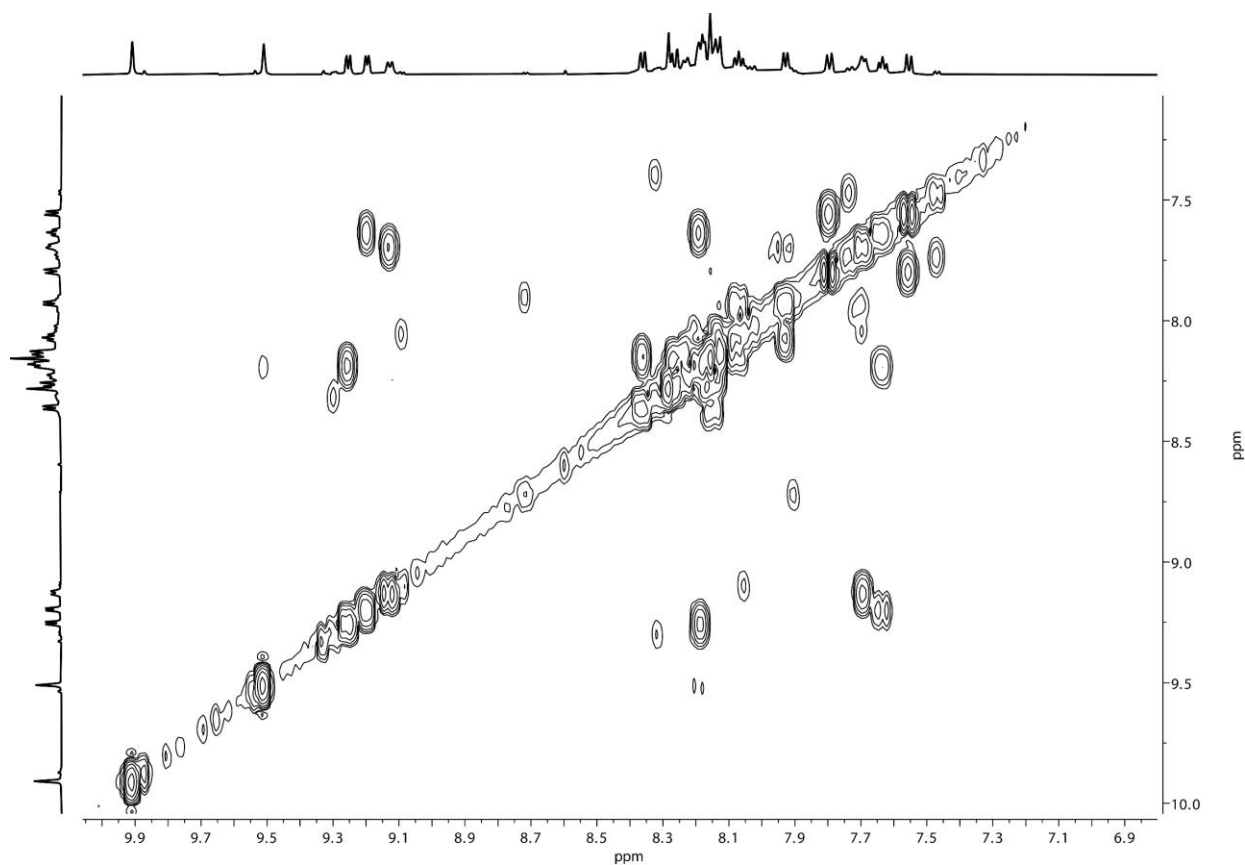


Figure S24: Enlargement of the aromatic region of the ¹H-¹H COSY spectrum in CD₃CN of the heteroleptic assembly Pd₂A₂(B5)₂.

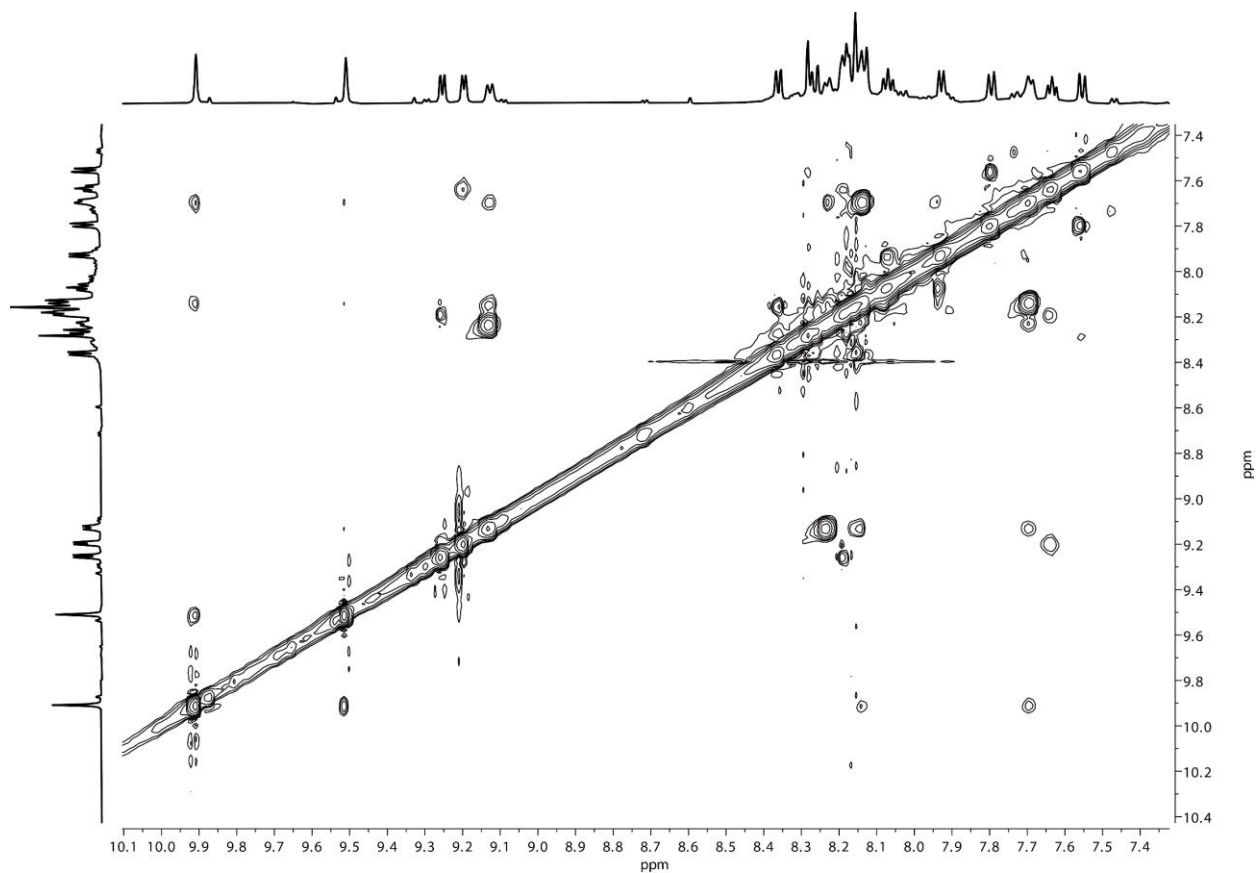


Figure S25: Enlargement of the aromatic region of the ¹H-¹H NOESY spectrum in CD₃CN of the heteroleptic assembly Pd₂A₂(B5)₂.

Synthesis of $\text{Pd}_2\text{A}_2(\text{B6})_2$

225 μL of 3.11 mM solutions of each ligand in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{B6})_2$ in the equilibrated solution.

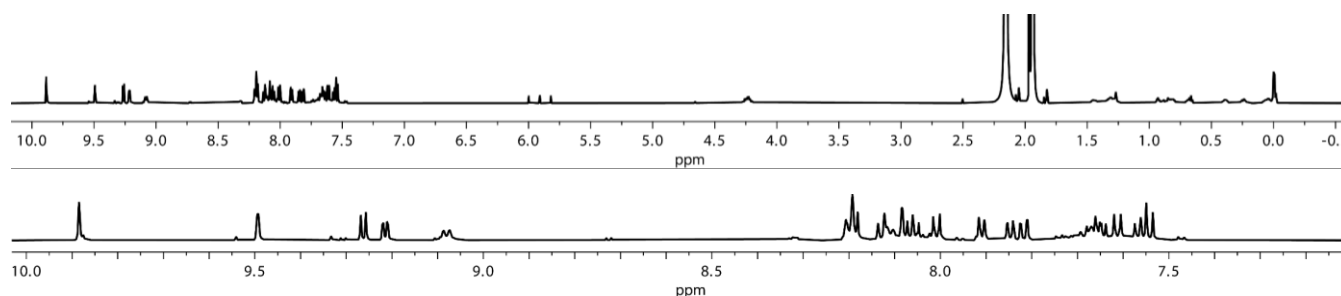


Figure S26: ^1H NMR spectrum (600 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B6})_2$.

Synthesis of $\text{Pd}_2\text{A}_2(\text{C1})_2$

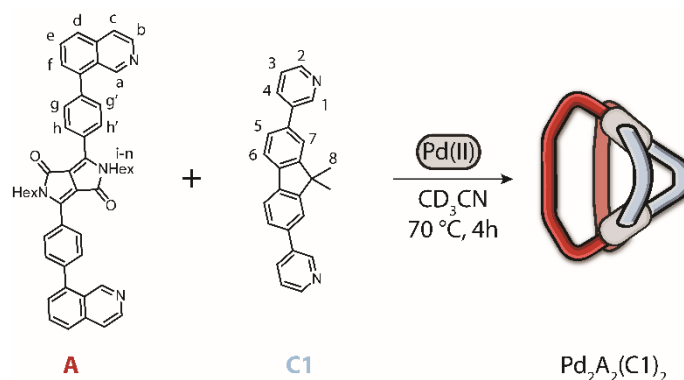


Figure S27: Formation of heteroleptic cage $\text{Pd}_2\text{A}_2(\text{C1})_2$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of both ligands.

225 μL of 3.11 mM solutions of each ligand in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{C1})_2$ in the equilibrated solution.

^1H NMR (700 MHz, CD_3CN), aromatic region δ 9.72 (s, 1H), 9.66 (s, 1H), 9.50 (s, 1H), 9.47 (s, 1H), 9.42 (d, $J = 6.6$ Hz, 1H), 9.26 (d, $J = 6.7$ Hz, 1H), 9.02 – 8.97 (m, 2H), 8.36 – 8.31 (m, 2H), 8.25 (d, $J = 6.7$ Hz, 1H), 8.17 (d, $J = 7.8$ Hz, 1H), 8.14 (d, $J = 8.5$ Hz, 1H), 8.13 (d, $J = 8.8$ Hz, 1H), 8.01 (ddd, $J = 8.2, 6.6, 1.4$ Hz, 2H), 7.93 (br, 2H), 7.90 – 7.84 (m, 2H), 7.77 (d, $J = 6.3$ Hz, 1H), 7.74 (d, $J = 6.6$ Hz, 1H), 7.67 (br, 2H), 7.65 (dd, $J = 7.6, 5.7$ Hz, 1H), 7.60 – 7.57 (m, 2H), 7.55 (dd, $J = 7.7, 5.8$ Hz, 1H), 7.44 (s, 1H), 7.31 (s, 1H).

HR ESI-MS (m/z): measured for $[\text{Pd}_2\text{A}_2(\text{C1})_2]^{4+}$: 582.7153
 expected: 582.7131

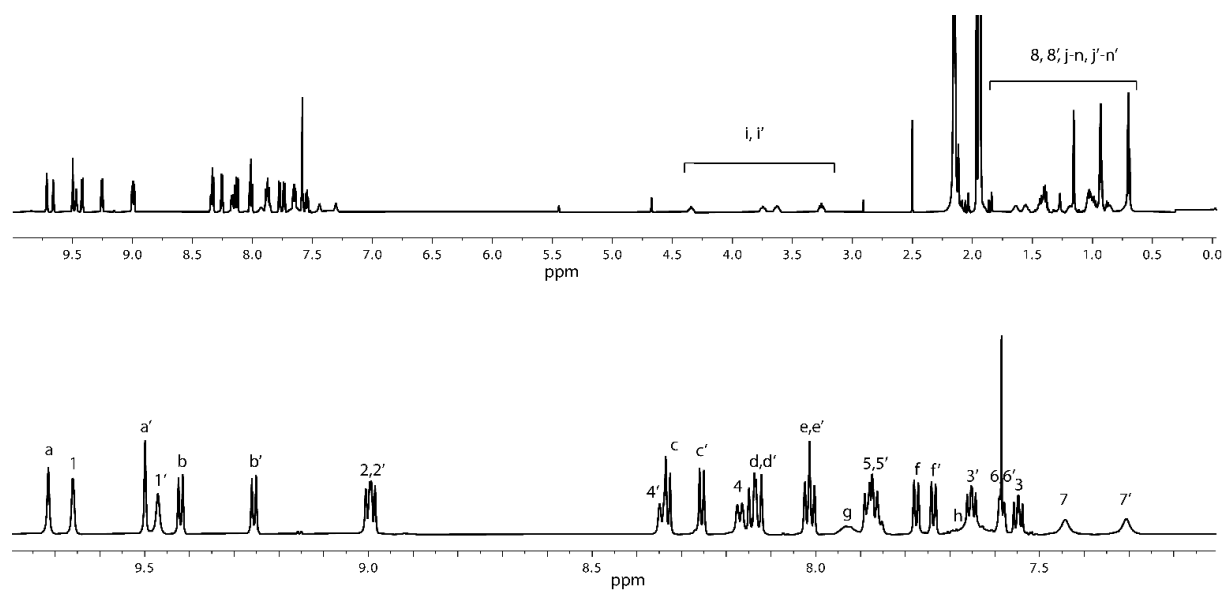


Figure S28: ^1H NMR spectrum (700 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C1})_2$.

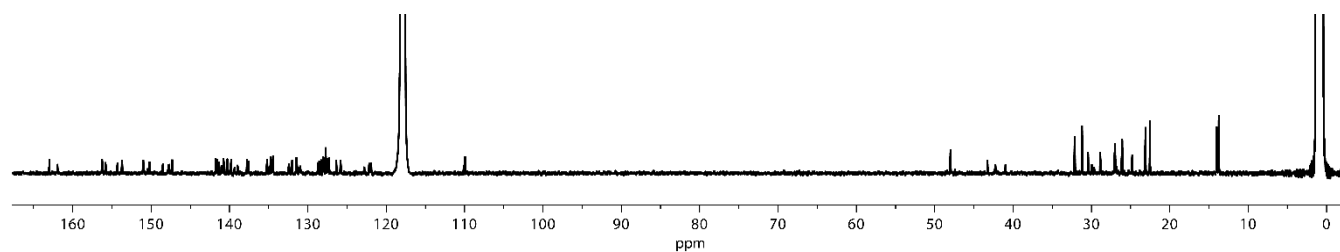


Figure S29: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B2})_2$.

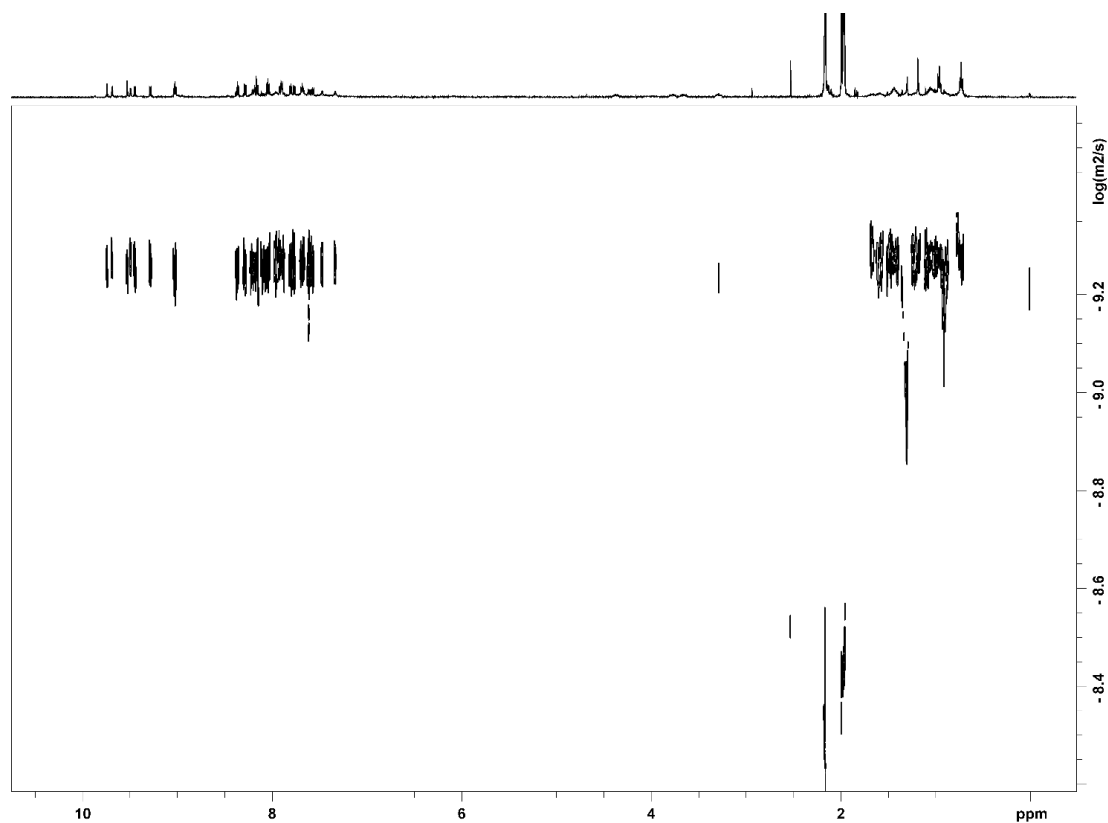


Figure S30: ^1H -DOSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{B2})_2$. $D = 5.23 \times 10^{-10} \text{ m}^2\text{s}^{-1}$, $R_h = 1.252 \text{ nm}$.

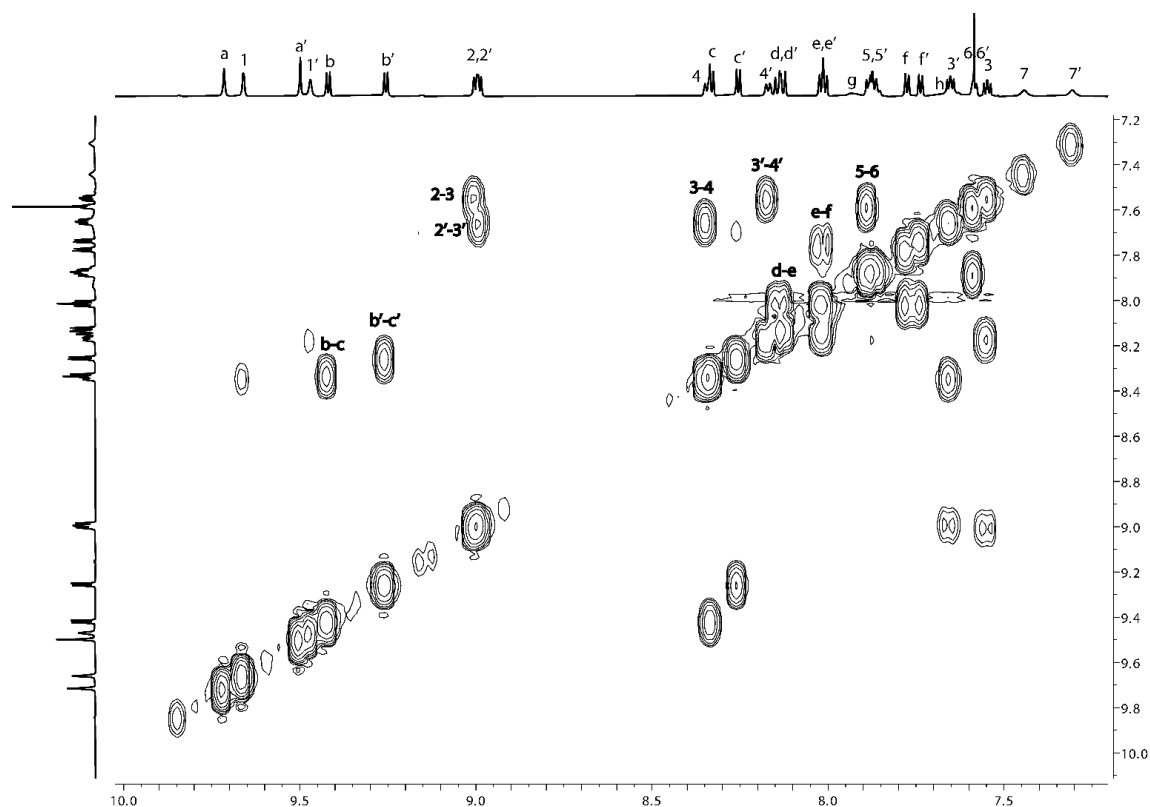


Figure S31: Enlargement of the aromatic region of the ^1H - ^1H COSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C1})_2$.

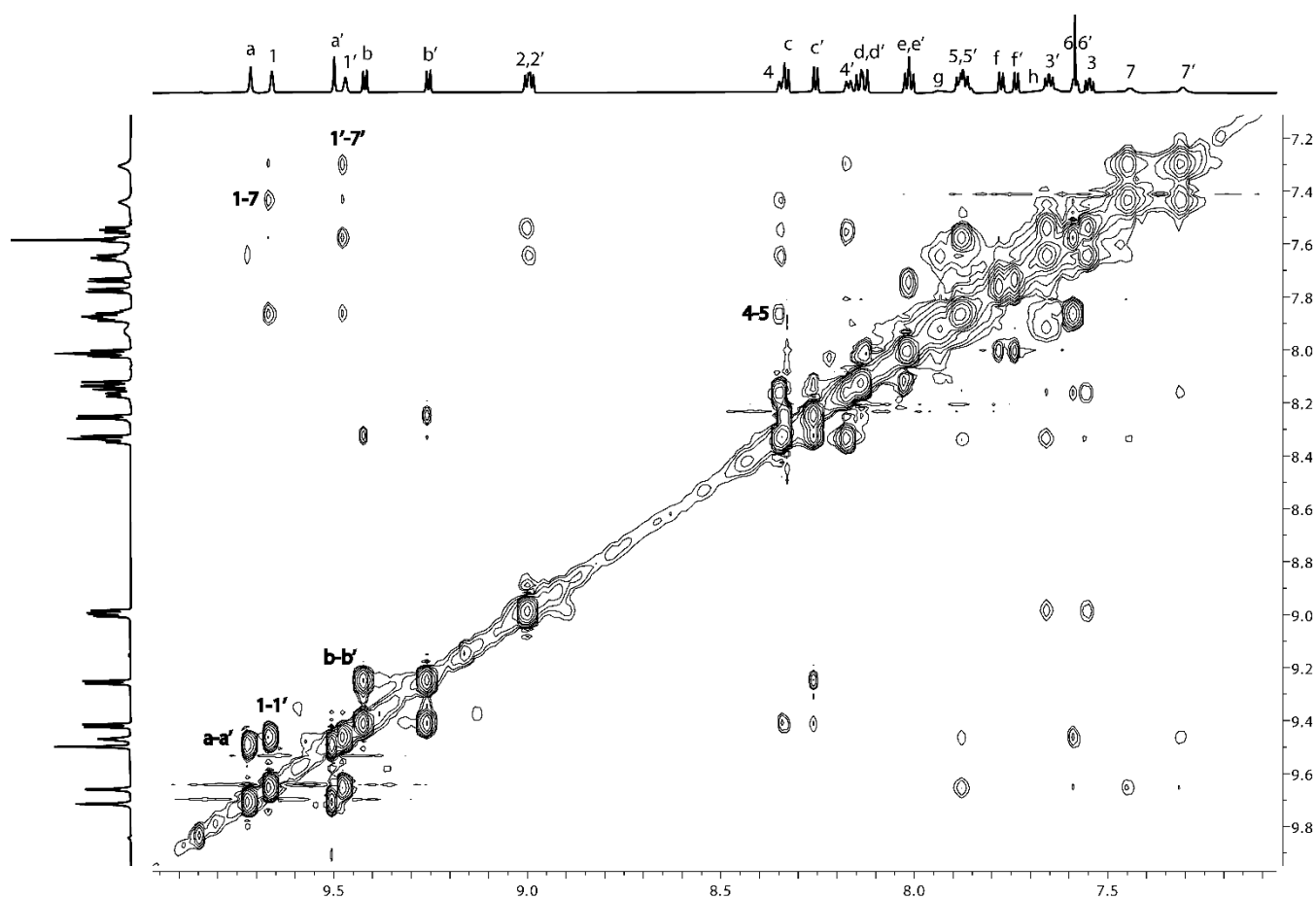


Figure S32: Enlargement of the aromatic region of the ^1H - ^1H NOESY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C1})_2$.

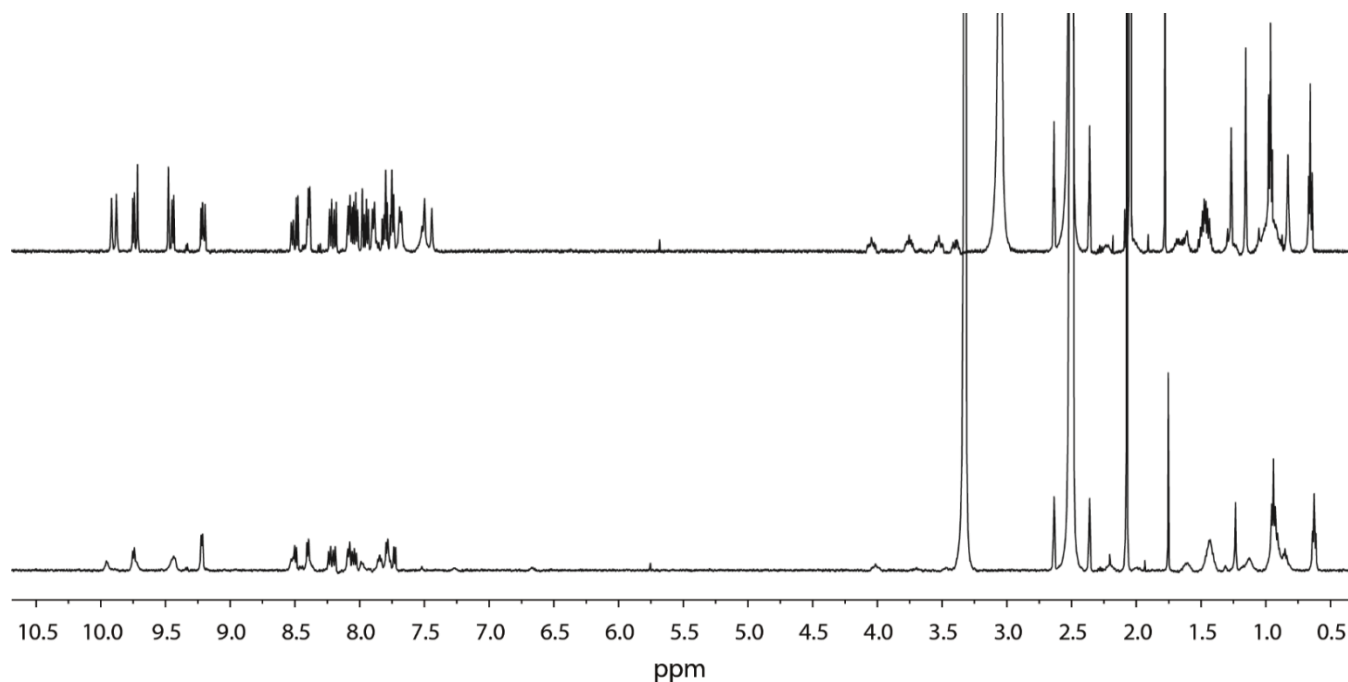


Figure S33: VT ^1H NMR spectrum of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C1})_2$ (500 MHz, DMSO-d_6). Bottom is 25 °C, with severe broadening of the signals. Up is 90 °C with clear splitting of all the signals indicative of the symmetry breaking of the cage.

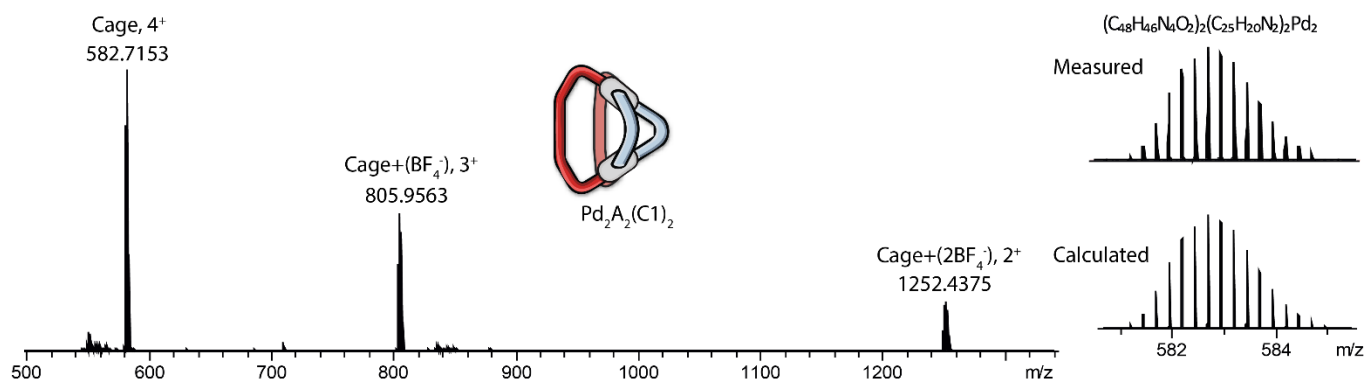


Figure S34: ESI-MS spectrum of an acetonitrile solution of A and C1 with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{A}_2(\text{C1})_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{A}_2(\text{C1})_2]^{4+}$ are shown in the inset.

Synthesis of $\text{Pd}_2\text{A}_2(\text{C2})_2$

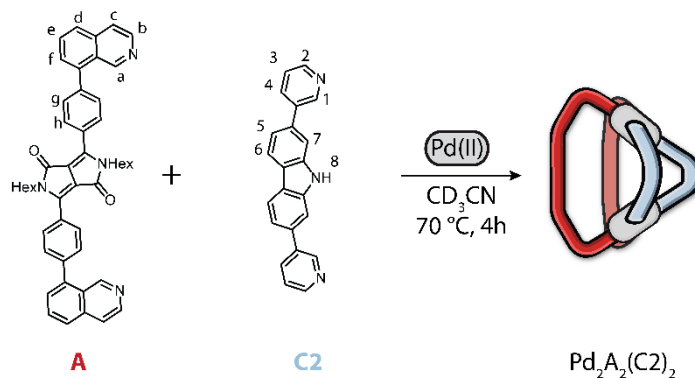


Figure S35: Formation of heteroleptic cage $\text{Pd}_2\text{A}_2(\text{C2})_2$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of both ligands.

225 μL of 3.11 mM solutions of each ligand in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{C2})_2$ in the equilibrated solution.

HR ESI-MS (m/z):	measured for $[\text{Pd}_2\text{A}_2(\text{C2})_2]^{4+}$:	569.1958
	expected:	569.1969

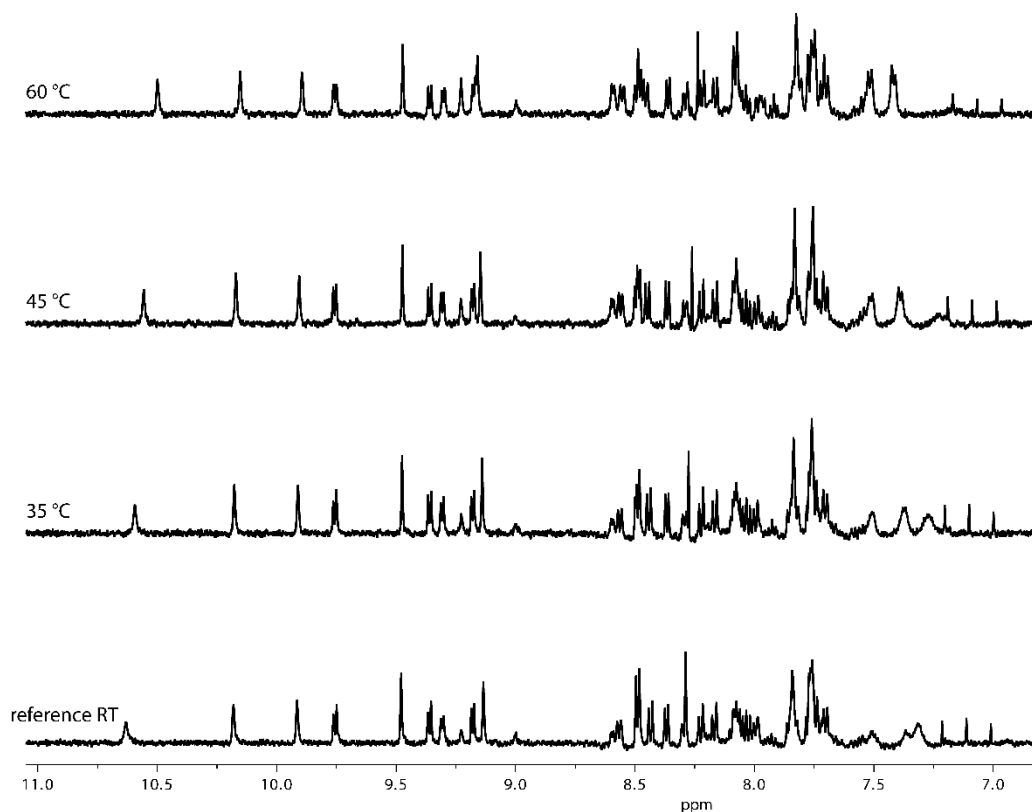


Figure S36: VT ^1H NMR spectrum (500 MHz, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C2})_2$. Zoomed of aromatic region with the same pattern observed for $\text{Pd}_2\text{A}_2(\text{C1})_2$ and no merging of the signals at higher temperature.

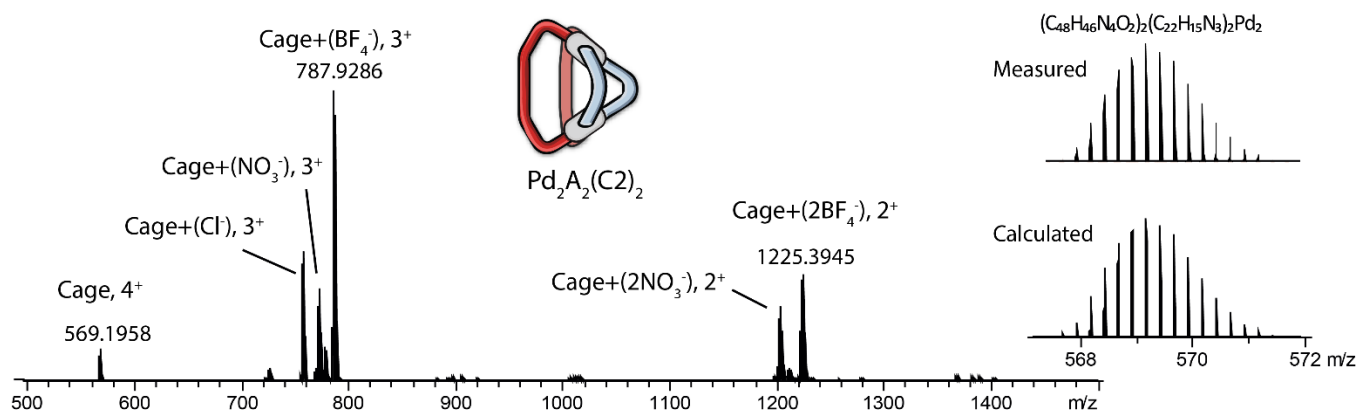


Figure S37: ESI-MS spectrum of an acetonitrile solution of **A** and **C2** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{A}_2(\text{C2})_2+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{A}_2(\text{C2})_2]^{4+}$ are shown in the inset.

Synthesis of Pd₂A₂(C3)₂

225 μL of 3.11 mM solutions of each ligand in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{C3})_2$ in the equilibrated solution.

HR ESI-MS (m/z): measured for $[\text{Pd}_2\text{A}_2(\text{C3})_2]^{4+}$: 575.6889

expected: 575.6890

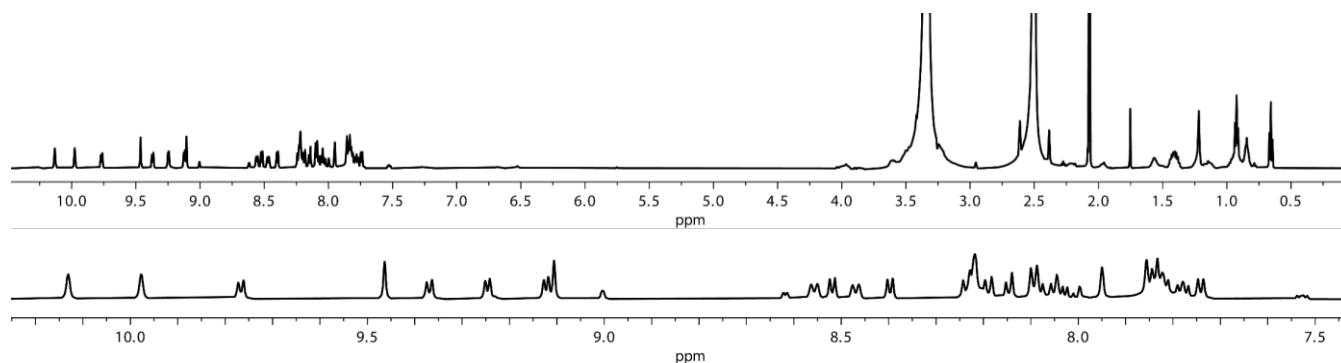


Figure S38: ^1H NMR spectrum (600 MHz, 298K, DMSO- d_6) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C3})_2$.

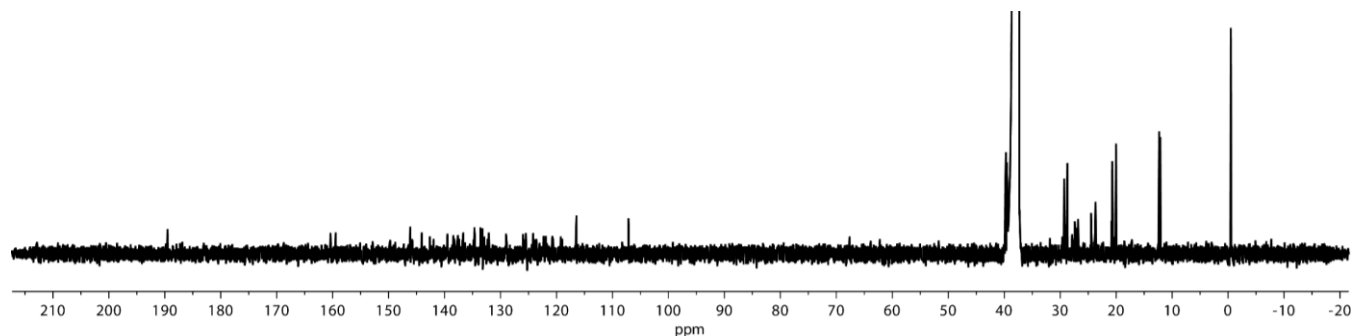


Figure S39: ^{13}C NMR spectrum (176 MHz, 298K, DMSO- d_6) of heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C3})_2$.

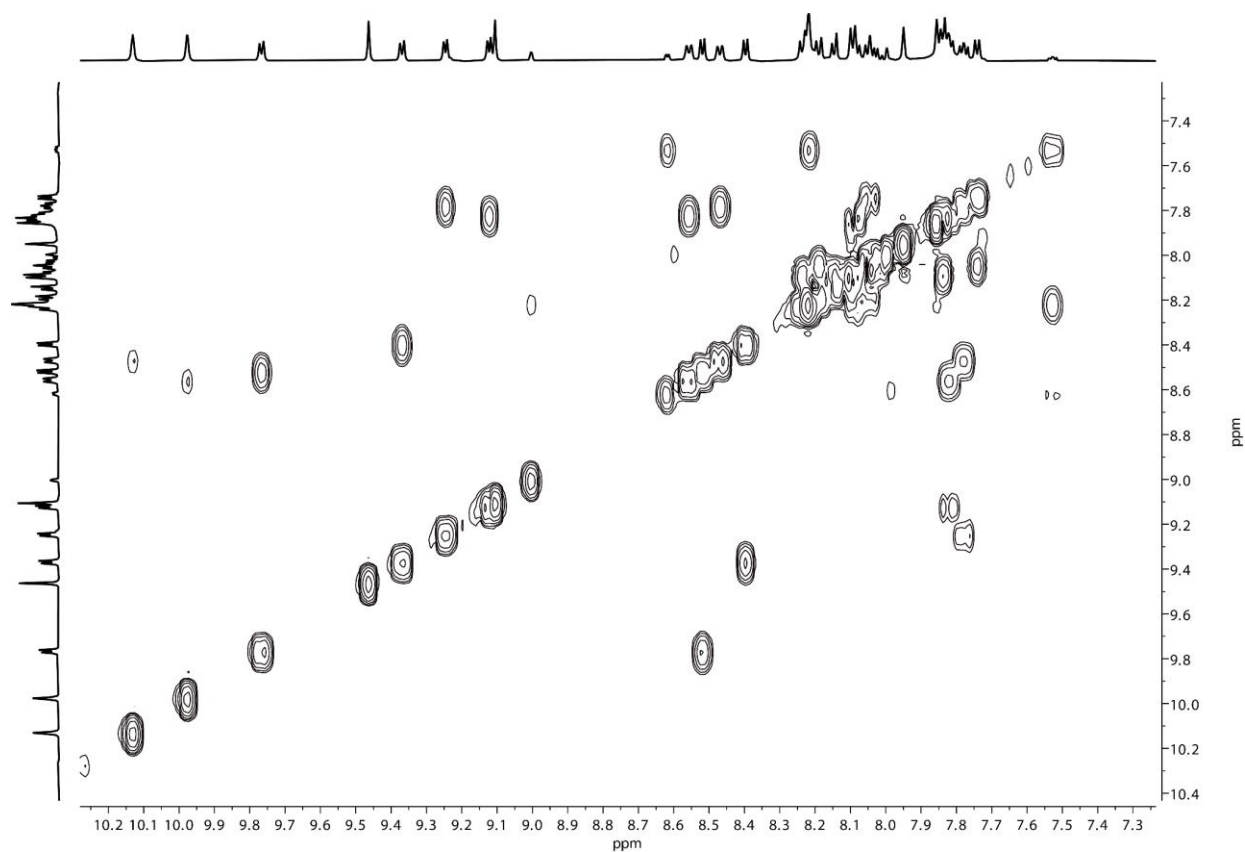


Figure S39: Enlargement of the aromatic region of the ^1H - ^1H COSY spectrum in DMSO- d_6 of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C3})_2$.

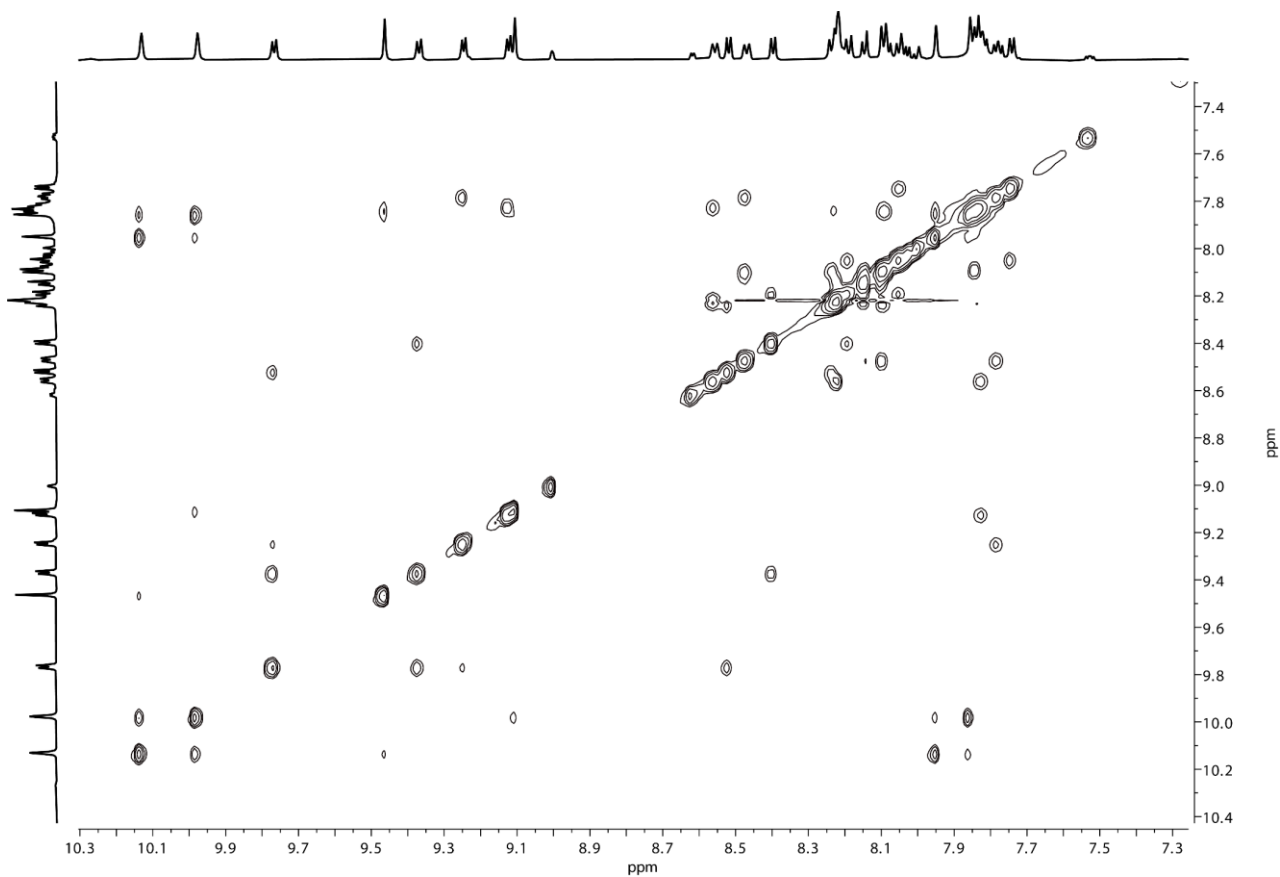


Figure S40: Enlargement of the aromatic region of the ^1H - ^1H NOESY spectrum in DMSO- d_6 of the heteroleptic assembly $\text{Pd}_2\text{A}_2(\text{C3})_2$.

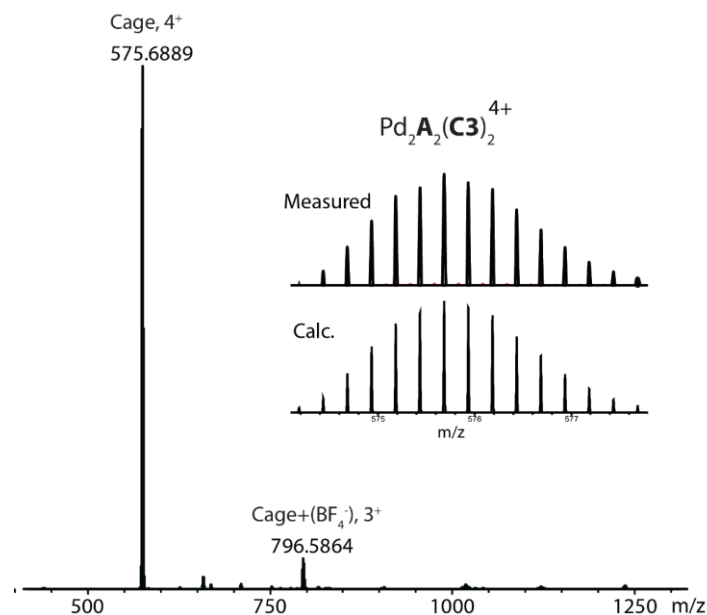


Figure S41: ESI-MS spectrum of a dimethyl sulfoxide solution of **A** and **C3** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{A}_2(\text{C3})_2+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{A}_2(\text{C3})_2]^{4+}$ are shown in the inset.

Synthesis of $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$

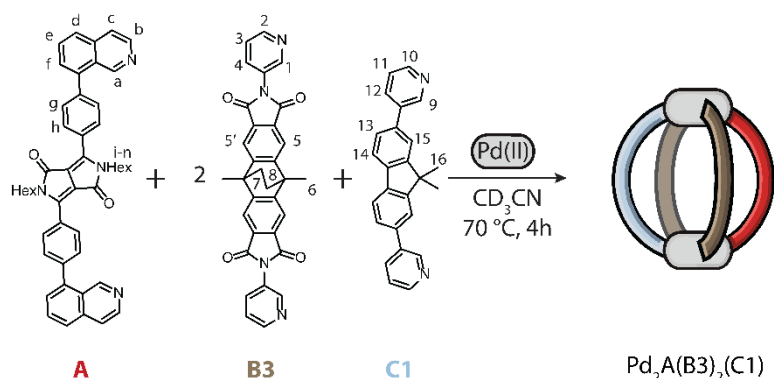


Figure S42: Formation of heteroleptic cage $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of ligands **A/B3/C1** in a 1:2:1 ratio.

224 μL of a 3.11 mM solution of **B3**, 112 μL of a 3.11 mM solution of **A** and 112 μL of a 3.11 mM solution of **C1** in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$ in the equilibrated solution.

^1H NMR (600 MHz, CD_3CN), aromatic region δ 9.75 (s, 1H), 9.50 (d, $J = 6.5$ Hz, 1H), 9.21 (dd, $J = 5.8, 1.2$ Hz, 1H), 9.19 (d, $J = 2.0$ Hz, 1H), 8.97 (s br, 2H), 8.75 (d, $J = 5.9$ Hz, 2H), 8.33 (d, $J = 6.5$ Hz, 2H), 8.26 (d, $J = 1.5$ Hz, 1H), 8.23 (d, $J = 7.5$ Hz, 2H), 8.16 (d, $J = 8.7$ Hz, 1H), 8.06 (dd, $J = 8.2, 7.0$ Hz, 1H), 8.01 (ddd, $J = 8.3, 2.2, 1.3$ Hz, 2H), 7.92 (d, $J = 8.7$ Hz, 2H), 7.88 (s, 2H), 7.86 – 7.81 (m, 2H), 7.70 (s, 1H), 7.68 – 7.61 (m, 3H), 7.55 (s, 2H), 7.50 (dd, $J = 7.7, 1.7$ Hz, 1H).

HR ESI-MS (m/z): measured for $[\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})]^{4+}$: 581.1618

expected: 581.1658

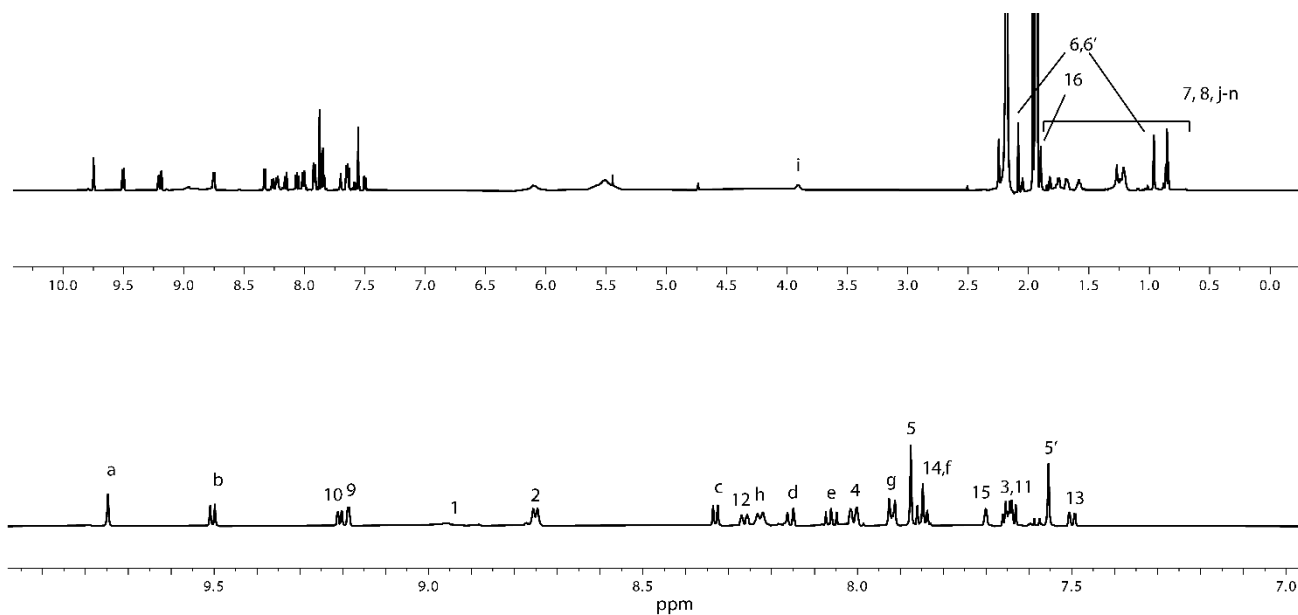


Figure S43: ^1H NMR spectrum (600 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$.

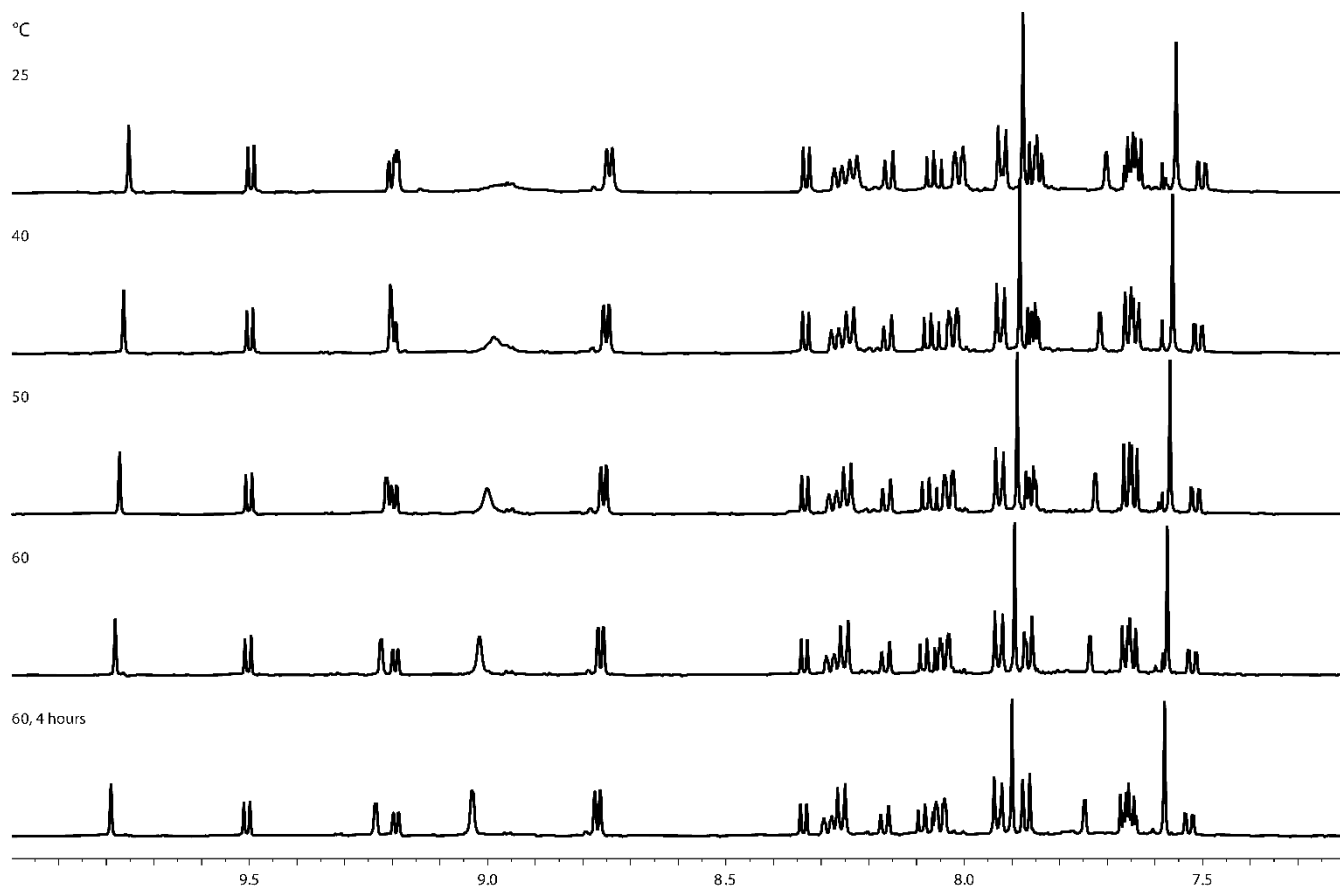


Figure S44: Variable temperature ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$.

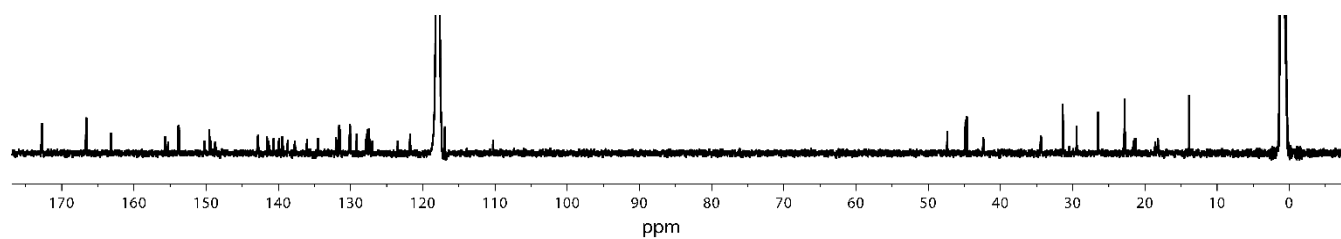


Figure S45: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of heteroleptic assembly $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$.

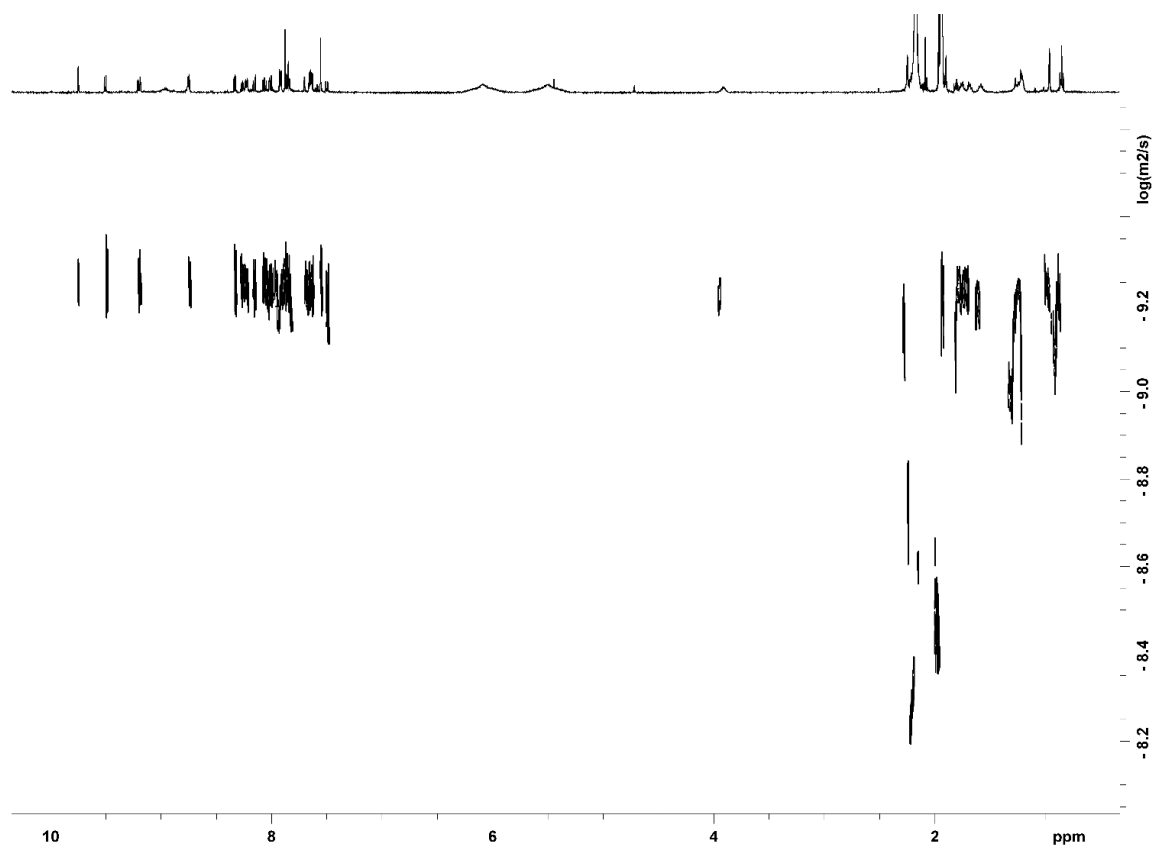


Figure S46: ^1H -DOSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$. $D = 5.60 \times 10^{-10} \text{ m}^2\text{s}^{-1}$, $R_h = 1.167 \text{ nm}$.

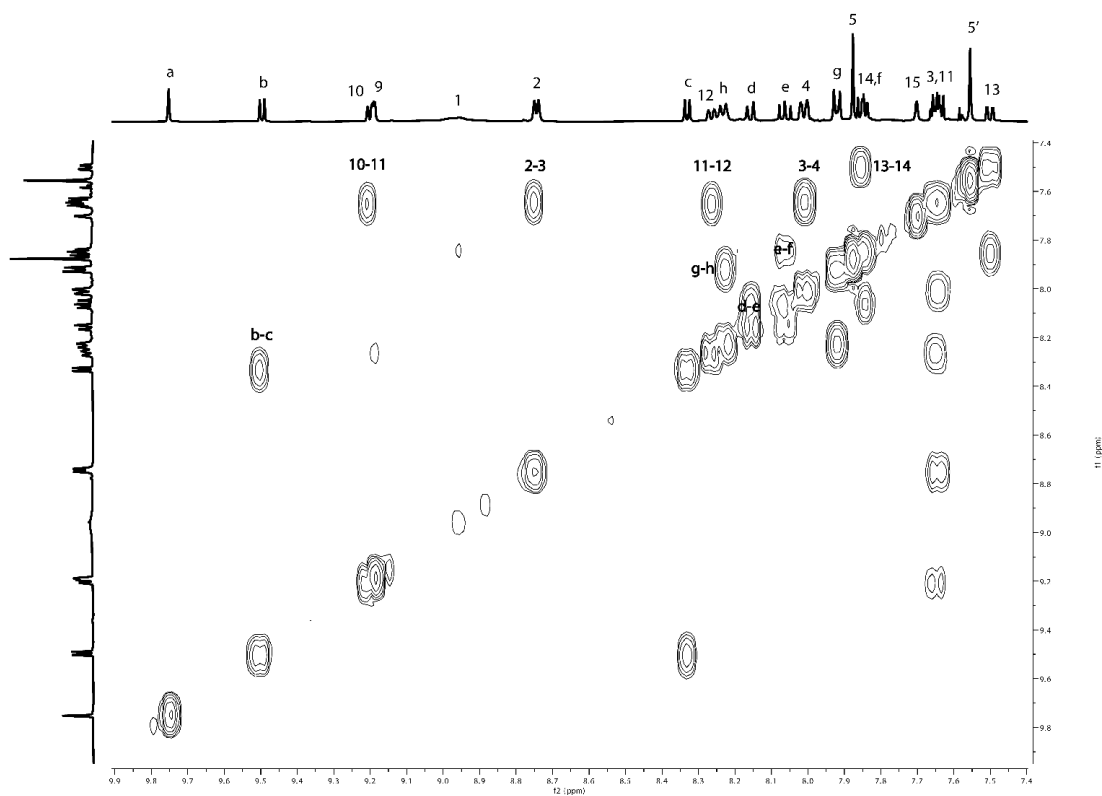


Figure S47: Enlargement of the aromatic region of the ^1H - ^1H COSY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$.

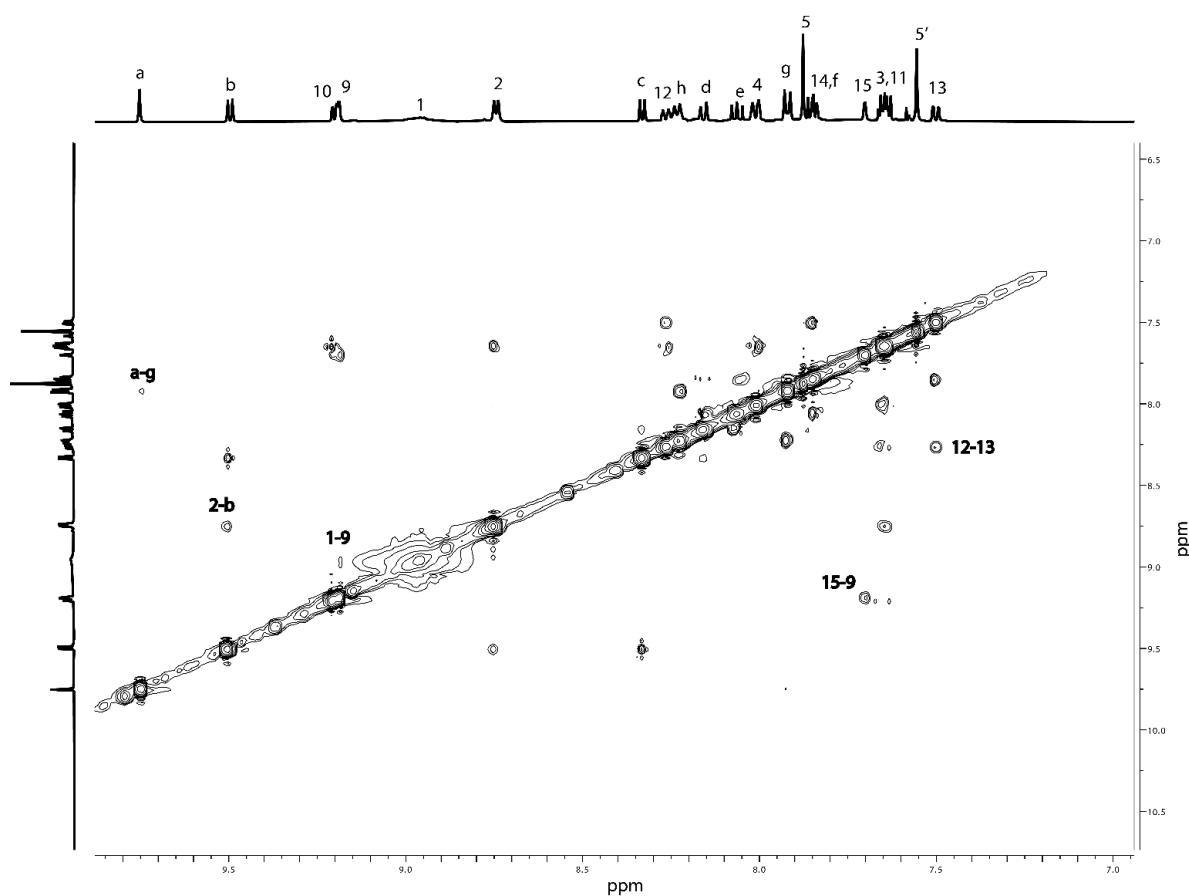


Figure S48: Enlargement of the aromatic region of the ^1H - ^1H NOESY spectrum in CD_3CN of the heteroleptic assembly $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$.

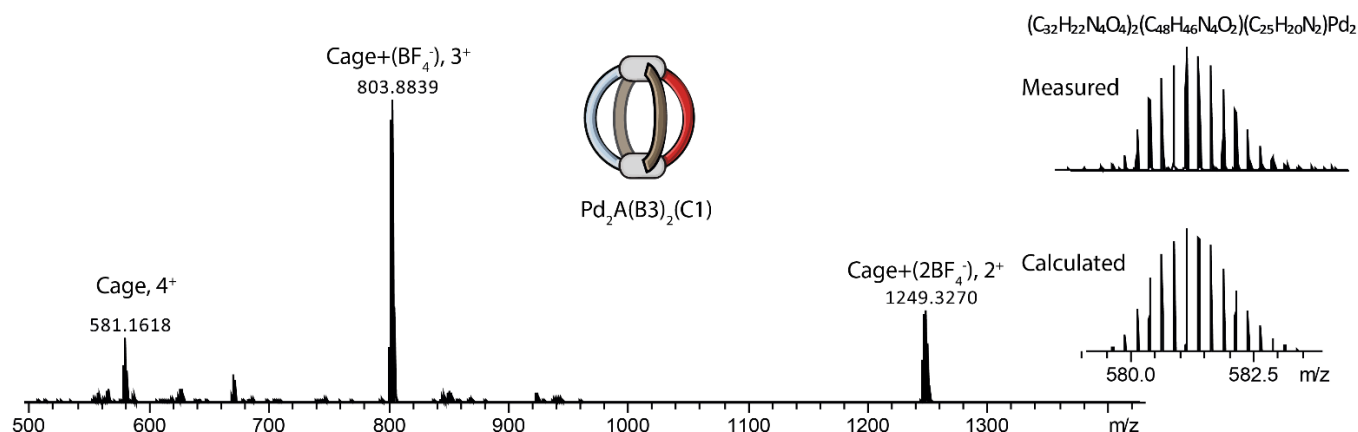


Figure S49: ESI-MS spectrum of an acetonitrile solution of **A**, **B3** and **C1** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{A}(\text{B3})_2(\text{C1}) + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})]^{4+}$ are shown in the inset.

Synthesis of the multi-cage systems

Pseudo statistical mixture formation to $\text{Pd}_2\text{A}_2(\text{B1})_2/\text{Pd}_2(\text{B1})\text{A}_2(\text{B2})/\text{Pd}_2\text{A}_2(\text{B2})_2$

250 μL of 0.7 mM solutions of $\text{Pd}_2\text{A}_2(\text{B1})_2$ and $\text{Pd}_2\text{A}_2(\text{B2})_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The solution was then heated to 70 $^\circ\text{C}$ for 4 h to afford the mixture of assemblies in the equilibrated solution. 50 μL of the mixture were collected to record ESI-MS data via direct injection.

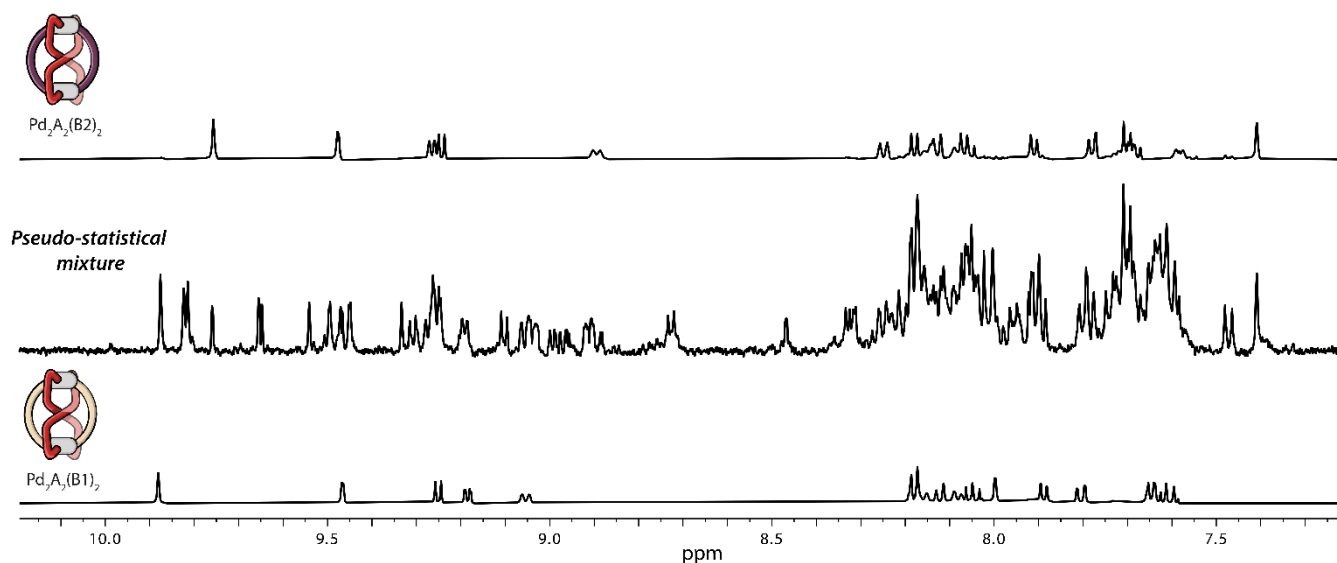


Figure S50: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of the pseudo-statistical mixture of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B1})_2$, $\text{Pd}_2\text{A}_2(\text{B2})_2$ and $\text{Pd}_2\text{A}_2(\text{B1})(\text{B2})$. The two isolated cages are stacked as references. No further solution state characterization methods were employed.

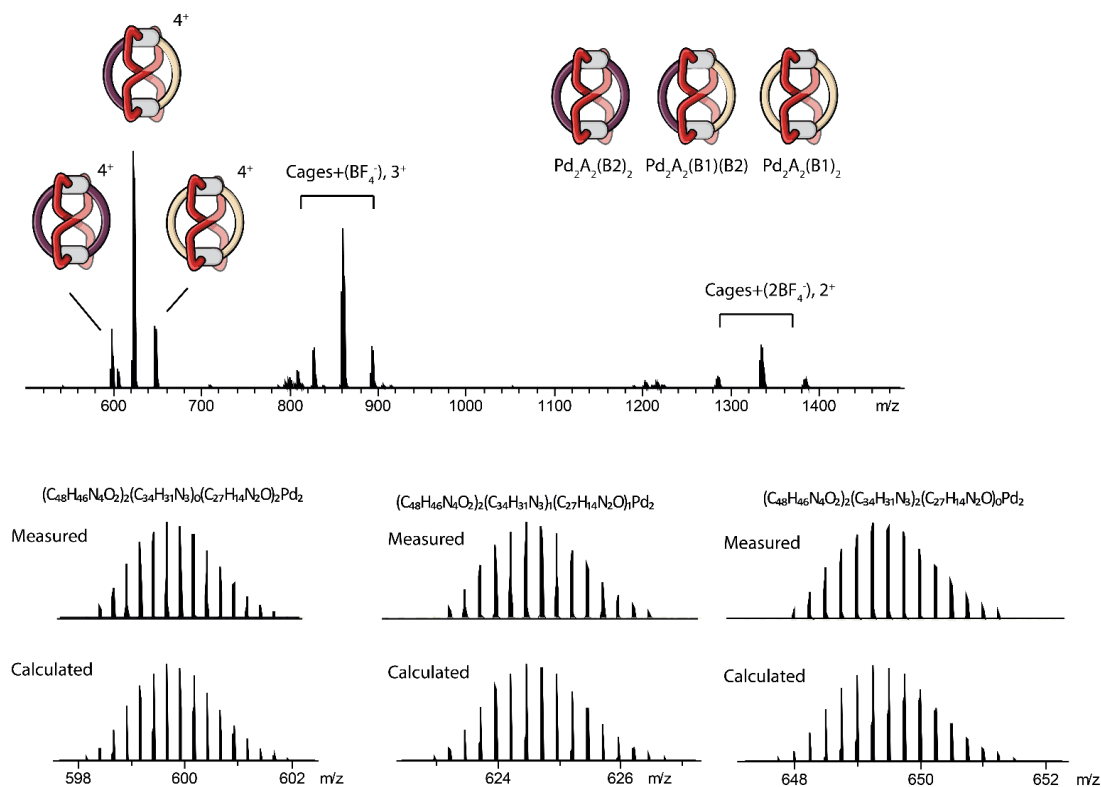


Figure S51: ESI-MS spectrum of an acetonitrile solution $\text{Pd}_2\text{A}_2(\text{B}_2)_2$, $\text{Pd}_2\text{A}_2(\text{B}_1)(\text{B}_2)$ and $\text{Pd}_2\text{A}_2(\text{B}_2)_2$. The observed peaks correspond to $[\text{cages} + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{A}_2(\text{B}_1)_2]^{4+}$, $[\text{Pd}_2\text{A}_2(\text{B}_1)(\text{B}_2)]^{4+}$ and $[\text{Pd}_2\text{A}_2(\text{B}_2)_2]^{4+}$ are shown in the insets.

Heteromeric complete self-sorting to $\text{Pd}_2\text{A}_2(\text{B}_2)_2$ (or $\text{Pd}_2\text{A}_2(\text{B}_1)_2$) + $\text{Pd}_2\text{A}_2(\text{B}_3)_2$

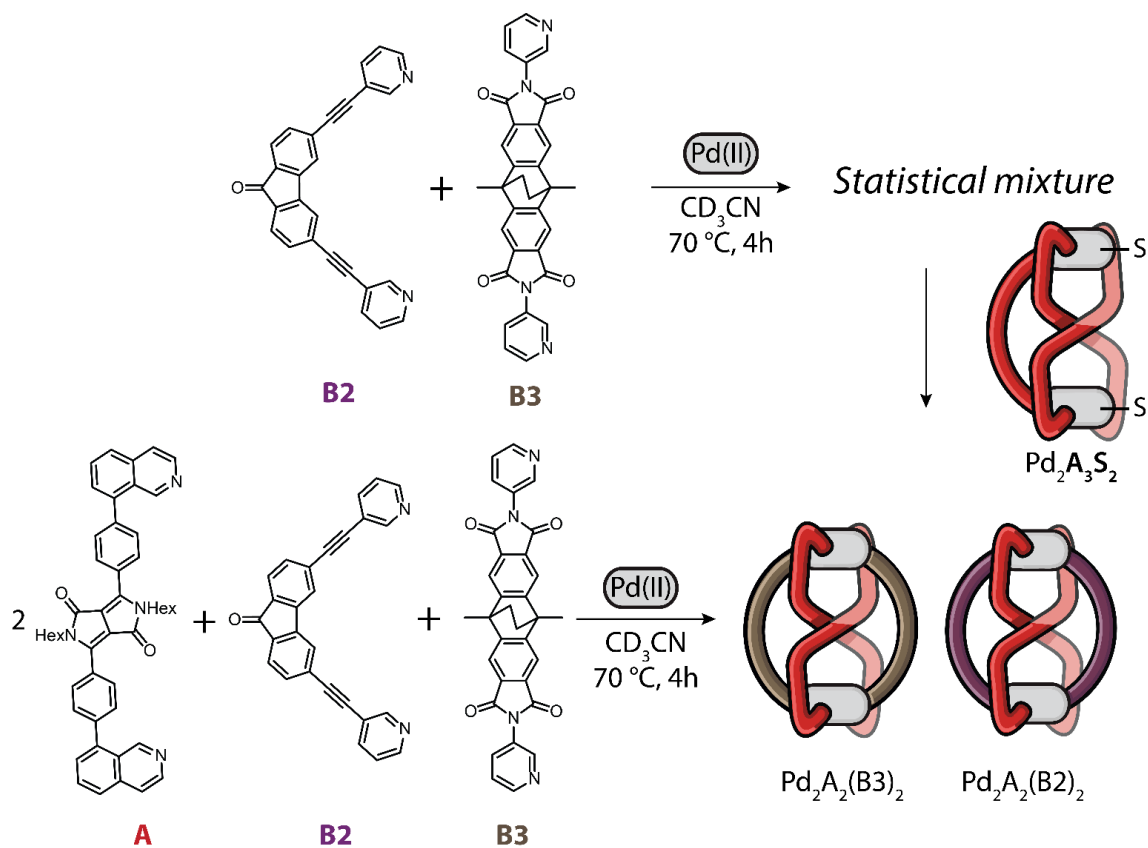


Figure S52: Heteromeric complete self-sorting between $\text{Pd}_2\text{A}_2(\text{B2})_2$ and $\text{Pd}_2\text{A}_2(\text{B3})_2$. The same results are obtained through sequential cage-to-cage transformation, from the statistical mixture between **B2** and **B3** or upon the addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of ligands **A/B2/B3** in a 2:1:1 ratio.

Cage to cage: 225 μL of a 3.11 mM solution of **B2**, 225 μL of a 3.11 mM solution **B3** in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford a statistical mixture of cages. Half of this solution was further mixed with 250 μL of a solution of $\text{Pd}_2\text{A}_3\text{S}_2$ (S = solvent molecule, ligand concentration 3.11 mM, 2 equiv of **A** as compared with **B2** and **B3**) and heated for 4 h at 70 $^\circ\text{C}$ to afford the coexisting heteroleptic cages $\text{Pd}_2\text{A}_2(\text{B2})_2 + \text{Pd}_2\text{A}_2(\text{B3})_2$ in the equilibrated solution.

One pot synthesis: 224 μL of a 3.11 mM solution of **A**, 112 μL of a 3.11 mM solution of **B2** and 112 μL of a 3.11 mM solution of **B3** in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford the coexisting heteroleptic cages $\text{Pd}_2\text{A}_2(\text{B2})_2 + \text{Pd}_2\text{A}_2(\text{B3})_2$ in the equilibrated solution.

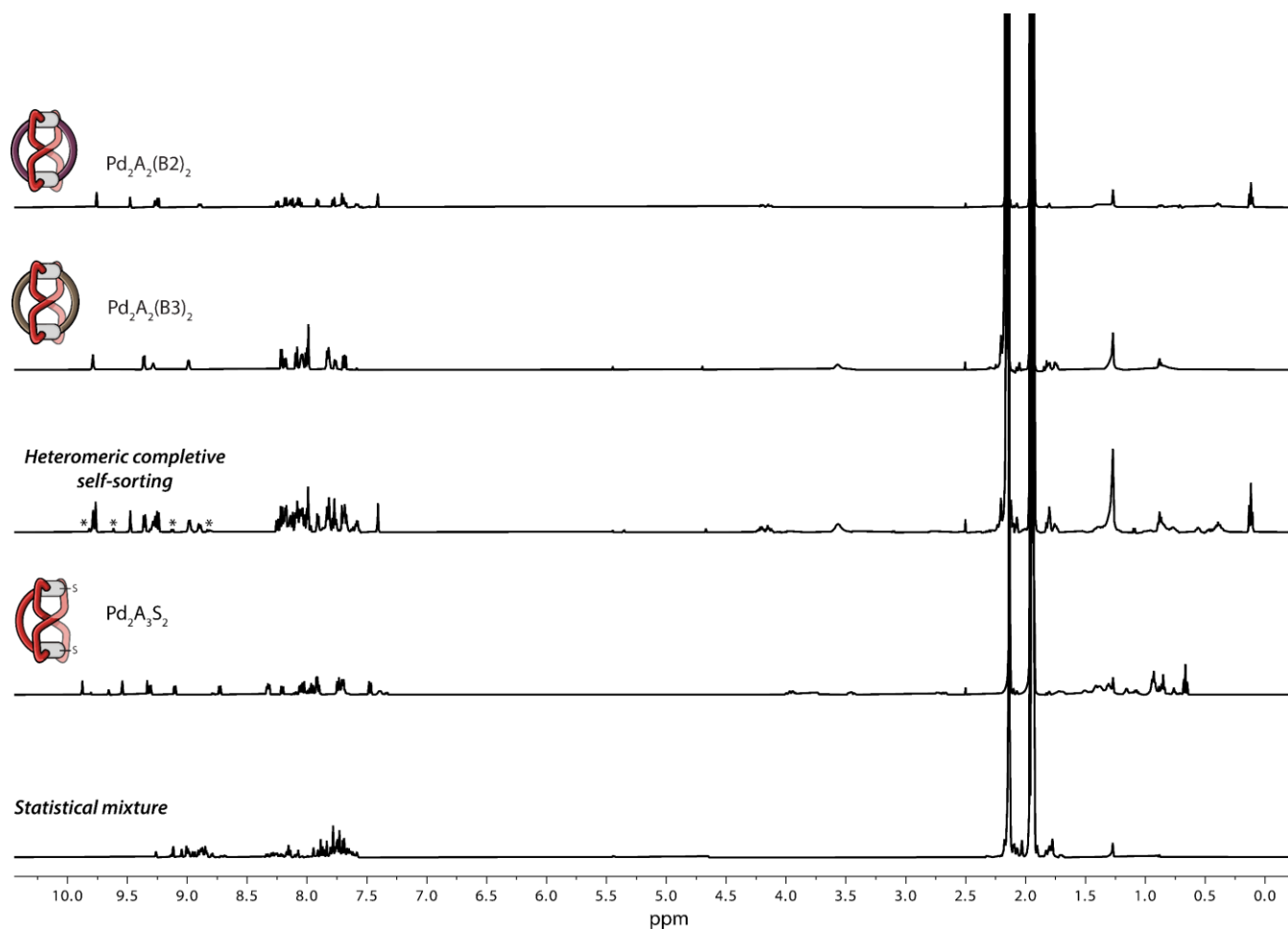


Figure S53: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B2})_2 \text{Pd}_2\text{A}_2(\text{B3})_2$ obtained by cage to cage transformation. ^1H NMR of cages are stacked for reference.

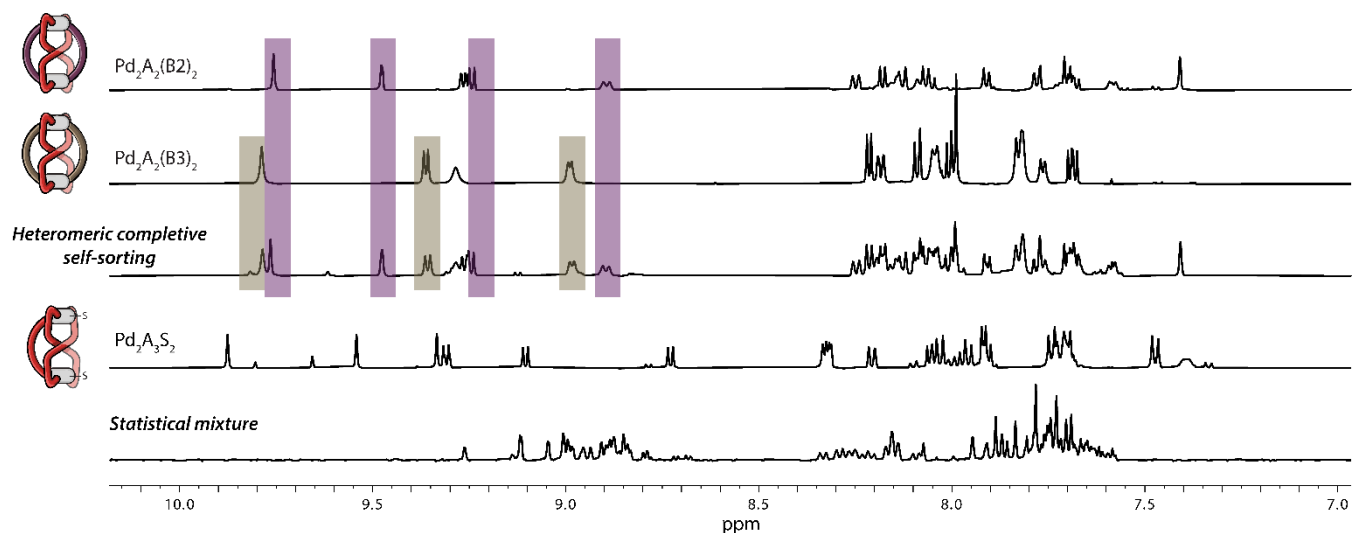


Figure S54: Aromatic region of the ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B}2)_2$ $\text{Pd}_2\text{A}_2(\text{B}3)_2$ obtained by cage to cage transformation. ^1H NMR of cages are stacked for reference. Colors serve to highlight the overlap of signals and showcase the coexistence of assemblies.

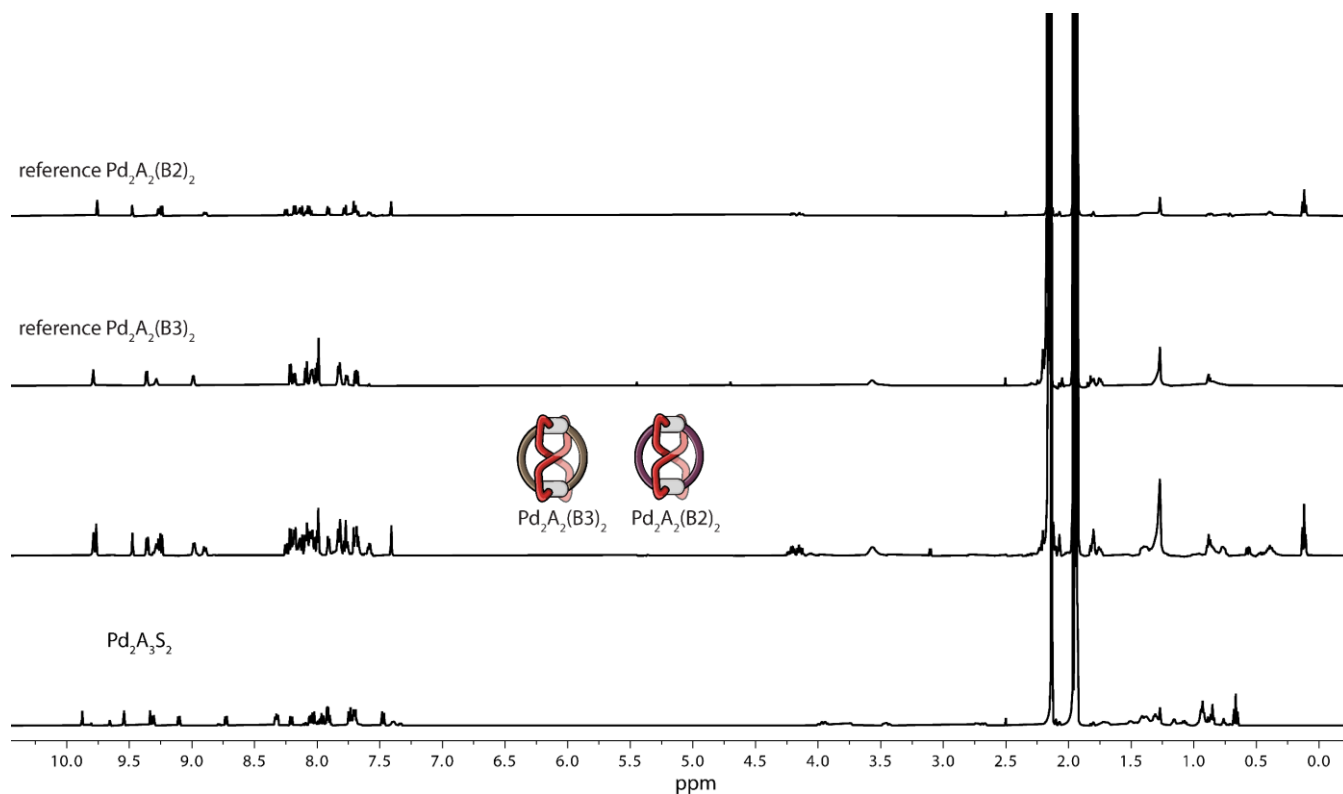


Figure S55: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B}2)_2$ $\text{Pd}_2\text{A}_2(\text{B}3)_2$ obtained by monitoring ligand and Pd(II) ratio. ^1H NMR of cages are stacked for reference. No side species can be observed in this case.

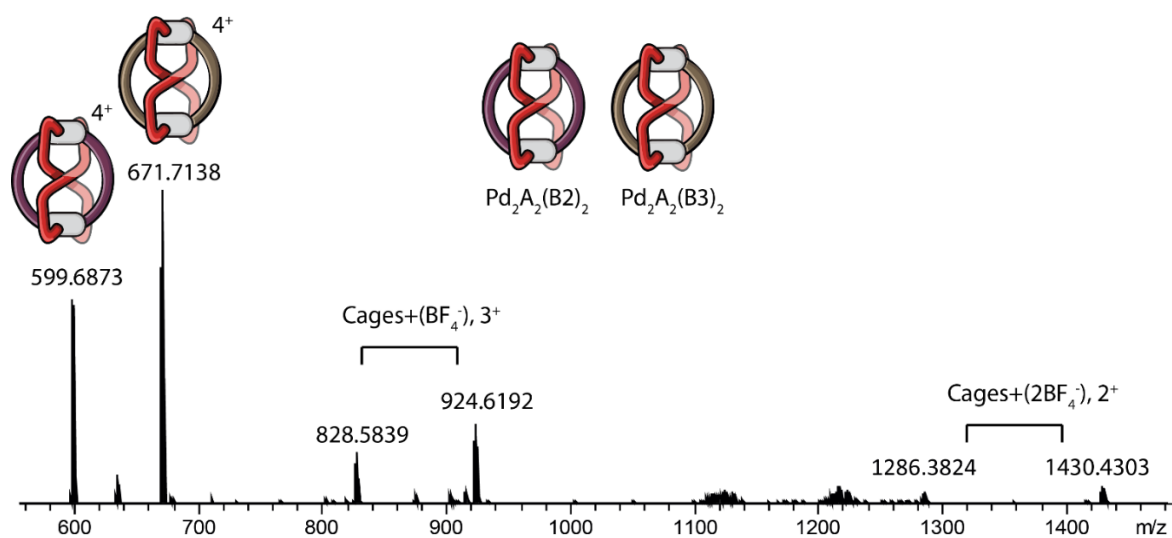


Figure S56: ESI-MS spectrum of an acetonitrile solution $\text{Pd}_2\text{A}_2(\text{B2})_2$ and $\text{Pd}_2\text{A}_2(\text{B3})_2$. The observed peaks correspond to $[\text{cages} + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$.

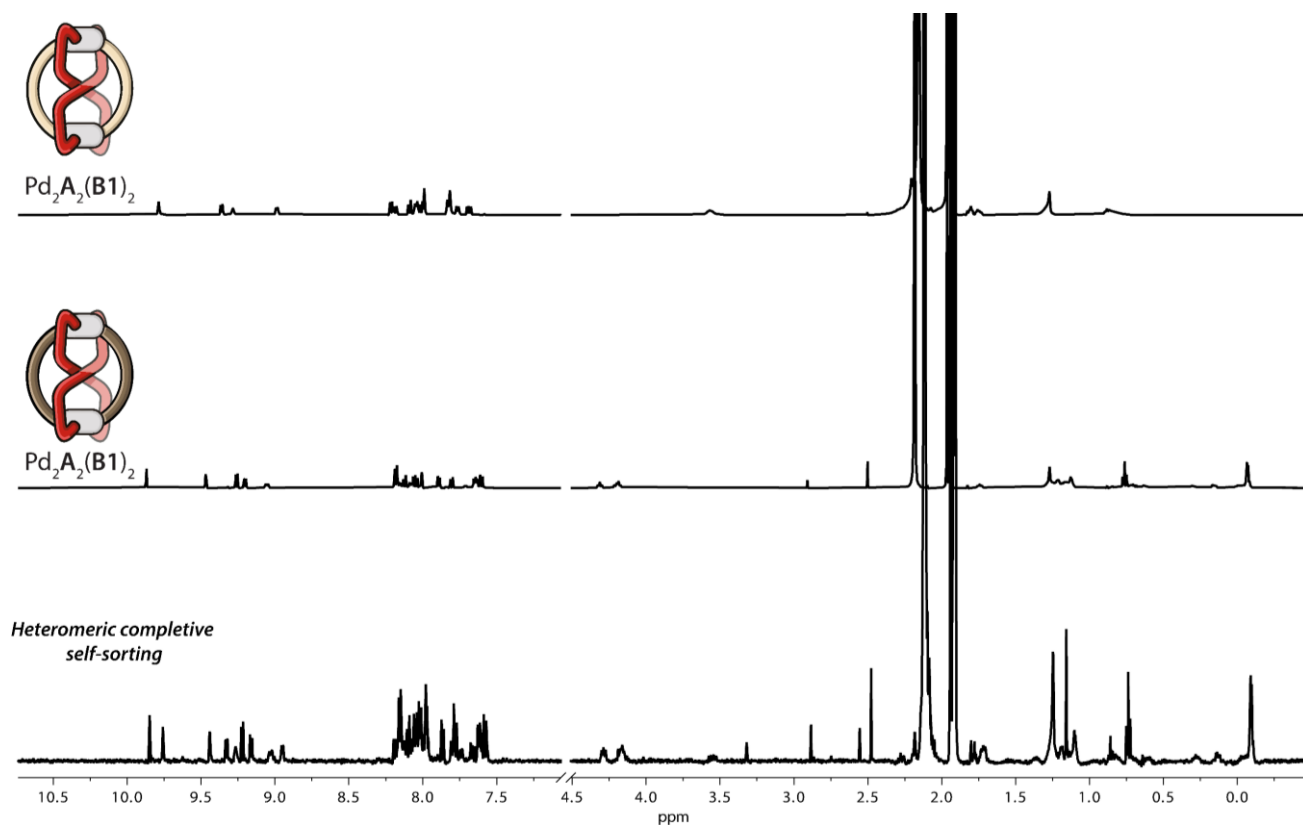


Figure S57: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B1})_2$ and $\text{Pd}_2\text{A}_2(\text{B3})_2$ obtained by mixing $\text{Pd}(\text{II})$, **A**, **B1** and **B3** in a 2:2:1:1 ratio. ^1H NMR of cages are stacked for reference.

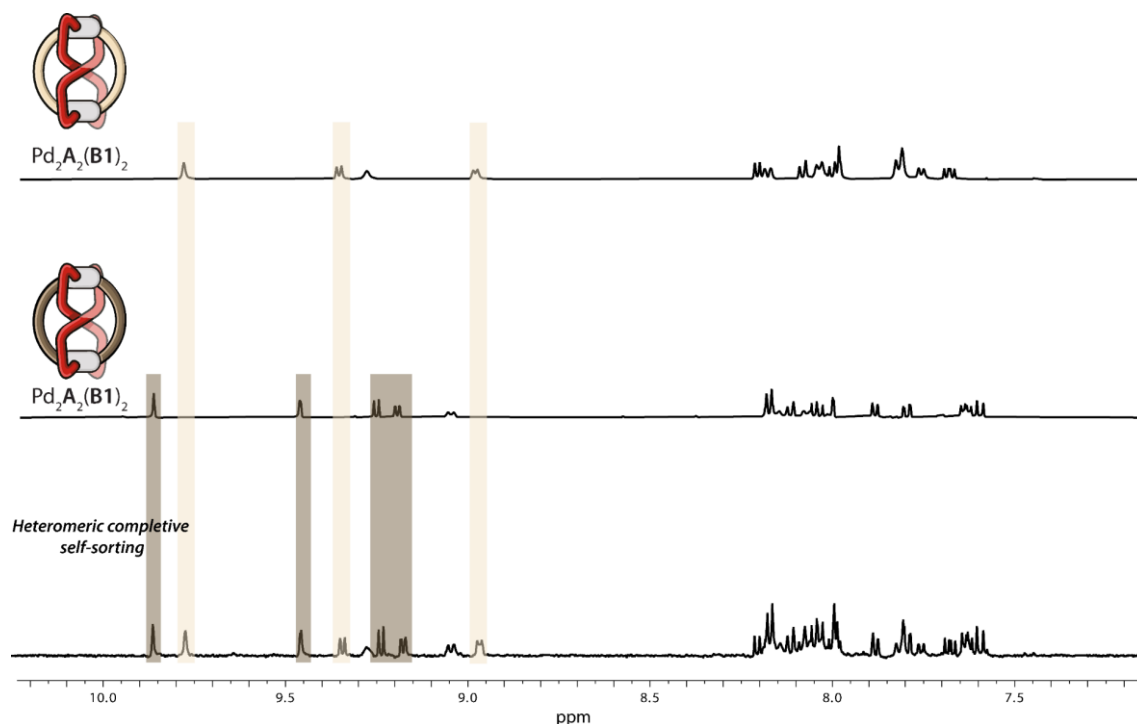


Figure S58: Aromatic region of the ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B1})_2$ and $\text{Pd}_2\text{A}_2(\text{B3})$ obtained by mixing $\text{Pd}(\text{II})$, **A**, **B1** and **B3** in a 2:2:1:1 ratio. ^1H NMR of cages are stacked for reference. Colors serve to highlight the overlap of signals and showcase the coexistence of assemblies.

Heteromeric complete self-sorting to $\text{Pd}_2\text{A}_2(\text{B1})_2 + \text{Pd}_2\text{A}_2(\text{C1})_2$

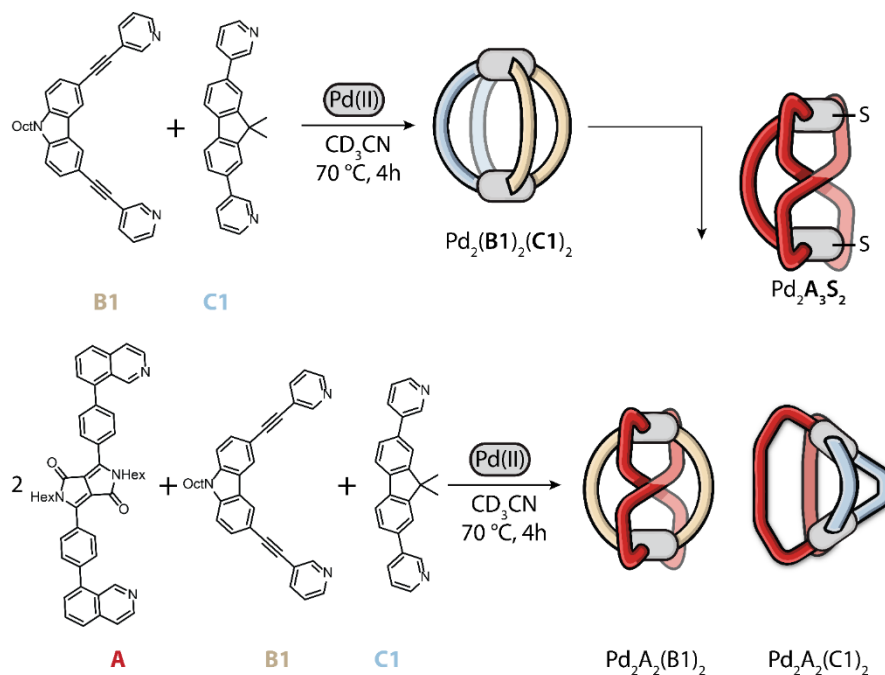


Figure S59: Heteromeric complete self-sorting between $\text{Pd}_2\text{A}_2(\text{B1})_2$ and $\text{Pd}_2\text{A}_2(\text{C1})_2$. The same results are obtained through the sequential cage-to-cage transformation, from heteroleptic cage $\text{Pd}_2(\text{B1})_2(\text{C1})_2$, or upon the addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of ligands **A/B1/C1** in a 2:1:1 ratio.

Cage to cage: 225 μL of a 3.11 mM solution of **B1**, 225 μL of a 3.11 mM solution **C1** in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford heteroleptic cage $\text{Pd}_2(\text{B1})_2(\text{C1})_2$. Half of this solution was further mixed with 250 μL of a solution of $\text{Pd}_2\text{A}_3\text{S}_2$ (ligand concentration 3.11 mM, 2 equiv. of **A** as compared with **B1** and **C1**) and heated for 4 h at 70 $^\circ\text{C}$ to afford $\text{Pd}_2\text{A}_2(\text{B1})_2 + \text{Pd}_2\text{A}_2(\text{C1})_2$ in the equilibrated solution.

One pot synthesis: 224 μL of a 3.11 mM solution of **A**, 112 μL of a 3.11 mM solution of **B1** and 112 μL of a 3.11 mM solution of **C1** in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2(\text{B1})_2 + \text{Pd}_2\text{A}_2(\text{C1})_2$ in the equilibrated solution.

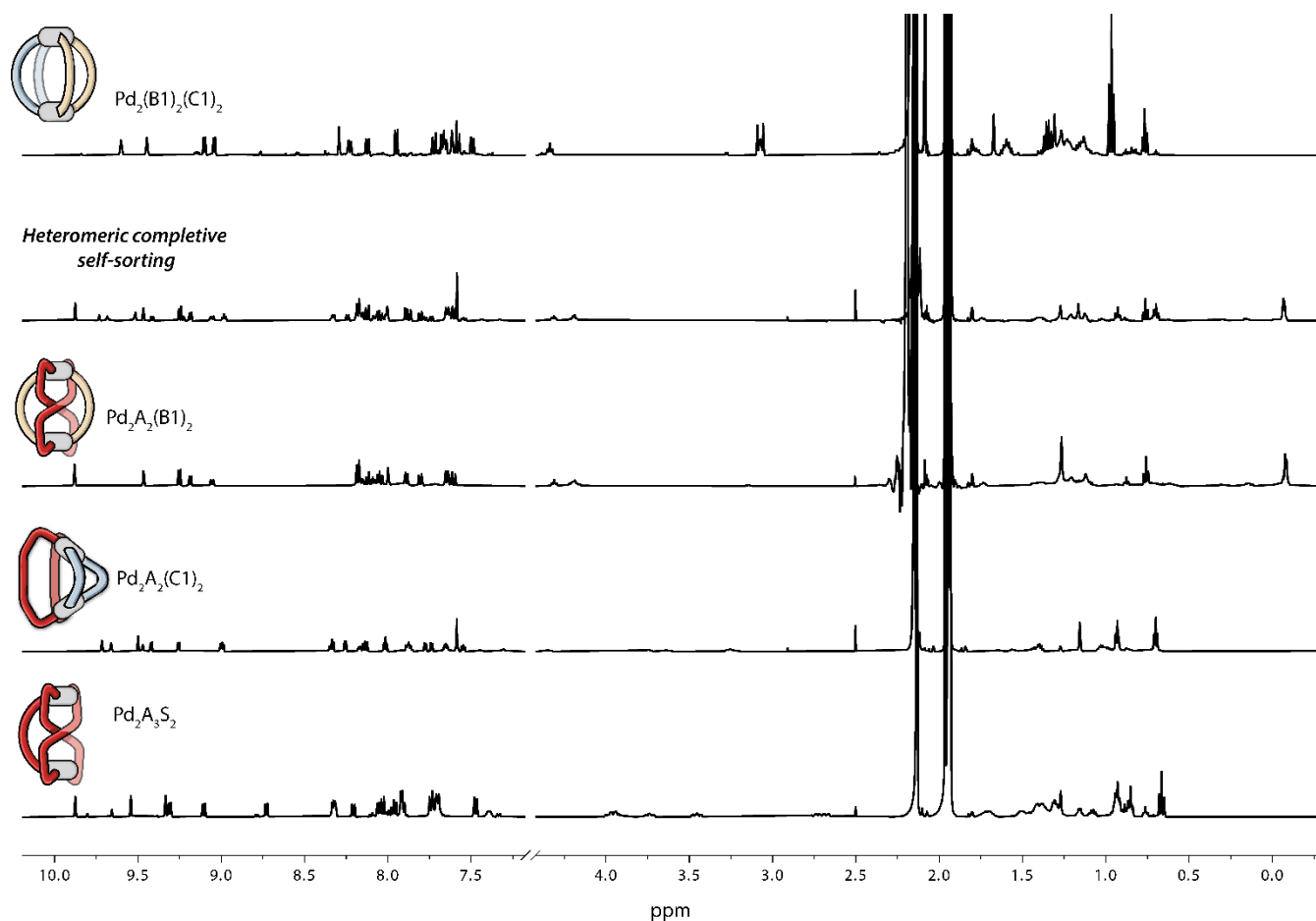


Figure S60: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B1})_2$ $\text{Pd}_2\text{A}_2(\text{C1})_2$. Isolated cages are stacked for reference.

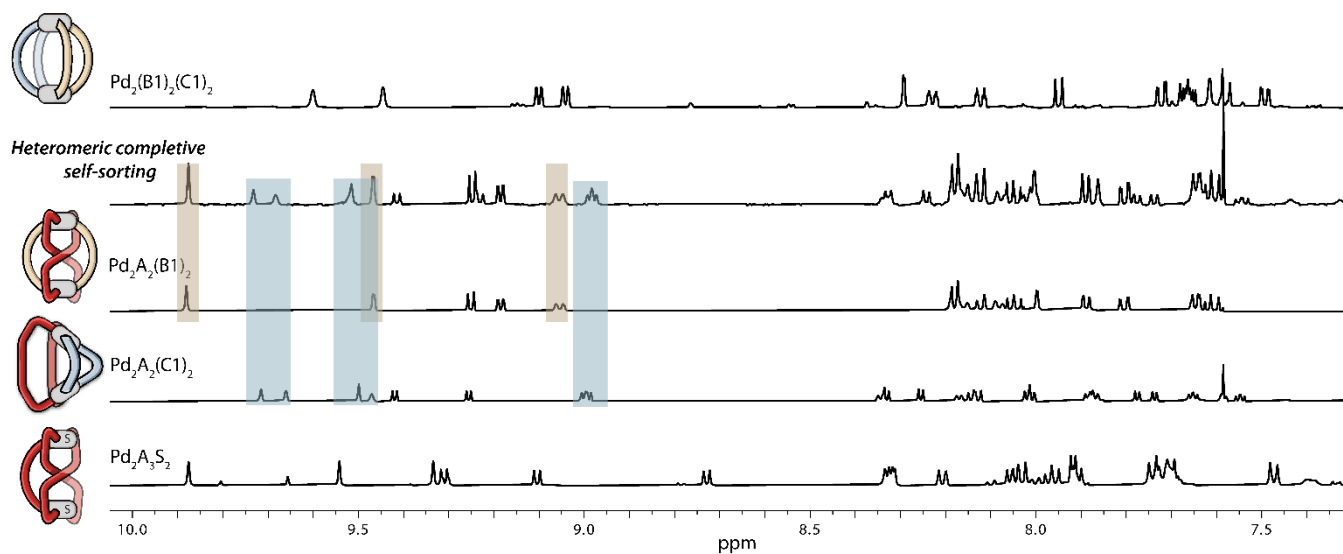


Figure S61: Aromatic region of the ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B1})_2$ $\text{Pd}_2\text{A}_2(\text{C1})_2$. Isolated cages are stacked for reference. Colors serve to highlight the overlap of signals and showcase the coexistence of assemblies.

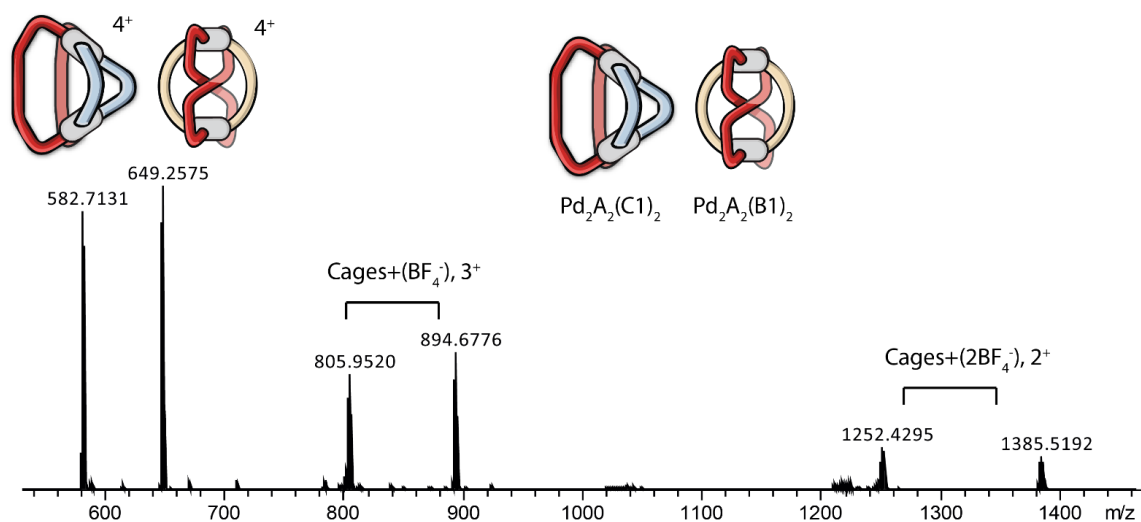


Figure S62: ESI-MS spectrum of an acetonitrile solution $\text{Pd}_2\text{A}_2(\text{B1})_2$ and $\text{Pd}_2\text{A}_2(\text{C1})_2$. The observed peaks correspond to $[\text{cages} + n\text{BF}_4^-]^{(4-n)+}$ with $n=0-2$.

Self-assembly conditions : (i) Pd:A:B1:C1= 2:1:2:1, (ii) Pd:A:B1:C1= 2:1:1:2, (iii) Pd:A:B1:C1 = 1:1:1:1 competitive experiment

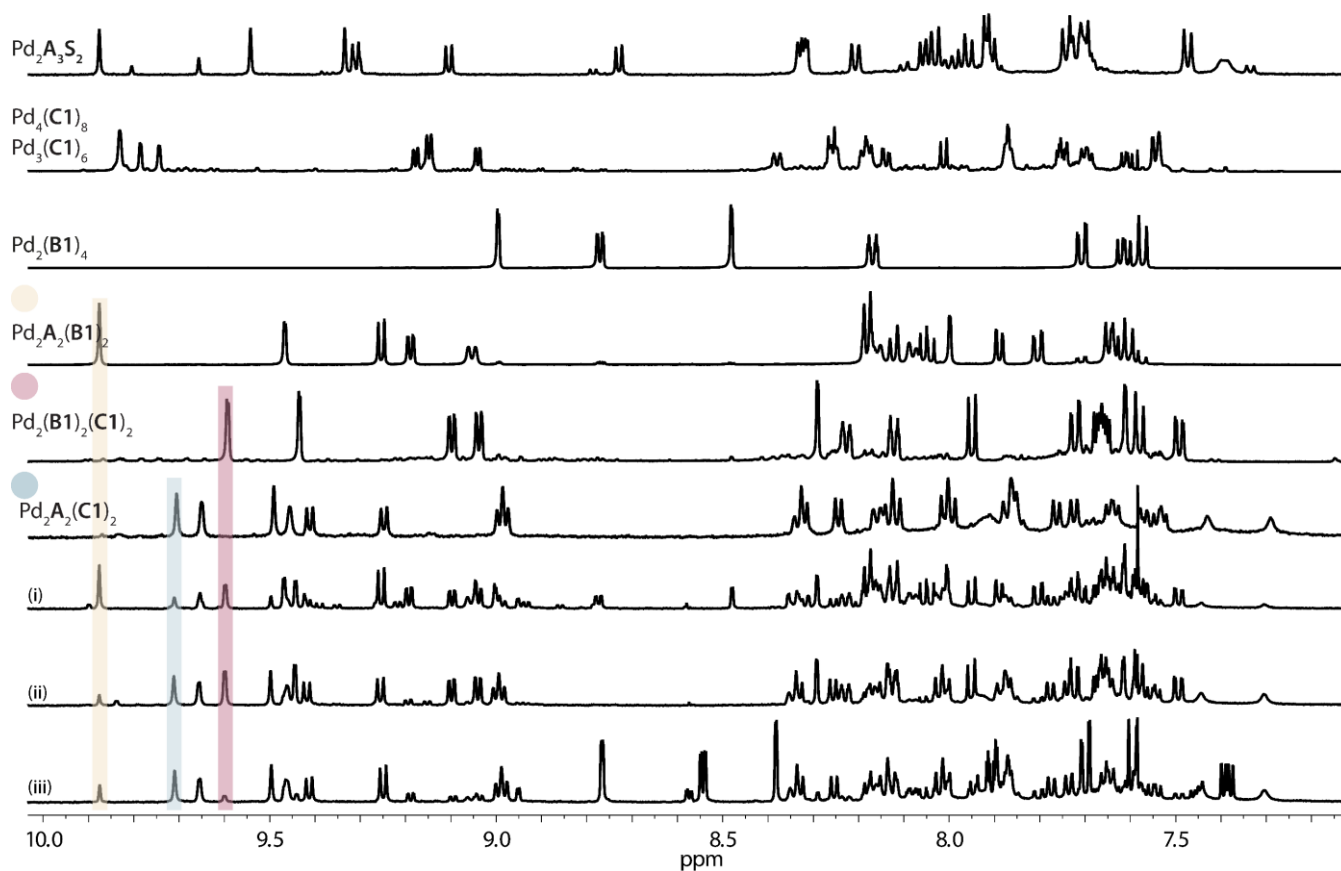


Figure S63: ^1H NMR stacked (500 MHz, 298K, CD_3CN) of the self-sorting outcome when varying the ligands **A**, **B1**, and **C1** ratio. Signature of $\text{Pd}_2\text{A}_2(\text{B1})_2$, $\text{Pd}_2(\text{B1})_2(\text{C1})_2$ and $\text{Pd}_2\text{A}_2(\text{C1})_2$ are highlighted in beige, red and blue respectively. No precise self-sorting can be observed. This further emphasize the stoichiometry role in the heteromeric competitive self-sorting outcome.

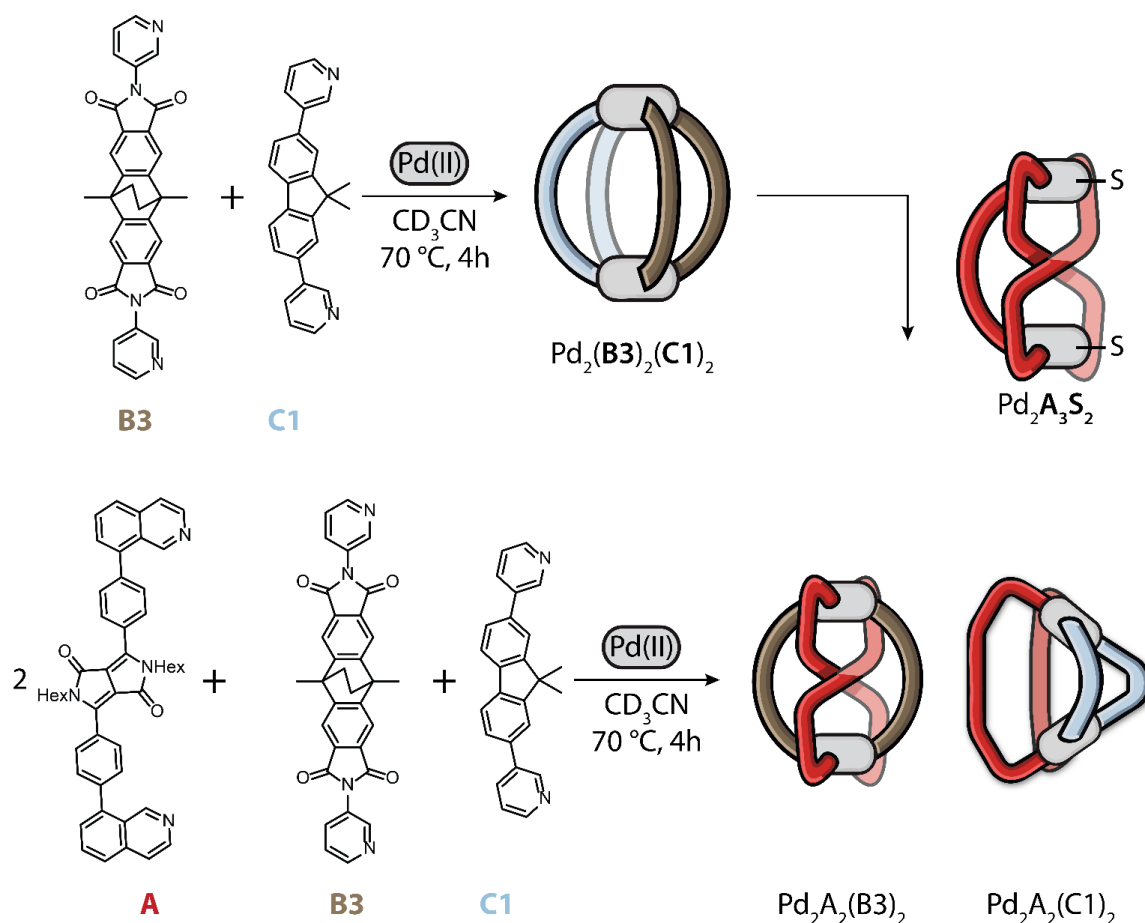
Heteromeric complete self-sorting to $\text{Pd}_2\text{A}_2(\text{B3})_2 + \text{Pd}_2\text{A}_2(\text{C1})_2$ 

Figure S63: Heteromeric complete self-sorting between $\text{Pd}_2\text{A}_2(\text{B3})_2$ and $\text{Pd}_2\text{A}_2(\text{C1})_2$. The same results are obtained through the sequential cage-to-cage transformation, from heteroleptic cage $\text{Pd}_2(\text{B3})_2(\text{C1})_2$, or upon the addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of ligands **A/B3/C1** in a 2:1:1 ratio.

Cage to cage: 225 μL of a 3.11 mM solution of **B3**, 225 μL of a 3.11 mM solution **C1** in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70°C for 4 h to afford heteroleptic cage $\text{Pd}_2(\text{B3})_2(\text{C1})_2$. Half of this solution was further mixed with 250 μL of a solution of $\text{Pd}_2\text{A}_3\text{S}_2$ (ligand concentration 3.11 mM, 2 equiv of **A** as compared with **B3** and **C1**) and heated for 4 h at 70°C to afford $\text{Pd}_2\text{A}_2(\text{B3})_2 + \text{Pd}_2\text{A}_2(\text{C1})_2$ in the equilibrated solution.

One pot synthesis: 224 μL of a 3.11 mM solution of **A**, 112 μL of a 3.11 mM solution of **B3** and 112 μL of a 3.11 mM solution of **C1** in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70°C for 4 h to afford $\text{Pd}_2\text{A}_2(\text{B3})_2 + \text{Pd}_2\text{A}_2(\text{C1})_2$ in the equilibrated solution.

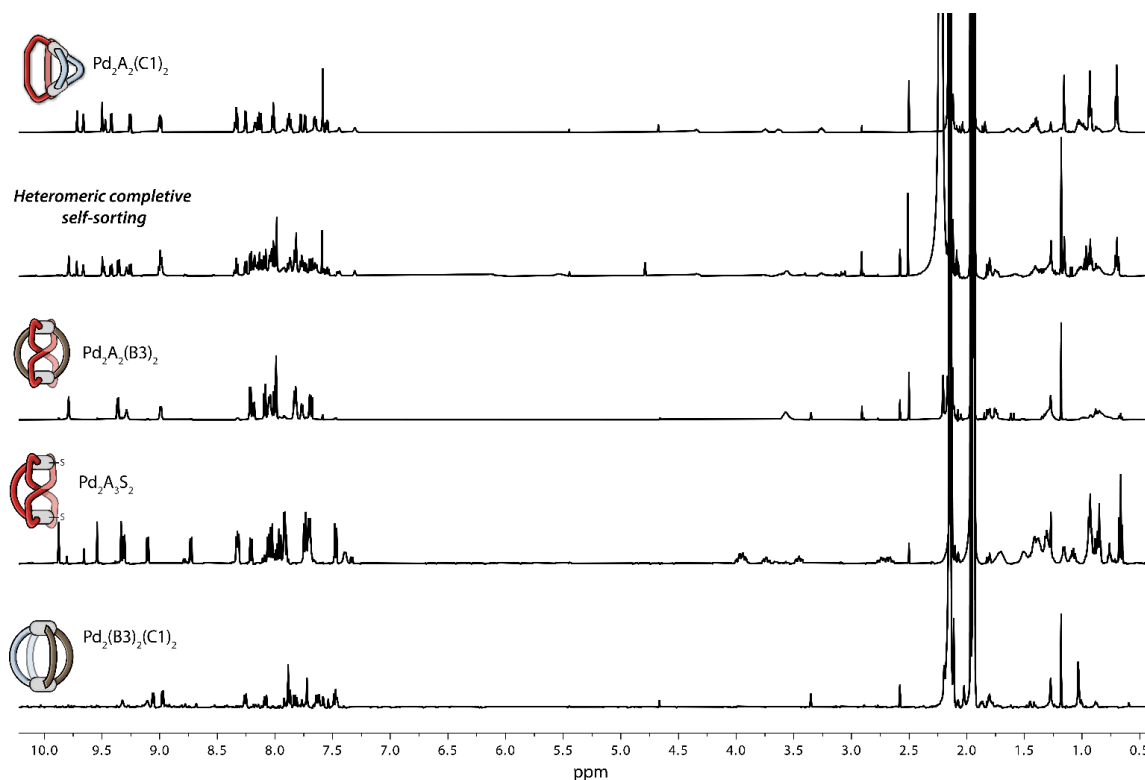


Figure S64: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B3})_2 \text{Pd}_2\text{A}_2(\text{C1})_2$. Isolated cages are stacked for reference.

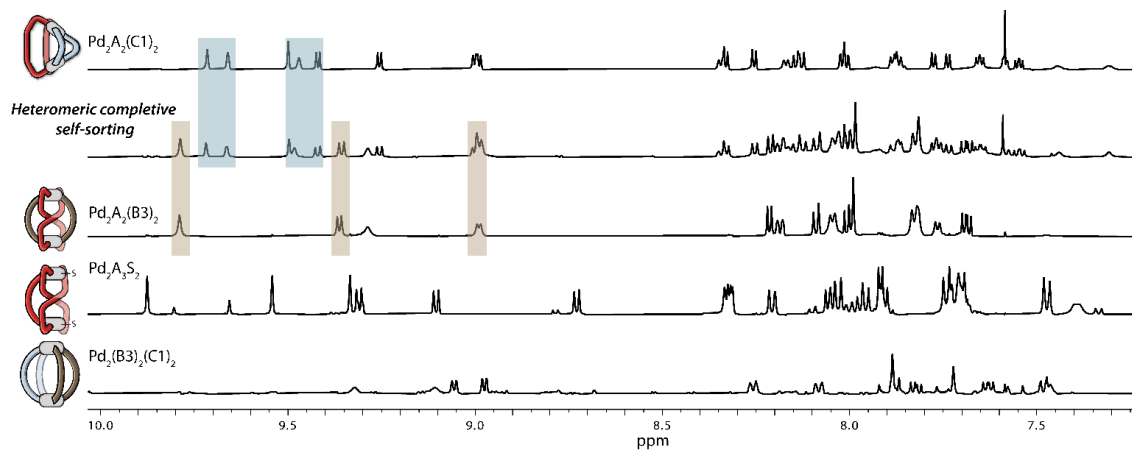


Figure S65: Aromatic region of the ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteromeric self-sorting of heteroleptic assemblies $\text{Pd}_2\text{A}_2(\text{B3})_2 \text{Pd}_2\text{A}_2(\text{C1})_2$. Isolated cages are stacked for reference. Colors serve to highlight the overlap of signals and showcase the coexistence of assemblies.

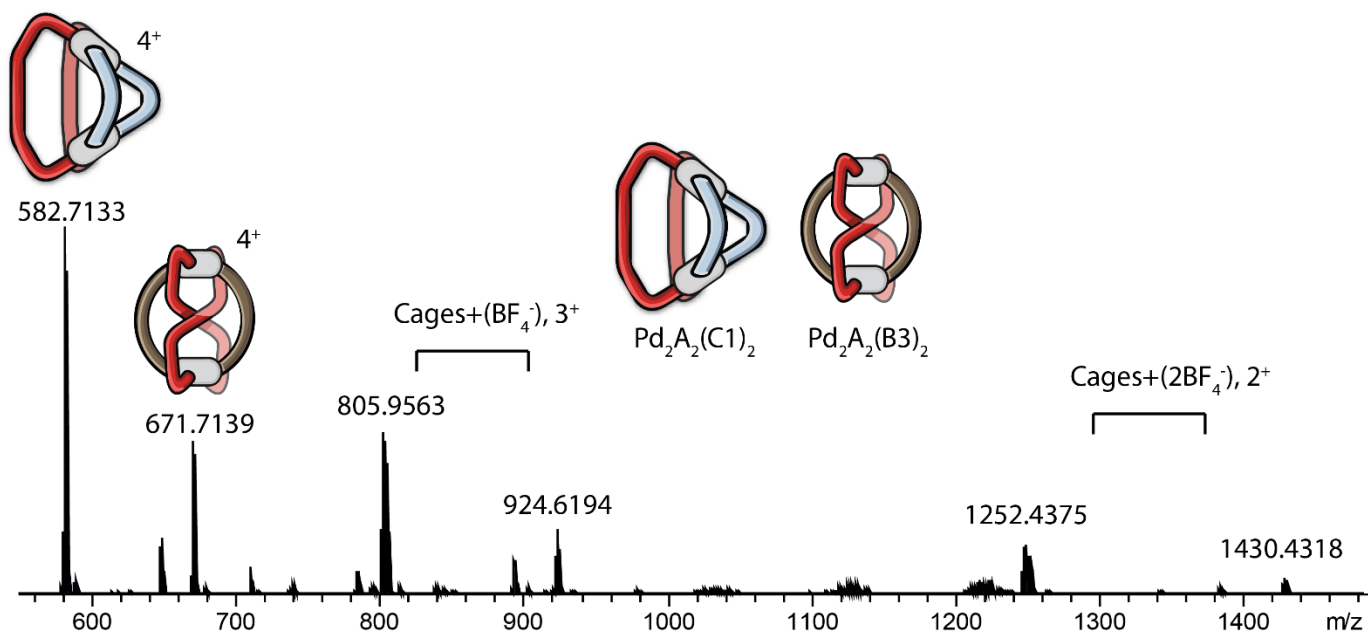
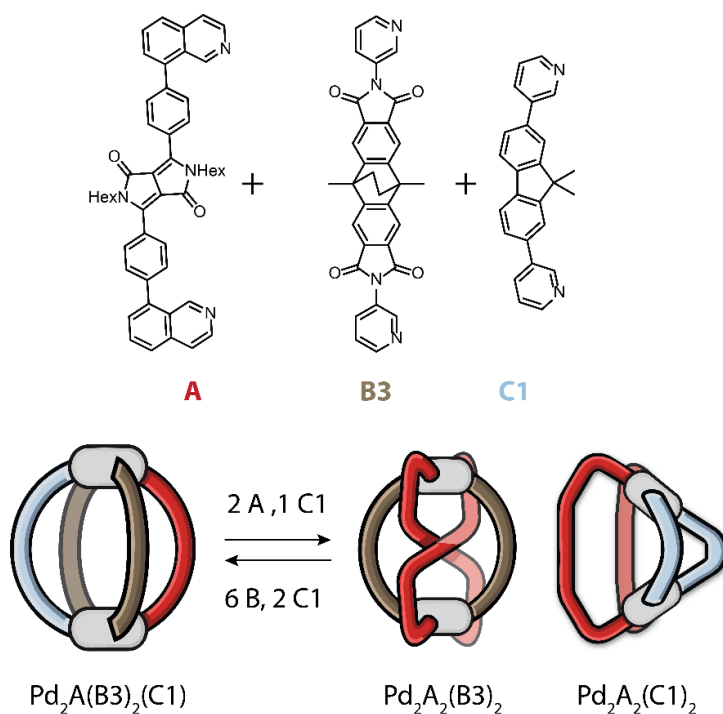


Figure S67: ESI-MS spectrum of an acetonitrile solution Pd₂A₂(B1)₂ and Pd₂A₂(C1)₂. The observed peaks correspond to [cages + nBF₄]⁽⁴⁻ⁿ⁾⁺ with n=0-2.

Self-sorting modulation by stoichiometry



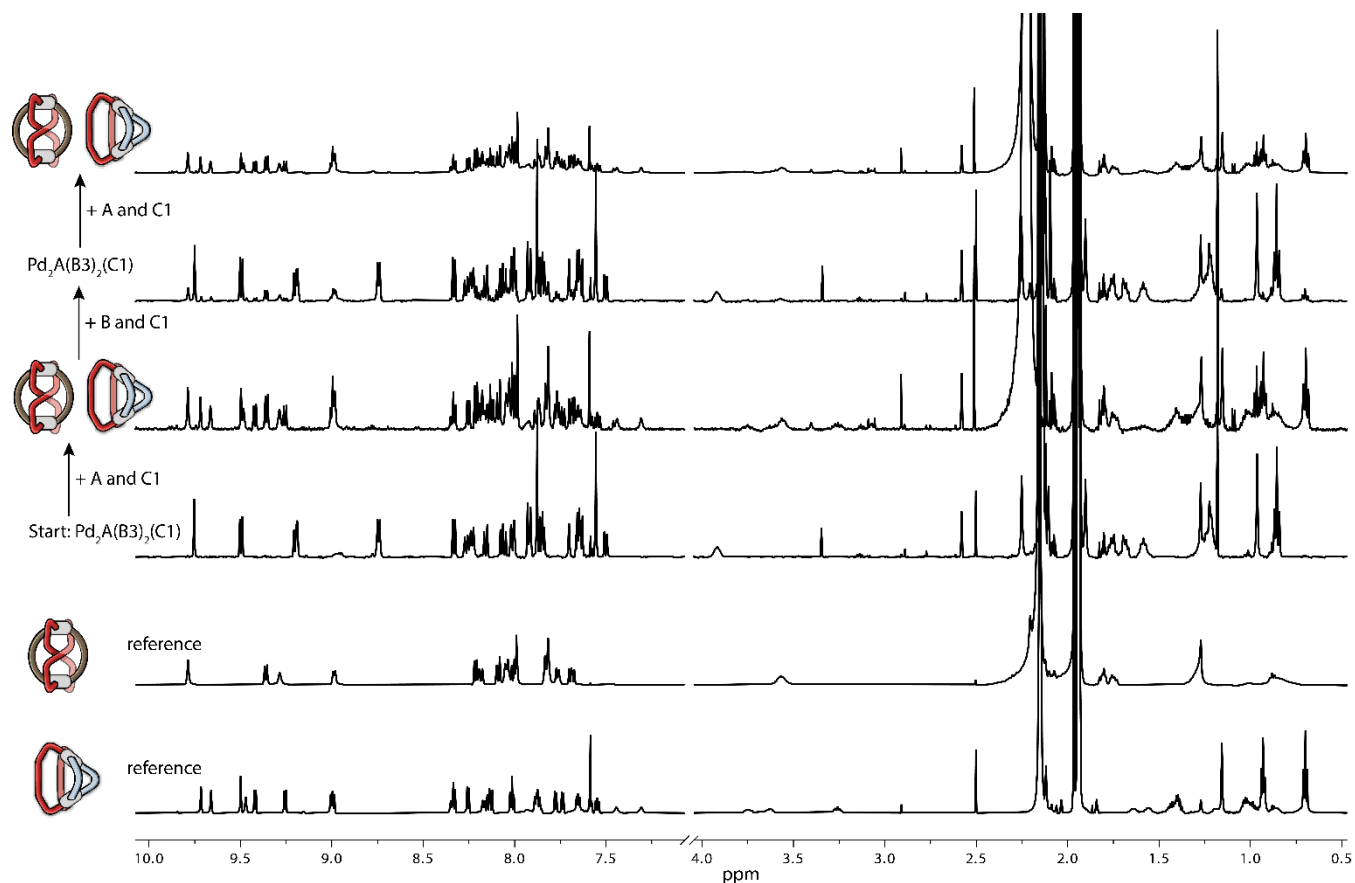


Figure S68: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) highlighting the self-sorting switch upon changing the stoichiometry. Starting from cage $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$, obtained by integrative self-sorting, the addition of components **A** and **C1** allows the switch into heteromeric self-sorting with $\text{Pd}_2\text{A}_2(\text{B3})_2$ and $\text{Pd}_2\text{A}_2(\text{C1})_2$ coexisting. This can be repeated for another cycle.

Computational studies for the sorting process

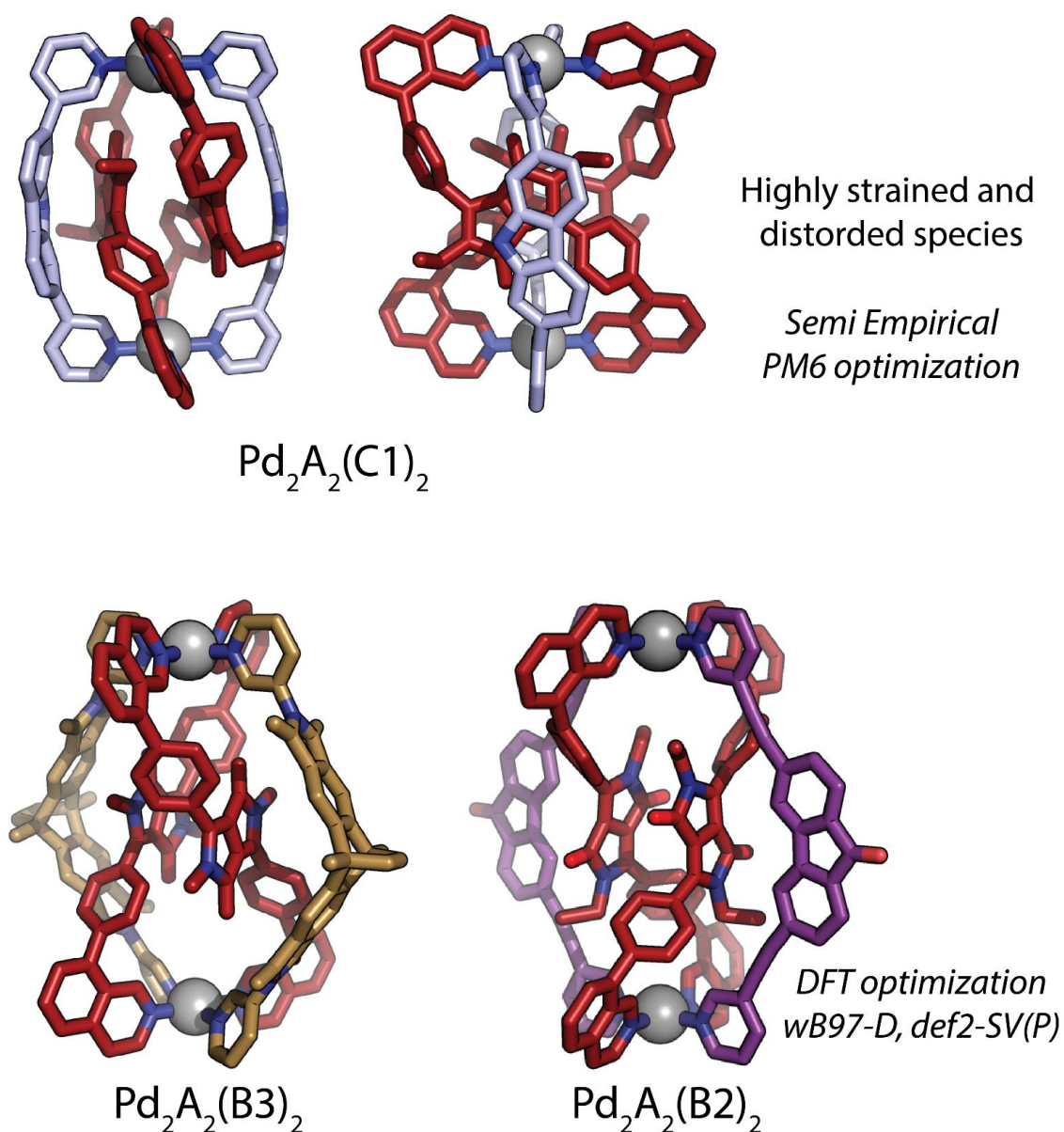


Figure S69: (Top) Front and lateral views of computed (semi-empirical PM6 calculation) $\text{Pd}_2\text{A}_2(\text{C1})_2$ heteroleptic cage in the *trans*-figure-of-eight topology. To adapt to this configuration both ligands have to be extremely distorted and therefore this topology was excluded after obtaining the crystal structure of $\text{Pd}_2\text{A}_2(\text{C2})_2$. $E(\text{cis-cage})=4797.61$ kJ/mol vs. $E(\text{trans-cage})=4947.39$ kJ/mol. $\Delta E= +149.78$ kJ/mol. (bottom) DFT (wB97X-D, def2-SV(P)) optimized structures of (left) $\text{Pd}_2\text{A}_2(\text{B3})_2$ and (right) $\text{Pd}_2\text{A}_2(\text{B2})_2$ cages in *trans*-figure-of-eight topology.

Structural analysis of ligand A in the different assemblies

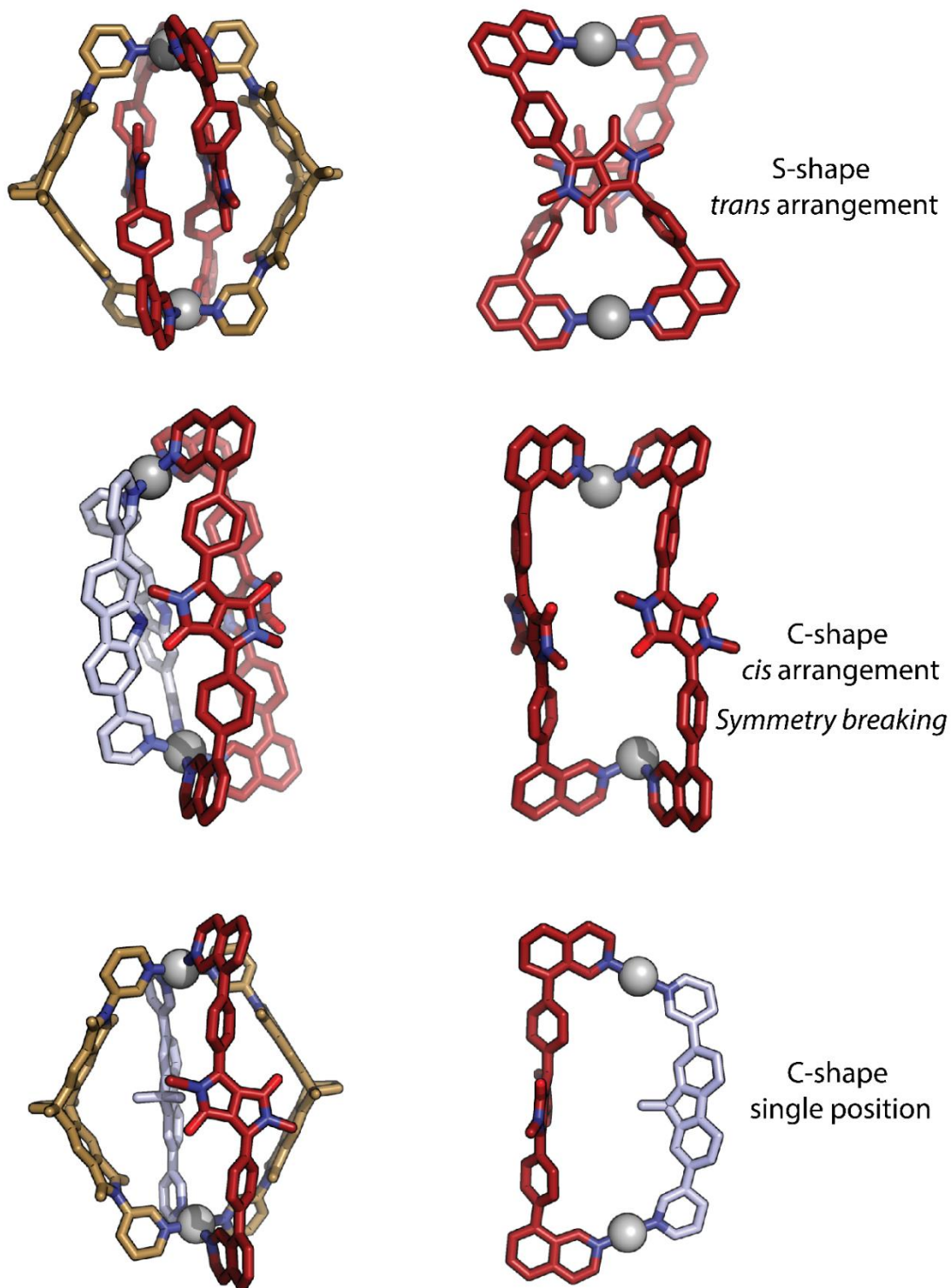


Figure S70: Positions and configurations of ligand **A** in the different assemblies (Top) DFT (ω B97X-D/def2-SV(P)) optimized structures of $\text{Pd}_2\text{A}_2(\text{B3})_2$. Ligand **A** adopts an S shape, with one quinoline donor fully rotating from the core, and coordinates to the Pd(II) cations in a *trans*-arrangement. (middle) Crystal structure of $\text{Pd}_2\text{A}_2(\text{C2})_2$. Ligand **A** adopts a C shape and coordinates in a *cis*-arrangement. The presence of the alkyl chains (omitted for clarity) as well as the strain, prevent the rotation of the core and lead to a symmetry breaking. (bottom) Crystal structure of $\text{Pd}_2\text{A}(\text{B3})_2(\text{C1})$. Ligand **A** is present only once and adopts its C shape to fit by shape complementarity with **C1**.

Photophysical properties

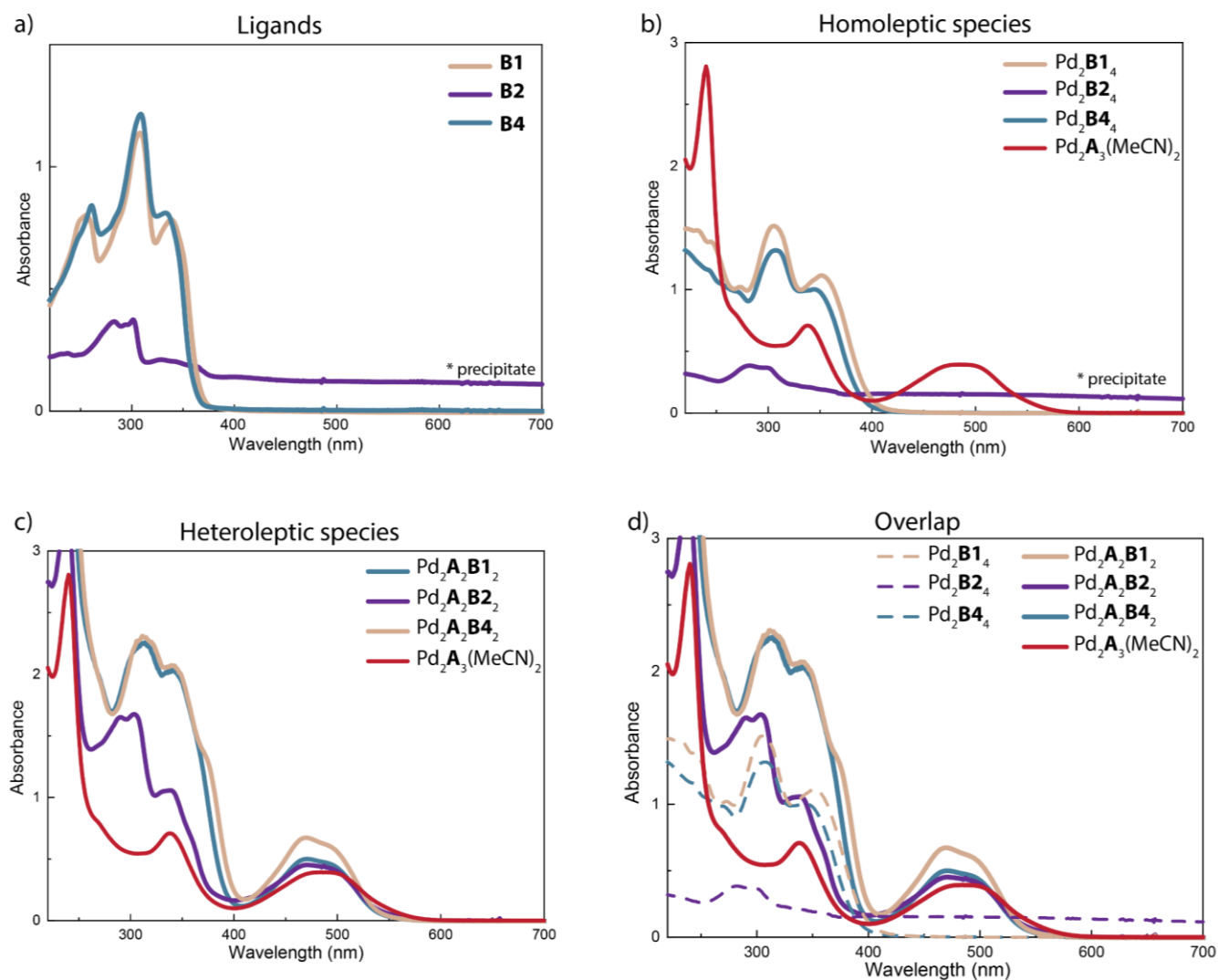


Figure S71: UV-Vis absorption spectra of a) ligands, b) homoleptic assemblies, c) heteroleptic assemblies and d) overlap of both homoleptics and heteroleptics. 2 mm cuvette, acetonitrile, 298 K, 0.15 mM chromophore concentration.

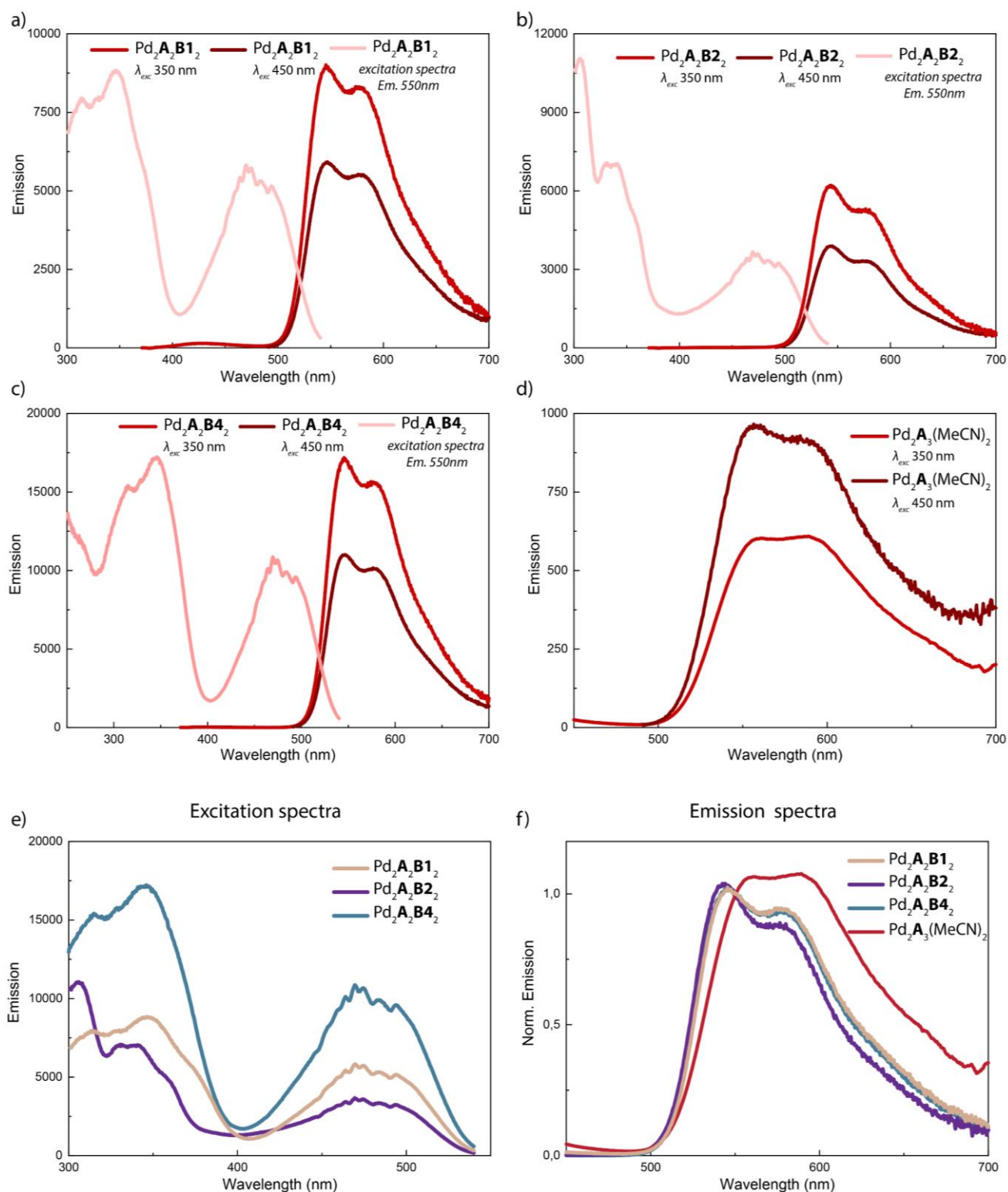


Figure 72: Emission and excitation spectra of a) $\text{Pd}_2\text{A}_2\text{B1}_2$, b) $\text{Pd}_2\text{A}_2\text{B2}_2$, c) $\text{Pd}_2\text{A}_2\text{B4}_2$ and d) $\text{Pd}_2\text{A}_3(\text{MeCN})_2$. e) Overlap of the excitation spectra of the three heteroleptic cages. f) Overlap of the normalized emission spectra of the heteroleptic cages and the homoleptic assemblies from **A**. Acetonitrile 2 mm cuvette, chromophore concentration 0.01 mM for emission

	λ_{PL} (nm)	τ (ns)	Φ (%)
A	550, 600	6.5	95
B4	540	5.8	85
B1	490	4.8	83
B2	500	3.6	71
$\text{Pd}_2\text{A}_3(\text{MeCN})_2$	550, 600	2.1	0.5
$\text{Pd}_2\text{A}_2\text{B4}_2$	550, 600	7.0	64
$\text{Pd}_2\text{A}_2\text{B1}_2$	550, 600	11.2	52
$\text{Pd}_2\text{A}_2\text{B2}_2$	550, 600	5.7	42

Table S1: Summary of emission wavelengths, emission lifetime and quantum yield of the different ligands compared with the homoleptic assembly $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ as well as the three heteroleptic assemblies. $\lambda_{\text{exc}} = 350$ nm. Those results were compiled by collaboration with Dr. Sascha Feldmann.

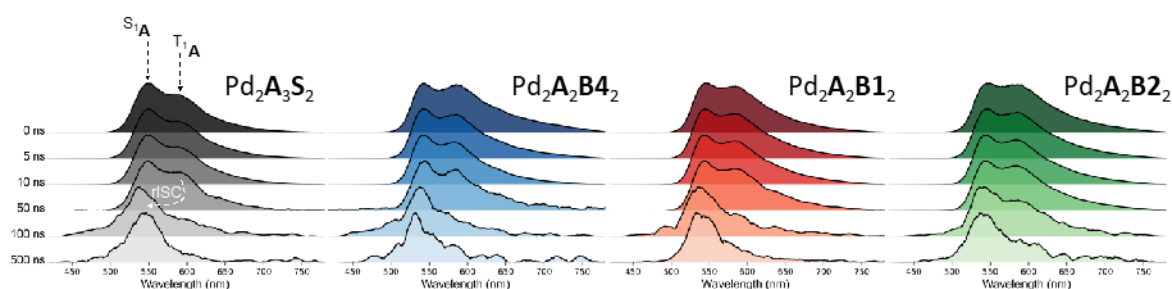


Figure S73: Transient photoluminescence spectral slices measured for (from left) $\text{Pd}_2\text{A}_3\text{S}_2$, $\text{Pd}_2\text{A}_2\text{B4}_2$, $\text{Pd}_2\text{A}_2\text{B1}_2$ and, $\text{Pd}_2\text{A}_2\text{B2}_2$. All the heteroleptic cages show emission from ligand **A** though we excite the higher absorbing donor-ligand band, this is due to fast FRET from donor to the acceptor (**A**) ligand. The singlet, $S_{1,A}$ and triplet, $T_{1,A}$ bands are labeled for the spectral slices from $\text{Pd}_2\text{A}_3\text{S}_2$ and the probable $r\text{ISC}$ process which leads to long-lived emission in the blue 550 nm band is shown to occur between 50-100 ns. This behavior is consistent in all heteroleptic cages. Those results were compiled by collaboration with Dr. Sascha Feldmann.

Electrochemistry

	Pd ₂ A ₂ B1 ₂		Pd ₂ A ₂ B4 ₂		Pd ₂ A ₂ B2 ₂		Pd ₂ A ₃ (MeCN) ₂	Pd ₂ B1 ₄
	B1	A	B4	A	B2	A		
E _{p/2} in V	1.06	-1.58	0.77	-1.51	-1.39	-1.58	-1.57	1.00
E _{HOMO} in eV ^[1]	-5.86		-5.57		-6.51 ^[2]			-5.80
E _{LUMO} in eV ^[1]	-3.22		-3.29		-3.22		-3.23	

Table S2: Summary of the electrochemical data for the heteroleptic species. E_{p/2} is referenced to Fc/Fc⁺. [1] E_{HOMO}/E_{LUMO} = -4.8 eV - e · E_{p/2}. [2] E_{HOMO} = E_{LUMO} - ΔE with ΔE the HOMO-LUMO gap obtained by UV-Vis abs. spectroscopy taking the 525 nm band in the heteroleptic cage. Those results were compiled with PhD colleague Laura Neukirch.

The reduction potential of **A** is similar in homo- and heteroleptic cages. This agrees with our studies on other heteroleptic cages (Measurement of Pd₂A₂B4₂ might be repeated). The value for the LUMO is also roughly in accordance with values reported in the literature (DPP usually comes with thiophene substituents making an exact comparison difficult, e.g. *Chem. Commun.*, **2012**, 48, 3039-3051).

The oxidation potential of **B1** is similar in homo- and heteroleptic cages. Again, agreeing with studies on other heteroleptic cages. The half-wave potential of **B3** is lower than the one of **B1** which is in agreement with the expected increased donor strength.

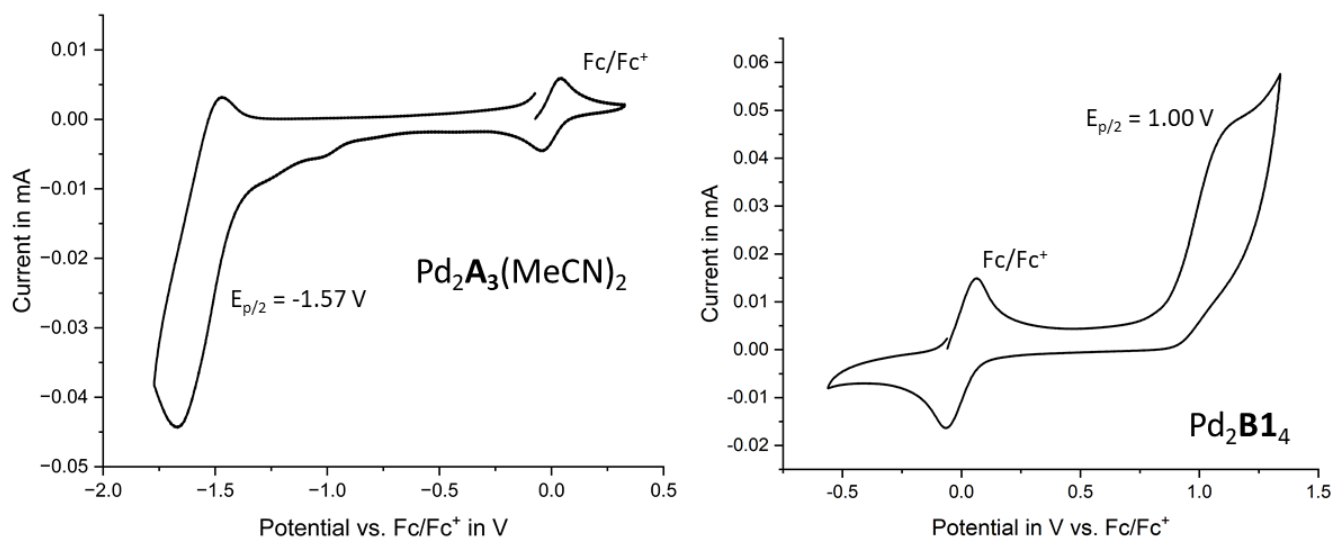


Figure S74: Cyclic voltammograms of sample recorded at a glassy carbon working electrode and Ag/AgNO₃ reference electrode of (left) Pd₂A₃(MeCN)₂ (XX mM in MeCN), (right) Pd₂B1₄ (XX mM in 0.1 M [NBu₄][PF₆] MeCN). The potentials are given with respect to the Fc/Fc⁺ potential. The CV plots of each sample are shown with ferrocene (1 mM) as an internal reference. Supporting electrolyte: 0.1 M [NBu₄][PF₆]. Scan rate: 0.1 V·s⁻¹.

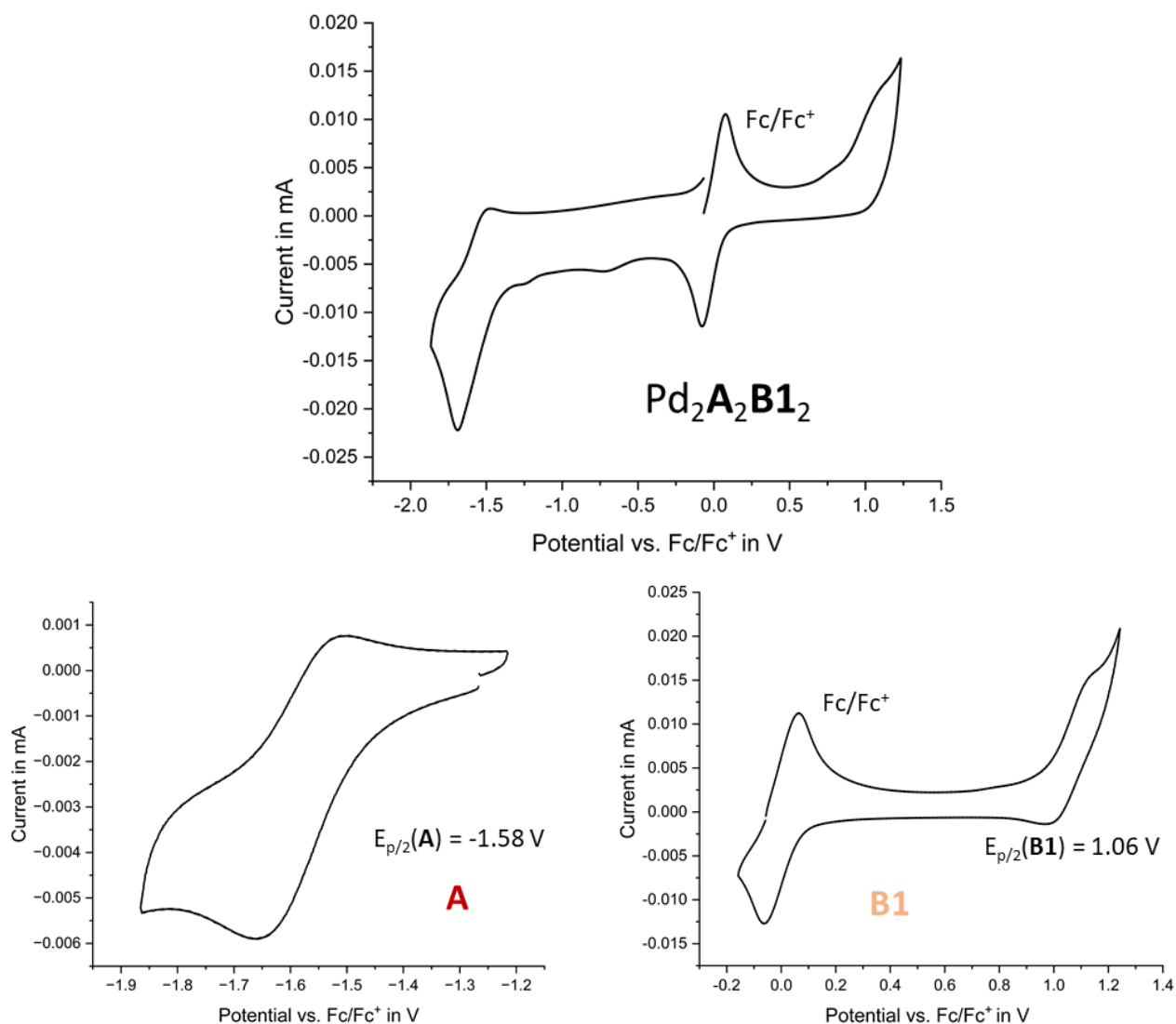


Figure S75: Cyclic voltammograms of sample recorded at a glassy carbon working electrode and Ag/AgNO_3 reference electrode of $\text{Pd}_2\text{A}_3\text{B1}_2$ (XX in 0.1 M $[\text{NBu}_4][\text{PF}_6]$ MeCN),. The potentials are given with respect to the Fc/Fc^+ potential. The CV plots of each part are shown with ferrocene (1 mM) as an internal reference. Supporting electrolyte: 0.1 M $[\text{NBu}_4][\text{PF}_6]$. Scan rate: $0.1 \text{ V}\cdot\text{s}^{-1}$.

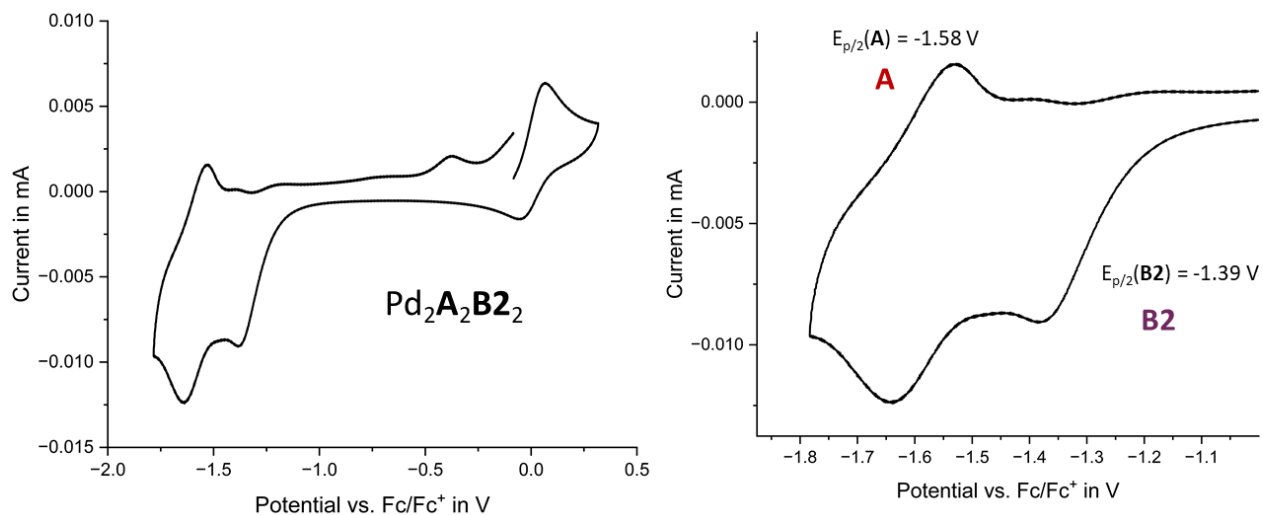


Figure S76: Cyclic voltammograms of sample recorded at a glassy carbon working electrode and Ag/AgNO₃ reference electrode of Pd₂A₂B₂₂ (XX in 0.1 M [NBu₄][PF₆] MeCN),. The potentials are given with respect to the Fc/Fc⁺ potential. The CV plots of each part are shown with ferrocene (1 mM) as an internal reference. Supporting electrolyte: 0.1 M [NBu₄][PF₆]. Scan rate: 0.1 V·s⁻¹.

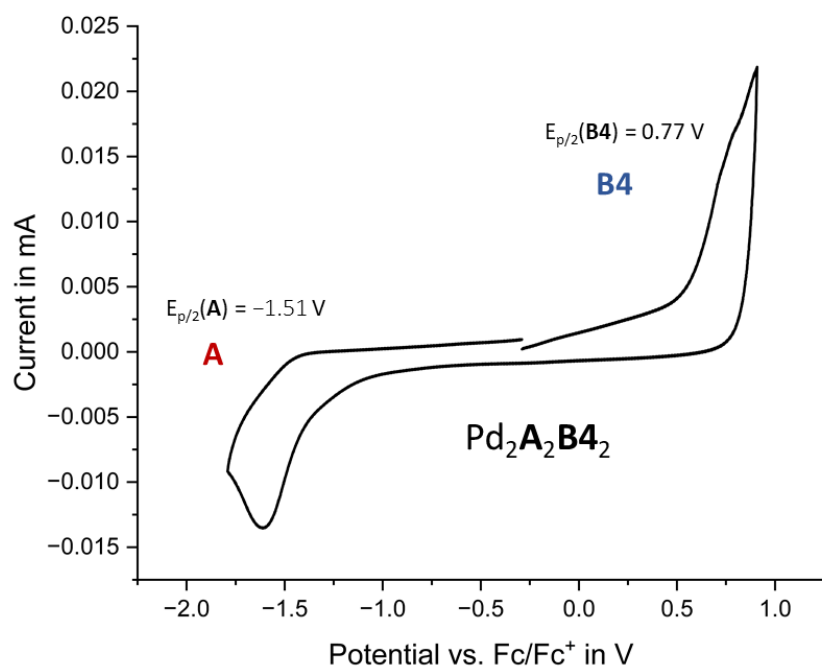


Figure S77: Cyclic voltammograms of sample recorded at a glassy carbon working electrode and Ag/AgNO₃ reference electrode of Pd₂A₂B₄₂ (XX in 0.1 M [NBu₄][PF₆] MeCN),. The potentials are given with respect to the Fc/Fc⁺ potential. The CV plots of each part are shown with ferrocene (1 mM) as an internal reference. Supporting electrolyte: 0.1 M [NBu₄][PF₆]. Scan rate: 0.1 V·s⁻¹.

DFT calculation and orbital modeling

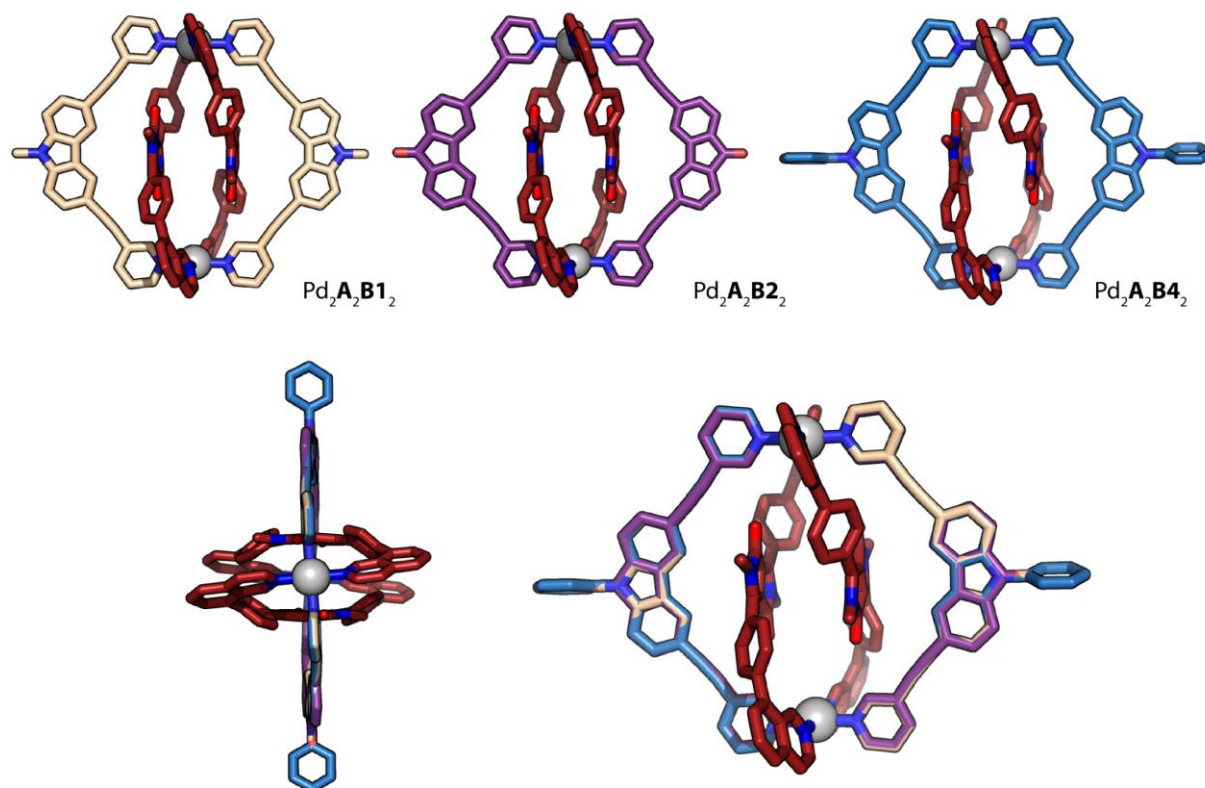


Figure S78: DFT geometry optimized (B3LYP/def2-SVP) structures of $\text{Pd}_2\text{A}_2\text{B}_{12}$, $\text{Pd}_2\text{A}_2\text{B}_{22}$ and $\text{Pd}_2\text{A}_2\text{B}_{42}$. At the bottom is displayed an overlap of the three optimized structures.

		Cages					
		$\text{Pd}_2\text{A}_2\text{B}_{12}$		$\text{Pd}_2\text{A}_2\text{B}_{22}$		$\text{Pd}_2\text{A}_2\text{B}_{32}$	
Energies (in eV)		HOMO	LUMO	HOMO	LUMO	HOMO	LUMO
	B3LYP/def2-SVP	-5.88	-3.22	-5.91	-3.4	-5.89	-3.22
	ω B97X-D/def2-TZVP	-7.66	-1.65	-7.68	-1.74	-7.66	-1.65
ΔE (in eV)	B3LYP/def2-SVP	2.67		2.51		2.67	
	ω B97X-D/def2-TZVP	6.01		5.94		6.01	

Table S3: Summary of the DFT calculations for the heteroleptic cages. The energies of frontiers orbitals with the two methods are given as well as the ΔE . Those calculations were compiled with PhD colleague Laura Neukirch.

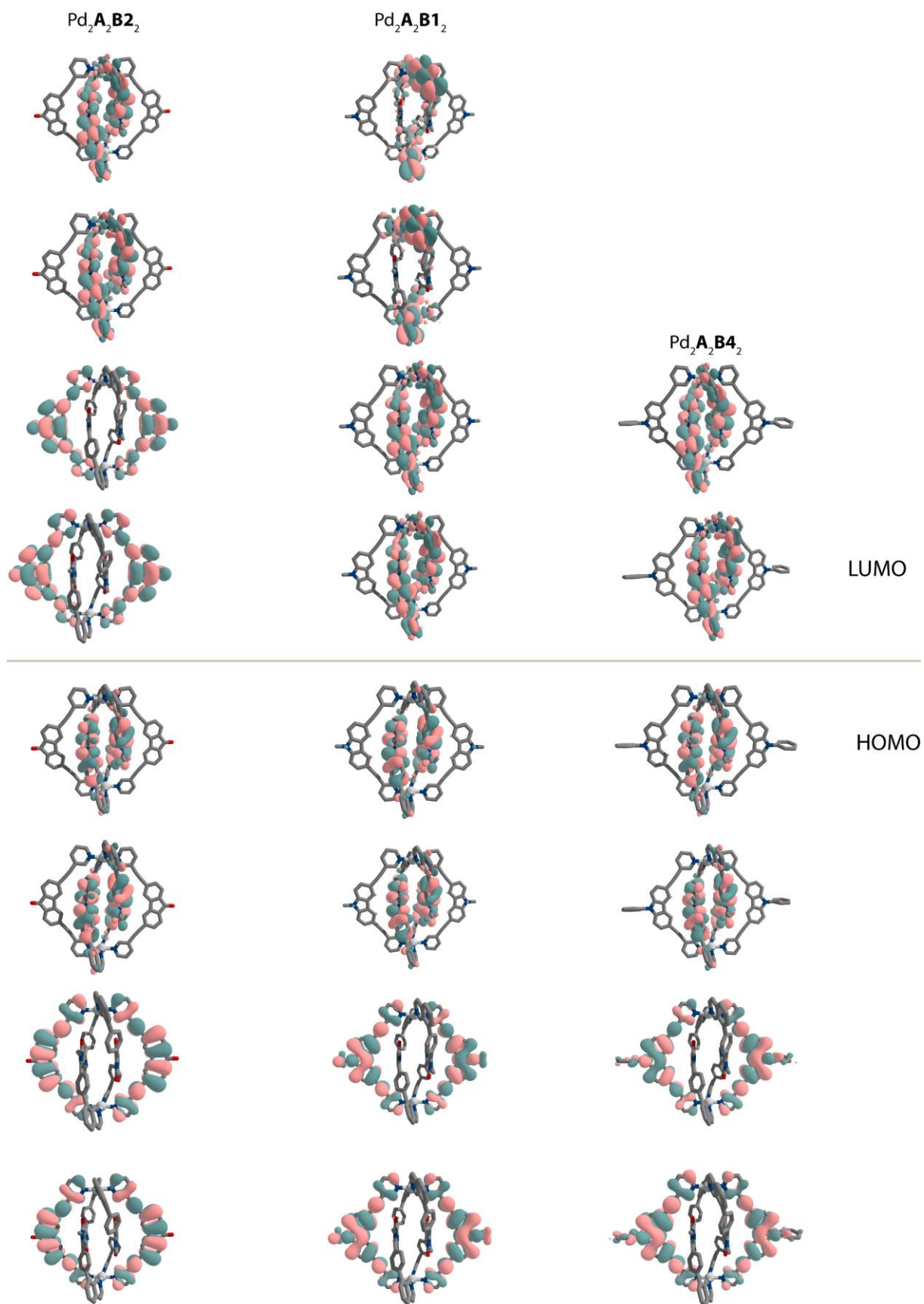


Figure S79: Representation of the frontier orbitals in the respective cages.

	Ligands							
	A		B1		B2		B4	
	HOMO	LUMO	HOMO	LUMO	HOMO	LUMO	HOMO	LUMO
Energies (in eV)	-5.6	-2.89	-5.65	-1.97	-6.31	-3.12	-5.69	-1.98
ΔE (in eV)	2.71		3.68		3.19		3.71	

Table S4: Summary of the DFT calculations for the cropped ligand in the optimized conformations. The energies of frontiers orbitals are given with the corresponding ΔE . Those calculations were compiled with PhD colleague Laura Neukirch

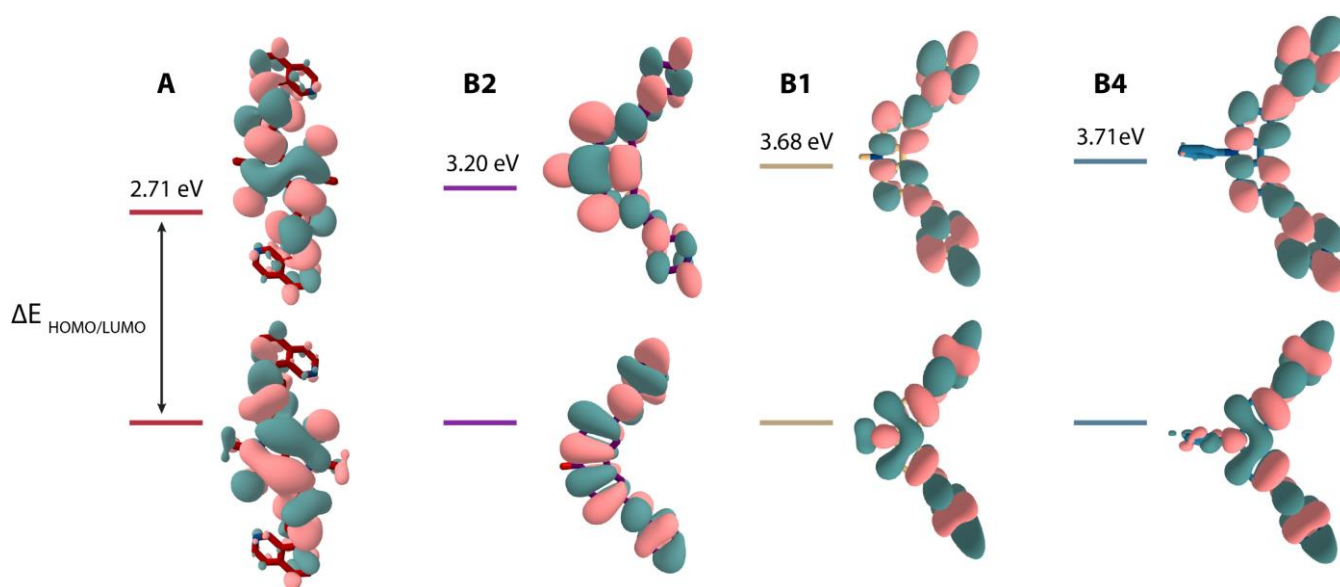


Figure S80: Representation of the frontier orbitals of the respective ligands **A**, **B1**, **B2** and **B4** in their conformation within the cages.

X-ray structure analysis

Four supramolecular assemblies $\text{Pd}_2\text{A}_2(\text{C2})_2$, $\text{Pd}_2\text{A}_1(\text{B3})_2(\text{C1})_1$, $\text{Pd}_2\text{A}_2(\text{B1})_1(\text{B2})_1$ and $\text{Pd}_2\text{A}_2(\text{B4})_2$ were analyzed using single-crystal X-ray crystallography. The crystals of the supramolecular assemblies were extremely sensitive to loss of organic solvent. Due to very tiny crystal volumes, the analysis was further hampered by the limited scattering power. Gaining detailed structural insight required cryogenic crystal handling and highly brilliant synchrotron radiation. Diffraction data was collected during two beamtime shifts at macromolecular synchrotron beamline P11, PETRA III, at DESY, Hamburg.⁶ Carefully adapted macromolecular refinement protocols employing geometrical restraint dictionaries, similarity restraints and restraints for anisotropic displacement parameters (ADPs) were applied. Details can be found in the discussions below.

Table S5: Crystallographic data of $[\text{Pd}_2\text{A}_2(\text{C2})_2]$, $[\text{Pd}_2\text{A}_1(\text{B3})_2(\text{C1})_1]$ and $[\text{Pd}_2\text{A}_2(\text{B1})_1(\text{B2})_1]$

Compound	$[\text{Pd}_2\text{A}_2(\text{C2})_2]$	$[\text{Pd}_2\text{A}_1(\text{B3})_2(\text{C1})_1]$	$[\text{Pd}_2\text{A}_2(\text{B1})_1(\text{B2})_1]$
CIF ID	eb16x4x8	eb14a	eb04b
CCDC number	2310126	2310127	2310128
Empirical formula	$\text{C}_{146}\text{H}_{129}\text{As}_2\text{BF}_{16}\text{N}_{17}\text{O}_4\text{Pd}_2$	$\text{C}_{143}\text{H}_{122}\text{B}_4\text{F}_{16}\text{N}_{16}\text{O}_{11}\text{Pd}_2$	$\text{C}_{162}\text{H}_{153}\text{B}_4\text{F}_{16}\text{N}_{13}\text{O}_8\text{Pd}_2$
Formula weight	2863.10	2800.60	2970.00
Temperature [K]	100(2)	100(2)	100(2)
Crystal system	triclinic	monoclinic	triclinic
Space group (number)	$P\bar{1}$ (2)	$P2_1/c$ (14)	$P\bar{1}$ (2)
a [Å]	19.437(8)	16.976(3)	18.422(5)
b [Å]	20.689(6)	26.421(5)	20.975(4)
c [Å]	21.247(6)	31.767(6)	26.104(5)
α [°]	91.425(6)	90	69.379(4)
β [°]	108.259(17)	96.62(3)	89.275(10)
γ [°]	107.475(7)	90	73.462(7)
Volume [Å ³]	7672(4)	14153(5)	9007(4)
Z	2	4	2
ρ_{calc} [gcm ⁻³]	1.239	1.314	1.095
μ [mm ⁻¹]	0.673	0.595	0.244
$F(000)$	2926	5744	3072
Crystal size [mm ³]	0.100×0.080×0.030	0.080×0.020×0.005	0.150×0.060×0.050
Crystal colour	orange	orange	orange
Crystal shape	plate	needle	block
Radiation	synchrotron ($\lambda=0.6888$ Å)	synchrotron ($\lambda=0.8856$ Å)	synchrotron ($\lambda=0.6888$ Å)
2 θ range [°]	1.97 to 55.56 (0.74 Å)	2.50 to 45.21 (1.15 Å)	1.62 to 49.03 (0.83 Å)
Index ranges	$-25 \leq h \leq 25$ $-26 \leq k \leq 26$ $-26 \leq l \leq 26$	$-14 \leq h \leq 14$ $-22 \leq k \leq 22$ $-27 \leq l \leq 27$	$-22 \leq h \leq 22$ $-24 \leq k \leq 24$ $-31 \leq l \leq 31$
Reflections collected	195089	61554	104311
Independent reflections	31314 $R_{\text{int}} = 0.0821$ $R_{\text{sigma}} = 0.0389$	9509 $R_{\text{int}} = 0.0850$ $R_{\text{sigma}} = 0.0500$	27806 $R_{\text{int}} = 0.0175$ $R_{\text{sigma}} = 0.0153$
Completeness	97.1 % ($\theta = 24.411^\circ$)	98.1 % ($\theta = 22.604^\circ$)	84.8 % ($\theta = 24.411^\circ$)

Data / Restraints / Parameters	31314/3831/1739	9509/3744/1776	27806/4280/2042
Goodness-of-fit on F^2	1.221	1.367	1.931
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.1092$ $wR_2 = 0.3128$	$R_1 = 0.1058$ $wR_2 = 0.3080$	$R_1 = 0.1302$ $wR_2 = 0.4563$
Final R indexes [all data]	$R_1 = 0.1340$ $wR_2 = 0.3415$	$R_1 = 0.1664$ $wR_2 = 0.3679$	$R_1 = 0.1503$ $wR_2 = 0.4768$
Largest peak/hole [$e\text{\AA}^{-3}$]	2.64/-0.53	0.85/-0.57	0.59/-0.67

Crystal structure of $[\text{Pd}_2\text{A}_2(\text{C2})_2]$

Orange plate-shaped crystals of $[\text{Pd}_2\text{A}_2(\text{C2})_2]$ were grown by slow vapor diffusion of diethylether into the solution of $[\text{Pd}_2\text{A}_2(\text{C2})_2]$ in acetonitrile at room temperature. Single crystals in mother liquor were pipetted onto a glass slide containing NVH oil. To avoid collapse of the crystal lattice, the crystal was quickly mounted onto a 0.2 mm nylon loop and immediately flash-cooled in liquid nitrogen. Crystals were stored at cryogenic temperature in dry shippers, in which they were safely transported to macromolecular beamline P11 at Petra III⁶, DESY, Hamburg, Germany. A wavelength of $\lambda = 0.6888 \text{ \AA}$ was chosen using a liquid N₂-cooled double-crystal monochromator. Single crystal X-ray diffraction data of several crystals was collected at 100 K on a single-axis goniometer, equipped with an Oxford Cryostream 800 and an Eiger 2x 16M detector. 3600 diffraction images were collected in a $360^\circ \phi$ sweep at a detector distance of 154 mm, 50% (crystal x4) or 70% (crystal x8) filter transmission, 0.1° step width and 0.1 seconds exposure time per image. Data integration and reduction were undertaken using XDS.⁷ Diffraction data of two crystals (x4 and x8) were merged using XPREP as the multi crystal data set has significantly higher completeness (97.1 %) compared to the best single crystal dataset (86,7 %). The structure was solved by intrinsic phasing/direct methods using SHELXT⁸ and refined with SHELXL⁹ using 22 CPU cores for full-matrix least-squares routines on F^2 and ShelXle¹⁰ as a graphical user interface and the DSR program plugin was employed for modeling.^{11,12}

Specific refinement details for $[\text{Pd}_2\text{A}_2(\text{C2})_2]$

The structure was solved and refined in orthorhombic space group $P\bar{1}$ (2) and therefore, contains one full cage molecule in the asymmetric unit. Three out of four tetrafluoroborate counterions were successfully modelled. Stereochemical restraint dictionaries for the ligands were generated by the GRADE2 program using the GRADE2 Web Server (<http://grade2.globalphasing.org>) and applied in the refinement. A GRADE2 dictionary for SHELXL contains target values and standard deviations for 1,2-distances (DFIX) and 1,3-distances (DANG), as well as restraints for planar groups (FLAT). All displacements for non-hydrogen atoms were refined anisotropically. The refinement of ADPs for carbon, nitrogen and oxygen atoms was enabled by a combination of similarity restraints (SIMU) and rigid bond restraints (RIGU).¹⁴ The contribution of the electron density from disordered counterions and solvent molecules, which could not be modeled with discrete atomic positions was handled using the SQUEEZE¹⁴ routine in PLATON.¹⁵ The solvent mask file (.fab) computed by PLATON was included in the SHELXL refinement via the ABIN instruction leaving the measured intensities untouched.

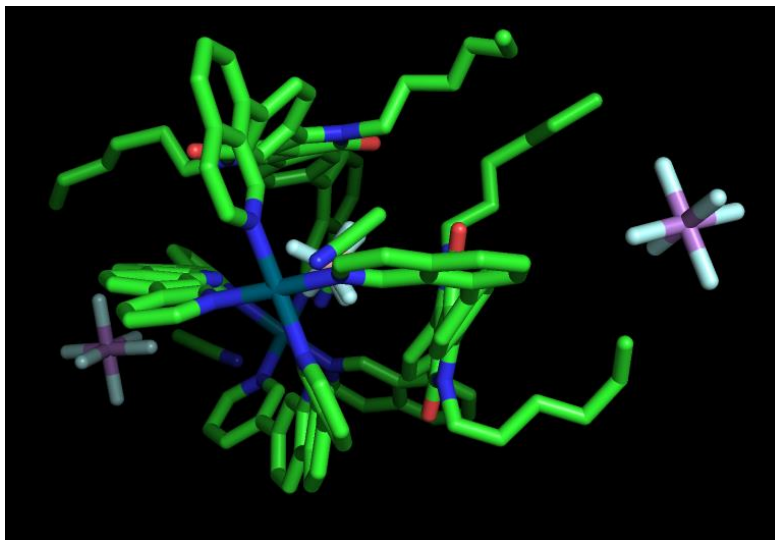


Figure S81: View of $[\text{Pd}_2\text{A}_2(\text{C2})_2]$ and modelled counterions along the Pd-Pd axis.

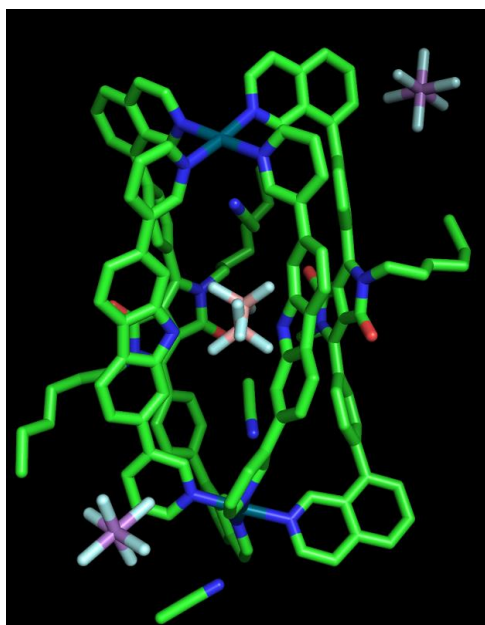


Figure S82: View of $[\text{Pd}_2\text{A}_2(\text{C2})_2]$ and modelled counterions from an axis orthogonal to the Pd-Pd axis revealing the ellipsoidal nature of the structure's cavity.

Crystal structure of $[\text{Pd}_2\text{A}_1(\text{B3})_2(\text{C1})_1]$

Orange plate-shaped crystals of $[\text{Pd}_2\text{A}_1(\text{B3})_2(\text{C1})_1]$ were grown by slow vapor diffusion of diethylether into the solution of $[\text{Pd}_2\text{A}_1(\text{B3})_2(\text{C1})_1]$ in acetonitrile at room temperature. Single crystals in mother liquor were pipetted onto a glass slide containing NVH oil. To avoid collapse of the crystal lattice, the crystal was quickly mounted onto a 0.1 mm nylon loop and immediately flash-cooled in liquid nitrogen. Crystals were stored at cryogenic temperature in dry shippers, in which they were safely transported to macromolecular beamline P11 at Petra III⁶, DESY, Hamburg, Germany. A wavelength of $\lambda = 0.8856 \text{ \AA}$ was chosen using a liquid N_2 cooled double crystal monochromator. Single crystal X-ray diffraction data was collected at 100(2) K on a single axis goniometer, equipped with an Oxford Cryostream 800 and an Eiger 2x 16M detector. 3600 diffraction images were collected in a $360^\circ \phi$ sweep at a detector distance of 154 mm, 100% filter transmission, 0.1° step width and 10 milliseconds exposure time per image. Data integration and reduction were undertaken using XDS.⁷ The structure was solved by intrinsic phasing/direct methods using SHELXT⁸ and refined with SHELXL⁹ using 22 CPU cores for full-matrix

least-squares routines on F^2 and ShelXle¹⁰ as a graphical user interface and the DSR program plugin was employed for modeling.^{11,12}

Specific refinement details for $[\text{Pd}_2\text{A}_1(\text{B3})_2(\text{C1})_1]$

The structure was solved and refined in monoclinic space group $P2_1/c$ (14) and contains one full cage molecule in the asymmetric unit. All four tetrafluoroborate counterions and one co-crystallized acetonitrile solvent molecule was successfully modelled. Stereochemical restraints for the three ligands (residues LFP, EAP and QPD), acetonitrile and diethylether solvent molecules (residue ACN and ETO) were generated by the GRADE2 program using the GRADE Web Server (<http://grade2.globalphasing.org>) and applied in the refinement. A GRADE dictionary for SHELXL contains target values and standard deviations for 1,2-distances (DFIX) and 1,3-distances (DANG), as well as restraints for planar groups (FLAT). All displacements for non-hydrogen atoms were refined anisotropically. The refinement of ADPs for carbon, nitrogen and oxygen atoms was enabled by a combination of similarity restraints (SIMU) and rigid bond restraints (RIGU).¹³ The contribution of the electron density from disordered counterions and solvent molecules, which could not be modeled with discrete atomic positions were handled using the SQUEEZE¹⁴ routine in PLATON.¹⁵ The solvent mask file (.fab) computed by PLATON was included in the SHELXL refinement via the ABIN instruction leaving the measured intensities untouched.

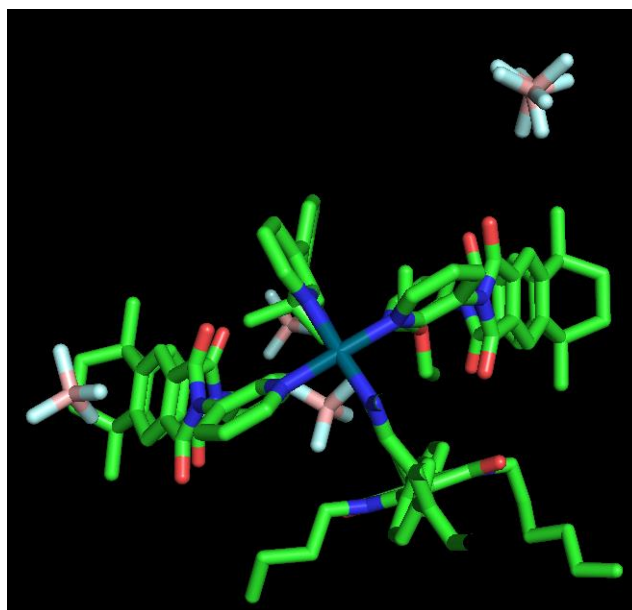


Figure S83: View of $[\text{Pd}_2\text{A}_1(\text{B3})_2(\text{C1})_1]$ and modelled counterions along the Pd-Pd axis.

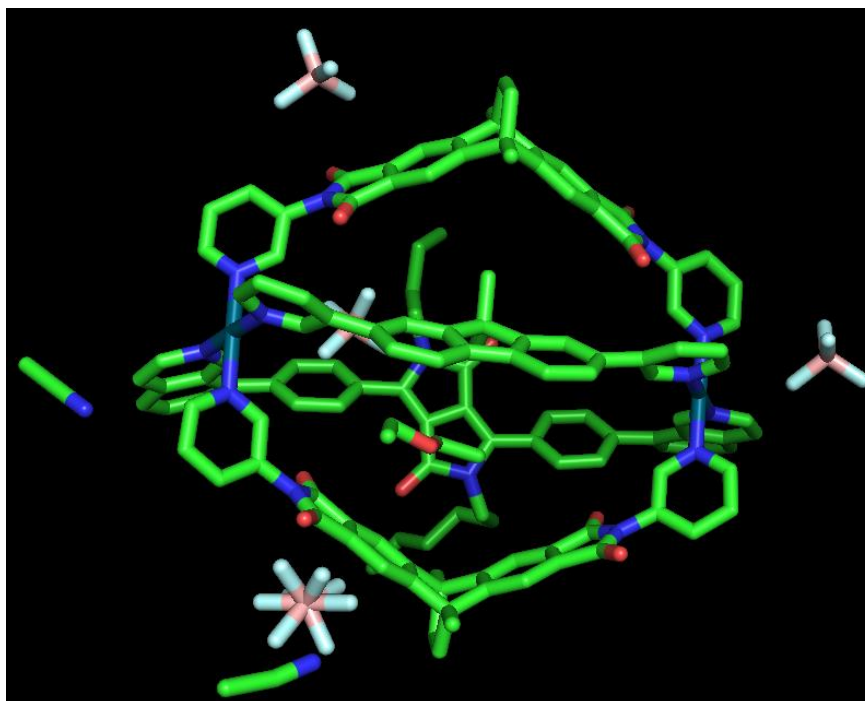


Figure S84: View of $[\text{Pd}_2\text{A}_1(\text{B}3)_2(\text{C}1)_1]$ and modelled counterions from an axis orthogonal to the Pd-Pd axis.

Crystal structure of $[\text{Pd}_2\text{A}_2(\text{B}1)_1(\text{B}2)_1]$

Orange block-shaped crystals of $[\text{Pd}_2\text{A}_2(\text{B}1)_1(\text{B}2)_1]$ were grown by slow vapor diffusion of *t*-butylmethylether into the solution of $[\text{Pd}_2\text{A}_2(\text{B}1)_1(\text{B}2)_1]$ in acetonitrile at room temperature. Single crystals in mother liquor were pipetted onto a glass slide containing NVH oil. To avoid collapse of the crystal lattice, the crystal was quickly mounted onto a 0.04 mm nylon loop and immediately flash-cooled in liquid nitrogen. Crystals were stored at cryogenic temperature in dry shippers, in which they were safely transported to macromolecular beamline P11 at Petra III⁶, DESY, Hamburg, Germany. A wavelength of $\lambda = 0.6888 \text{ \AA}$ was chosen using a liquid N₂ cooled double crystal monochromator. Single crystal X-ray diffraction data was collected at 100 K on a single axis goniometer, equipped with an Oxford Cryostream 800 and an Eiger 2x 16M detector. 3600 diffraction images were collected in a $360^\circ \phi$ sweep at a detector distance of 154 mm, 100% filter transmission, 0.1° step width and 20 milliseconds exposure time per image. Data integration and reduction were undertaken using XDS.⁷ The structure was solved by intrinsic phasing/direct methods using SHELXT⁸ and refined with SHELXL⁹ using 22 CPU cores for full-matrix least-squares routines on F^2 and ShelXle¹⁰ as a graphical user interface and the DSR program plugin was employed for modeling.^{11,12}

Specific refinement details for $[\text{Pd}_2\text{A}_2(\text{B}1)_1(\text{B}2)_1]$

The structure was solved and refined in triclinic space group $P\bar{1}$ (2) and contains the one full cage molecule in the asymmetric unit. All four disordered tetrafluoroborate counterions and the co-crystallised *t*-butylmethylether solvent molecule were successfully modelled. Stereochemical restraints for the two ligands (residues COP and QPD) *t*-butylmethylether solvent molecules (residue TME) were generated by the GRADE2 program using the GRADE2 Web Server (<http://grade2.globalphasing.org>) and applied in the refinement. A GRADE2 dictionary for SHELXL contains target values and standard deviations for 1,2-distances (DFIX) and 1,3-distances (DANG), as well as restraints for planar groups (FLAT). All displacements for non-hydrogen atoms were refined anisotropically. The refinement of ADPs for carbon, nitrogen and oxygen atoms was enabled by a combination of similarity restraints (SIMU) and rigid bond restraints (RIGU).¹³ The contribution of the electron density from disordered counterions and solvent molecules, which could not be modeled with discrete atomic positions were handled

using the SQUEEZE¹⁴ routine in PLATON.¹⁵ The solvent mask file (.fab) computed by PLATON was included in the SHELXL refinement via the ABIN instruction leaving the measured intensities untouched.

In the assembly's cavity, there are two small-volume binding sites close to each of the Pd(II) cations. These appear to be occupied by a water molecule as the scattering factor of oxygen is fitting well. The positions of hydrogen atoms for the two encapsulated water molecules in the entire structure were refined with the help of 1.2 and 1.3 distance restraints using DFIX and DANG from a GRADE dictionary for water. Additionally, distance restraints (DFIX) from hydrogen atoms to their oxygen acceptor atoms were used, employing target value of 1.85(8) Å.

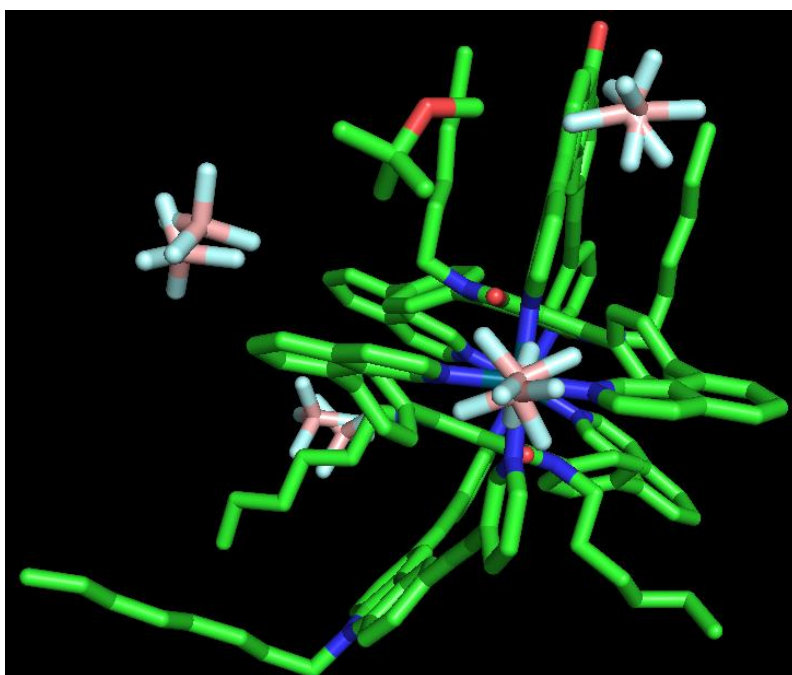


Figure S85: View of $[\text{Pd}_2\text{A}_2(\text{B1})_2(\text{B2})_1]$ and modeled counterions along the Pd-Pd axis.

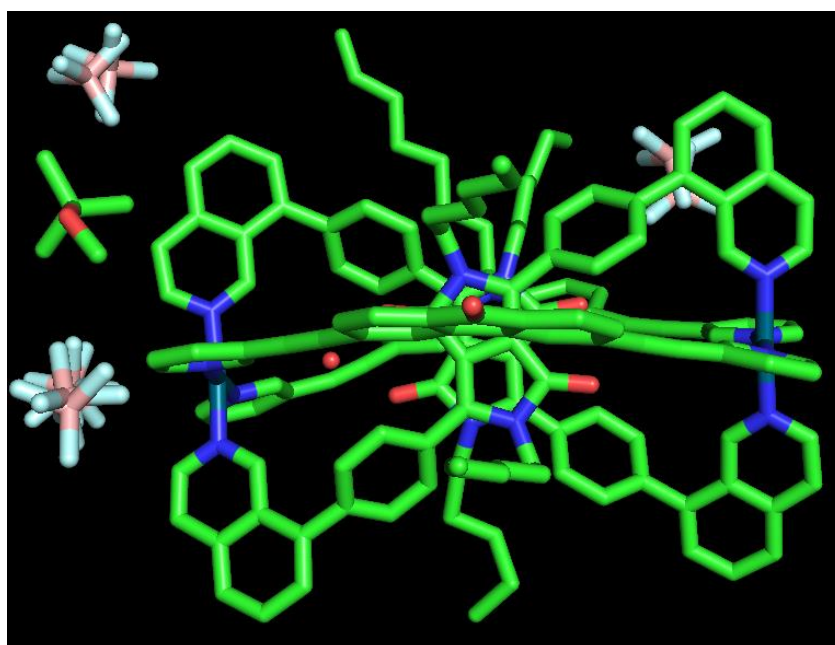


Figure S86: View of $[\text{Pd}_2\text{A}_2(\text{B1})_2(\text{B2})_1]$ and modeled counterions from an axis orthogonal to the Pd-Pd axis.

Specific refinement details for $[\text{Pd}_2\text{A}_2(\text{B4})_2]$

A red, block-shaped crystal of $\text{Pd}_2\text{A}_2(\text{B4})_2$ was mounted on a MiTeGen micromount with perfluoroether oil. Data were collected from a shock-cooled single crystal at 100(2) K on a Bruker D8 VENTURE dual wavelength Mo/Cu four-circle diffractometer with a microfocus sealed X-ray tube using a mirror optics as monochromator and a Bruker PHOTON II detector. The diffractometer was equipped with a low temperature device and used $\text{CuK}\alpha$ radiation ($\lambda = 1.54178 \text{ \AA}$). All data were integrated with SAINT and a multi-scan absorption correction using SADABS was applied.^[1,2] The structure was solved by direct methods using SHELXT and refined by full-matrix least-squares methods against F^2 by SHELXL-2018/3.^[3,4] All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined with isotropic displacement parameters. Some of their coordinates were refined freely and some on calculated positions using a riding model with their U_{iso} values constrained to 1.5 times the U_{eq} of their pivot atoms for terminal sp^3 carbon atoms and 1.2 times for all other carbon atoms. Disordered moieties were refined using bond lengths restraints and displacement parameter restraints. Crystallographic data for the structures reported here have been deposited with the Cambridge Crystallographic Data Centre.^[5] CCDC XXX contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures. This report and the CIF file were generated using FinalCif.^[6]

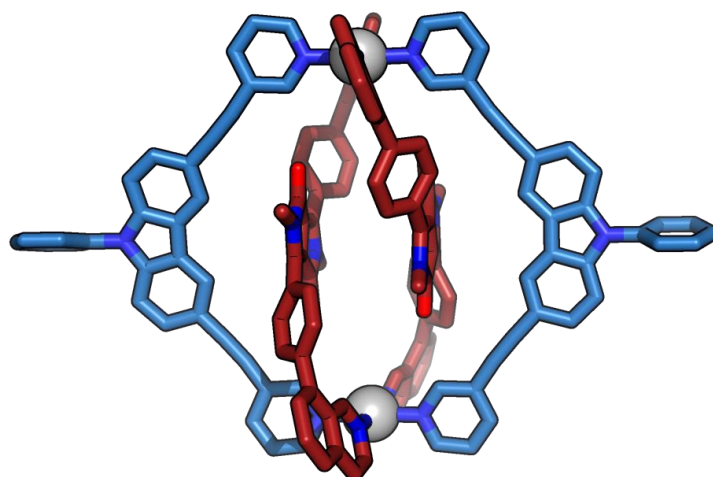


Figure S87: View of $[\text{Pd}_2\text{A}_2(\text{B1})_2(\text{B2})_1]$ and modeled counterions from an axis orthogonal to the Pd-Pd axis.

Table S6: Crystallographic data of $[\text{Pd}_2\text{A}_2(\text{B4})_2]$

CCDC number	x
Empirical formula	$\text{C}_{154}\text{H}_{122}\text{BF}_4\text{N}_{14}\text{O}_6\text{Pd}_2$
Formula weight	2564.26
Temperature [K]	100(2)
Crystal system	trigonal
Space group (number)	$P3_2$ (145)
a [$\text{\AA}$]	23.5835(8)
b [$\text{\AA}$]	23.5835(8)
c [$\text{\AA}$]	26.1238(14)
α [$^\circ$]	90

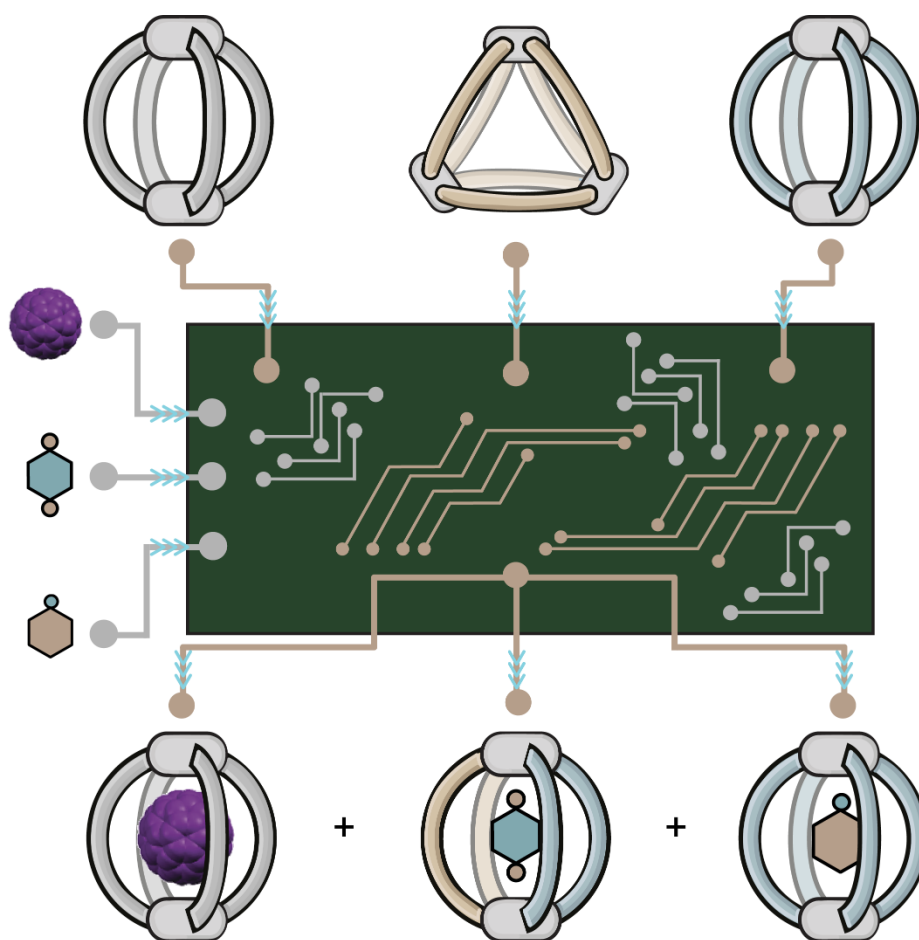
β [°]	90
γ [°]	120
Volume [Å ³]	12583.0(11)
<i>Z</i>	3
ρ_{calc} [gcm ⁻³]	1.015
μ [mm ⁻¹]	2.160
<i>F</i> (000)	3975
Crystal size [mm ³]	0.050×0.050×0.020
Crystal colour	red
Crystal shape	block
Radiation	CuK α (λ =1.54178 Å)
2 θ range [°]	4.33 to 90.31 (1.09 Å)
Index ranges	–19 ≤ <i>h</i> ≤ 21 –21 ≤ <i>k</i> ≤ 21 –23 ≤ <i>l</i> ≤ 23
Reflections collected	65987
Independent reflections	13570 $R_{\text{int}} = 0.1009$ $R_{\text{sigma}} = 0.1044$
Completeness to $\theta = 45.153^\circ$	99.8 %
Data / Restraints / Parameters	13570/5272/2220
Absorption correction $T_{\text{min}}/T_{\text{max}}$ (method)	0.5622/0.7489 (multi-scan)
Goodness-of-fit on F^2	1.052
Final <i>R</i> indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.1003$ $wR_2 = 0.2614$
Final <i>R</i> indexes [all data]	$R_1 = 0.1549$ $wR_2 = 0.3054$
Largest peak/hole [eÅ ⁻³]	0.53/–0.58
Flack X parameter	0.118(9)

7. References

- [1] J. Lehn, *Angew. Chem. Int. Ed.* **1990**, *29*, 1304–1319.
- [2] J.-M. Lehn, *Chem. Soc. Rev.* **2007**, *36*, 151.
- [3] M. M. Safont-Sempere, G. Fernández, F. Würthner, *Chem. Rev.* **2011**, *111*, 5784–5814.
- [4] Z. He, W. Jiang, C. A. Schalley, *Chem. Soc. Rev.* **2014**, *44*, 779–789.
- [5] A. Wu, L. Isaacs, *J. Am. Chem. Soc.* **2003**, *125*, 4831–4835.
- [6] P. T. Corbett, J. Leclaire, L. Vial, K. R. West, J.-L. Wietor, J. K. M. Sanders, S. Otto, *Chem. Rev.* **2006**, *106*, 3652–3711.
- [7] J. Tessarolo, H. Lee, E. Sakuda, K. Umakoshi, G. H. Clever, *J. Am. Chem. Soc.* **2021**, *143*, 6339–6344.
- [8] M. L. Saha, M. Schmittel, *Org. Biomol. Chem.* **2012**, *10*, 4651–4684.
- [9] S. Gaikwad, M. L. Saha, D. Samanta, M. Schmittel, *Chem. Commun.* **2017**, *53*, 8034–8037.
- [10] K. Mahata, M. Schmittel, *J. Am. Chem. Soc.* **2009**, *131*, 16544–16554.
- [11] M. L. Saha, M. Schmittel, *J. Am. Chem. Soc.* **2013**, *135*, 17743–17746.
- [12] K. Mahata, M. L. Saha, M. Schmittel, *J. Am. Chem. Soc.* **2010**, *132*, 15933–15935.
- [13] M. Schmittel, B. He, P. Mal, *Org. Lett.* **2008**, *10*, 2513–2516.
- [14] A. Ghosh, M. Schmittel, *Beilstein J. Org. Chem.* **2020**, *16*, 2831–2853.
- [15] J. Lehn, *Chem. Eur. J.* **1999**, *5*, 2455–2463.
- [16] Z. Yang, F. Esteve, C. Antheaume, J.-M. Lehn, *Chem. Sci.* **2023**, *14*, 6631–6642.
- [17] P. Baxter, J. Lehn, A. DeCian, J. Fischer, *Angew. Chem. Int. Ed.* **1993**, *32*, 69–72.
- [18] J.-F. Ayme, J.-M. Lehn, *Chem. Sci.* **2020**, *11*, 1114–1121.
- [19] F. B. L. Cougnon, J. K. M. Sanders, *Acc. Chem. Res.* **2012**, *45*, 2211–2221.
- [20] S. Otto, R. L. E. Furlan, J. K. M. Sanders, *J. Am. Chem. Soc.* **2000**, *122*, 12063–12064.
- [21] I. Regeni, R. Chowdhury, K. Terlinden, S. Horiuchi, J. J. Holstein, S. Feldmann, G. H. Clever, *Angew. Chem. Int. Ed.* **2023**, *62*, e202308288.
- [22] R. Zhu, J. Lübken, B. Dittrich, G. H. Clever, *Angew. Chem. Int. Ed.* **2015**, *54*, 2796–2800.
- [23] K. Wu, B. Zhang, C. Drechsler, J. J. Holstein, G. H. Clever, *Angew. Chem. Int. Ed.* **2020**, *60*, 6403–6407.
- [24] K. E. Ebbert, L. Schneider, A. Platzek, C. Drechsler, B. Chen, R. Rudolf, G. H. Clever, *Dalton T.* **2019**, *48*, 11070–11075.
- [25] B. Chen, J. J. Holstein, S. Horiuchi, W. G. Hiller, G. H. Clever, *J. Am. Chem. Soc.* **2019**, *141*, 8907–8913.
- [26] K. Wu, E. Benchimol, A. Baksi, G. H. Clever, *Nat. Chem.* **2024**, *16*, 584–591.
- [27] W. M. Bloch, J. J. Holstein, W. Hiller, G. H. Clever, *Angew. Chem. Int. Ed.* **2017**, *56*, 8285–8289.
- [28] T. Abe, N. Sanada, K. Takeuchi, A. Okazawa, S. Hiraoka, *J. Am. Chem. Soc.* **2023**, *145*, 28061–28074.
- [29] Y. Liu, S. Liao, W. Dai, Q. Bai, S. Lu, H. Wang, X. Li, Z. Zhang, P. Wang, W. Lu, Q. Zhang, *Angew. Chem. Int. Ed.* **2023**, *62*, e202217215.
- [30] N. Kishi, Z. Li, K. Yoza, M. Akita, M. Yoshizawa, *J. Am. Chem. Soc.* **2011**, *133*, 11438–11441.
- [31] M. A. Auwalu, S. Cheng, *Chemosensors* **2021**, *9*, 44.
- [32] W. Li, L. Wang, H. Tang, D. Cao, *Dye. Pigment.* **2019**, *162*, 934–950.
- [33] Q. Liu, S. E. Bottle, P. Sonar, *Adv. Mater.* **2019**, *32*, e1903882.
- [34] N. Luo, G. Zhang, Z. Liu, *Org. Chem. Front.* **2021**, *8*, 4560–4581.
- [35] D. Dalmau, E. P. Urriolabeitia, *Molecules* **2023**, *28*, 2663.
- [36] K. Ebbert, *Systematic Studies on Heteroleptic Coordination Cages*, TU Dortmund, **2024**.
- [37] A. B. S. Elliott, J. E. M. Lewis, H. van der Salm, C. J. McAdam, J. D. Crowley, K. C. Gordon, *Inorg. Chem.* **2016**, *55*, 3440–3447.
- [38] A. Schmidt, M. Hollering, J. Han, A. Casini, F. E. Kühn, *Dalton T.* **2016**, *45*, 12297–12300.

Chapter II

Guests segregation in multi-cage systems



Guests segregation in multi-cage systems

This chapter has benefited from the previous work of Dr. Bo Zhang and the help of Dr. Andrea Rivoli, exchange student from Prof. Pablo Ballester Group, for conducting part of the experimental work.

Introduction

Engineering specific host-guest interactions, akin to those of enzyme-substrate complexes, has been the central topic of supramolecular chemistry for the past decades. In order to mimic biological systems, a plethora of receptors have been developed to elucidate the principles of such binding events. Among those supramolecular hosts, metal-organic cages are of particular interest because of their inner shielded cavity and the dynamic nature of the metal-ligand bond allowing potential induced fit and reorganization of the host upon guest encapsulation. Binding of one particular guest in a cage is now a common phenomenon and, as seen in the general introduction of this dissertation, they have been used to separate,^[1] catalyze,^[2,3] or stabilize^[4] those molecules inside their inner available space. However, systems with the ability to bind multiple guest molecules or to transform upon binding have recently started to emerge.^[5] This process mirrors the ability of biological systems to compartmentalize functionalities to process either in an orthogonal or cooperative fashion. Moreover, bringing several distinct guests within one host offers exciting possibilities for the use of cages as nano-vessels. Multi-cavity assemblies have been employed to bind several substrates such as *cisplatin* and anions or multiple neutral aromatics.^[6–8] They present spatially segregated empty spaces, that can be equivalent or different and therefore bind several identical or chemically discernible guests. Interlocked cages are, in a similar fashion, capable of encapsulating diverse guests, the catenation creating distinguishable cavities within the higher-ordered structure.^[9–12] Finally, single homoleptic cage structures have also shown the ability to uptake different guests in their cavities leveraging a collection of effects such as guest interaction, hydrophobic effect, or unsaturated metal centers.^[13–18] Recent examples based on narcissistic self-sorting have begun to emerge, taking a systems approach where multiple assemblies can coexist and uptake different guests orthogonally or by preferential association.^[19,20]

The previous chapter has highlighted that it is now possible to make several heteroleptic assemblies coexist in a non-interfering manner through heteromeric complete self-sorting. While our previous examples lacked proper function or properties and served as a proof of concept of this newly encountered sorting, we now introduced a system where the diverse assemblies —one heteroleptic cage coexisting with either one or two homoleptic cages— are capable of segregating guests within their cavities. Guests also play a crucial role in the self-sorting process as fullerene C₆₀ or quinuclidine-N-oxide (**Q**) respectively drive it to completion or alter it in a *guest-driven narcissistic sorting* fashion.

1. Assembly characterization

Acridine-based ligand **L1** was synthesized from its dibromo precursor through a one-step Sonogashira cross-coupling reaction with 3-ethynylpyridine. **L2** and **L3** were obtained following the reported procedure by reacting their respective dianhydride precursors with 3-aminopyridine.^[21] Note that, the ligand named **L3** in this chapter corresponds to **B3** in the other ones. When mixed in a 1:1 ratio with Pd(II) in acetonitrile, **L1** led to the formation of a Pd₂**L1**₄ lantern-shape assembly which was fully characterized by NMR, ESI-MS as well as X-ray structure previously obtained by Dr. Bo Zhang (Figure 1a-b). On the other hand, owing to the more diverging vectors of **L2** a Pd₃**L2**₆ ring structure was obtained (Figure 1c-d). This assembly was confirmed by ESI-MS analysis as well as by a bigger hydrodynamic radius $r_h=1.31$ nm calculated from the diffusion coefficient measured with ¹H DOSY NMR. Eventually, **L3** affords a Pd₂**L3**₄ capsule as already reported by our group and mentioned in the previous chapter.^[21]

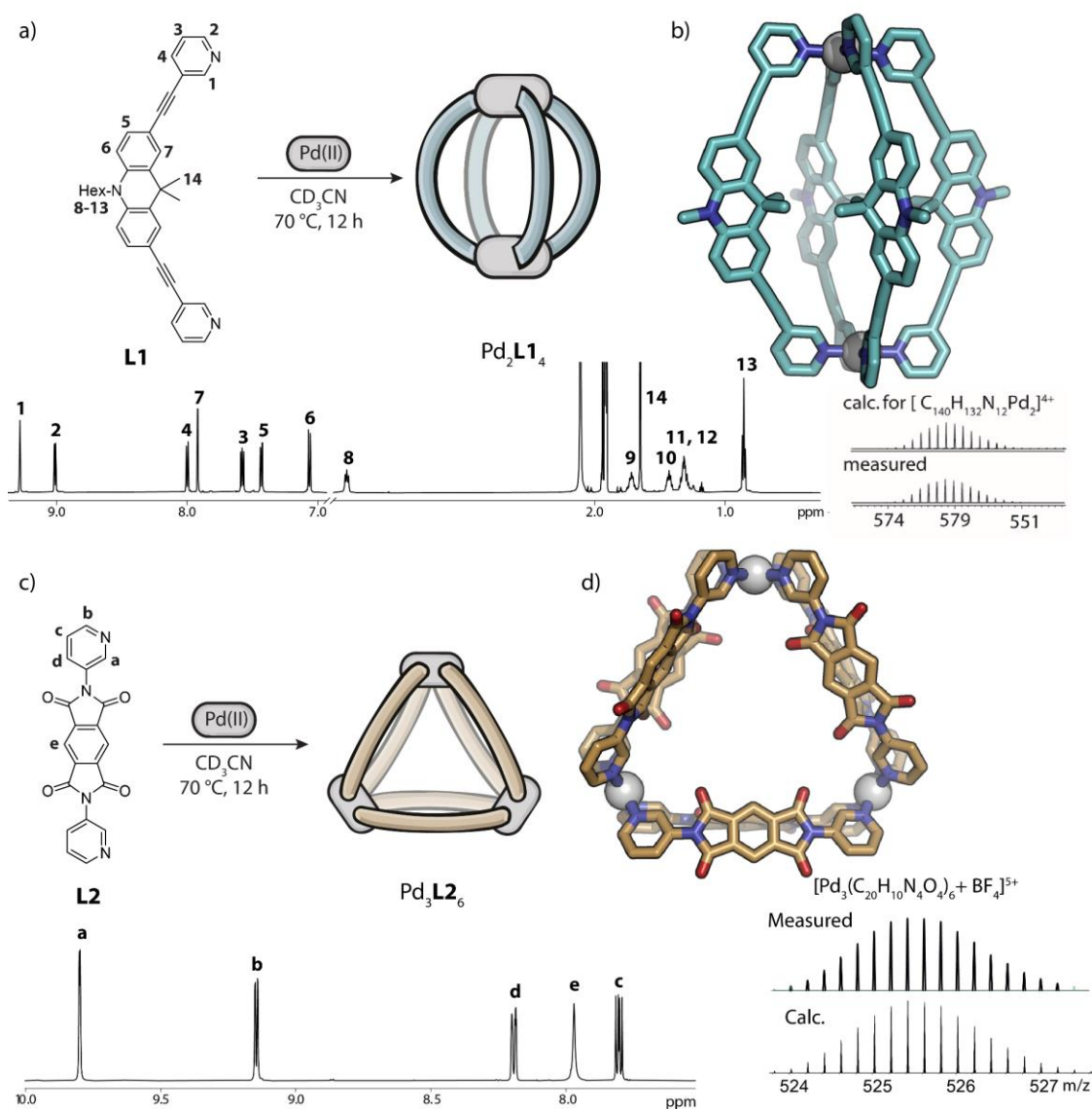


Figure 1: a) Formation of homoleptic cage Pd₂L₁₄ with assigned ¹H NMR (CD₃CN, 500 MHz) and isotopic pattern of the HR-ESI-MS. b) X-ray structure of the cage Pd₂L₁₄. Hexyl chains are omitted for clarity. c) Formation of homoleptic ring Pd₃L₂₆ with assigned ¹H NMR (CD₃CN, 500 MHz) and isotopic pattern of the HR-ESI-MS. d) DFT model (ωB97X-D/ def2-SVP) of the Pd₃L₂₆ ring.

When mixed in a ratio ensuring the same ligand's concentration, Pd₂L₁₄ and Pd₃L₂₆ give rise to a new set of signals in ¹H NMR (Figure 2a). All these signals belong to a single species with a hydrodynamic radius of $r_h=1.15$ nm,

determined by diffusion experiment and matching previously reported $\text{Pd}_2\text{A}_2\text{B}_2$ type assemblies. The formation of a heteroleptic cage $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$ was unambiguously confirmed by ESI-MS as prominent peaks corresponding to $[\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2 + n \text{BF}_4]^{(4-n)+}$ could be detected in the gas phase. No crystals suitable for synchrotron diffraction analysis could be grown and instead, DFT modeling was carried out to visualize the species (Figure 2c). The cage structure explained the pronouncedly broad character of proton **He** in the heteroleptic cage, which was further deciphered by VT NMR analysis. The two ligands **L2** face each other and a probable interligand *CH*- π interaction affects the ligand's free rotation, leading to the broadening of the signal. Host-guest experiments were performed and uncovered the binding of 1,4-benzene disulfonate (**G1**) and 1,3-benzene disulfonate (**G2**) in the cavity of the heteroleptic cage. The anions are bound in a slow exchange regime with respect to the NMR timescale and the addition of one equivalent of guest resulted in the complete conversion into the host-guest species witnessing a strong binding ($K > 10^5 \text{ M}^{-1}$ from the integrals at 0.5 equiv. of guest) (Figure 2a). This binding event is mostly driven by electrostatic interactions. ESI-MS provided more information and a 1:1 binding can be confirmed by detecting a distinct peak corresponding to $[\text{G1}@\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2]^{2+}$ (Figure 2b).

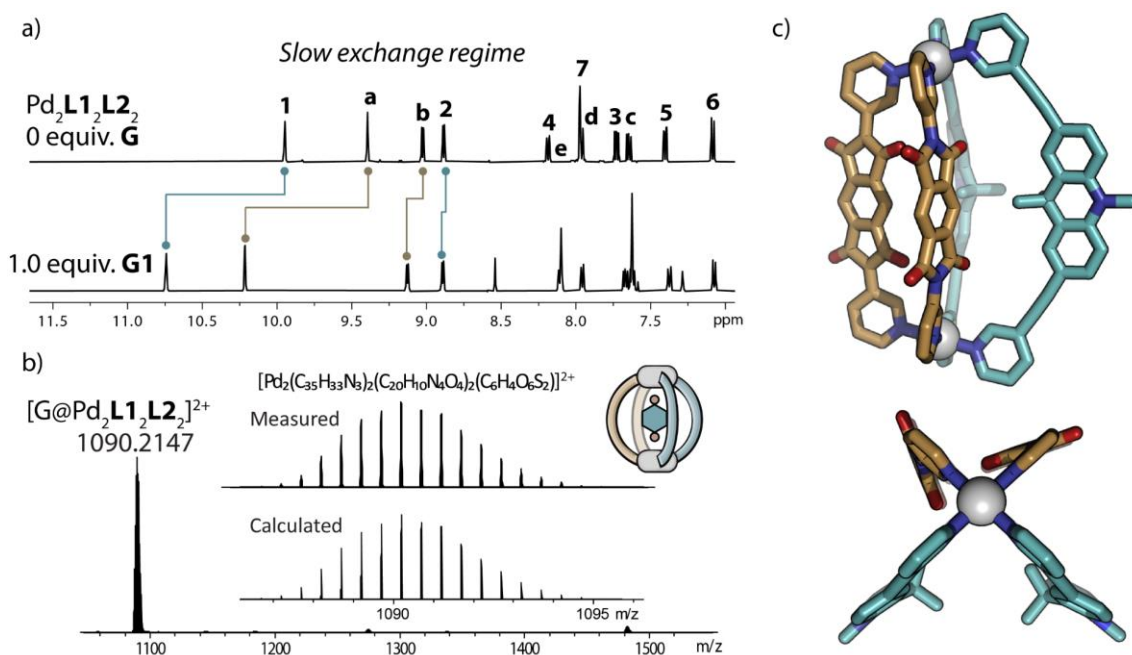


Figure 2: a) ^1H NMR (CD_3CN , 500 MHz) stack of heteroleptic cage $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$ and $\text{G1}@\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$ after the addition of 1 equivalent **G1**. b) HR-ESI-MS of the host-guest complex $\text{G1}@\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$ with the corresponding isotopic pattern. c) DFT model ($\omega\text{B97X-D/def2-SVP}$) of the $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$ cage.

2. Guest-induced multi-cage system

In a different fashion, neither **L1** nor **L2** gave a discrete species when combined with **L3** and Pd(II) in a 1:1:1 ratio. Mixing **L1** and **L3** affords a statistical mixture that could be anticipated as their coordination vectors do not match each other by shape complementary assembly. Further addition of fullerene C_{60} did not result in a precise sorting either but only in the emergence of the $\text{C}_{60}@\text{Pd}_2\text{L}_3\text{L}_4$ host-guest complex among diverse other species (Figure 3a-c). Prolonged heating did not result in narcissistic self-sorting, the mixture staying identical. It also demonstrates that this state is not a kinetic trap of the system related to a slow kinetic of the biphasic fullerene uptake process. We also proceeded to the experiment in which a preformed $\text{C}_{60}@\text{Pd}_2\text{L}_3\text{L}_4$ host-guest complex was mixed with $\text{Pd}_2\text{L}_1\text{L}_4$ and observed the same mixture, thus resulting in a partial fullerene release.

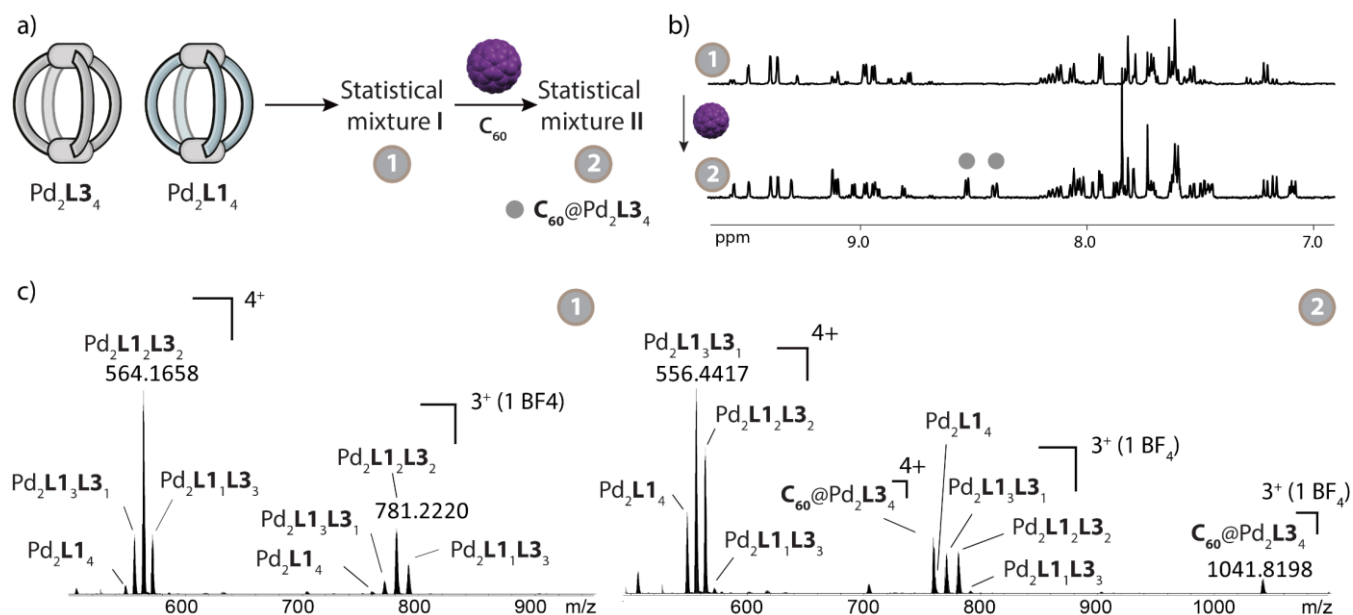


Figure 3: a) Schematic representation of the formation of the two statistical mixtures. b) ^1H NMR (CD_3CN , 500 MHz) of the *statistical mixture I* from $\text{Pd}_2\text{L}_1\text{L}_4$ and $\text{Pd}_2\text{L}_3\text{L}_4$ and formation of the *statistical mixture II* upon the addition of fullerene C_{60} . c) HR-ESI-MS of the two statistical mixtures.

However, when ligand **L2** (via $\text{Pd}_3\text{L}_2\text{L}_6$) was introduced in the balance, the mixture underwent self-sorting and eventually equilibrated with the coexistence of $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$ and $\text{C}_{60}@\text{Pd}_2\text{L}_3\text{L}_4$ in a 1:1 ratio (**Path I**) (note that the fullerene molecules that were previously released were therefore reuptaken by the Pd_2L_3 hosts in solution) (Figure 4a-b). This case differs from our previously reported *heteromeric completive self-sorting* where we had demonstrated that two heteroleptic cages could coexist orthogonally in a 1:1 ratio. Herein, driven by the fullerene affinity of $\text{Pd}_2\text{L}_3\text{L}_4$ the mixture can converge into a primary homoleptic species and a binary heteroleptic one. To the best of my knowledge, this self-sorting is not yet described in the current literature. The importance of the fullerene in the sorting process was further demonstrated by using the other possible routes leading to a similar outcome (**Path II**) (Figure 4c-e). When **L2** and **L3** are mixed together in presence of $\text{Pd}(\text{II})$, they also do not lead to a single species by integrative self-sorting. However, additional fullerene addition induced a narcissistic sorting and led to a 1:1 mixture of $\text{Pd}_3\text{L}_2\text{L}_6$ and $\text{C}_{60}@\text{Pd}_2\text{L}_3\text{L}_4$. This can then give the same aforementioned primary/binary cage association by introducing $\text{Pd}_2\text{L}_1\text{L}_4$. Eventually, when the three ligands are mixed together with $\text{Pd}(\text{II})$ in acetonitrile, no self-sorting can be observed at first. However, heating the sample in the presence of fullerene C_{60} directly results in the sorting (**Path III**) (Figure 5 (vi)). The presence of the guest and the last introduced ligand act in a cooperative fashion on the self-sorting outcome.

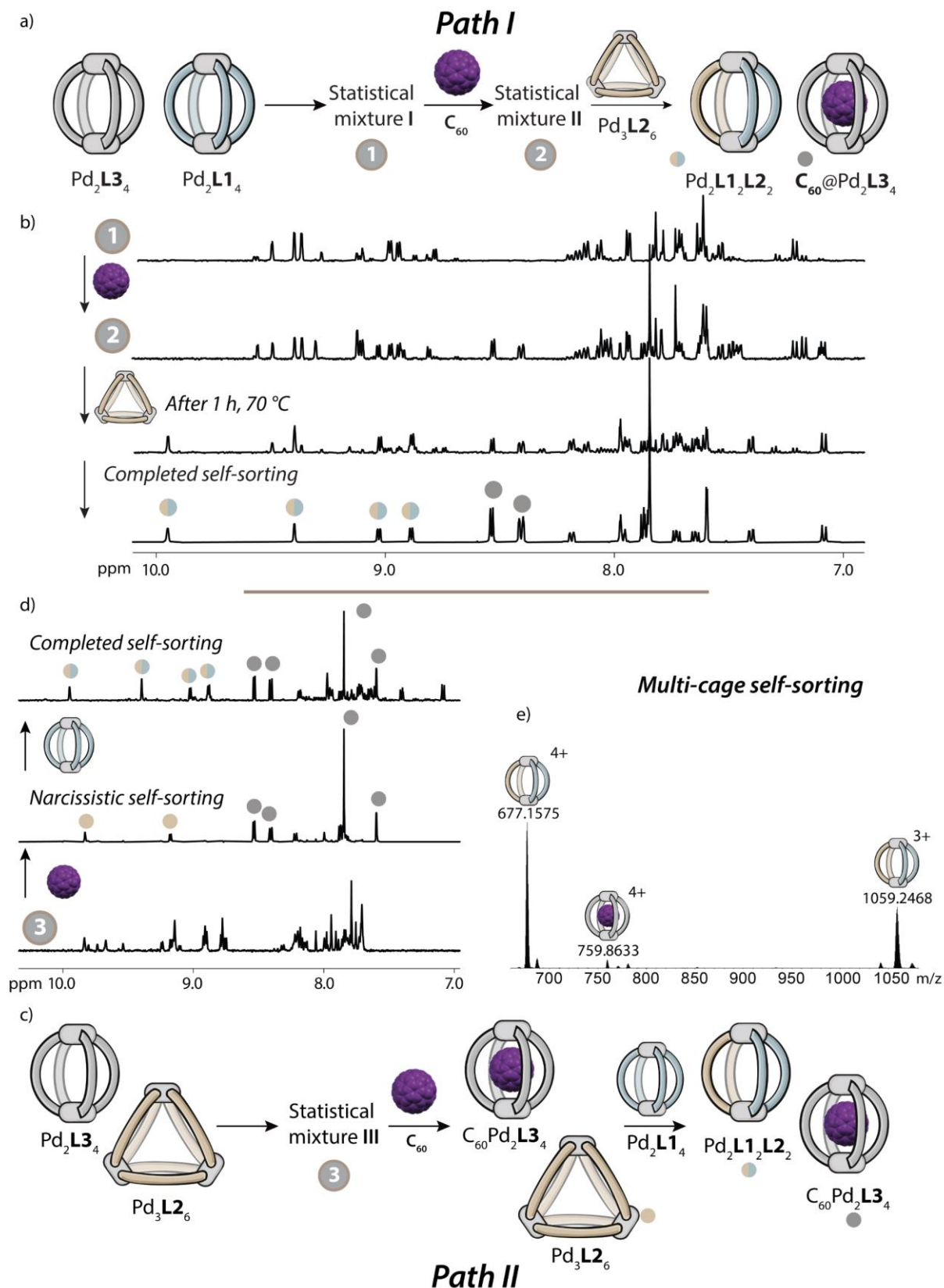


Figure 4: Multi-cage system. a) Schematic representation of *Path I* to the formation of the multi-cage system. b) Stacked ^1H NMR (CD_3CN , 500 MHz) of the sequential formation of statistical mixture I and II and the self-sorting upon introduction of Pd_3L_2_6 . c) Schematic representation of *Path II* to the formation of the multi-cage system. d) Stacked ^1H NMR (CD_3CN , 500 MHz) of the sequential transformation of statistical mixture III to narcissistic self-sorting upon introduction of C_{60} and to the multi-cage state after mixing of Pd_2L_{14} . e) HR-ESI-MS of the final outcome displaying peaks from $\text{Pd}_2\text{L}_{12}\text{L}_{22}$ and $\text{C}_{60}@\text{Pd}_2\text{L}_{34}$.

In alignment with the terminology introduced by Schmittl and coworkers,^[22] the current classification for such a process is termed "incomplete" sorting. However, it's crucial to note that this designation might here be prone to misinterpretation. The "incompleteness" refers (in Schmittl terminology) to the fact that not all the components assemble in pairs or together. Herein, they do so in a way that the primary host-guest and the binary heteroleptic cage undergo a narcissistic self-sorting which is what is considered incomplete. It is however an interesting case, as the outcome of the self-sorting is dependent on the level of complexity of the mixture, the highest one affording eventually a defined and sorted state. This could then be seen as an example of *simplicity*. Mixing of the three ligands in a 1:1:1 ratio in presence of Pd(II) (Figure 5 (vi)) did not yield a discrete outcome but a mix of species. This was still the case when ligands were mixed in 2:1:1 ratio (Figure 5 (i-iii)). And, only with the introduction of the 4th component, the fullerene guest, can the sorting be *complete* (this time meaning it happens precisely) (Figure 5 (vi)). Interesting to note that as long as **L1** and **L2** were present in equimolar amounts, the introduction of the fullerene drives the self-sorting to completion. Therefore, the final ratio between the C₆₀@Pd₂**L3**₄ host guest and Pd₂**L1**₂**L2**₂ heteroleptic cage has no influence, which is characteristic of a narcissistic self-sorting phenomenon between two assemblies. On the other hand, addition of **G1** to the mixture containing the three ligands in equimolar ratio (Figure 5 (v)) did not result in a fully selective self-sorting. Despite the clear emergence of signals corresponding to **G1**@Pd₂**L1**₂**L2**₂ other species were present in the mixture. Eventually, a last path can be envisaged and logically led to the same outcome. It starts by forming the heteroleptic cages Pd₂**L1**₂**L2**₂ which is then not responsive to the introduction of fullerene. In the second step, Pd₂**L3**₄ is added to the solution and the uptake fullerene results in the same outcome. Therefore, while the four potential paths described herein lead to the same final mixture, it is interesting to realize that they pass by very distinct routes, containing all different defined or undefined states (referring to their self-sorting nature).

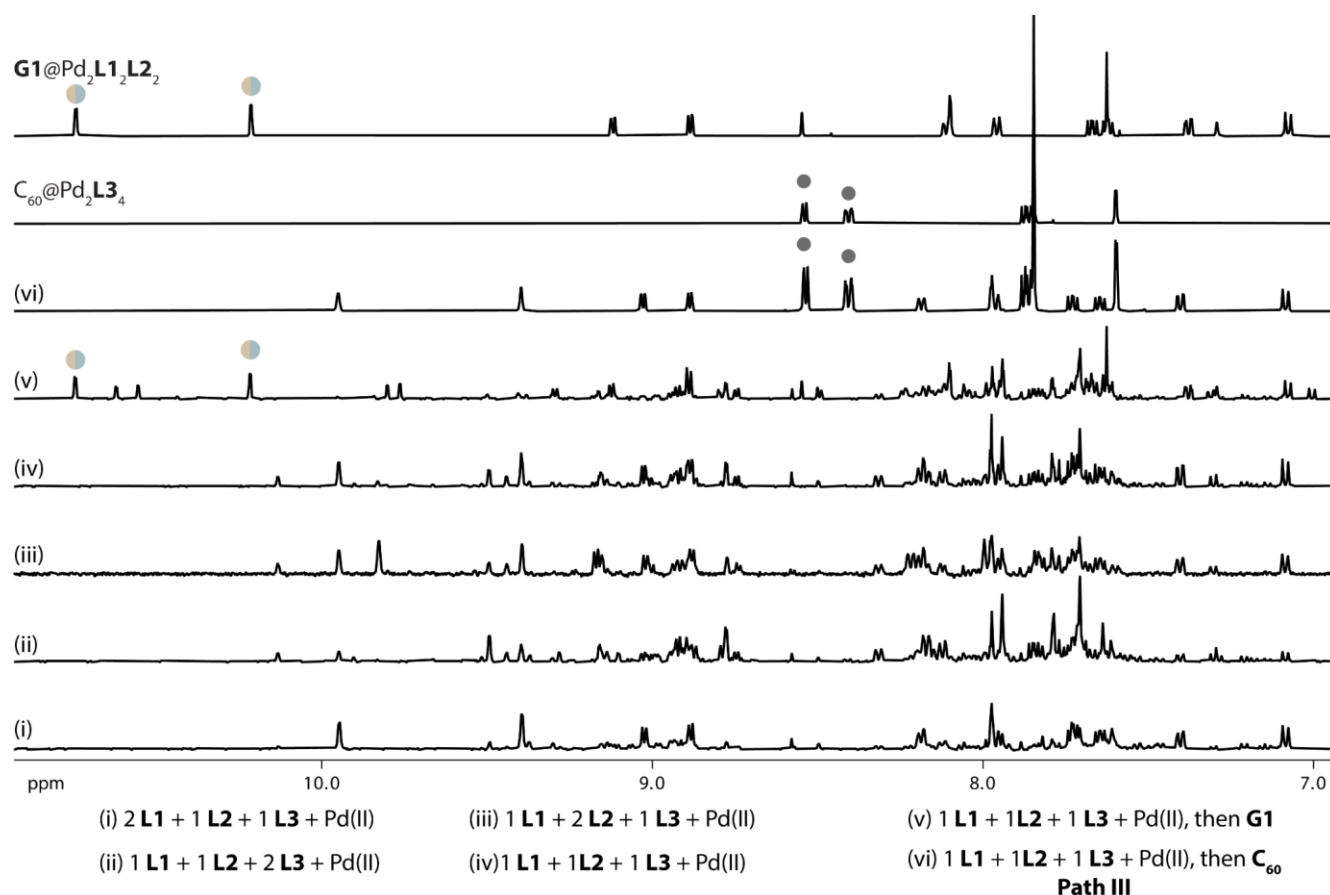


Figure 5: Stacked ¹H NMR (CD₃CN, 500 MHz) of the different outcomes of self-sorting when varying the ratio of ligands. The respective traces of **G1**@Pd₂**L1**₂**L2**₂ and C₆₀@Pd₂**L3**₄ are given as references.

3. Guests segregation I in multi-cage system

Advancing into higher complexity, I realized that guests could be selectively separated into host cavities coexisting in the same solution. Adding one equivalent of **G1** into the previously described mixtures results in its exclusive binding within the cavity of Pd₂**L1**₂**L2**₂ (Figure 6a). Remarkably, this binding event did not disrupt the existing cage assemblies (which stayed narcissistic) and demonstrated orthogonality to fullerene binding. Another outcome could have been a guest-induced transformation into a statistical mixture or a discrete species. To validate this, a one-pot reaction was conducted by combining all components and stirring them at 70 °C in acetonitrile overnight. Consequently, the selective *guest segregation* into two distinct hosts was observed, confirming the robustness of this process (Figure 4). The ¹H NMR of the final state was shown to be a perfect overlap of the two traces from host-guest assemblies (Figure 6b). Additionally, ESI-MS analysis provided further confirmation of their coexistence in the gas phase (Figure 6c). The presence of both empty hosts can be observed in the gas phase but this is inferred to be the sole consequence of ionization conditions. The process was quantitative and fully selective in the solution state as highlighted by the NMR data. Thus, in comparison with the system presented in the first chapter of this dissertation, an emergent property in populations of non-homoleptic coordination cages can be observed. Not only can the cages coexist in an orthogonal fashion but they can also segregate two different substrates in their respective cavities. This step further into functional cage populations. The present case also has the advantage of featuring two coexisting assemblies presenting real cavities as opposed to the figure-of-eight presented in the previous chapter. It is, however, important to note that the formation of the cage population and the guest segregation are somehow interdependent here as only in the presence of fullerene can the mixture be fully driven towards a defined sorting.

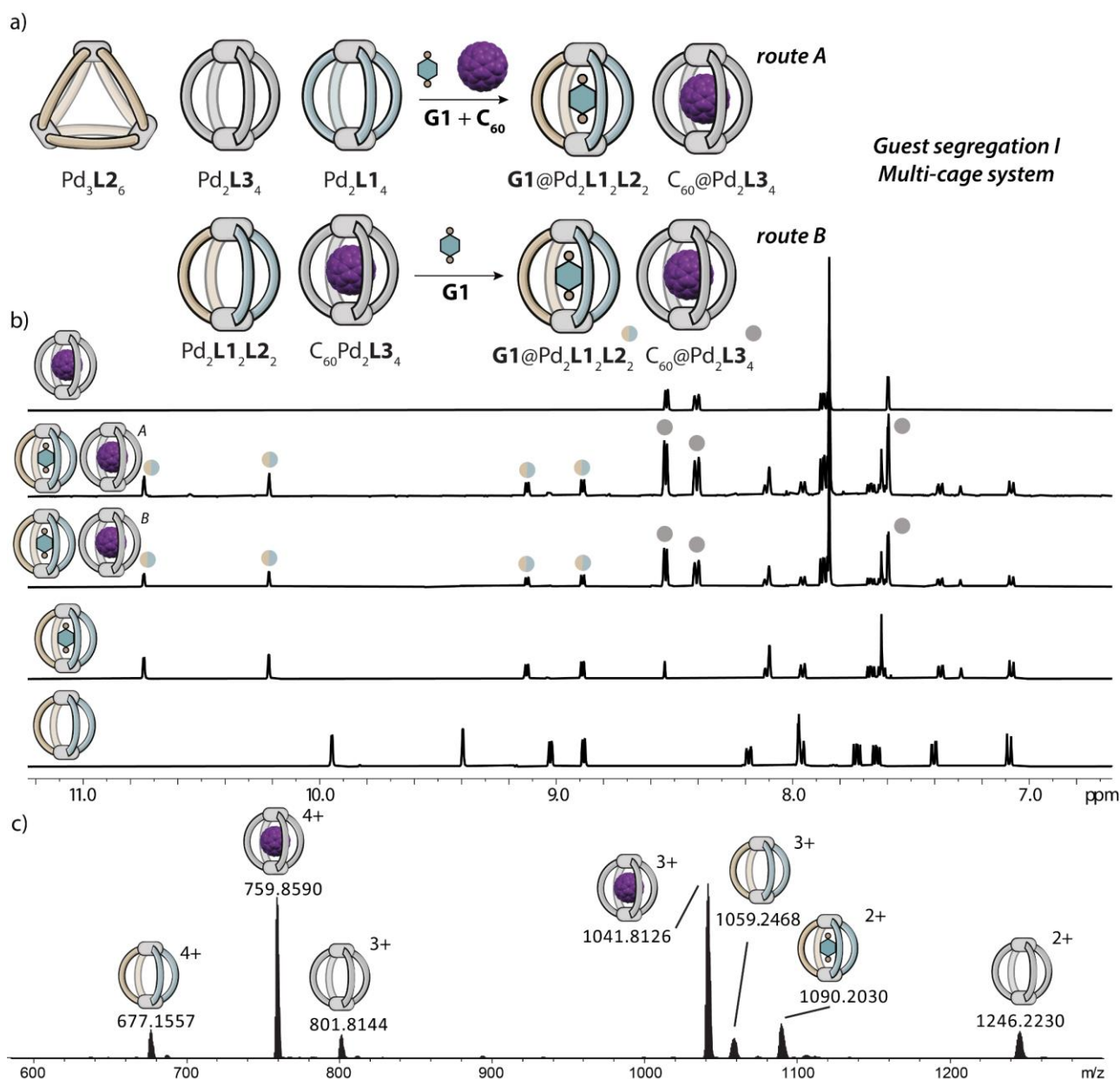


Figure 6: Guest segregation I. a) Schematic representations of the two routes employed for the formation of the multi-cage system capable of guest segregation. b) Stacked ^1H NMR (CD₃CN, 500 MHz) $\text{C}_{60}@Pd_2L_3_4$ (top), $\text{G1}@Pd_2L_1L_2L_2$ and $\text{Pd}_2L_1L_2L_2$ (bottom), and the two outcomes in the middle. c) HR-ESI-MS of the final outcome displaying peaks from $\text{G1}@Pd_2L_1L_2L_2$ and $\text{C}_{60}@Pd_2L_3_4$.

As I delved into exploring the host-guest capabilities of the different cages, I discovered that the homoleptic $\text{Pd}_2\text{L}_1\text{L}_4$ could interact with zwitterionic quinuclidine-N-oxide (**Q**). Although the interaction is weak, a clear shift of the inward-pointing pyridine proton H_a of **L1** was observed upon titration of an increasing amount of **Q** in a solution of the cage (Figure 7b). However, when more than 1.5 equivalents of **Q** were introduced, as compared to cage concentration, the same proton underwent a severe broadening and a stronger shift. In the meantime, new signals corresponding to free ligand in solution appeared upfield witnessing partial cage decomposition. It is therefore challenging to determine properly the binding constant, as well as the stoichiometry of binding of quinuclidine in the cavity of $\text{Pd}_2\text{L}_1\text{L}_4$ but the two species are undeniably interacting. Further analysis by HR-ESI-MS also reveals peaks corresponding to $\text{Q}@Pd_2L_1\text{L}_4$ and $2\text{Q}@Pd_2L_1\text{L}_4$ (Figure 7a). One can easily imagine a 2:1 guests/host stoichiometry in which the negatively charged oxygen atoms of **Q** point towards the positively charged Pd(II) cations holding the assembly together. Unfortunately, no crystal structure could be obtained from these samples and therefore some aspects stayed unclear.

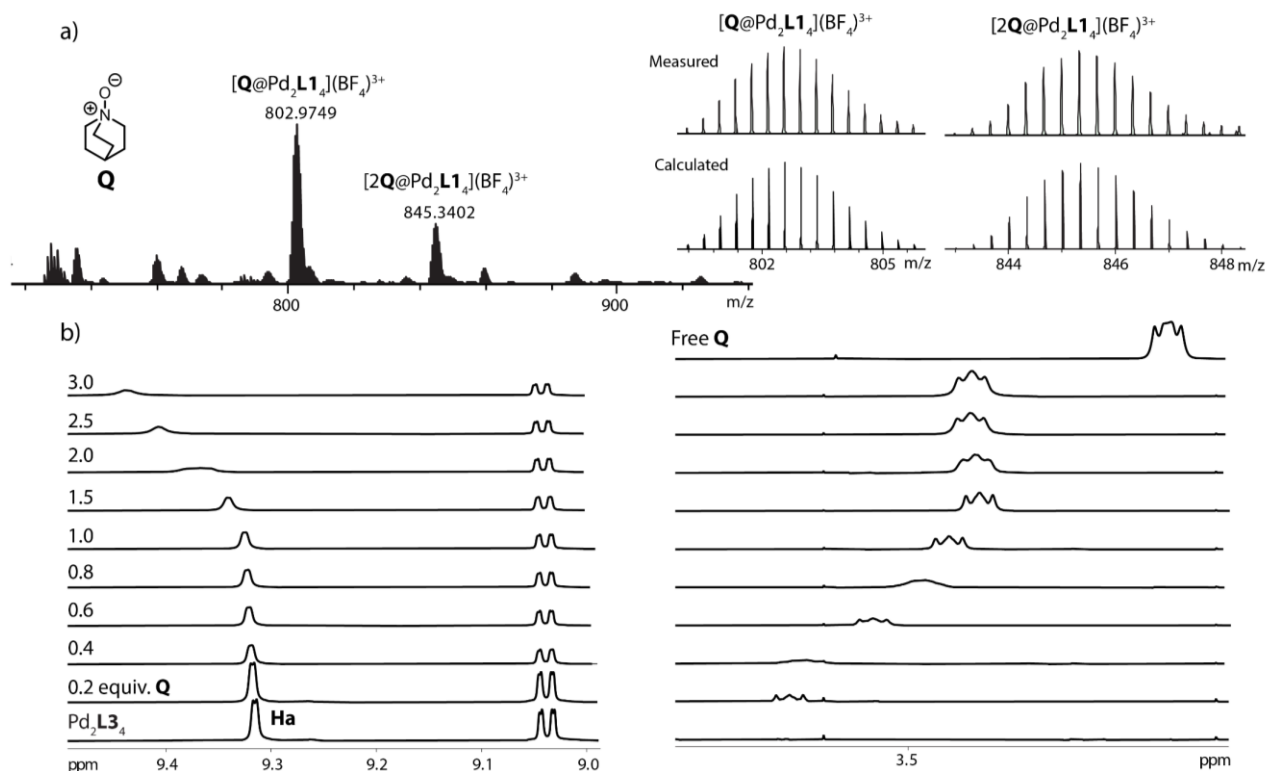


Figure 7: a) HR-ESI-MS of the $\text{Pd}_2\text{L1}_4$ cage in the presence of 2 equivalents of **Q** and displaying peaks $[\text{Q}@\text{Pd}_2\text{L1}_4](\text{BF}_4)^{3+}$ and $[2\text{Q}@\text{Pd}_2\text{L1}_4](\text{BF}_4)^{3+}$. b) Stacked ^1H NMR (CD_3CN , 500 MHz) of the titration of a solution of **Q** into a solution of $\text{Pd}_2\text{L1}_4$ showing a clear shift of inward pointing proton Ha upon an increase of **Q**. The right part displays the influence of the titration on the signal corresponding to quinuclidine **Q**.

Nevertheless, when quinuclidine N-oxide(**Q**) was employed as a guest in cage mixtures, a distinct change in the self-sorting outcome was observed (Figure 8). Introducing **Q** into the statistical mixture obtained from ligands **L1** and **L3**, in the presence of C_{60} , resulted in the converging towards a narcissistic self-sorting upon stirring for a few hours. Despite the weak binding interaction of **Q** within $\text{Pd}_2\text{L1}_4$, this interaction was sufficient to bias the self-sorting outcome, ultimately leading to the formation of two separate homoleptic host-guest complexes (Figure 8b). This stable 1:1 mixture persisted for several days at room temperature. However, when heated over a long period of time, a complete decomposition of the sample occurred. This phenomenon arises from the low thermal stability of N-oxide molecules.

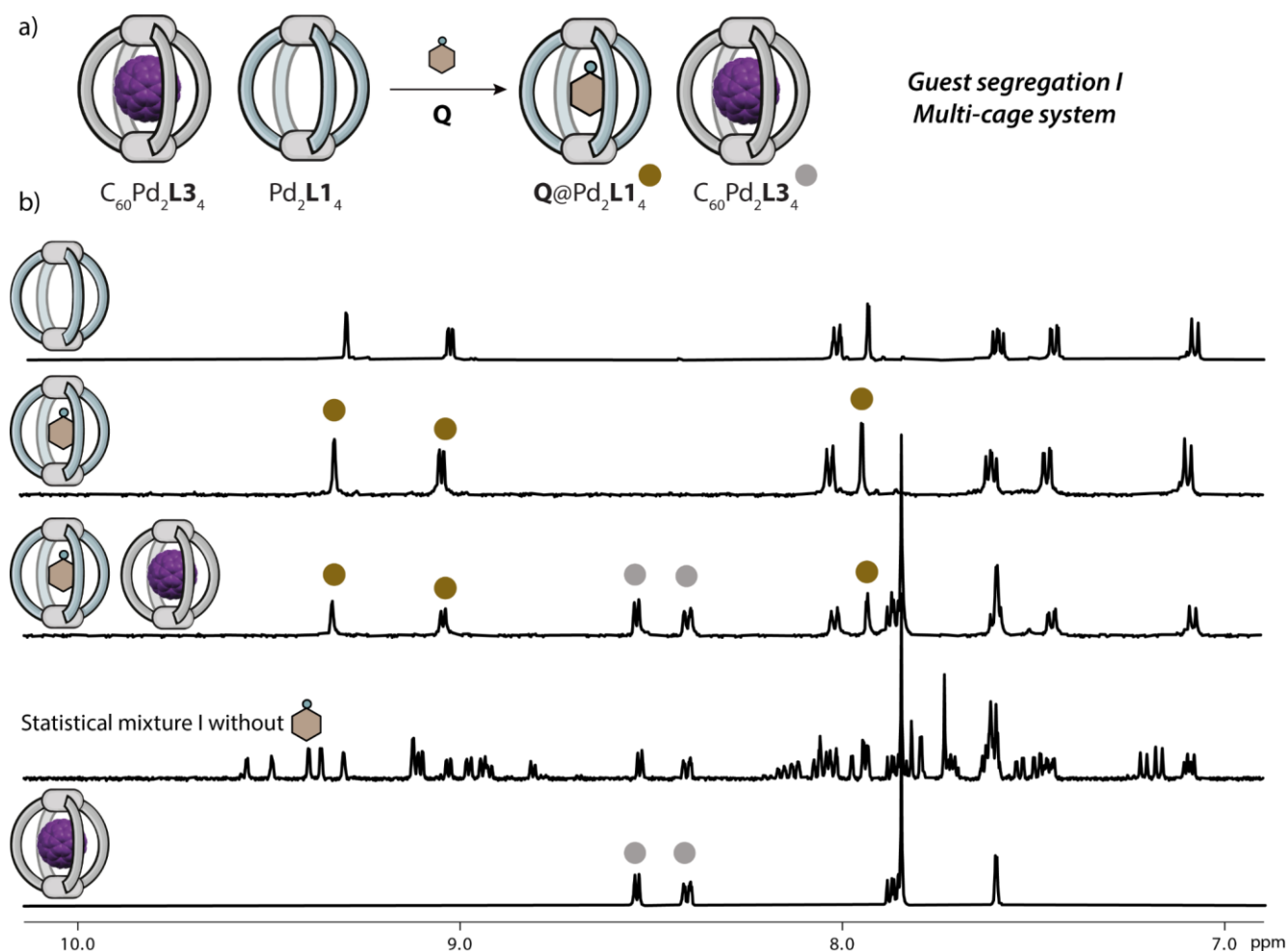


Figure 8: Guest segregation I. a) Schematic representations of the formation of the multi-cage system capable of guest segregation. b) Stacked 1H NMR (CD₃CN, 500 MHz) (top to bottom) of Pd_2L1_4 , $Q@Pd_2L1_4$, self-sorting outcome with **Q1**, self-sorting outcome without **Q** and $C_{60}@Pd_2L3_4$.

In a similar fashion, I realized that the binding of **Q** and **G1**, respectively, in Pd_2L1_4 and $Pd_2L1_2L2_2$ occurred orthogonally (Figure 9). This finding indicated that changes in stoichiometry such as a greater amount of Pd(II) and **L1** with respect to **L2**, did not disrupt the formation of the heteroleptic cage or its host-guest complex (Figure 9b). Herein, in the absence of any guest, Pd_2L1_4 and $Pd_2L1_2L2_2$ could still coexist orthogonally and no other heteroleptic species with a different **L1**:**L2** ratio was formed. In the same manner, when only **G1** is introduced into the mixture containing Pd_2L1_4 and $Pd_2L1_2L2_2$, it was selectively and solely encapsulated within $Pd_2L1_2L2_2$ resulting in the coexistence of $G1@Pd_2L1_2L2_2$ and Pd_2L1_4 . These experiments illustrate guest segregation into separate hosts, where the guest plays a pivotal role in driving the self-sorting process to completion. Thus far, we have observed two hosts coexisting and selectively uptaking respective guests into their cavities, representing the first level of segregation. Building on the insights gained from these experiments, we envisioned the possibility of creating a second level of segregation in a more complex system.

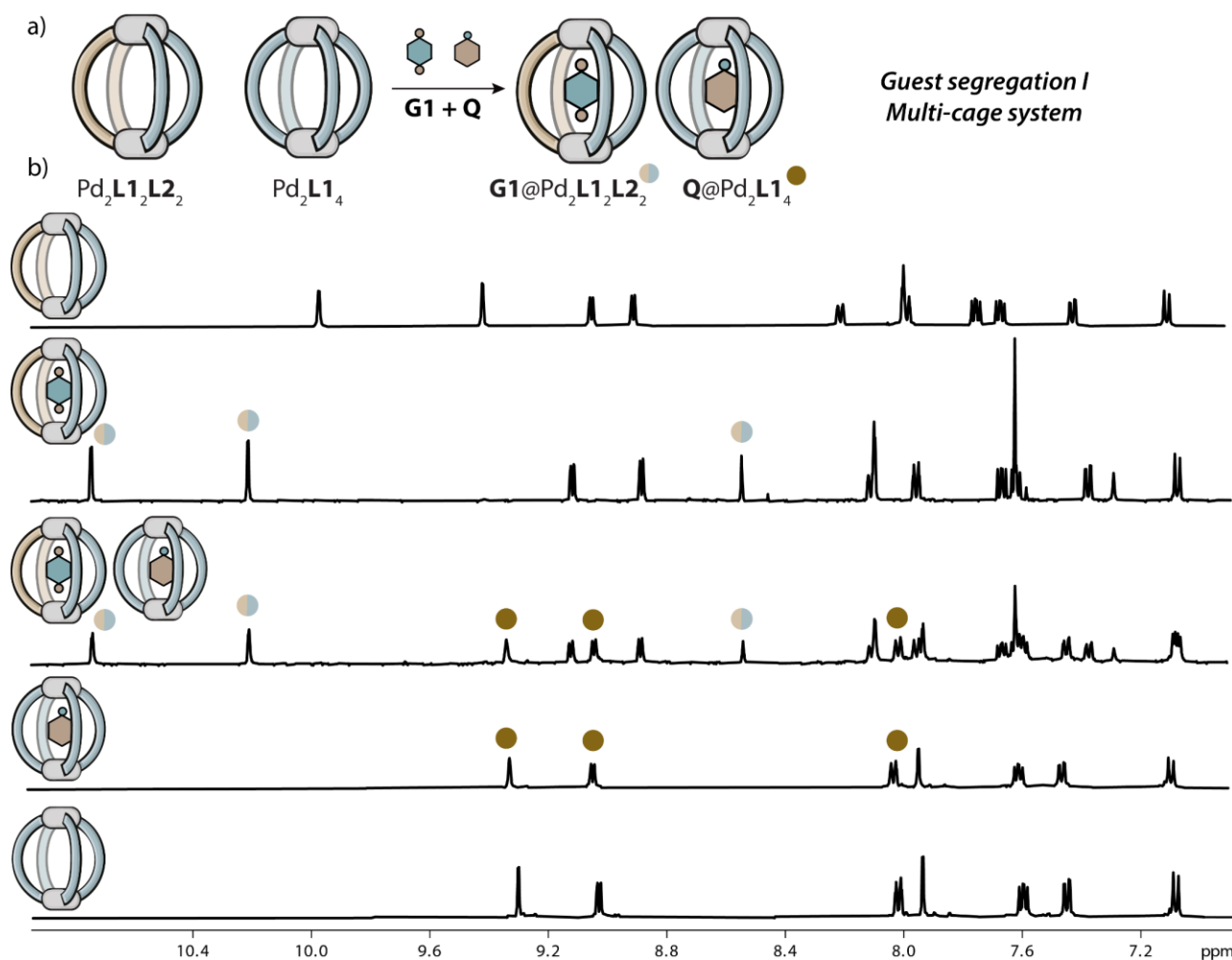


Figure 9: Guest segregation I. a) Schematic representations of the formation of the multi-cage system capable of guest segregation. b) Stacked ^1H NMR (CD₃CN, 500 MHz) (top to bottom) of $\text{Pd}_2\text{L}_1\text{L}_2$, $\text{G1}@Pd_2\text{L}_1\text{L}_2$, self-sorting outcome with **Q1** and **G**, $\text{Q}@Pd_2\text{L}_1$ and Pd_2L_1 .

4. Guest segregation II in multi-cage system

Mixing together Pd_2L_3 and $\text{Pd}_2\text{L}_1\text{L}_2$ in presence of C_{60} and **G1** yields a 1:1 mixture of $\text{C}_{60}@Pd_2\text{L}_3$ and $\text{G1}@Pd_2\text{L}_1\text{L}_2$, as already described. Addition of Pd_2L_1 alone to this mixture would result in a partial fullerene release and the disruption of the first segregation level as described in Figure 3. But mixing **Q** in this system led to novel guest segregation, wherein three cages coexisted, each containing a different guest molecule (Figure 10). Given our prior observation of each host-guest complex's ability to coexist orthogonally, it followed logically that the three host-guest complexes could also do so in this scenario. This represents a case where a population of three assemblies performs a defined function, leveraging the unique characteristics of each cavity. Notably, these assemblies do not undergo further component shuffling, and the self-sorting can be described as *guest-driven narcissistic*, despite one of the assemblies being a heteroleptic species. Of particular interest is the ability to manipulate stoichiometry, leading to an unprecedented level of self-sorting from a 2:1:1 ratio of ligands (**L1/L2/L3**). We had previously described that this can lead to *integrative* self-sorting and it would here result in the formation of a $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_3$ cage. This was never observed with these components. In the first chapter of this thesis we saw that it can also lead to *heteromeric complete* self-sorting, which would yield a discrete mixture of $\text{Pd}_2\text{L}_1\text{L}_2$ and $\text{Pd}_2\text{L}_1\text{L}_3$. This case was also not obtained with the presented ligands. However, I did succeed in obtaining a population of three cages composed of $\text{Q}@Pd_2\text{L}_1$, $\text{G1}@Pd_2\text{L}_1\text{L}_2$, and $\text{C}_{60}@Pd_2\text{L}_3$ (Figure 10b). When combined in a 1:2:1 ratio, a new self-sorting outcome occurs, marking a significant development in the quest of complex systems.

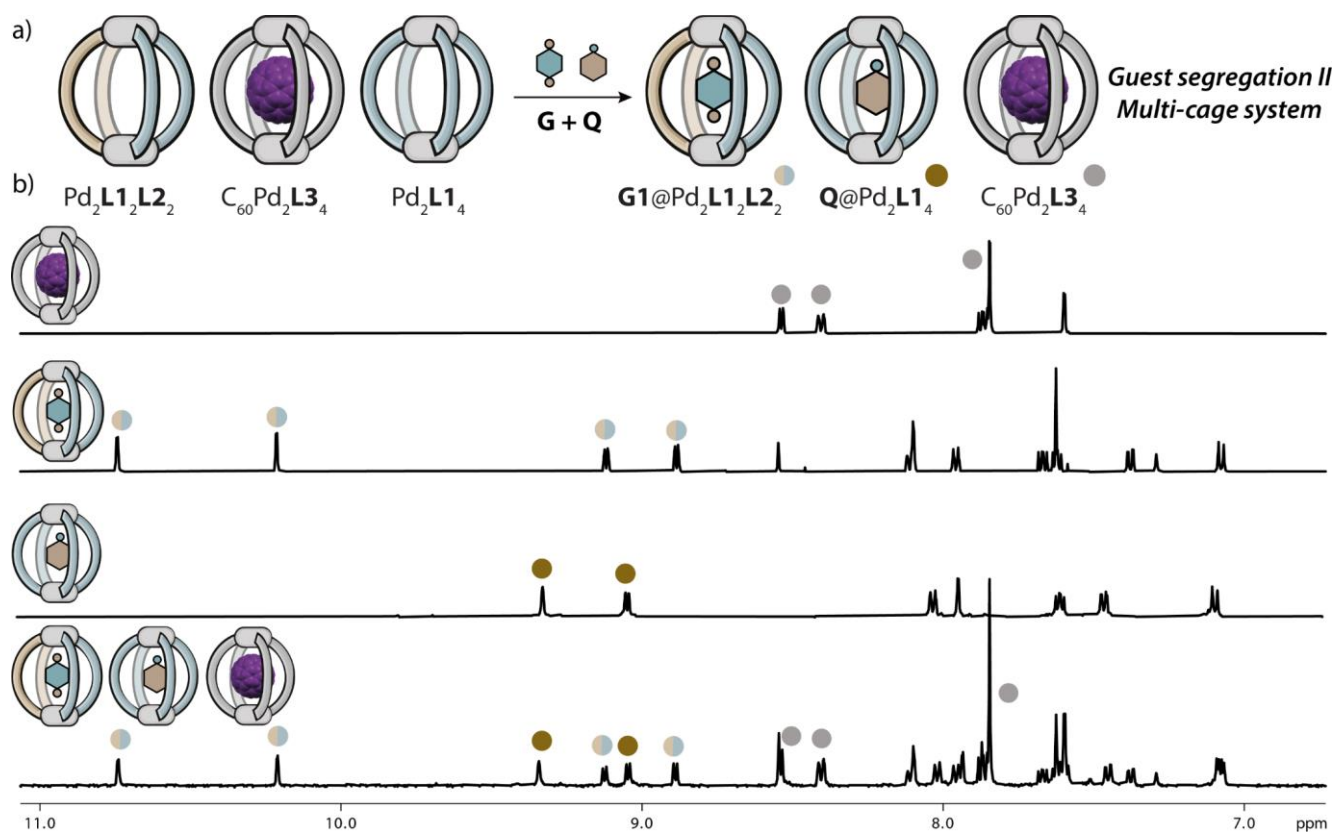


Figure 10: Guest segregation II. a) Schematic representations of the formation of the multi-cage system capable of guest segregation. The three host-guest systems coexist orthogonally. b) Stacked ^1H NMR (CD₃CN, 500 MHz) (top to bottom) of $\text{C}_{60}\text{Pd}_2\text{L3}_4$, $\text{G@Pd}_2\text{L1}_2\text{L2}_2$, $\text{Q@Pd}_2\text{L1}_4$ the final outcome where the three assemblies formed a population of cages capable of segregating guests within their respective cavities.

Conclusion and outlook

In **Chapter II**, I demonstrated the formation of another type of multi-cage system in which fullerene C_{60} acted as the driving force to complete the self-sorting phenomena. This differed from the case of **Chapter I** as a similar 2:1:1 ratio between ligands led to the coexistence of a heteroleptic cage and homoleptic host-guest complex. Additionally, the heteroleptic cage was capable of encapsulating an anionic disulfonate guest in an orthogonal fashion to the fullerene leading to guest segregation in a multi-cage system. It was also showed that very low affinity between host and guest could lead to drastic differences in self-sorting outcomes. Making use of a zwitterionic N-oxide quinuclidine (**Q**) I highlighted the same type of double guest segregation in either narcissistic (homoleptic/homoleptic) or heteroleptic/homoleptic multi-cage systems. Eventually, the combination of the aforementioned processes allowed the creation of a population containing one heteroleptic and two homoleptic species each capable of uptaking a distinct guest leading to the orthogonal coexistence of three host-guest complexes in solution. This could have implications for chemical separation and the use of multi-cage mixtures to selectively extract multiple cargoes from complex mixtures. One could also envisage the use of such phenomenon for dual or sequential catalytic systems making use of the respective cavities of coexisting assemblies in solution, a phenomenon reminiscent of biological systems.

5. Experimental section

General Method

NMR

NMR spectroscopic data was measured on the spectrometers Bruker AV 500 Avance NEO and AV 600 Avance III HD. For ^1H and ^{13}C NMR spectra, chemical shifts were calibrated to the solvent lock signal. Chemical shifts δ are given in ppm, coupling constants J in Hz. The following abbreviations are used to describe signal multiplicity for ^1H NMR spectra: s: singlet, d: doublet, t: triplet, dd: doublet of doublets; dt: doublet of triplets; m: multiplet, br: broad. All proton signals were assigned with the aid of 2D NMR spectra. All spectra were recorded in standard 5 mm NMR tubes at the indicated temperature.

Mass Spectrometry

Mass spectra were measured on Bruker ESI-timsTOF (electrospray ionization-trapped ion mobility-time of flight) and Bruker compact high-resolution LC mass spectrometers (positive mode). For calibration of the TIMS and TOF devices, Agilent ESI-Low Concentration Tuning Mix was used.

Computational analysis

Models of the structures $\text{Pd}_2\text{L1}_2\text{L2}_2$ and $\text{Pd}_3\text{L2}_6$ were constructed using Wavefunction SPARTAN '18.1 The MMFF-optimized model was then optimized on semi-empirical PM6 level of theory without constraints and then further refined by DFT optimization on the $\omega\text{B97X-D/def2-SVP}$ level.

Experimental Procedures

Ligand **L3** was synthesized following procedure described in the literature.

Synthesis of **L1**

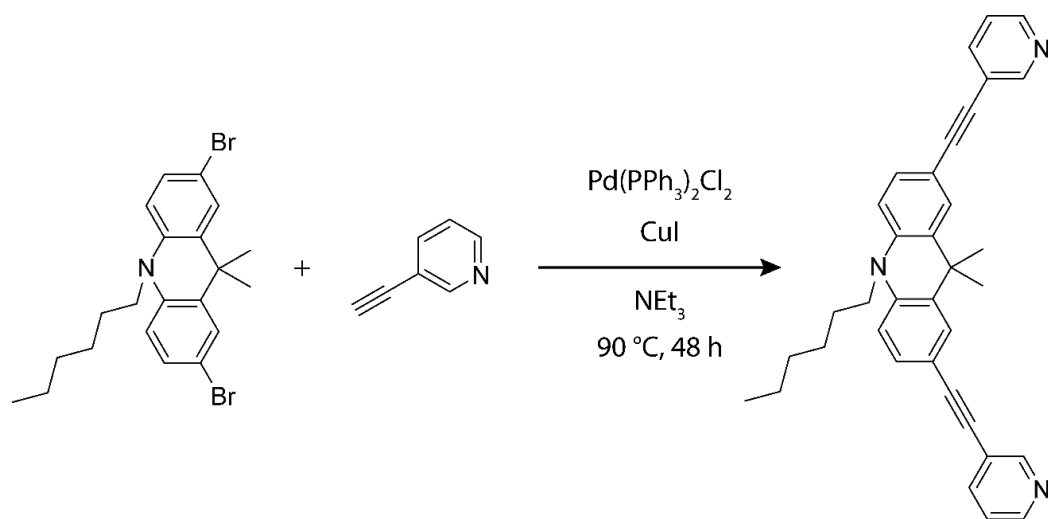


Figure S1: Reaction scheme of the synthesis of **L1**.

2,7-dibromo-9,9-dimethylacridine (350 mg, 0.77 mmol, 1.0 equiv.), 3-ethynylpyridine (238 mg, 2.31 mmol, 3.0 equiv.), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (26.3 mg, 38.5 μmol , 5 mol%) and CuI (17.5 mg, 0.92 mmol, 12 mol%) were suspended in triethylamine (4 ml). After degassing (via freeze-thaw cycles), the mixture was heated to 90 °C and stirred for 48 h. Subsequently, the mixture was cooled to ambient temperature. The solvent was removed under reduced pressure. The crude product was purified by column chromatography (DCM: EtOAc=1:4) and then further purified by GPC to provide the clean **L1** as a light-yellow solid (157 mg, 41 % yield).

^1H NMR (500 MHz, CD_3CN) δ 9.31 (d, J = 1.8 Hz, 2H), 9.03 (d, J = 5.9 Hz, 2H), 8.02 (dt, J = 8.1, 1.6 Hz, 2H), 7.94 (d, J = 1.9 Hz, 2H), 7.60 (dd, J = 8.0, 5.8 Hz, 2H), 7.46 (dd, J = 8.5, 1.9 Hz, 2H), 7.09 (d, J = 8.6 Hz, 2H), 3.92 (t, J = 8.0 Hz, 2H), 1.75 (m, 2H), 1.67 (s, 6H), 1.45 (m, 2H), 1.34 (m, 4H), 0.88 (t, J = 7.0 Hz, 4H).

^{13}C NMR (151 MHz, CD_3CN) δ 152.23, 149.00, 140.98, 138.58, 132.66, 131.08, 128.75, 123.97, 121.17, 114.77, 114.06, 93.56, 85.49, 46.46, 36.55, 31.82, 29.05, 26.89, 26.16, 22.98, 13.90.

HR-ESI MS (m/z) ($\text{C}_{35}\text{H}_{33}\text{N}_3$): measured: 495.2669, calculated: 495.2669

Synthesis of $\text{Pd}_2\text{L1}_4$

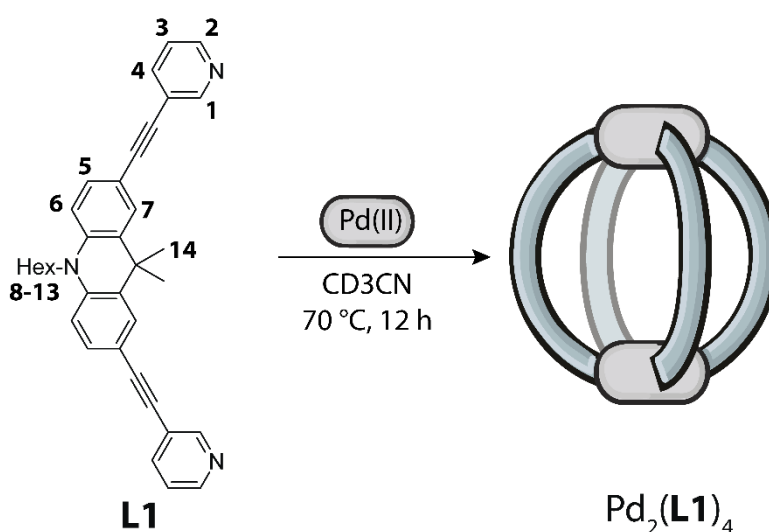


Figure S2: Formation of homoleptic cage $\text{Pd}_2\text{L1}_4$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in a CD_3CN solution of **L1**.

^1H NMR (600 MHz, CD_3CN) δ 9.28 (d, J = 1.9 Hz, 1H), 9.01 (dd, J = 5.9, 1.3 Hz, 1H), 8.00 (dt, J = 8.0, 1.6 Hz, 1H), 7.92 (d, J = 2.0 Hz, 1H), 7.58 (dd, J = 8.0, 5.9 Hz, 1H), 7.43 (dd, J = 8.4, 2.0 Hz, 1H), 7.06 (d, J = 8.6 Hz, 1H), 3.93 – 3.87 (m, 1H), 1.77 – 1.68 (m, 1H), 1.42 (q, J = 7.5 Hz, 1H), 1.37 – 1.26 (m, 2H), 0.86 (t, J = 7.1 Hz, 1.5H).

^{13}C NMR (151 MHz, CD_3CN) δ 152.38, 149.60, 142.80, 141.03, 132.37, 132.29, 131.94, 129.81, 129.29, 127.96, 125.29, 117.89, 114.26, 113.49, 97.49, 83.35, 46.72, 36.64, 31.76, 30.65, 26.71, 26.01, 22.93, 13.85

HR ESI-MS (m/z): measured for $[\text{Pd}_2\text{L1}_4]^{4+}$: 548.228, Calculated: 548.225

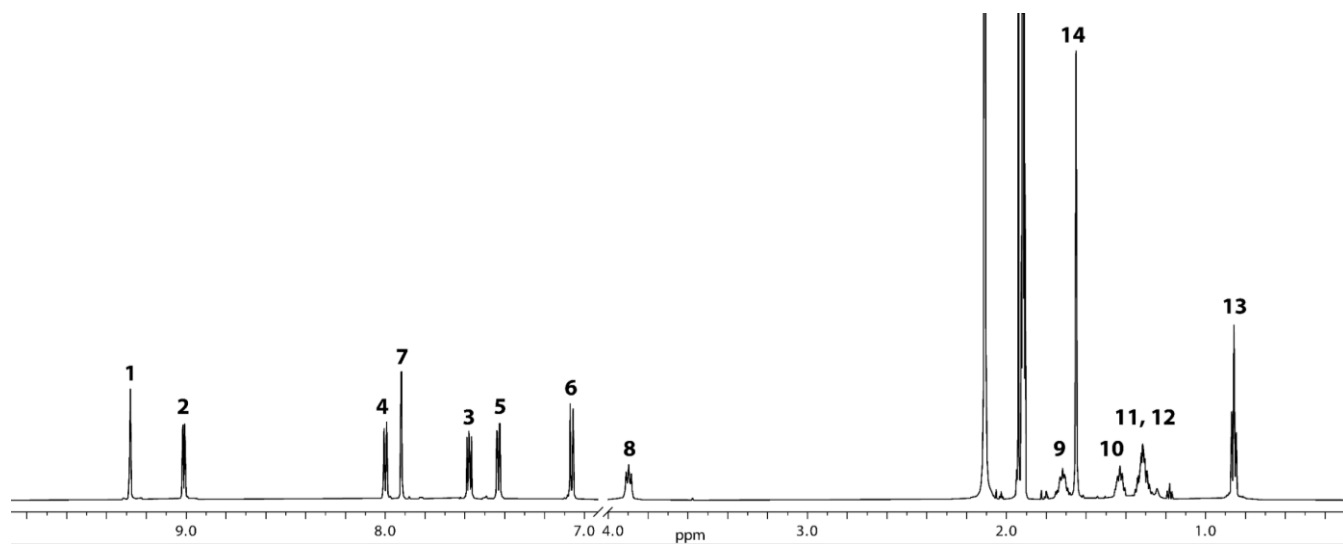


Figure S3: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_2\text{L1}_4$.

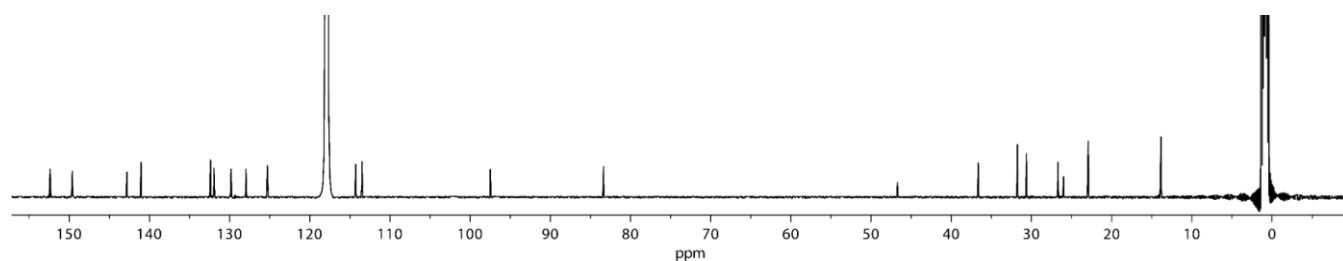


Figure S4: ^{13}C NMR spectrum (171 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_2\text{L1}_4$.

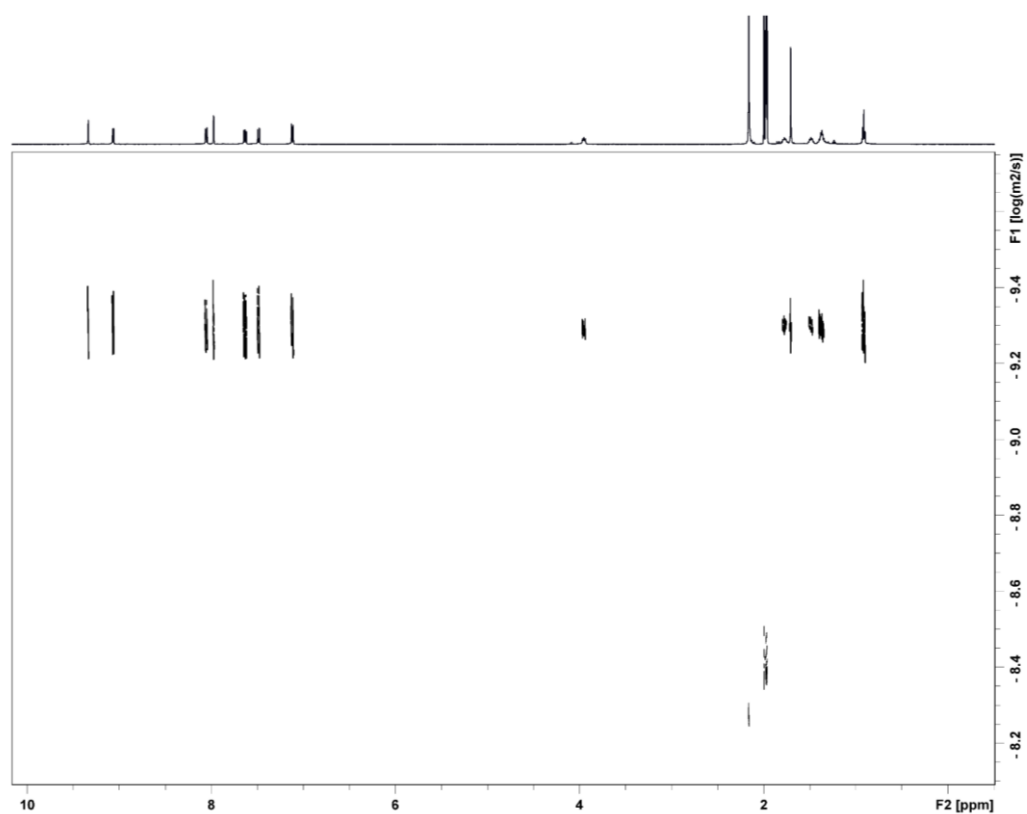


Figure S5: ^1H -DOSY spectrum (500 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_2\text{L1}_4$. $D = 5.18 \cdot 10^{-10} \text{ m}^2 \cdot \text{s}^{-1}$, $R_h = 1.26 \text{ nm}$.

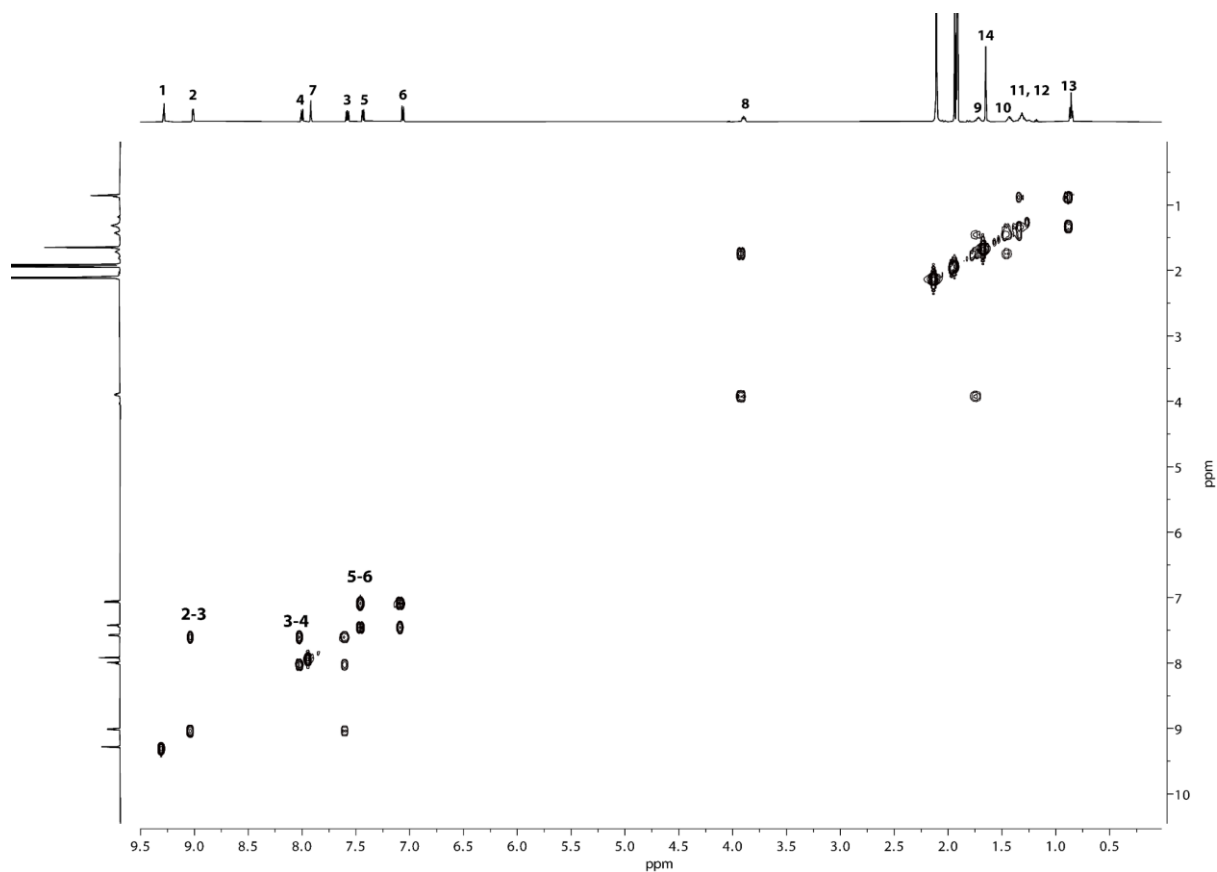


Figure S6: ^1H - ^1H COSY spectrum (500 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_2\text{L14}$.

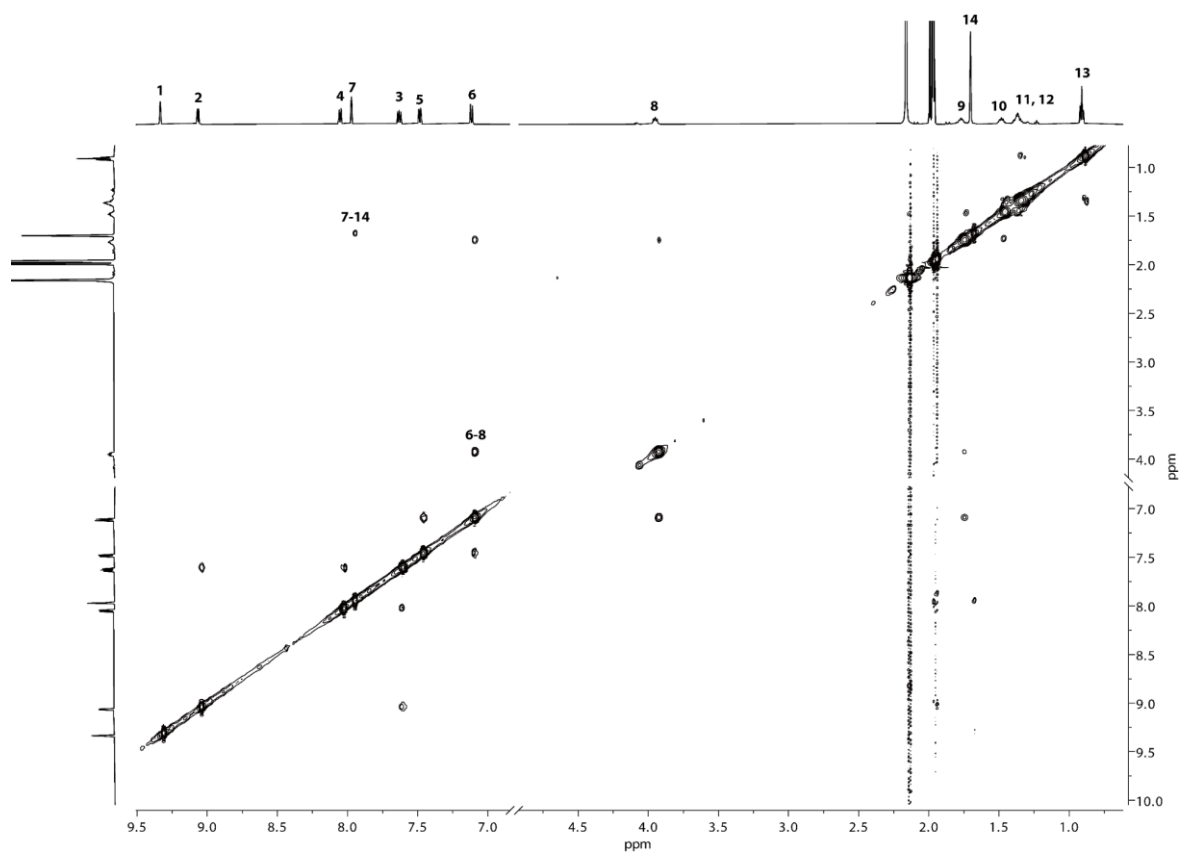


Figure S7: ^1H - ^1H NOESY spectrum (500 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_2\text{L14}$.

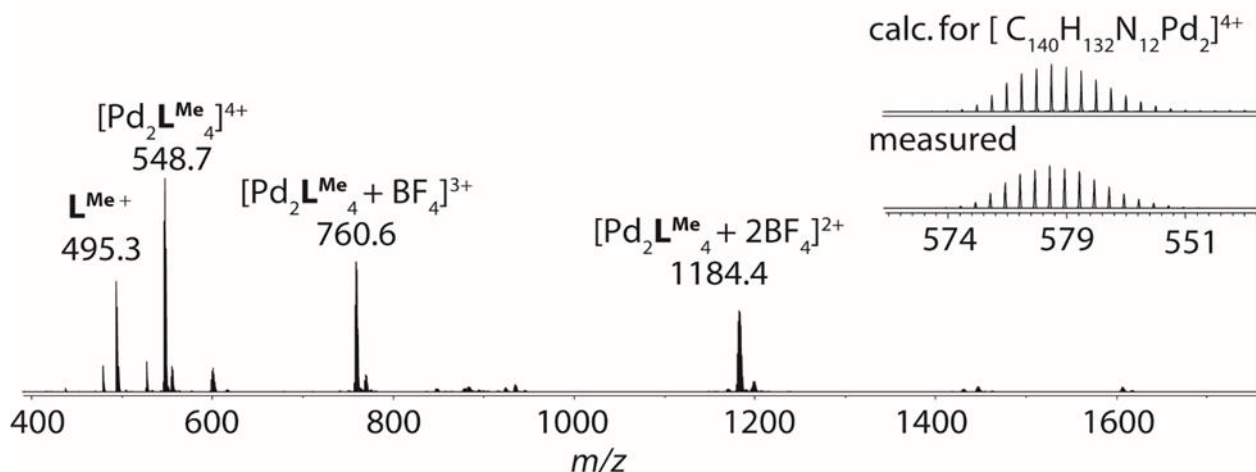


Figure S8: ESI-MS spectrum of a MeCN solution of **L1** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{L1}_4 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{L1}_4]^{4+}$ are shown in the inset.

Synthesis of L2

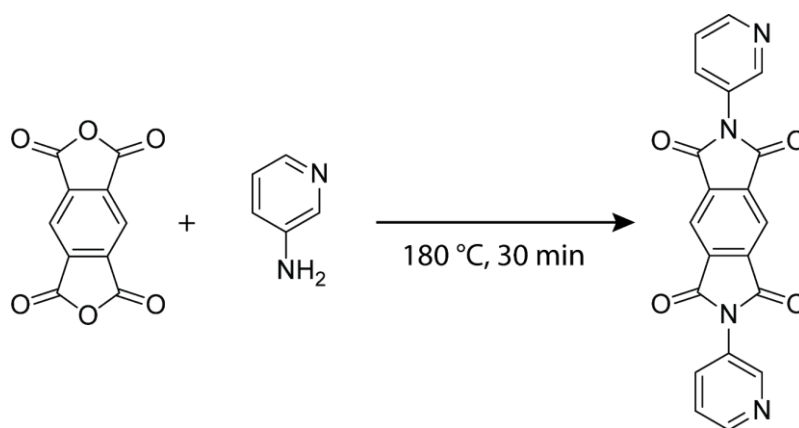


Figure S9: Reaction scheme for the synthesis of **L2**.

Under a nitrogen atmosphere, bis-pyridyl ligand **L3** was prepared from commercially available bis-anhydride (300 mg, 1.40 mmol, 1 eq.) and powdered 3-aminopyridine (3.88 g, 42 mmol, 30 eq.) by heating the mixture of solids without solvent in a preheated oil bath to 180 °C for 30 min. After the black melt cooled to room temperature, it was taken up into 10 mL DCM, sonicated and the suspension was immediately subjected to flash column chromatography on silica gel (0–2 % MeOH in CHCl_3) to give the crude product. This was further purified via recycling gel permeation chromatography and the solvent was removed under reduced pressure to yield the desired product as a colorless powder (288.2 mg, 57 %)

Because of its very low solubility in acetonitrile, the full NMR characterization is given through the assembly formation.

HR-ESI MS (m/z) (L3**+H):** measured: 371.0742, calculated: 371.0723

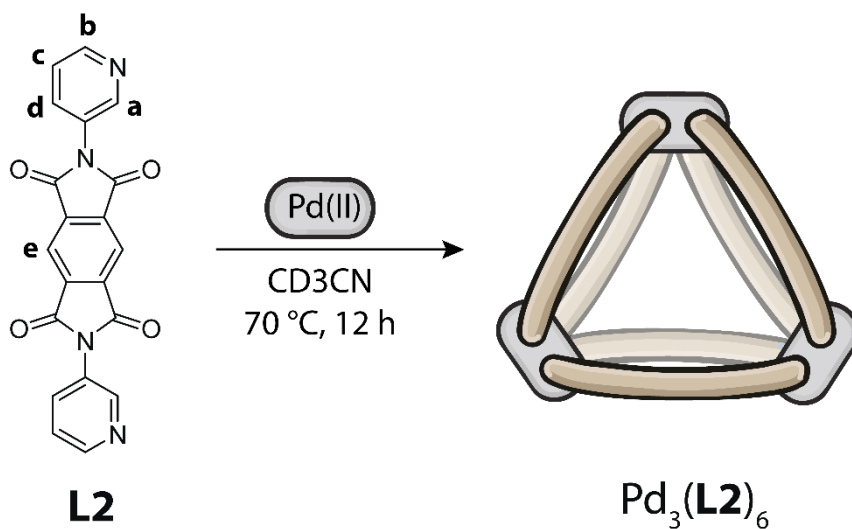
Synthesis of Pd_3L_2_6 

Figure S10: Formation of homoleptic cage Pd_3L_2_6 upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in a CD_3CN solution of **L2**.

^1H NMR (500 MHz, CD_3CN) δ 9.83 (s, 1H), 9.17 (d, $J = 5.8$ Hz, 1H), 8.22 (ddd, $J = 8.4, 2.2, 1.2$ Hz, 1H), 8.00 (s, 1H), 7.83 (dd, $J = 8.4, 5.7$ Hz, 1H).

^{13}C NMR (151 MHz, CD_3CN) δ 164.97, 150.48, 148.58, 137.79, 137.65, 131.47, 128.36, 119.89, 117.89.

HR-ESI MS (m/z) measured for $[\text{Pd}_3\text{L}_2_6]^{6+}$: 423.5189, calculated: 423.5225.

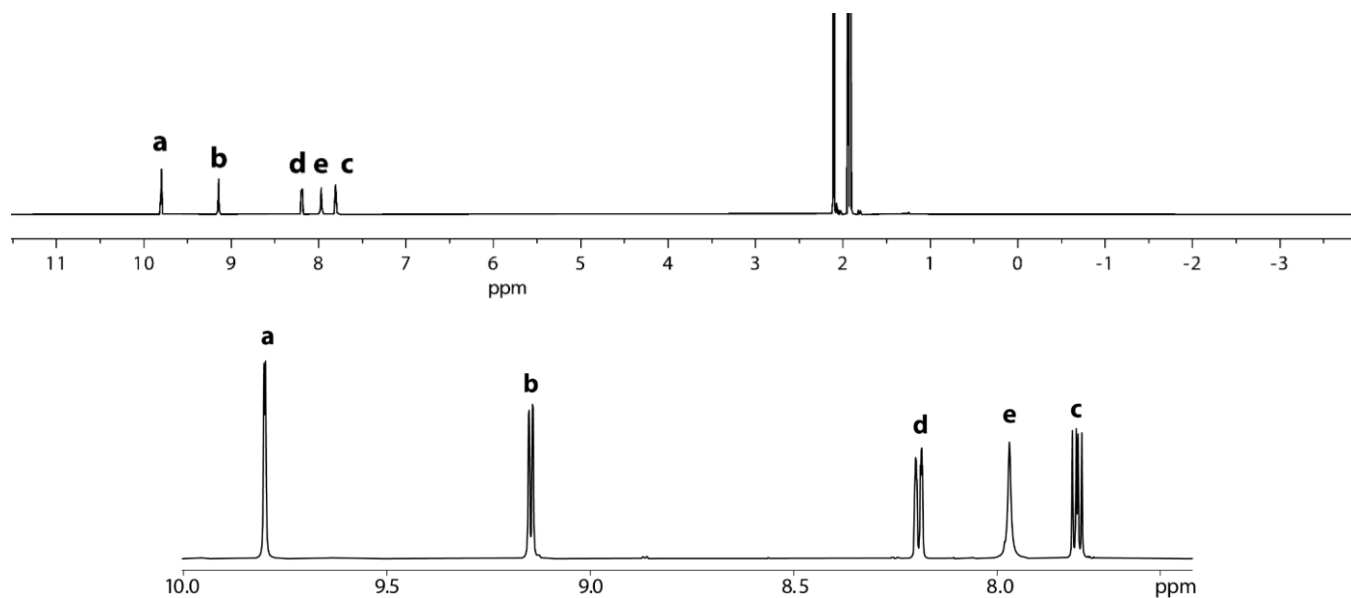


Figure S11: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of homoleptic cage Pd_3L_2_6 .

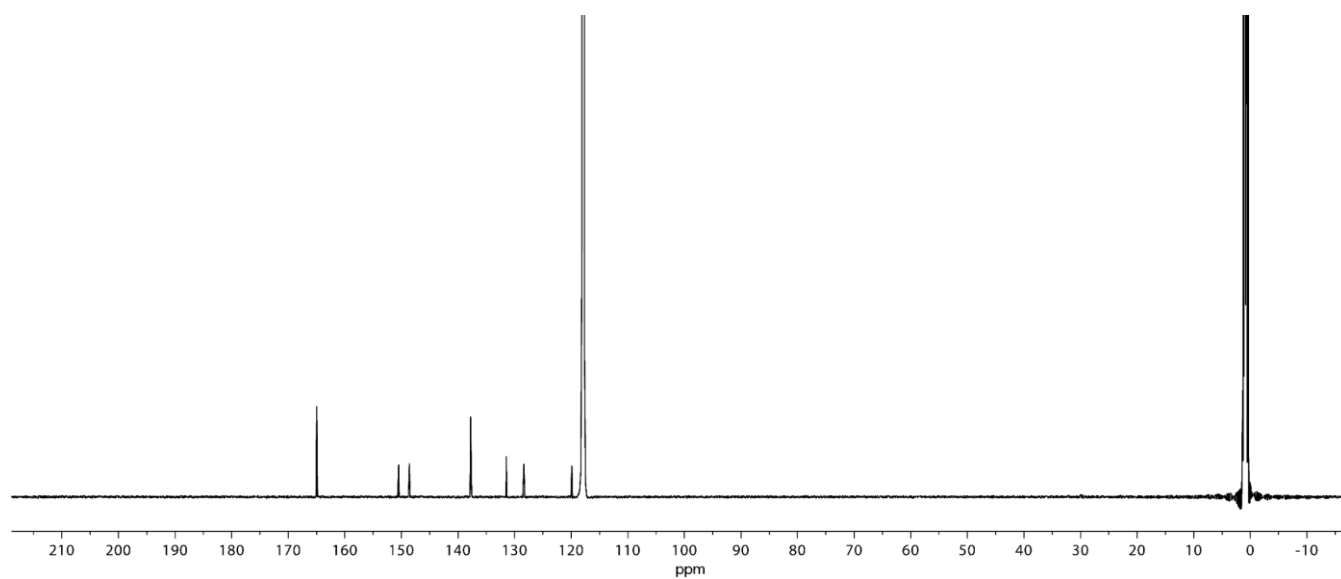


Figure S12: ^{13}C NMR spectrum (171 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_3\text{L}_2\mathbf{6}$.

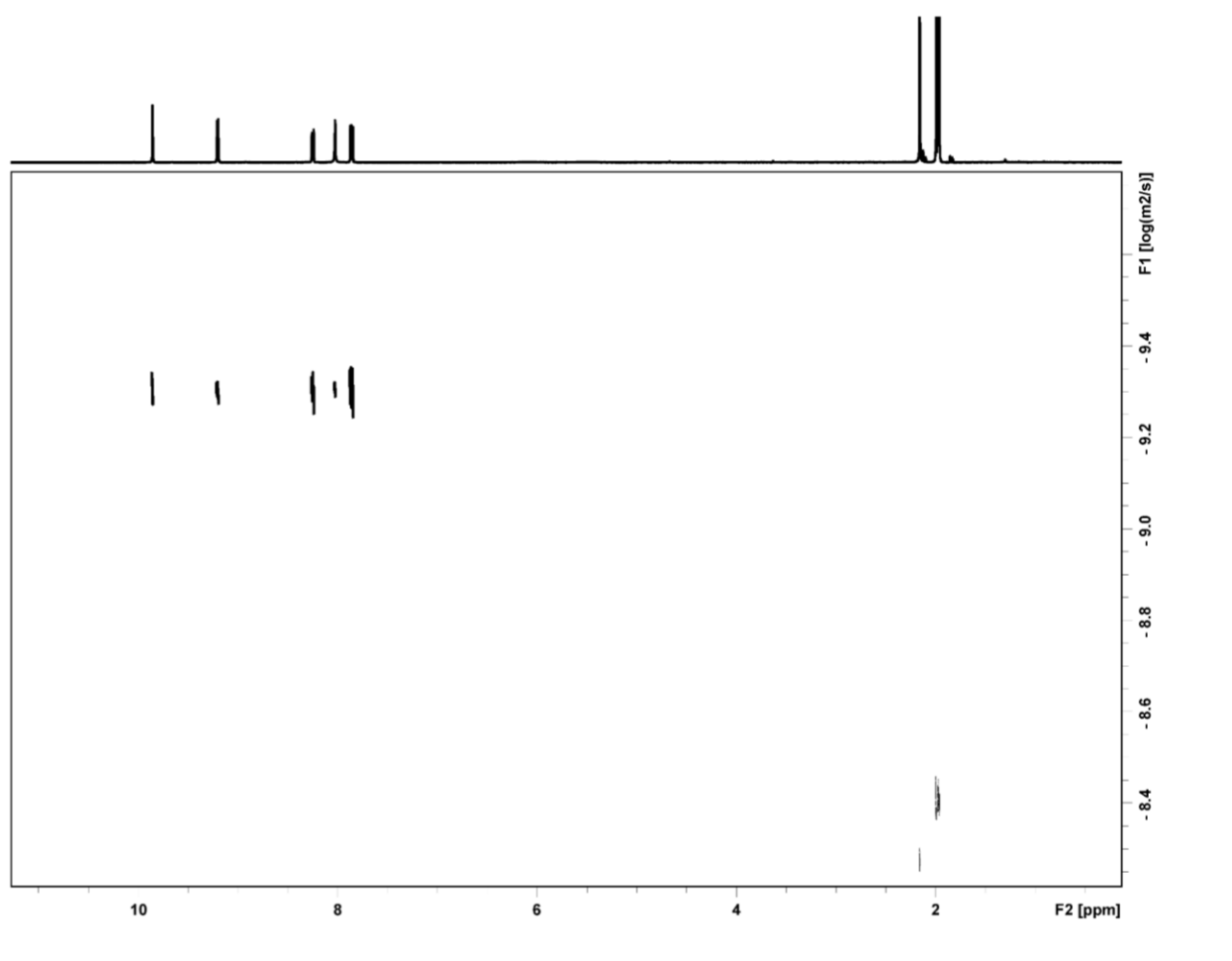


Figure S13: ^1H -DOSY spectrum (500 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_3\text{L}_2\mathbf{6}$. $D = 4.98 \cdot 10^{-10} \text{ m}^2 \cdot \text{s}^{-1}$, $R_h = 1.31 \text{ nm}$.

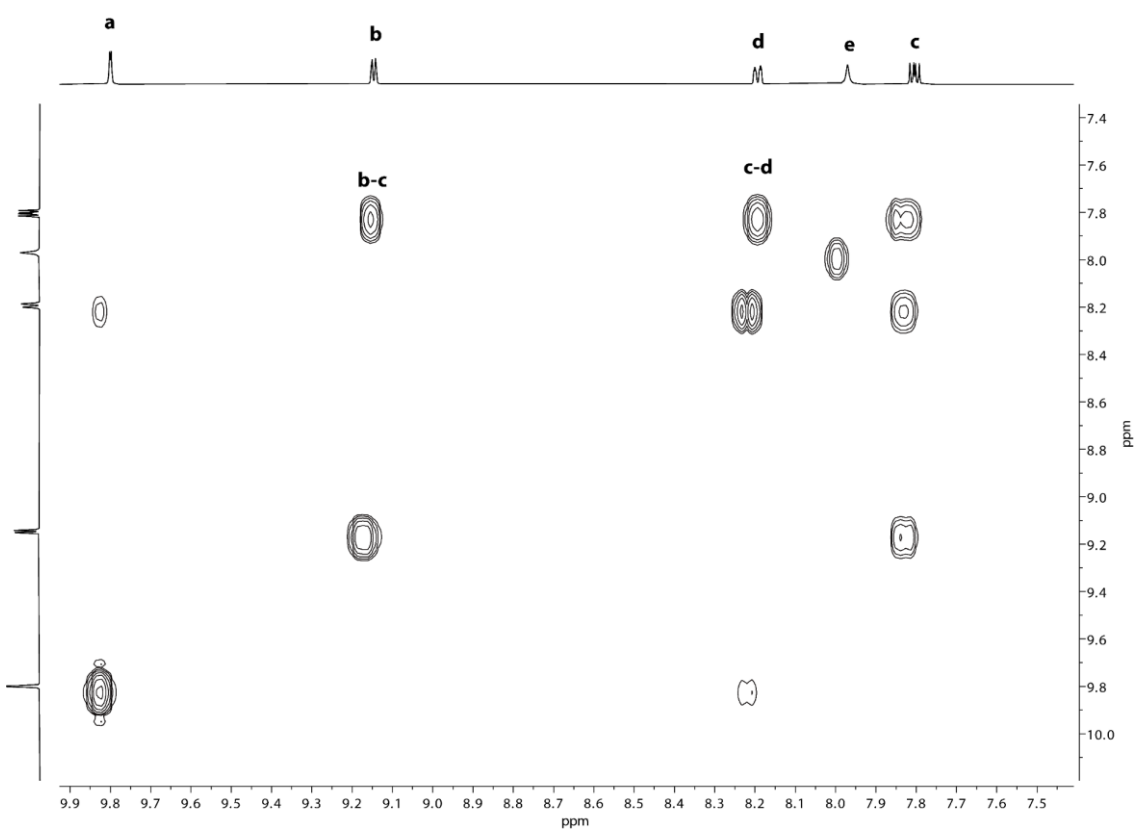


Figure S14: ^1H - ^1H COSY spectrum (500 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_3\text{L}_2\mathbf{6}$.

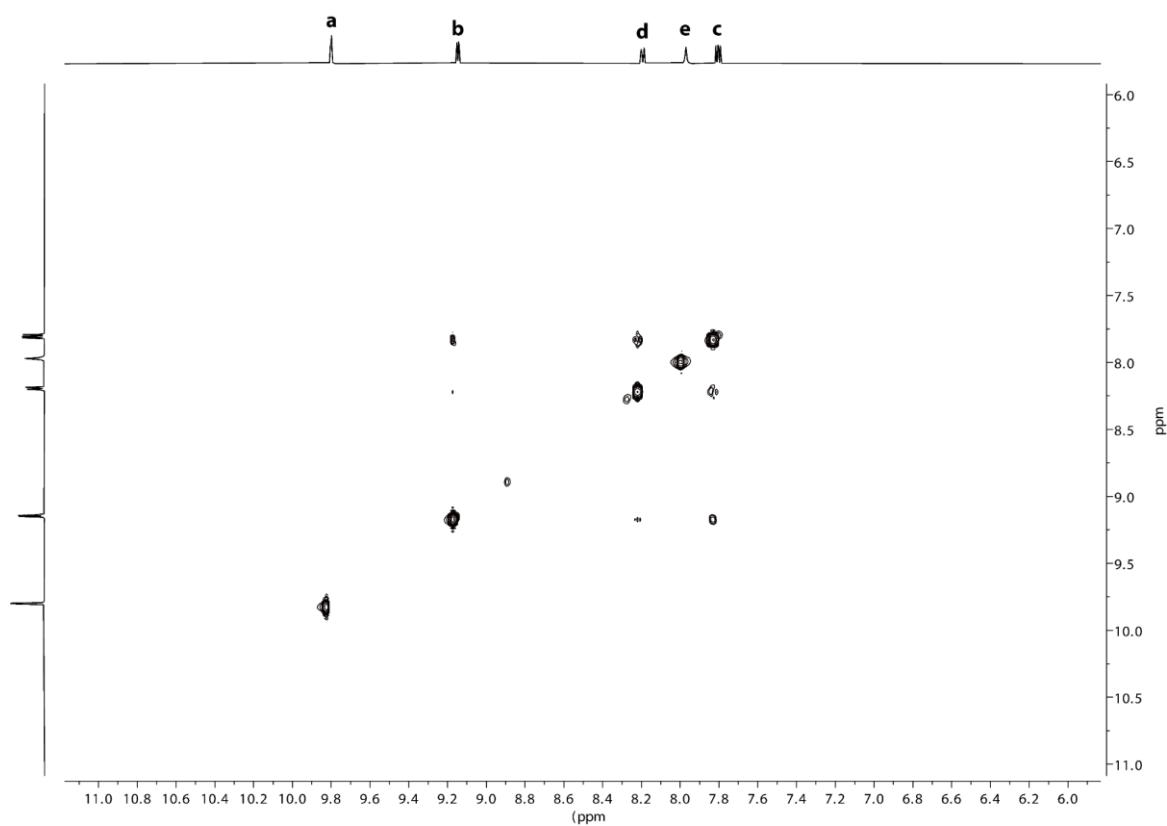


Figure S16: ^1H - ^1H NOESY spectrum (500 MHz, 298K, CD_3CN) of homoleptic cage $\text{Pd}_3\text{L}_2\mathbf{6}$.

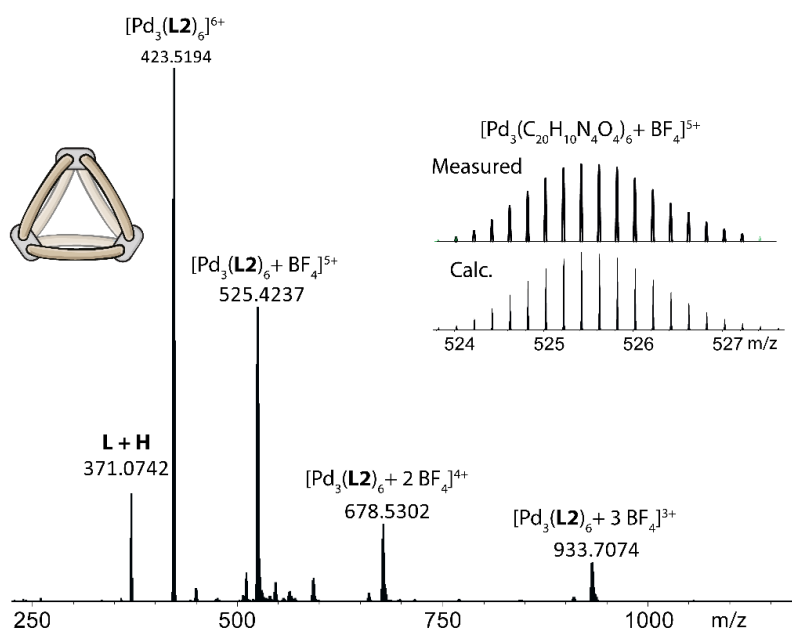


Figure S17: ESI-MS spectrum of a MeCN solution of **L2** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_3\text{L}_2\text{L}_6 + n\text{BF}_4]^{(6-n)+}$ with $n=0-3$. The observed and calculated isotopic patterns of $[\text{Pd}_3\text{L}_2\text{L}_6 + \text{BF}_4]^{5+}$ are shown in the inset.

Synthesis of $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$

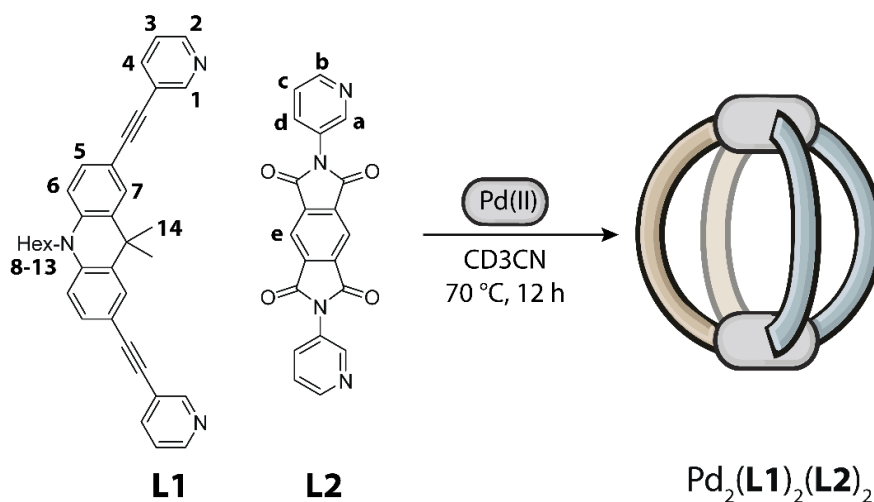


Figure S18: Formation of homoleptic cage $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in a CD_3CN solution of **L1** and **L2**.

^1H NMR (500 MHz, CD_3CN) δ 9.95 (d, $J = 2.2$ Hz, 1H), 9.39 (d, $J = 1.8$ Hz, 1H), 9.02 (dd, $J = 5.9, 1.3$ Hz, 1H), 8.88 (dd, $J = 5.8, 1.2$ Hz, 1H), 8.19 (ddd, $J = 8.2, 2.2, 1.2$ Hz, 1H), 8.01 – 7.93 (m, 2H), 7.73 (dd, $J = 8.2, 5.7$ Hz, 1H), 7.68 – 7.61 (m, 1H), 7.40 (dd, $J = 8.5, 1.9$ Hz, 1H), 7.09 (d, $J = 8.5$ Hz, 1H), 3.97 – 3.91 (m, 1H), 1.78 – 1.70 (m, 1H), 1.49 (s, 2H), 1.48 – 1.43 (m, 1H), 1.39 – 1.29 (m, 2H), 0.89 (t, $J = 7.0$ Hz, 1.5H).

^{13}C NMR (151 MHz, CD_3CN) δ 153.68, 150.76, 149.18, 148.90, 141.53, 141.22, 137.96, 137.86, 132.60, 131.72, 130.83, 128.29, 128.11, 125.14, 117.90, 114.16, 113.55, 97.48, 83.62, 46.58, 36.52, 32.69, 31.76, 28.49, 26.75, 26.11, 22.93, 13.85

HR-ESI MS (m/z) measured for $[\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2]^{4+}$: 486.1212, calculated: 486.1207

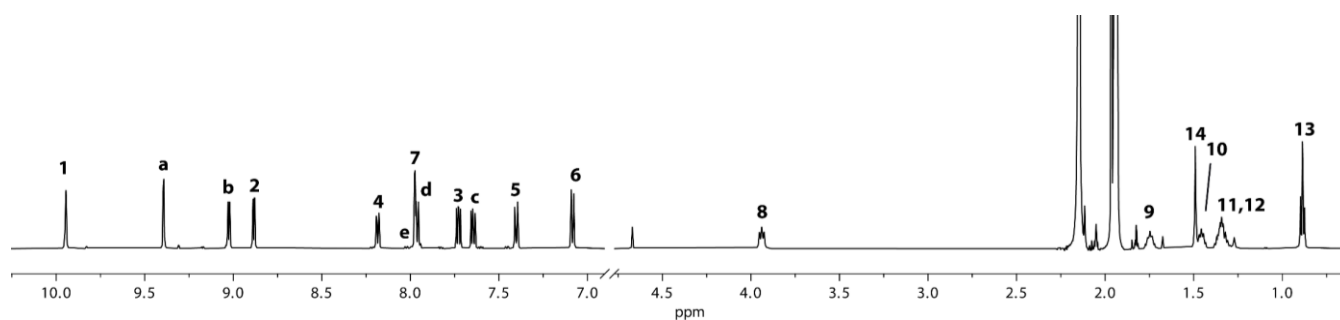


Figure S19: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$.

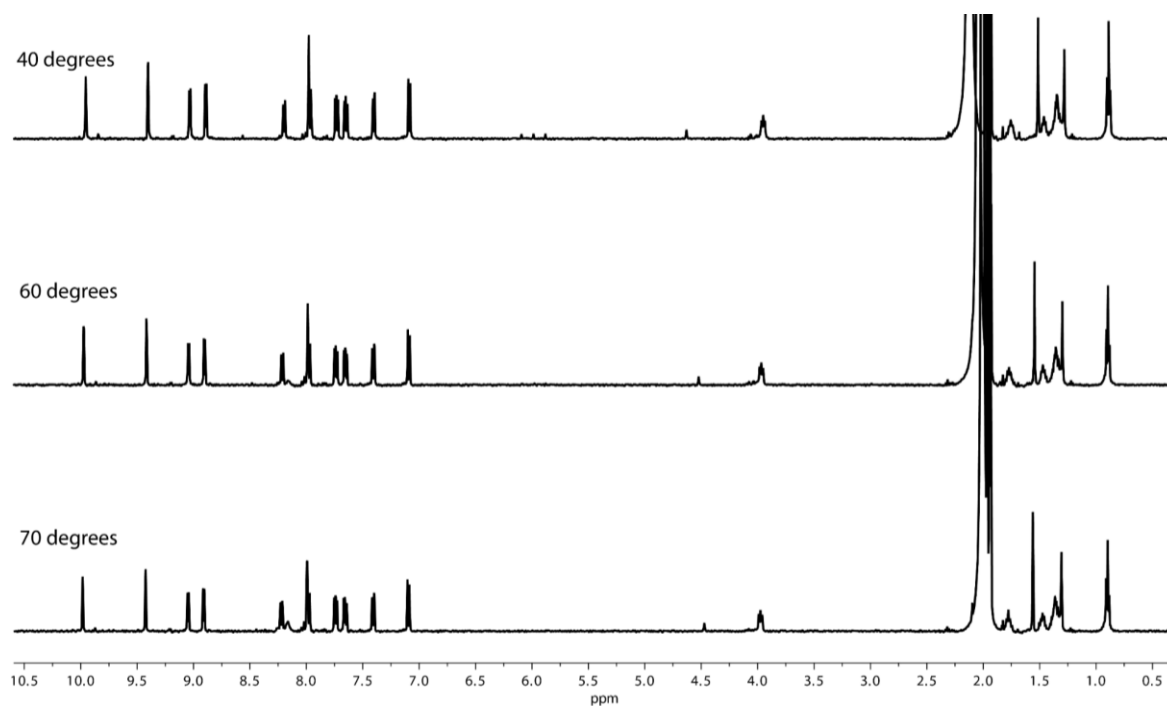


Figure S20: Variable temperature ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$.

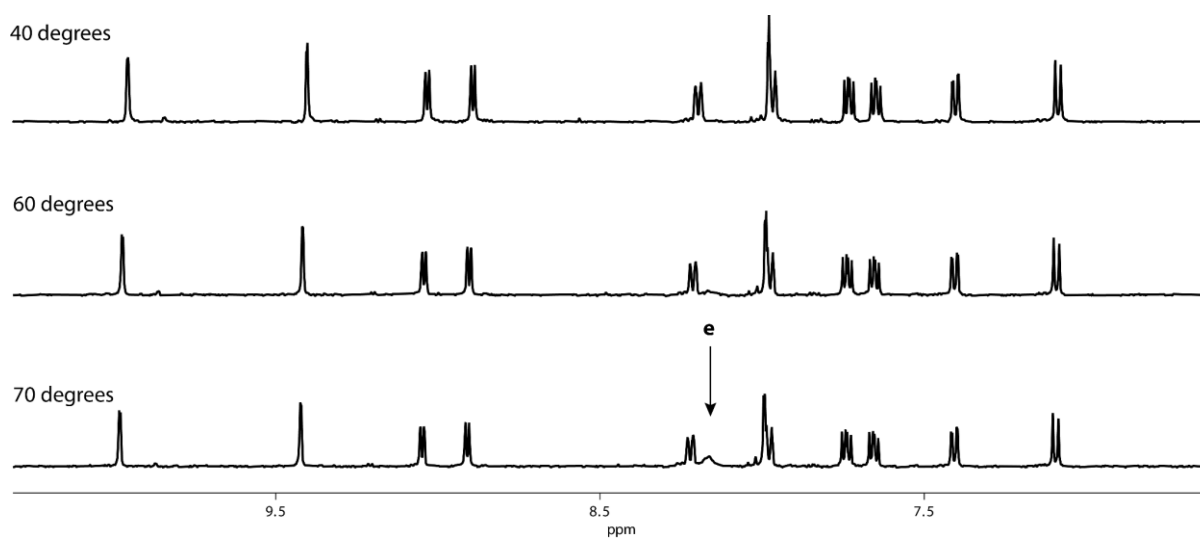


Figure S21: Variable temperature ^1H NMR spectrum (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of heteroleptic cage $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$.

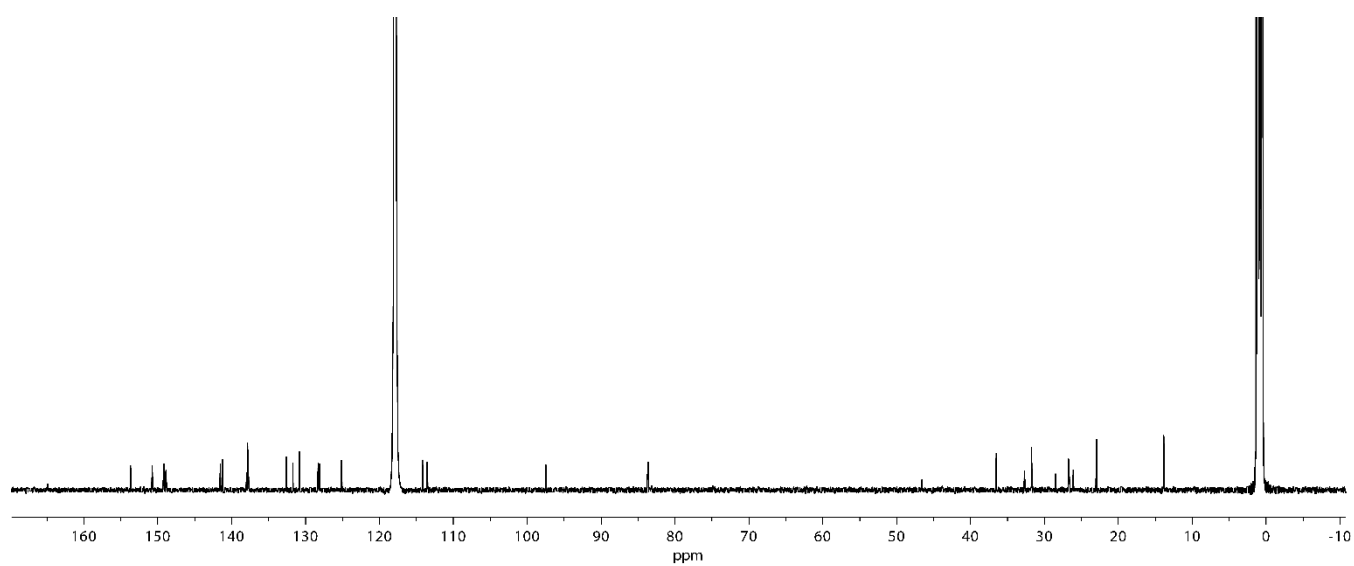


Figure S22: ^{13}C NMR spectrum (171 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$.

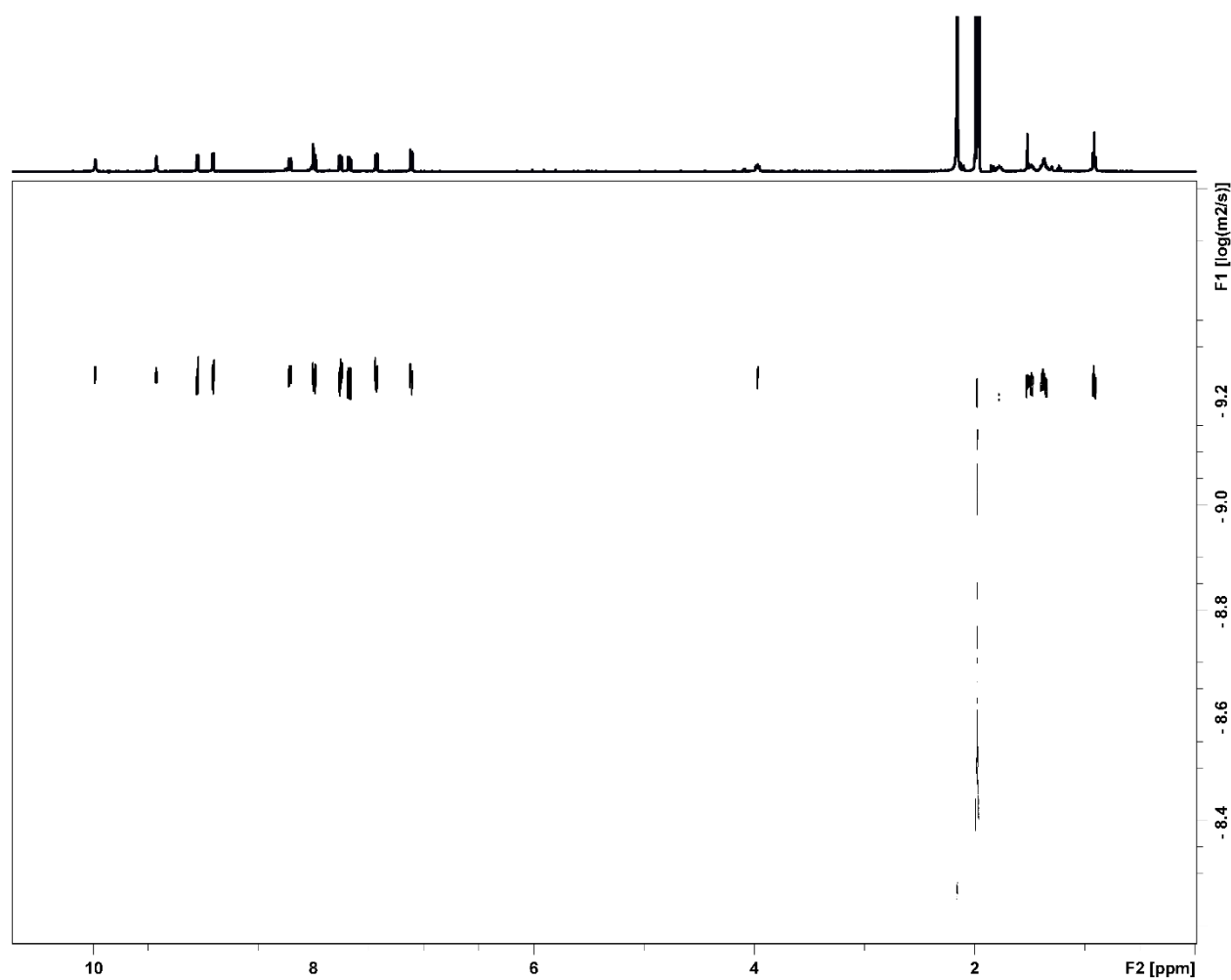


Figure S23: ^1H DOSY NMR spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{L}_1\text{L}_2\text{L}_2$. $D = 5.64 \cdot 10^{-10} \text{ m}^2 \cdot \text{s}^{-1}$, $R_h = 1.15 \text{ nm}$.

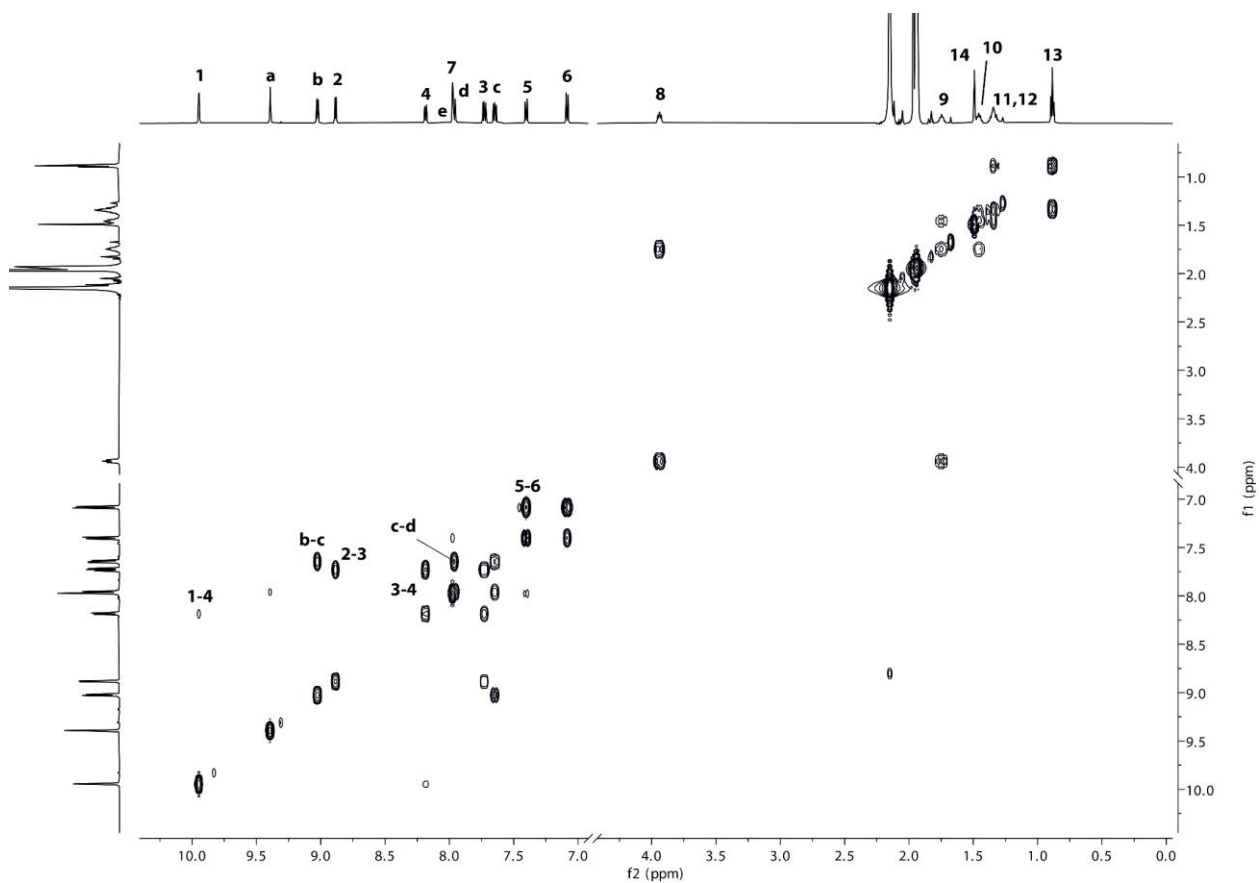


Figure S24: ^1H COSY NMR spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{L1}_2\text{L2}_2$.

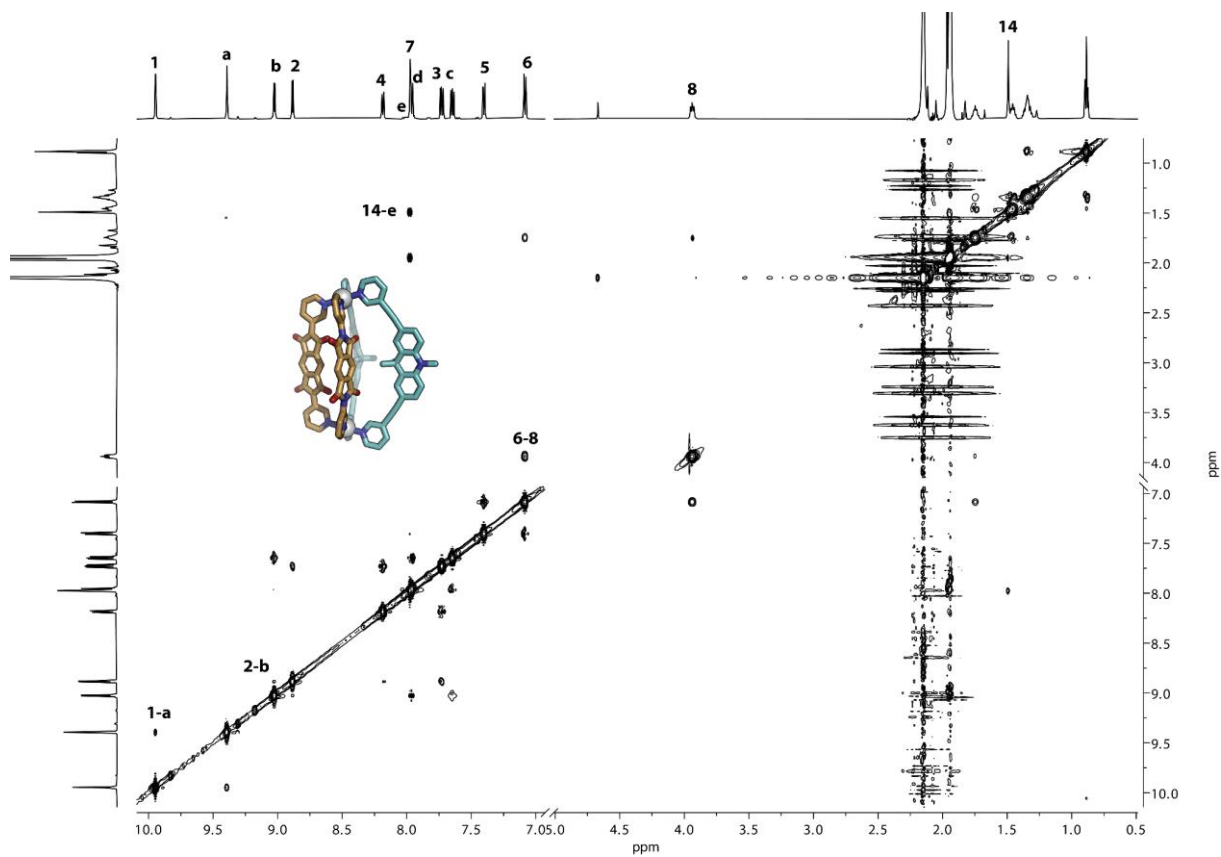


Figure S25: ^1H NOESY NMR spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{L1}_2\text{L2}_2$.

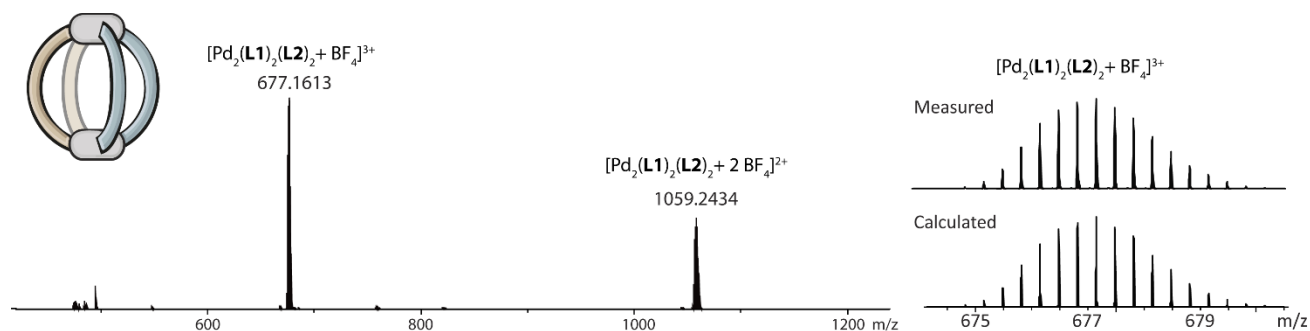


Figure S26: ESI-MS spectrum of a MeCN solution of **L1** and **L2** with 0.5 equiv. Pd(II). The observed peaks correspond to $[\text{Pd}_2\text{L1L2}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=1-2$. The observed and calculated isotopic patterns of $[\text{Pd}_2\text{L1L2}_2 + \text{BF}_4]^{3+}$ are shown in the inset.

Encapsulation of G1/G2 in $\text{Pd}_2\text{L1L2}_2$

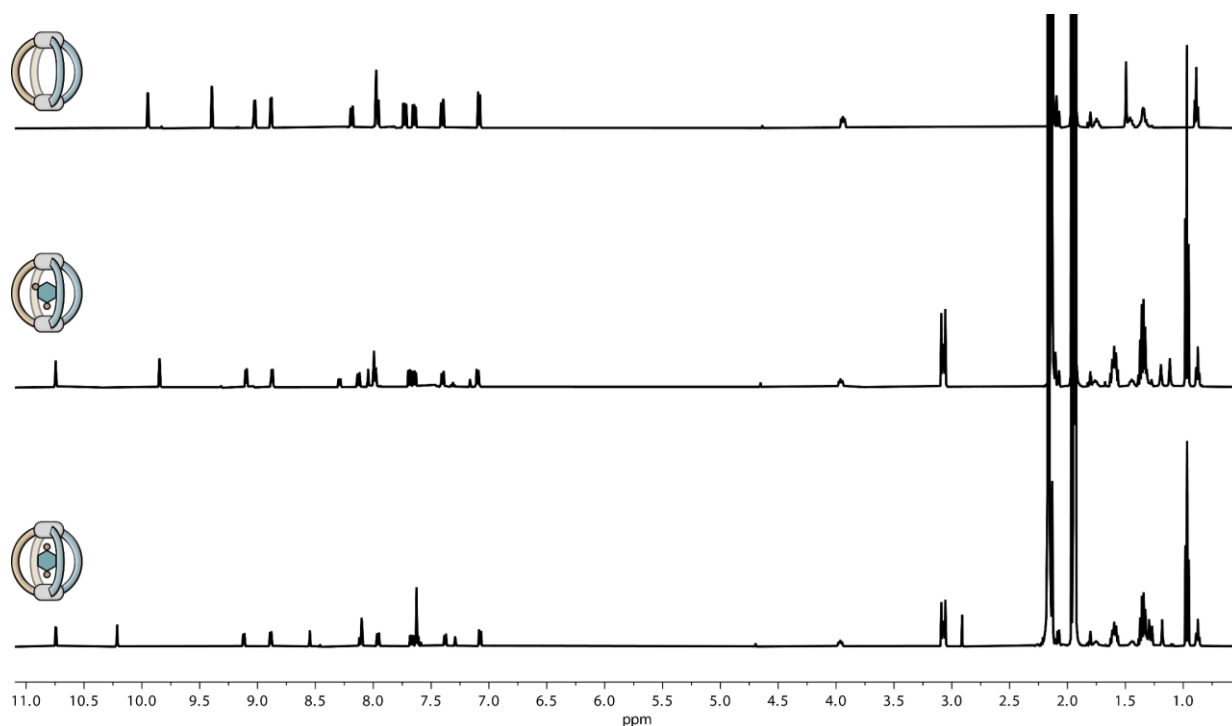


Figure S27: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) stack of heteroleptic cage $\text{Pd}_2\text{L1L2}_2$ and after encapsulation of 1,3/1,4-benzene disulfonate guest.

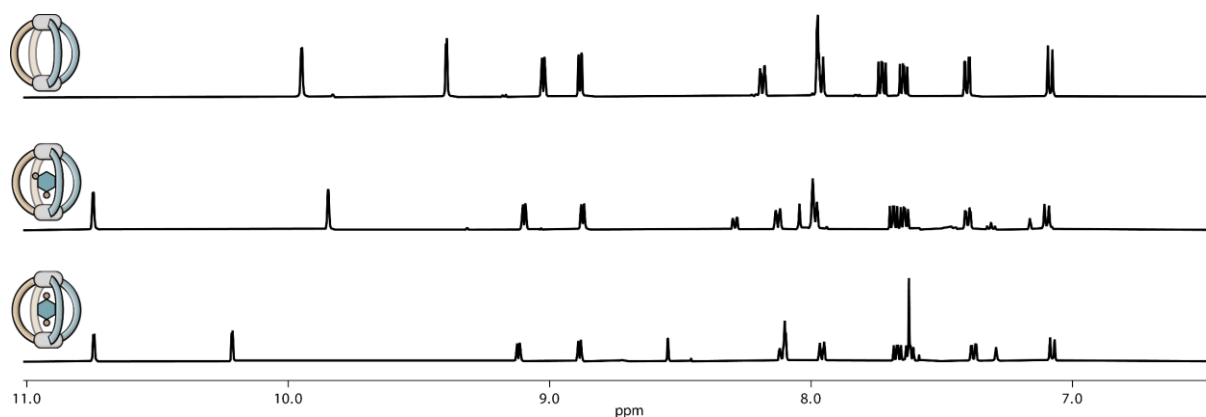


Figure S28: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) stack enlarged on the aromatic region of heteroleptic cage $\text{Pd}_2\text{L1L2}_2$ and after encapsulation of 1,3/1,4-benzene disulfonate guest.

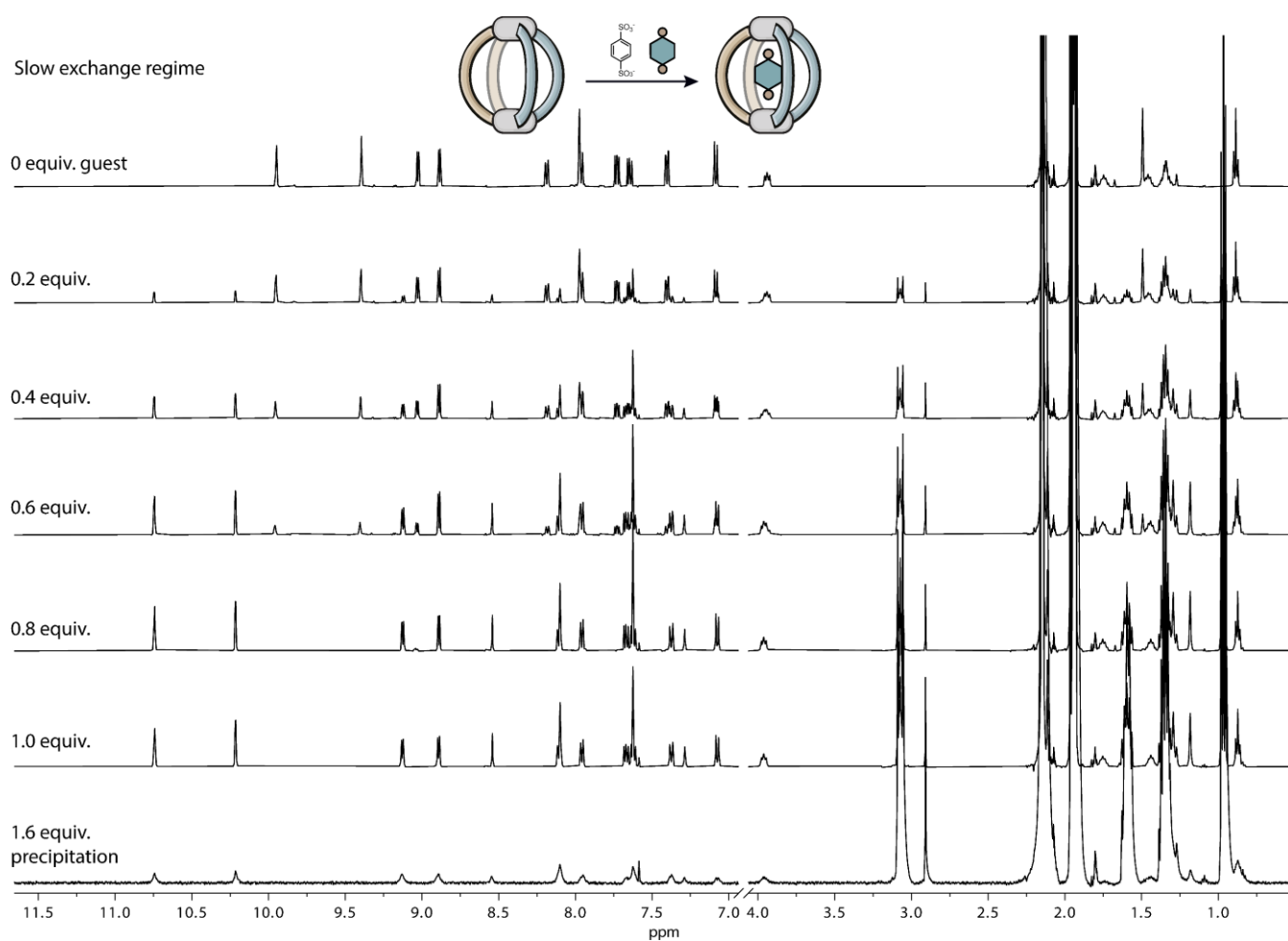


Figure S29: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the titration of **G1** into a solution of heteroleptic cage $\text{Pd}_2\text{L}_1\text{L}_2$. A slow exchange regime can be observed.

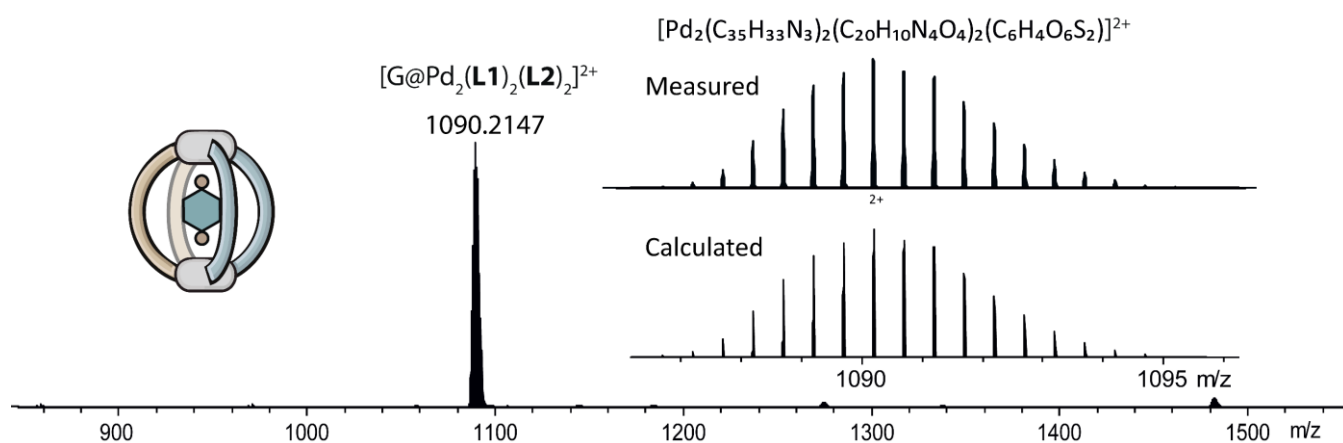


Figure S30: ESI-MS spectrum of a MeCN solution of **L1** and **L2** with 0.5 equiv. $\text{Pd}(\text{II})$ and 1 equiv. of **G**. The observed peak correspond to $[\text{G}@\text{Pd}_2\text{L}_1\text{L}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0$. The observed and calculated isotopic patterns of $[\text{G}@\text{Pd}_2\text{L}_1\text{L}_2]^{2+}$ are shown in the inset.

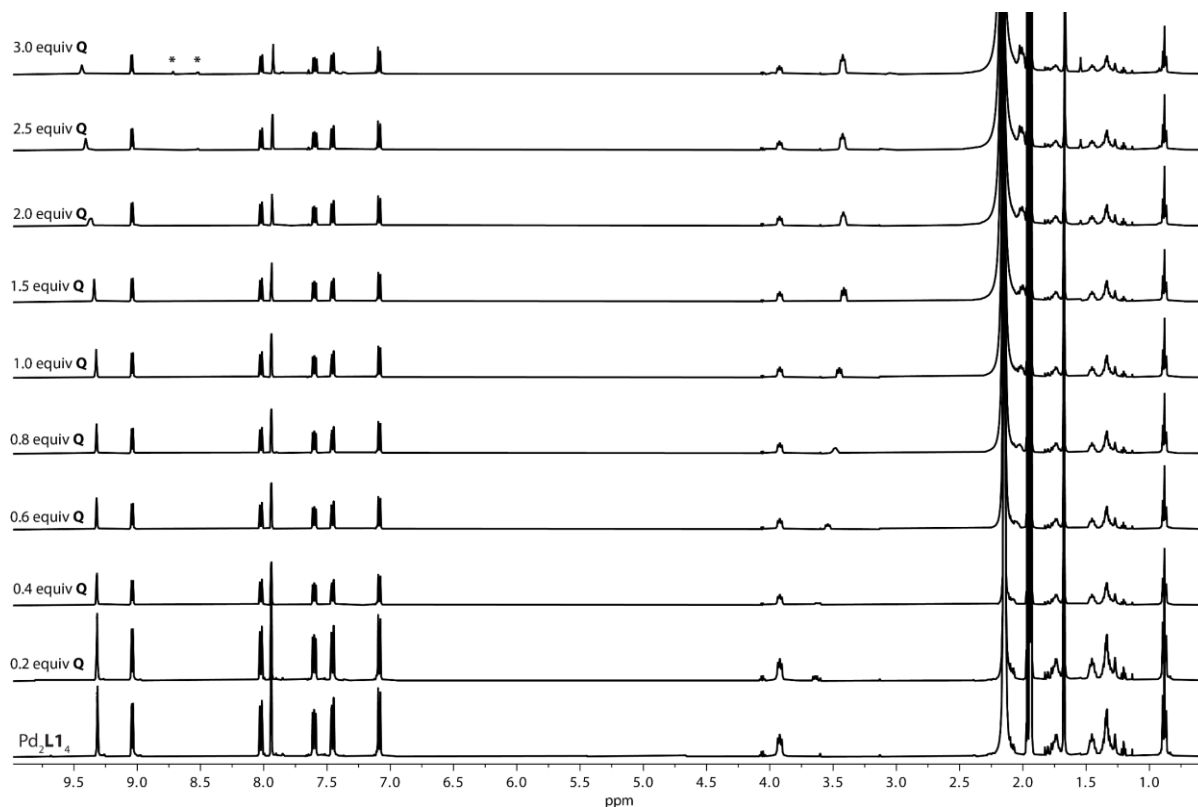
Interaction of **Q** with Pd₂L1₄

Figure S31: Stacked ¹H NMR spectra (500 MHz, 298K, CD₃CN) of the titration of **Q** into a solution of homoleptic cage Pd₂L1₄. After 2.0 equivalent, some free ligand can be observed and is marked with an asterisk.

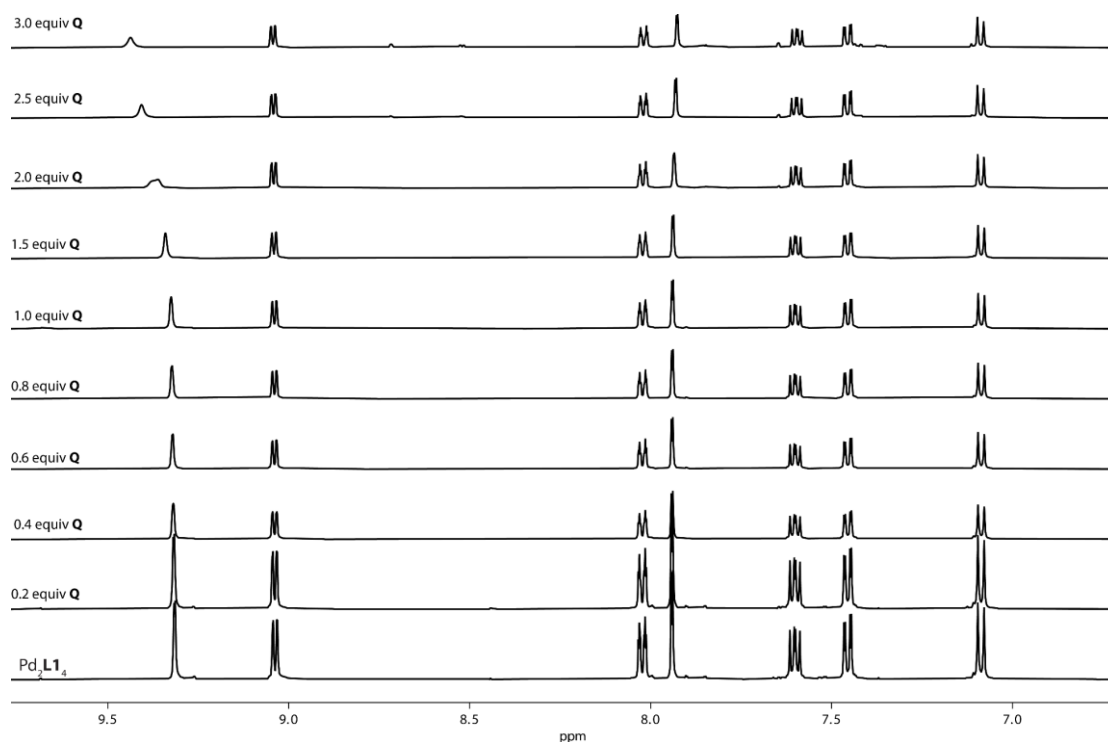


Figure S32: Stacked ¹H NMR spectra (500 MHz, 298K, CD₃CN) enlarged on the aromatic region of the titration of **Q** into a solution of homoleptic cage Pd₂L1₄.

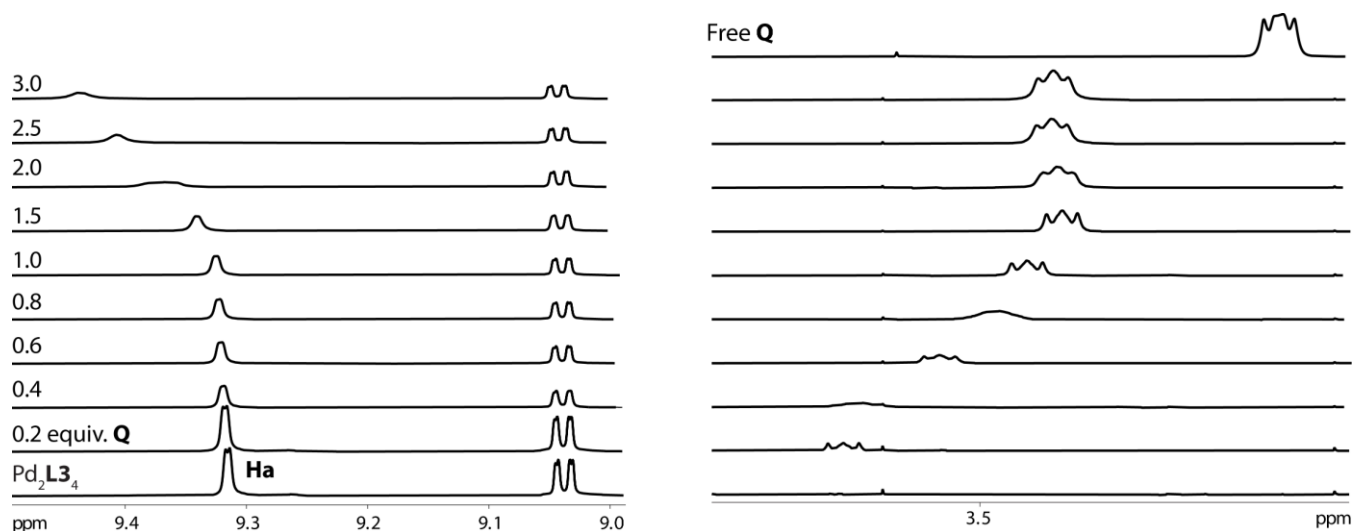


Figure S33: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN), enlarged on the region of proton α and quinuclidine, of the titration of **Q** into a solution of homoleptic cage $\text{Pd}_2\text{L1}_4$.

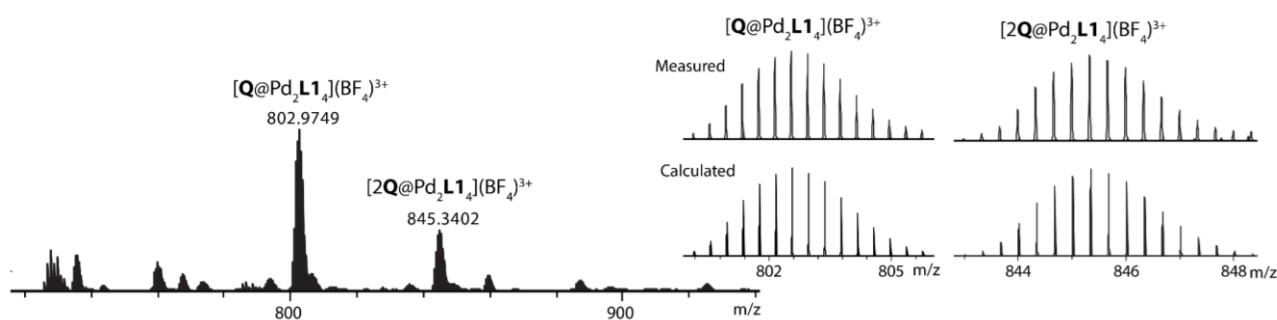


Figure S34: ESI-MS spectrum of a MeCN solution of **L1** with 0.5 equiv. $\text{Pd}(\text{II})$ and 2 equiv. of **G**. The observed peak correspond to $[\text{Q}@\text{Pd}_2\text{L1}_4+\text{BF}_4]^{3+}$ and $[2\text{Q}@\text{Pd}_2\text{L1}_4+\text{BF}_4]^{3+}$. The observed and calculated isotopic patterns are shown in the inset.

Guest segregation of Type I

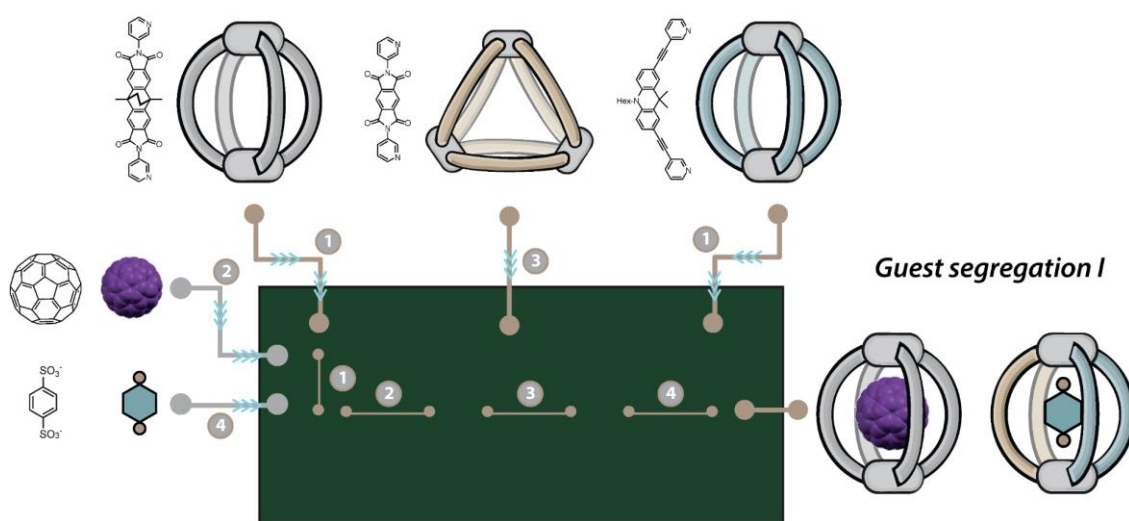


Figure S35: General scheme of the stepwise sorting and guest segregation I.

Multi-cage system sorting

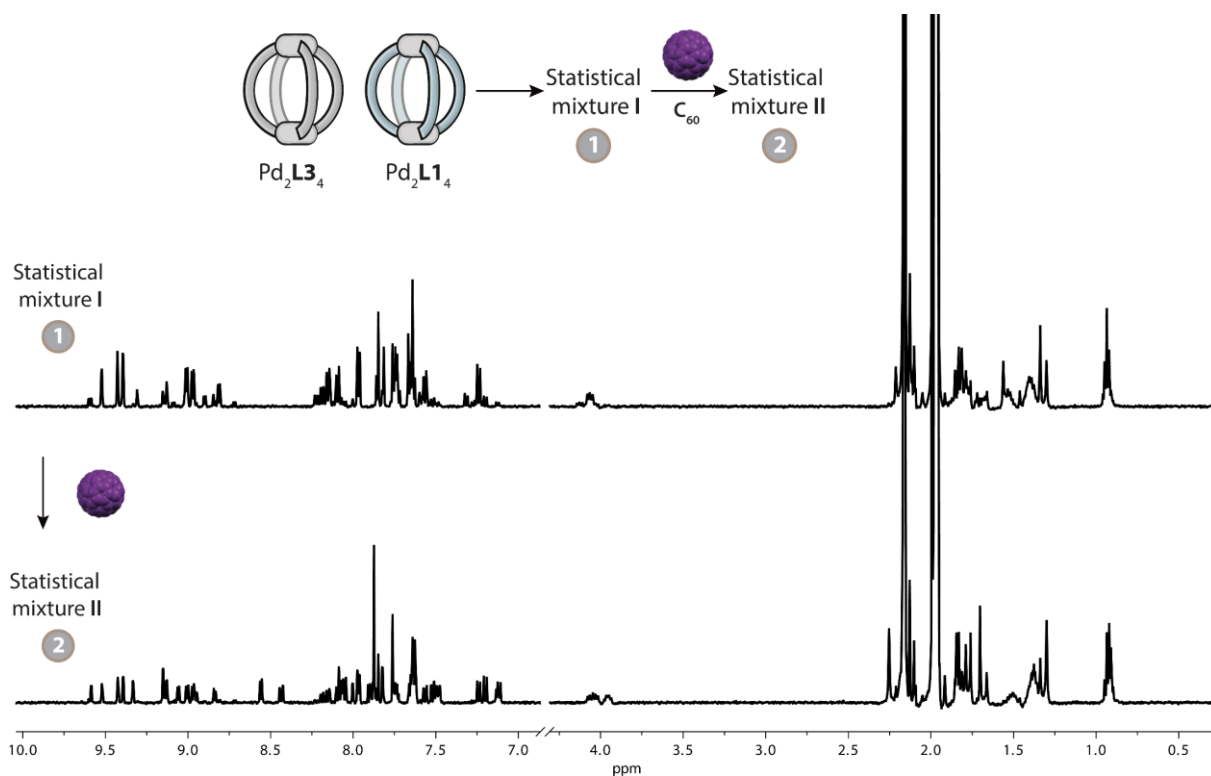


Figure S36: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the two types of statistical mixtures obtained when mixing $\text{Pd}_2\text{L1}_4$ and $\text{Pd}_2\text{L3}_4$ and after the addition of C_{60} .

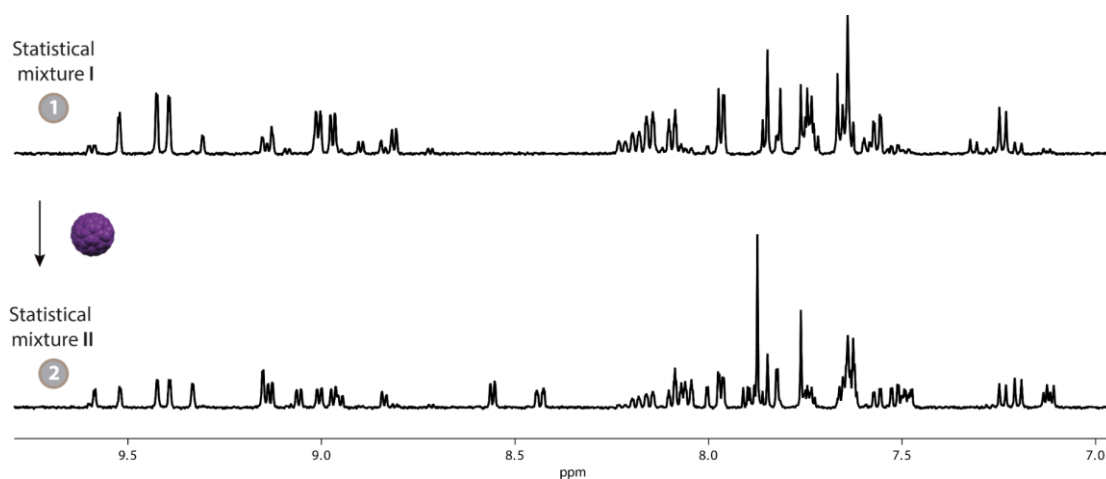


Figure S37: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the two types of statistical mixtures obtained when mixing $\text{Pd}_2\text{L1}_4$ and $\text{Pd}_2\text{L3}_4$ and after the addition of C_{60} .

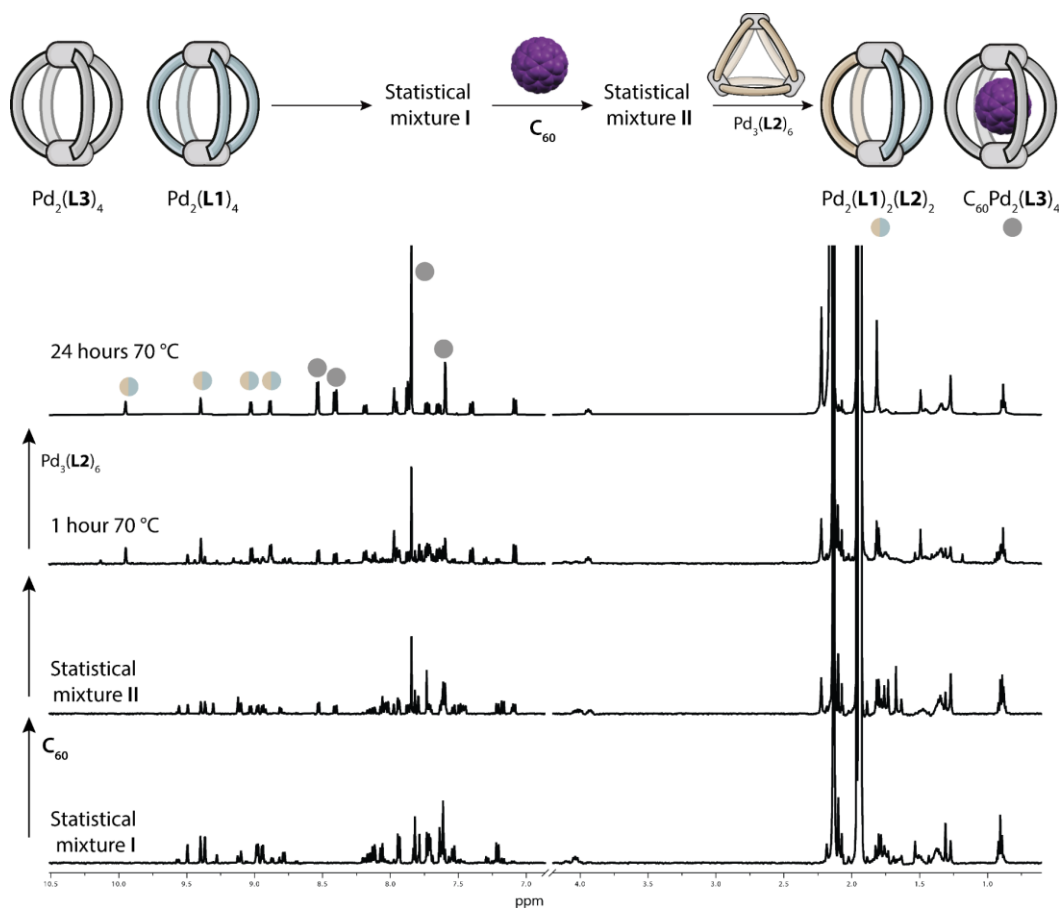


Figure S38: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the stepwise process towards coexistence of the two assemblies and self-sorting of a discrete cage mixture. This represents **Path I**.

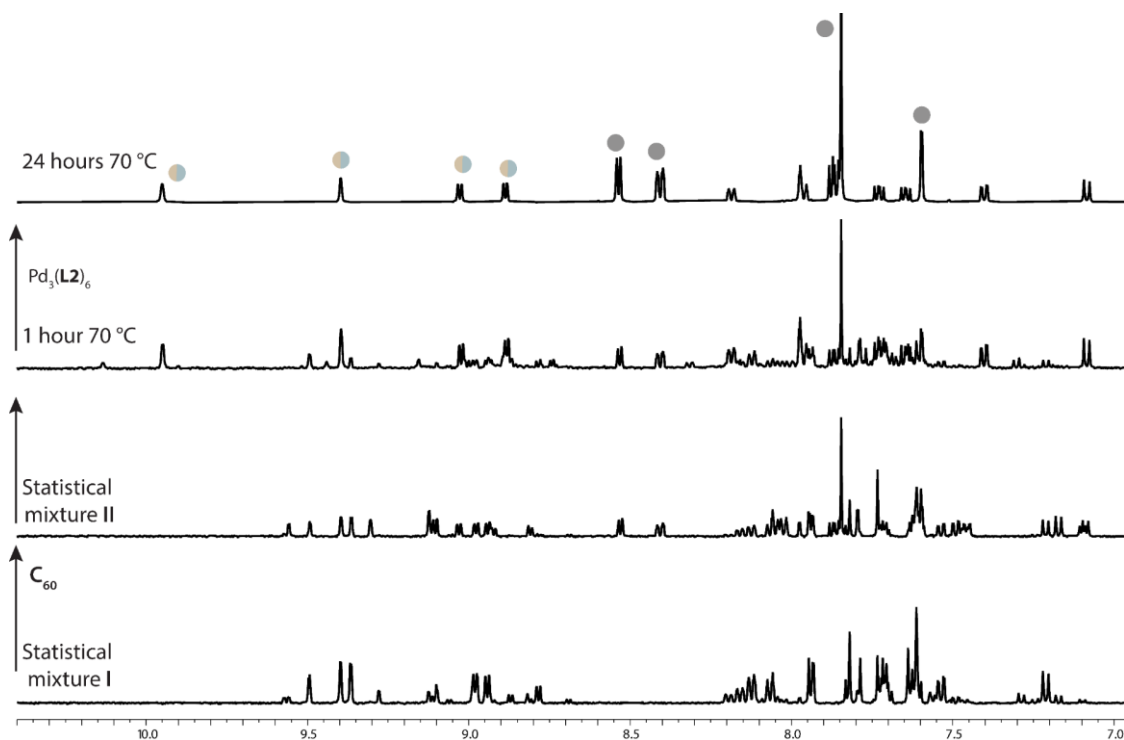


Figure S39: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN), zoomed on the aromatic region, of the stepwise process towards coexistence of the two assemblies and self-sorting of a discrete cage mixture.

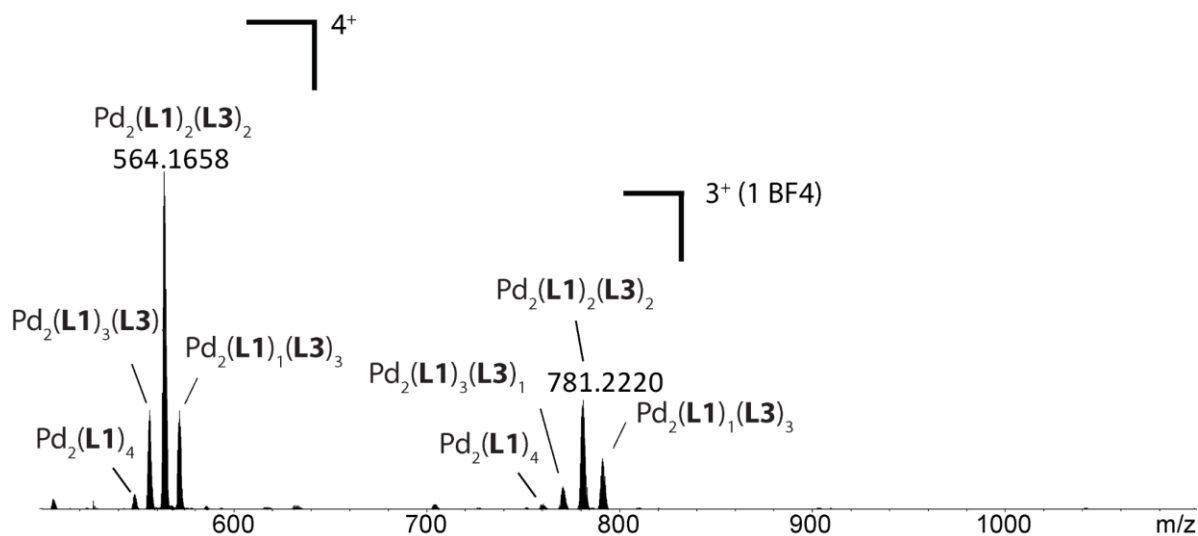


Figure S40: ESI-MS spectrum of a MeCN solution of **L1** and **L3** with 0.5 equiv. Pd(II). The observed peaks correspond to the different cages from the statistical mixture I.

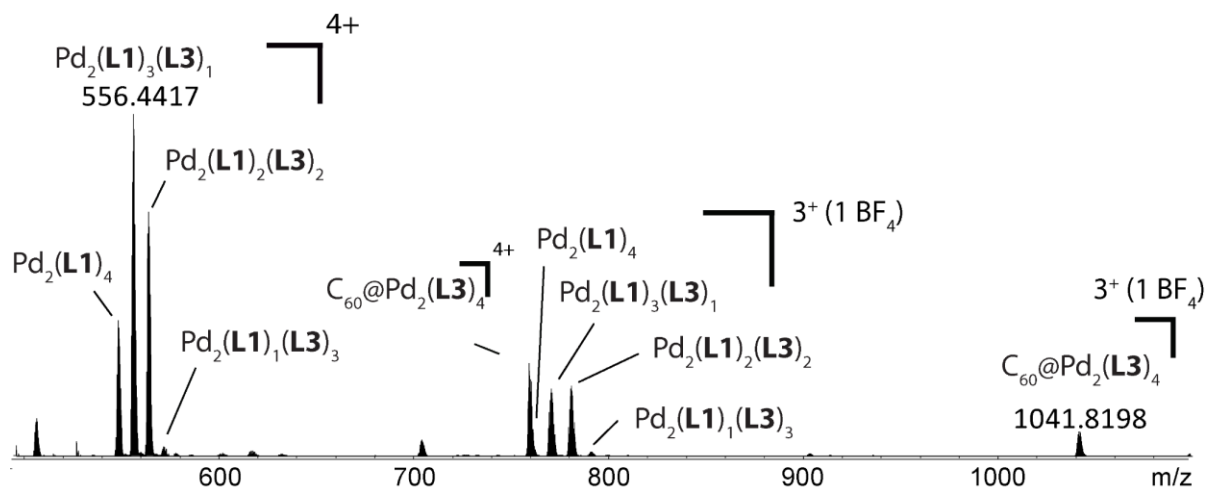


Figure S41: ESI-MS spectrum of a MeCN solution of **L1** and **L3** with 0.5 equiv. Pd(II) in the presence of fullerene C_{60} . The observed peaks correspond to the different cages and host-guest species from the statistical mixture II.

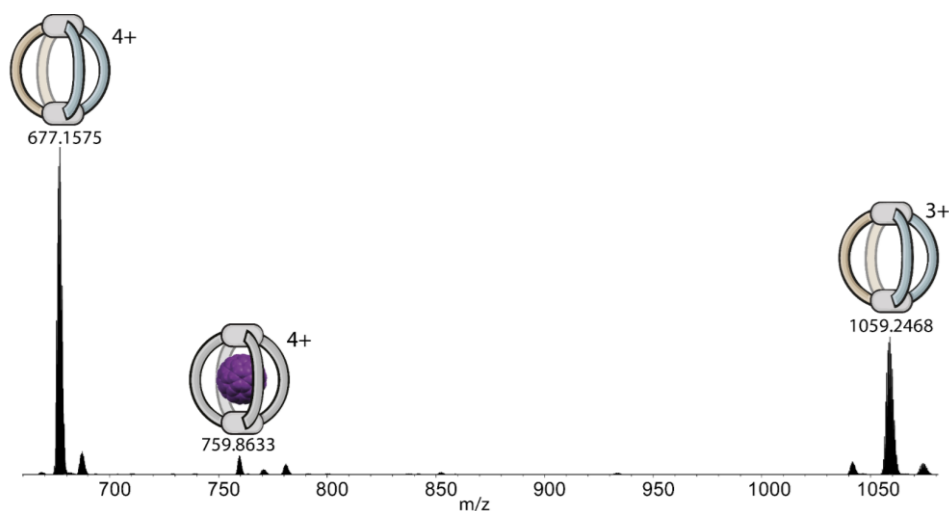


Figure S42: ESI-MS spectrum of a MeCN solution of **L1**, **L2** and **L3** with 0.5 equiv. Pd(II) in the presence of fullerene C_{60} . The observed peaks correspond to the different cages and host-guest species from the sorted final mixture of $Pd_2L_1L_2L_3$ and $C_{60}@Pd_2L_3$.

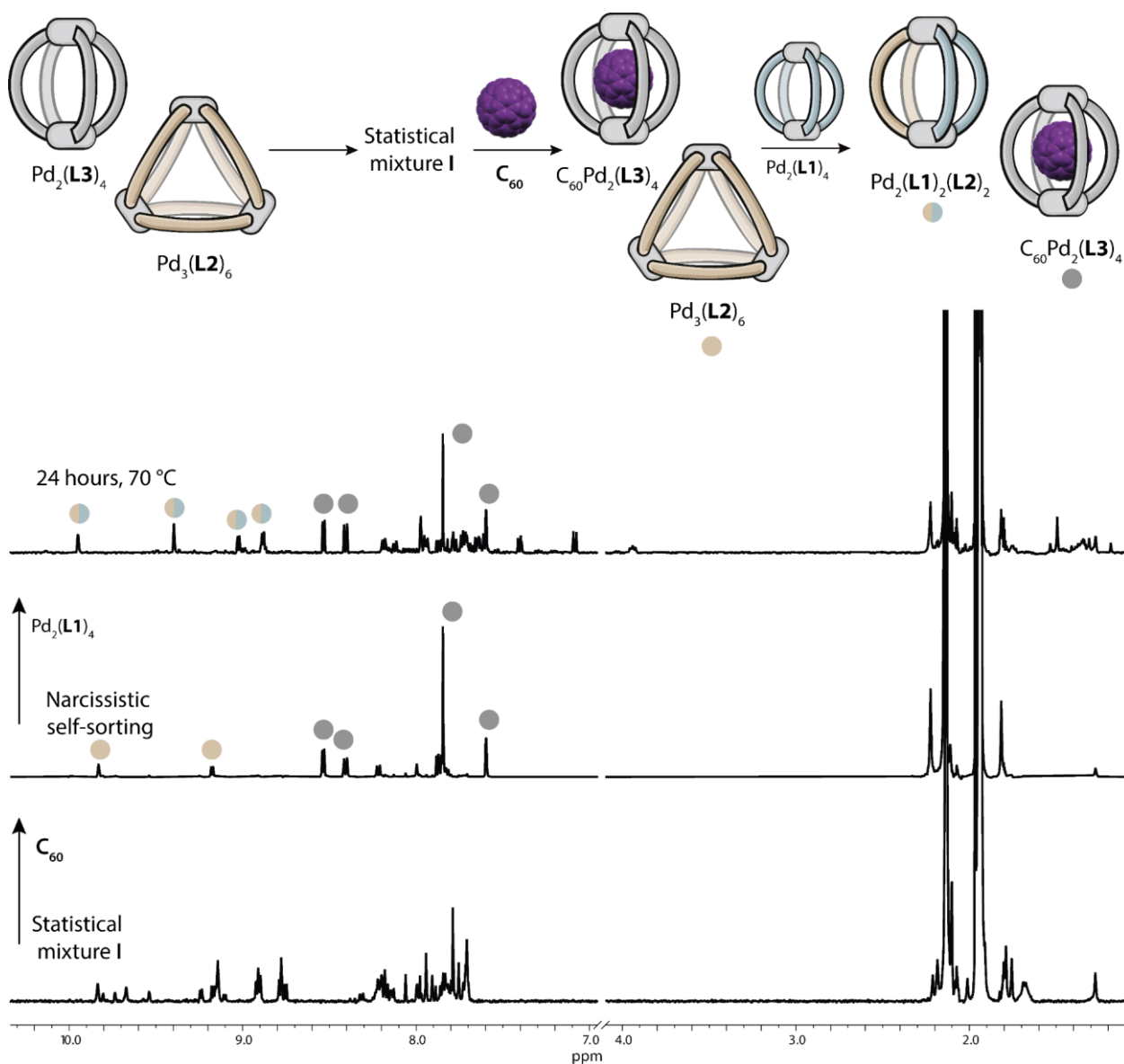


Figure S43: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the stepwise process towards coexistence of the two assemblies and self-sorting of a discrete cage mixture. This represents *Path II*.

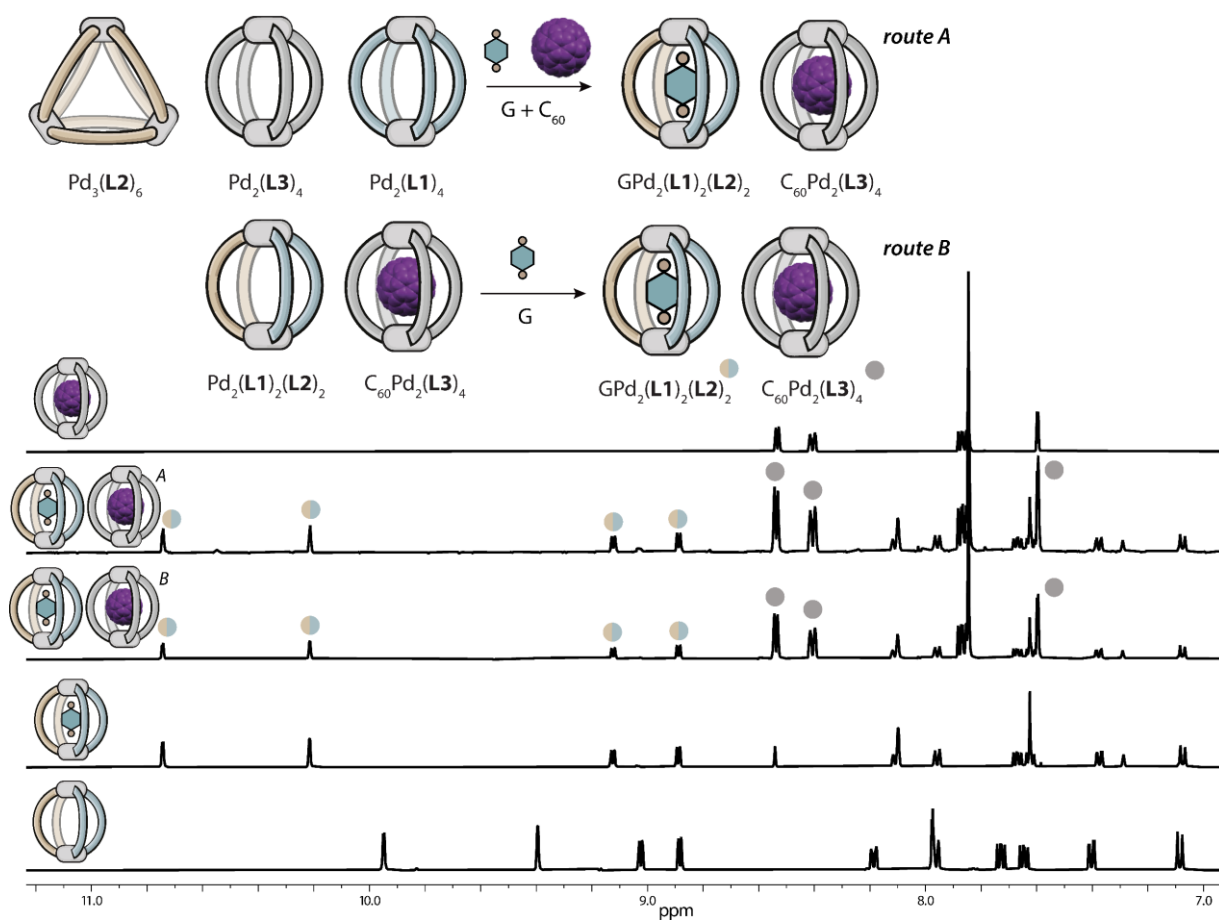


Figure S44: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the final step of the **Guest segregation I**. Two different routes A or B can be used in order to demonstrate that the final outcome is the thermodynamic state. **Route A:** 1 equivalent of 1,4-benzene disulfonate is added in a preformed mixture of $\text{Pd}_2\text{L1}_2\text{L2}_2$ and $\text{C}_{60}@\text{Pd}_2\text{L3}_4$. **Route B:** 1 equivalent of 1,4-benzene disulfonate and fullerene C_{60} are added to a NMR tube in which the three cages were premixed (in an amount assuring that the final ligand ratio is 1:1:1). The outcome of the self-sorting is similar and results in the guest segregation and coexistence of one heteroleptic host-guest complex $\text{G}@\text{Pd}_2\text{L1}_2\text{L2}_2$ and one homoleptic host-guest complex $\text{C}_{60}@\text{Pd}_2\text{L3}_4$.

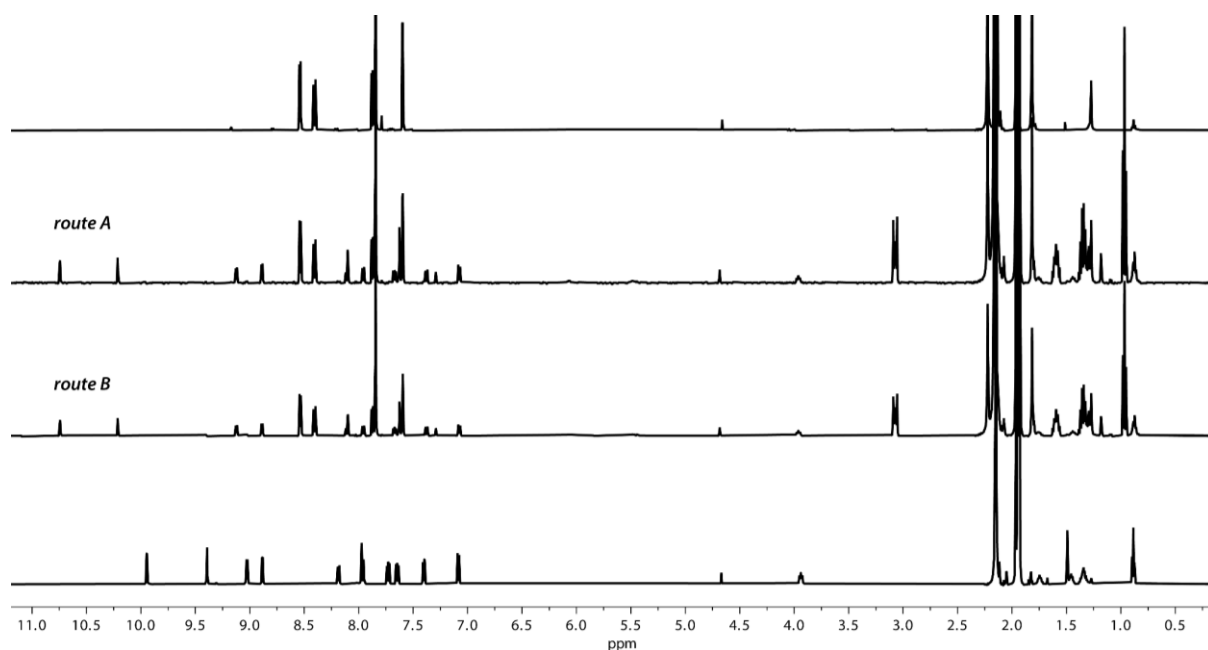


Figure S45: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the final step of the **Guest segregation I**.

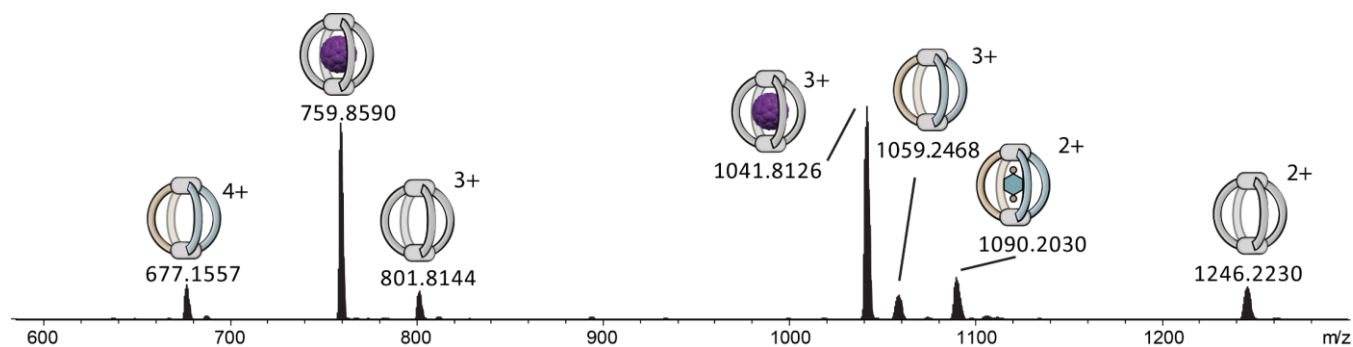


Figure S46: HR-ESI-MS of the final outcome displaying peaks from **G1@Pd₂L₁₂L₂₂** and **C₆₀@Pd₂L₃₄**

Stoichiometry and guest driven self-sorting

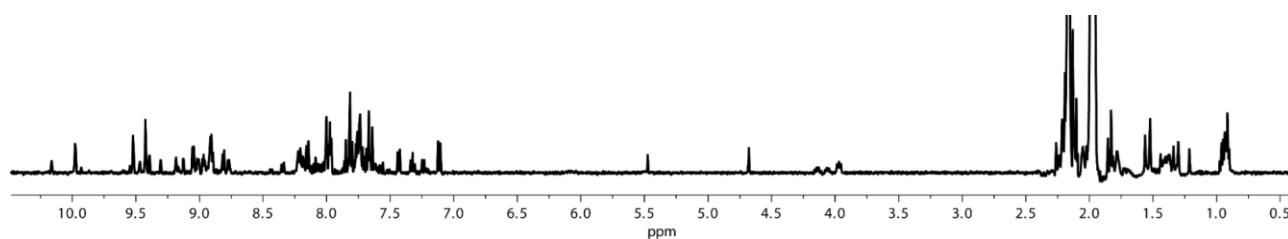


Figure S47: Stacked ¹H NMR spectra (500 MHz, 298K, CD₃CN) of the outcome of sorting when mixing the three ligands **L1**, **L2**, **L3** in equimolar ratio with Pd(II). No precise self-sorting is obtained.

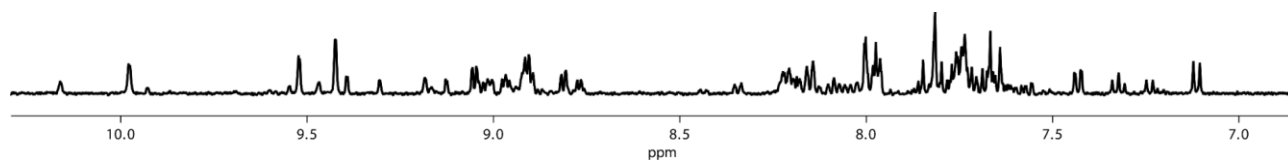


Figure S48: Stacked ¹H NMR spectra (500 MHz, 298K, CD₃CN) enlarged on the aromatic region of the outcome of sorting when mixing the three ligands **L1**, **L2**, **L3** in equimolar ratio with Pd(II). No precise self-sorting is obtained.

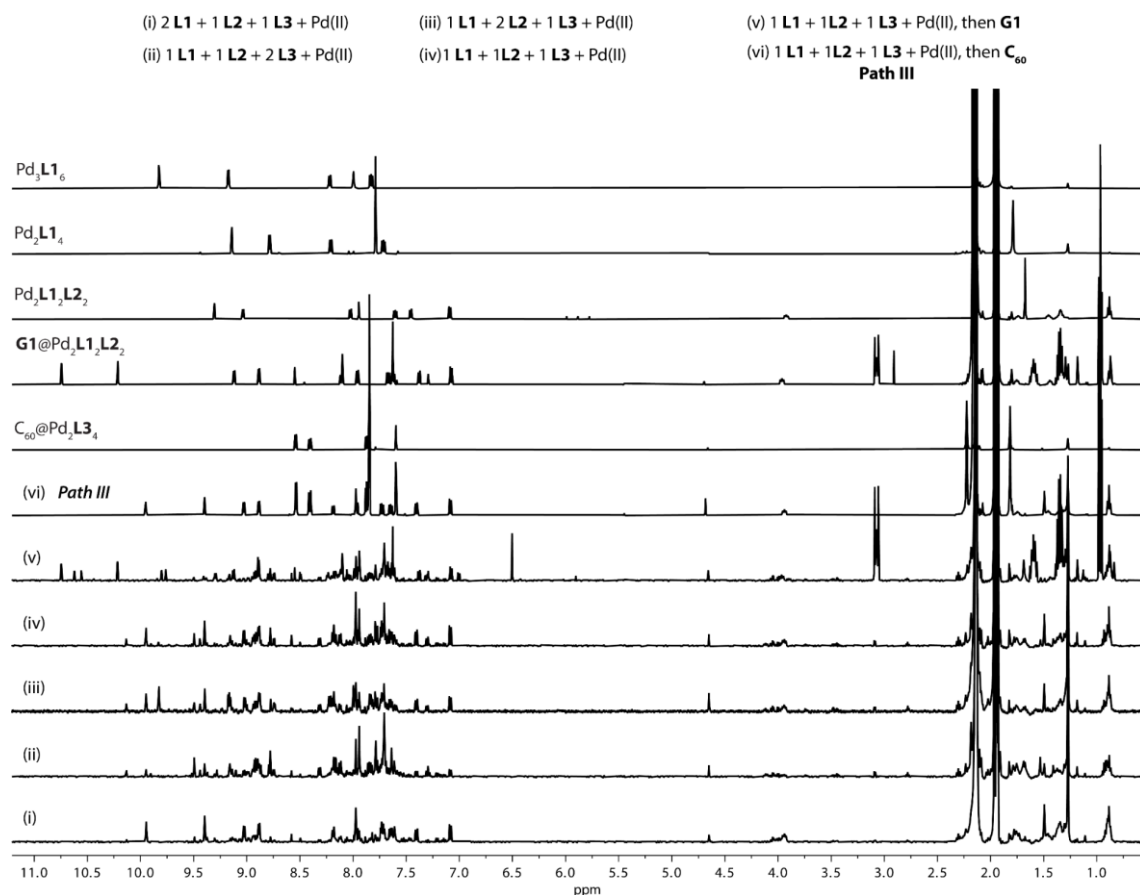


Figure S49: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the outcome of sorting when mixing the three ligands **L1**, **L2**, **L3** in different ratios and in the presence of either fullerene C_{60} or guest **G1**.

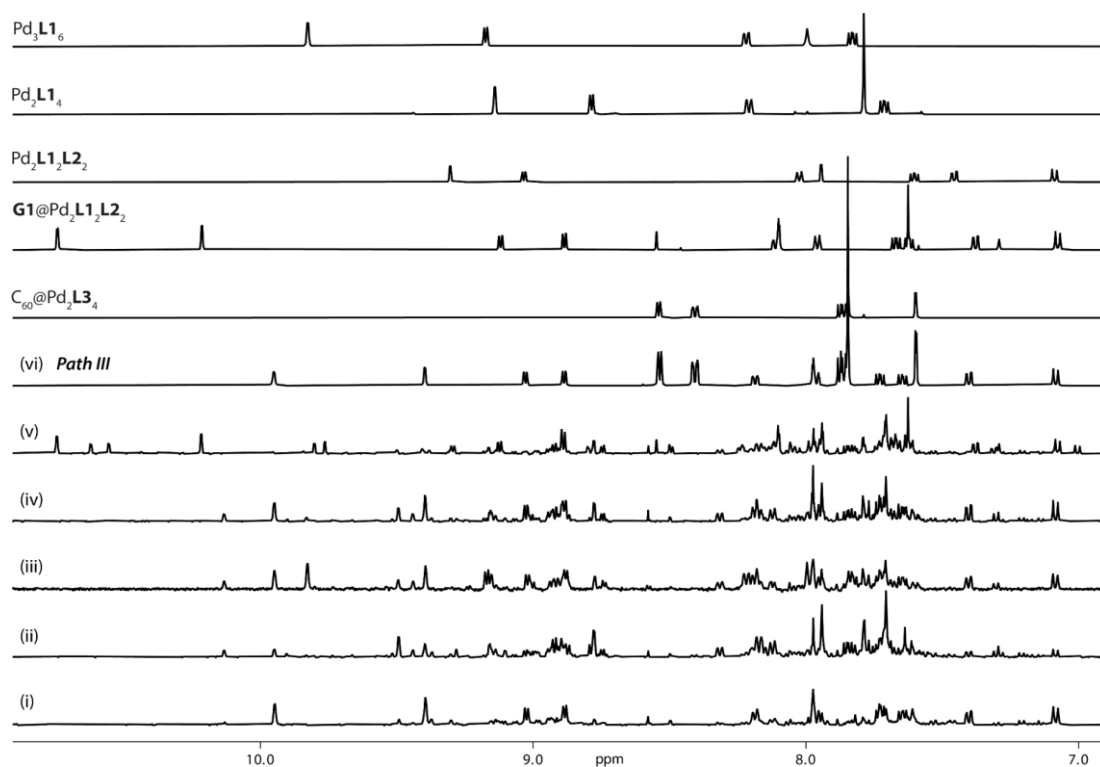


Figure S50: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) enlarged aromatic region of the outcome of sorting when mixing the three ligands **L1**, **L2**, **L3** in different ratios and in the presence of either fullerene C_{60} or guest **G1**.

Guest-induced narcissistic self-sorting and guest segregation

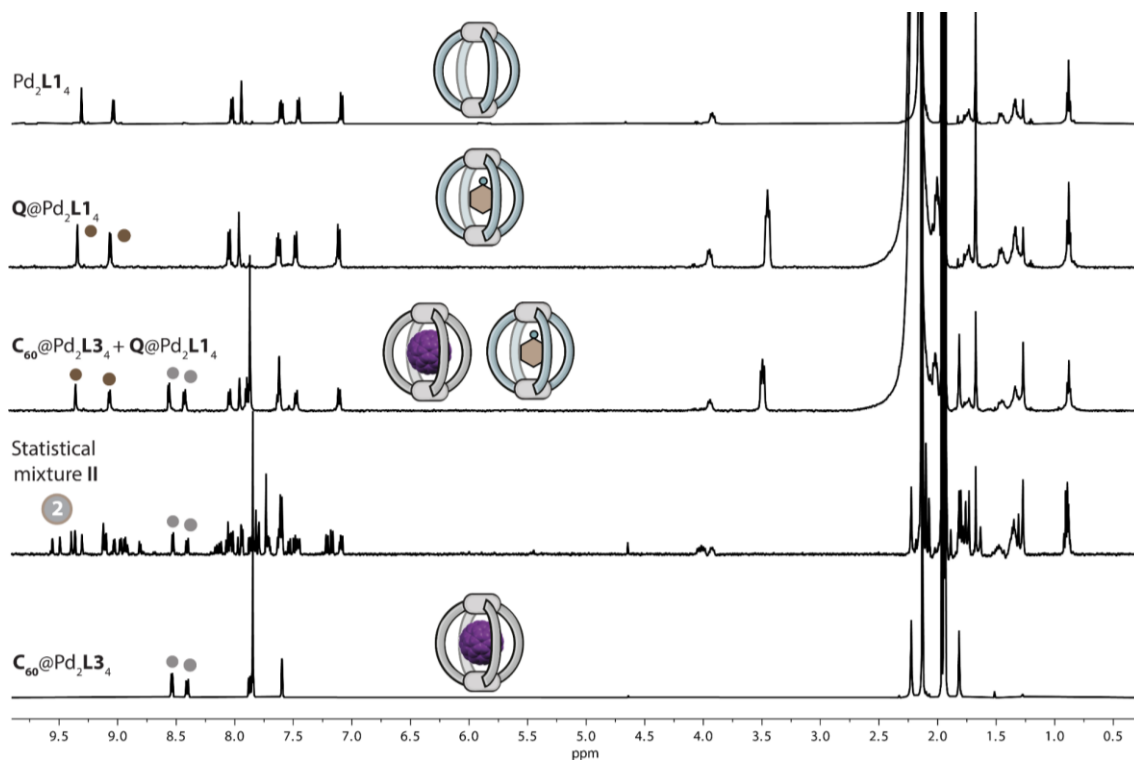


Figure S51: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the guest-induced narcissistic self-sorting in the presence of **Q**. The statistical mixture disappears to give rise to two distinct host-guest complexes. This also corresponds to a **Guest segregation of type I**.

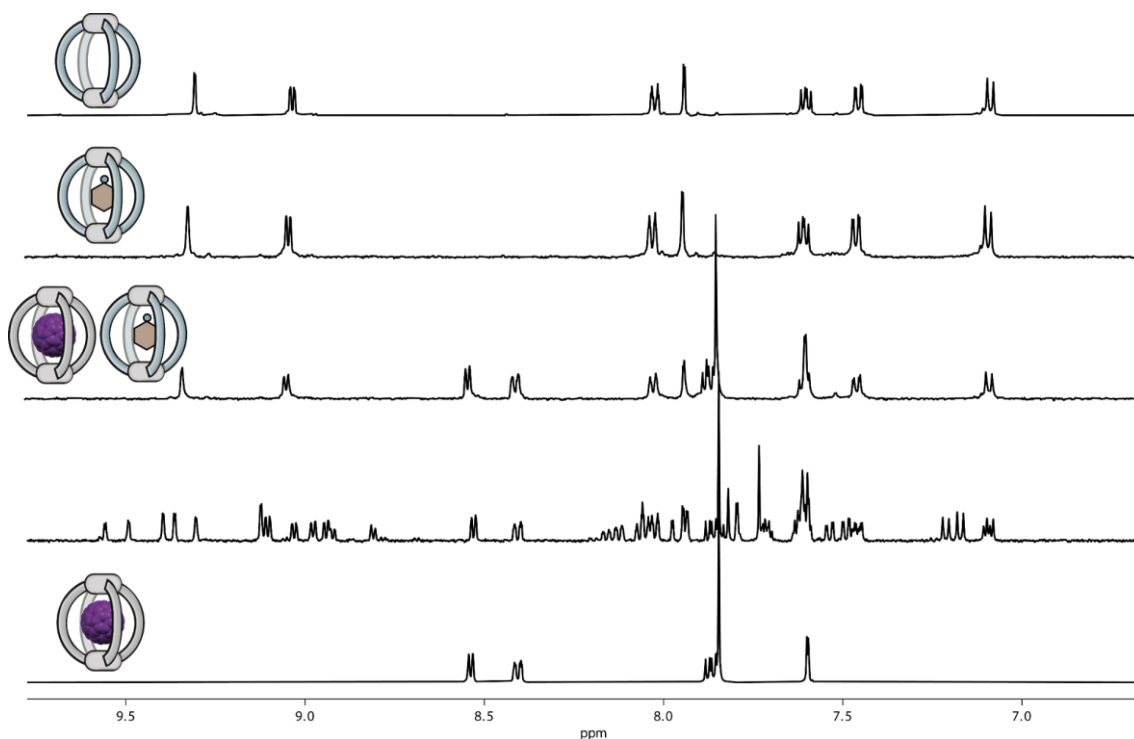


Figure S52: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the guest-induced narcissistic self-sorting in the presence of **Q**. The statistical mixture disappears to give rise to two distinct host-guest complexes. This also corresponds to a **Guest segregation of type I**.

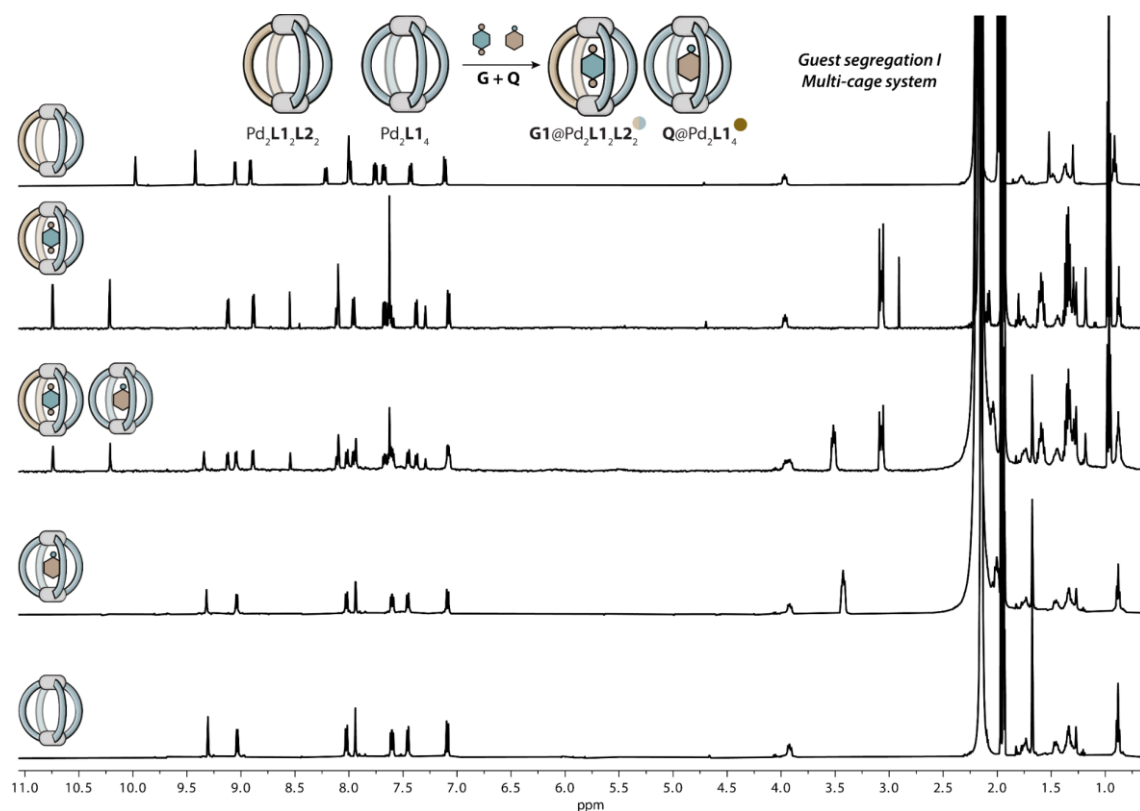


Figure S53: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the two coexisting host-guest complexes with **G1** and **Q**. This also corresponds to a **Guest segregation of type I**.

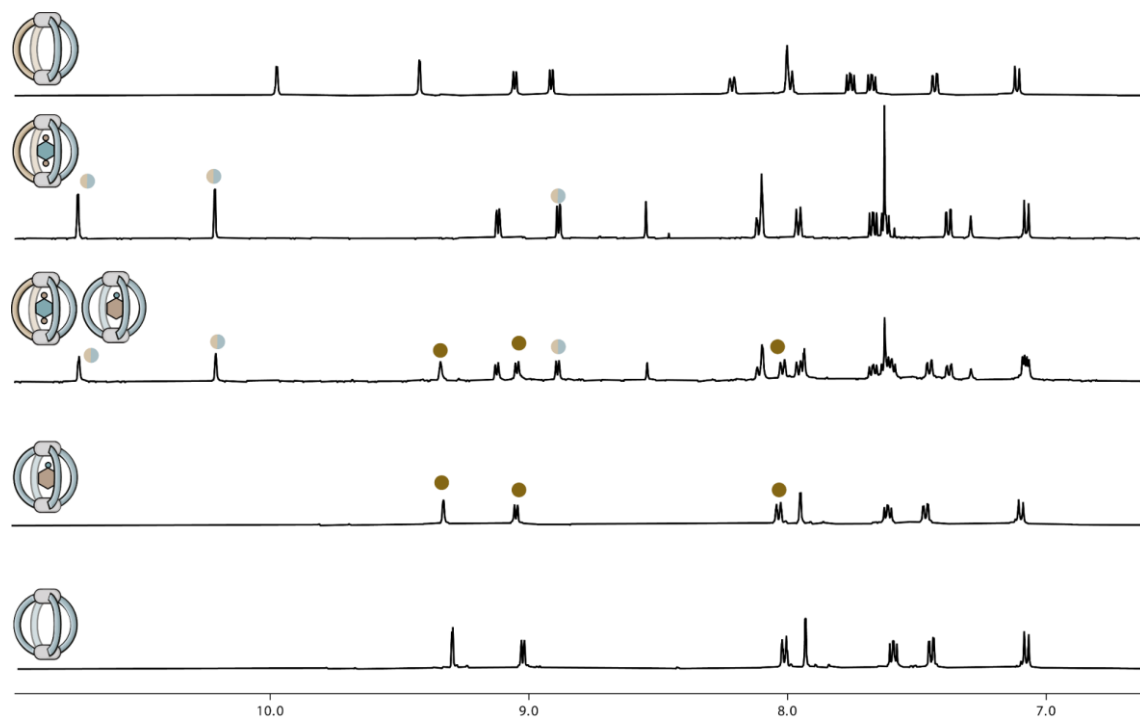


Figure S54: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the two coexisting host-guest complexes with **G1** and **Q**. This also corresponds to a **Guest segregation of type I**.

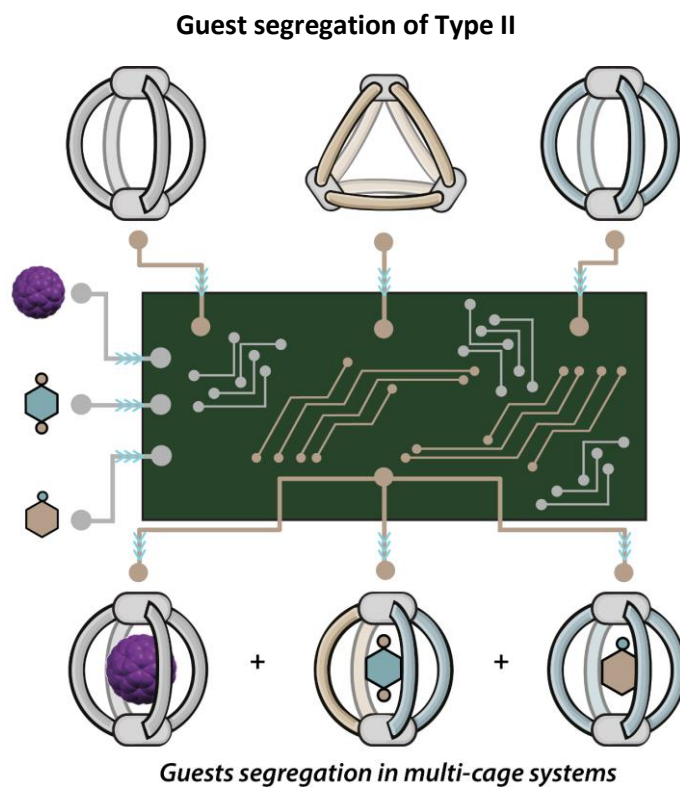


Figure S55: General scheme of the stepwise sorting and guest segregation II.

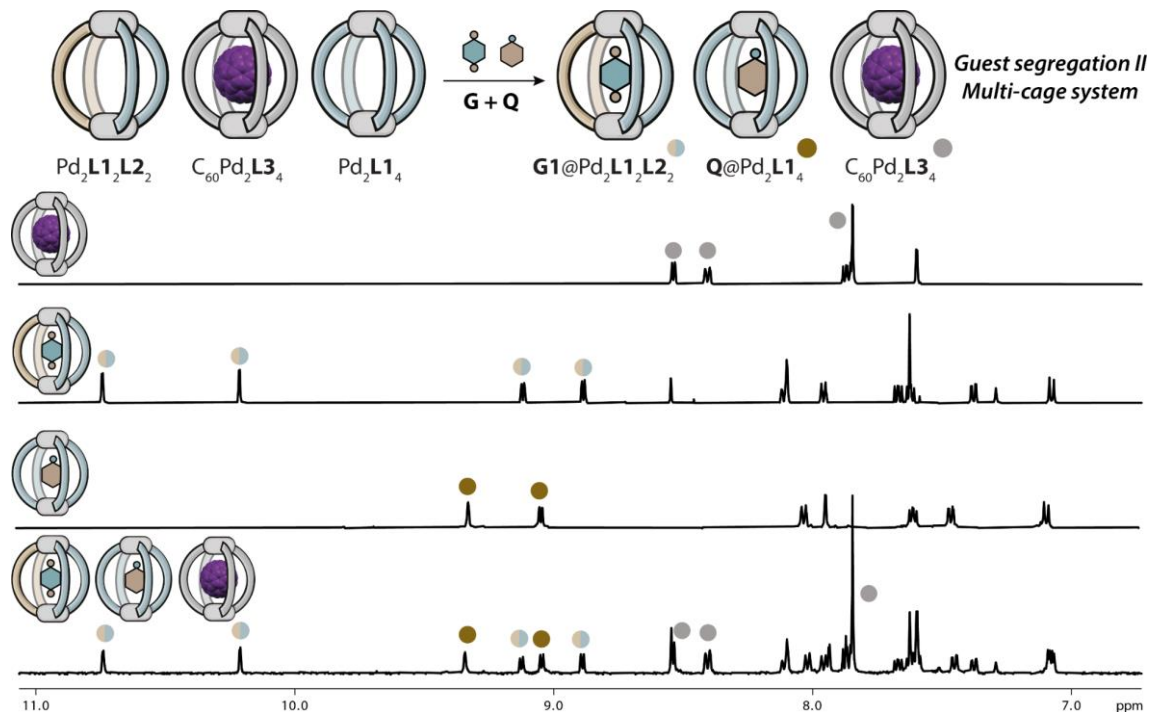


Figure S56: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the three orthogonally coexisting host-guest complexes with **G1** and **Q** and **C₆₀**. This corresponds to a **Guest segregation of type II**.

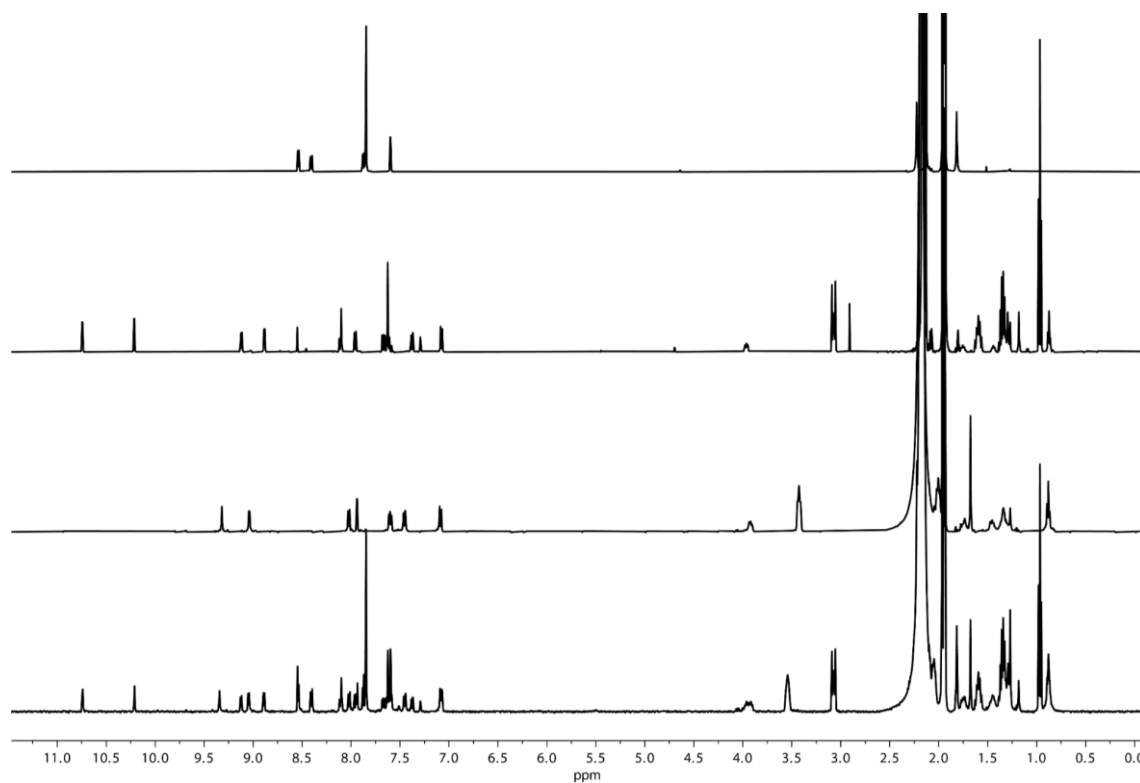


Figure S57: Stacked ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the three orthogonally coexisting host-guest complexes with **G1**, **Q** and **C₆₀**. This corresponds to a **Guest segregation of type II**.

X-ray structure and DFT models

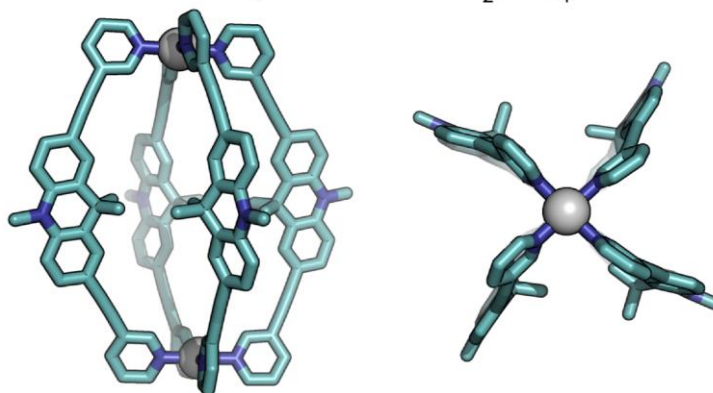
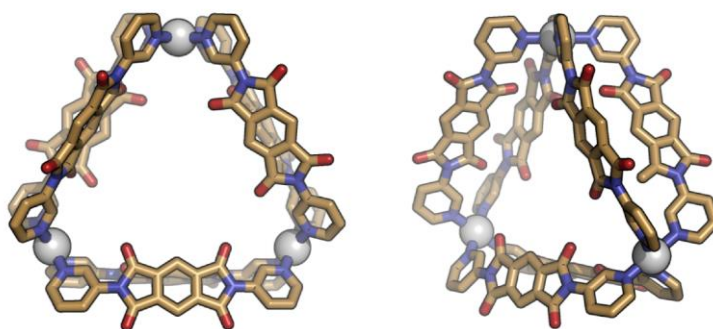
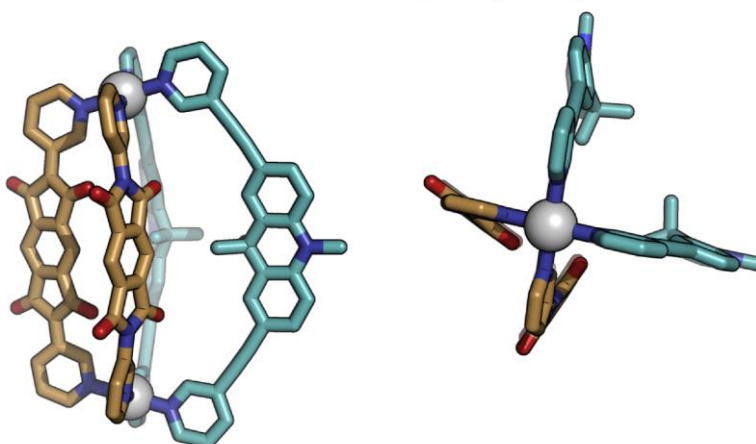
X-ray structure $\text{Pd}_2(\text{L1})_4$ DFT-Model $\text{Pd}_3(\text{L2})_6$ DFT-Model $\text{Pd}_2(\text{L1})_2(\text{L2})_2$ 

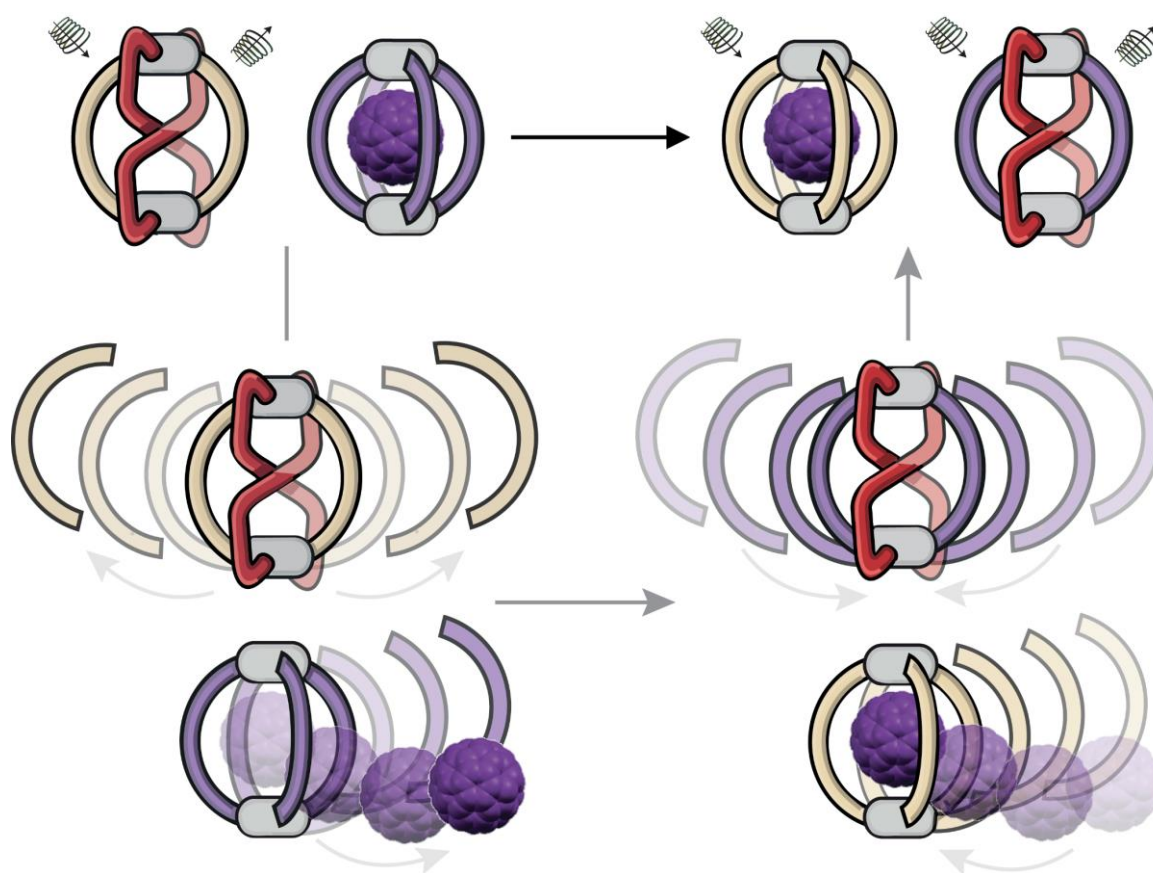
Figure S58: Structure of the three new assemblies reported in this study. (Top) X-ray structure of $\text{Pd}_2\text{L1}_4$, side and top view. Hexyl chains of the ligand are omitted for clarity. (middle) DFT (wB97X-D, def2-SV(P)) optimized structure of $\text{Pd}_3\text{L2}_6$ ring, side and top view. (bottom) DFT (wB97X-D, def2-SV(P)) optimized structure $\text{Pd}_2\text{L1}_2\text{L2}_2$, side and top view. Hexyl chains of the ligand are omitted for clarity.

6. References

- [1] D. Zhang, T. K. Ronson, Y.-Q. Zou, J. R. Nitschke, *Nat. Rev. Chem.* **2021**, *5*, 168–182.
- [2] Y. Xue, X. Hang, J. Ding, B. Li, R. Zhu, H. Pang, Q. Xu, *Coordin. Chem. Rev.* **2020**, *430*, 213656.
- [3] T. K. Piskorz, V. Martí-Centelles, R. L. Spicer, F. Duarte, P. J. Lusby, *Chem. Sci.* **2023**, *14*, 11300–11331.
- [4] A. Galan, P. Ballester, *Chem. Soc. Rev.* **2016**, *45*, 1720–1737.
- [5] F. J. Rizzuto, L. K. S. von Krbek, J. R. Nitschke, *Nat. Rev. Chem.* **2019**, *1*.
- [6] S. Sharma, M. Sarkar, D. K. Chand, *Chem. Commun.* **2022**, *59*, 535–554.
- [7] D. Preston, J. E. M. Lewis, J. D. Crowley, *J. Am. Chem. Soc.* **2017**, *139*, 2379–2386.
- [8] K. Yazaki, M. Akita, S. Prusty, D. K. Chand, T. Kikuchi, H. Sato, M. Yoshizawa, *Nat. Commun.* **2017**, *8*, 15914.
- [9] S. Sato, O. Morohara, D. Fujita, Y. Yamaguchi, K. Kato, M. Fujita, *J. Am. Chem. Soc.* **2010**, *132*, 3670–3671.
- [10] S. Löffler, J. Lübken, L. Krause, D. Stalke, B. Dittrich, G. H. Clever, *J. Am. Chem. Soc.* **2015**, *137*, 1060–1063.
- [11] S. Löffler, A. Wuttke, B. Zhang, J. J. Holstein, R. A. Mata, G. H. Clever, *Chem. Commun.* **2017**, *53*, 11933–11936.
- [12] S. Watanabe, M. Yamashina, E. Tsurumaki, S. Toyota, *ChemistryEurope* **2023**, *1*, e202300047.
- [13] Y. Yang, T. K. Ronson, Z. Lu, J. Zheng, N. Vanthuyne, A. Martinez, J. R. Nitschke, *Nat. Commun.* **2021**, *12*, 4079.
- [14] F. J. Rizzuto, W.-Y. Wu, T. K. Ronson, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2016**, *55*, 7958–7962.
- [15] S. H. A. M. Leenders, R. Becker, T. Kumpulainen, B. de Bruin, T. Sawada, T. Kato, M. Fujita, J. N. H. Reek, *Chem. Eur. J.* **2016**, *22*, 15468–15474.
- [16] M. Yamashina, M. M. Sartin, Y. Sei, M. Akita, S. Takeuchi, T. Tahara, M. Yoshizawa, *J. Am. Chem. Soc.* **2015**, *137*, 9266–9269.
- [17] I. A. Riddell, T. K. Ronson, J. K. Clegg, C. S. Wood, R. A. Bilbeisi, J. R. Nitschke, *J. Am. Chem. Soc.* **2014**, *136*, 9491–9498.
- [18] G. H. Clever, W. Kawamura, S. Tashiro, M. Shiro, M. Shionoya, *Angew. Chem. Int. Ed.* **2012**, *51*, 2606–2609.
- [19] A. M. Castilla, T. K. Ronson, J. R. Nitschke, *J. Am. Chem. Soc.* **2016**, *138*, 2342–2351.
- [20] A. Jiménez, R. A. Bilbeisi, T. K. Ronson, S. Zarra, C. Woodhead, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2014**, *53*, 4556–4560.
- [21] B. Chen, J. J. Holstein, S. Horiuchi, W. G. Hiller, G. H. Clever, *J. Am. Chem. Soc.* **2019**, *141*, , 8907–8913
- [22] M. L. Saha, M. Schmittel, *Org. Biomol. Chem.* **2012**, *10*, 4651–4684.

Chapter III

Dynamic cage populations and emergent behaviors



This chapter relies on a ligand synthesized by Dr. Helen O'Connor in Prof. Thorfinnur Gunnlaugsson's group and has benefited from the support of Björn Schmidt.

Introduction

The Tröger base backbone has been known for decades and has already been introduced in supramolecular assemblies by the Lützen group mostly.^[1–6] The core possesses two nitrogens bridged by a methylene preventing their inversion through strain and thus creating two stereogenic centers. The two enantiomers have a propeller shape and can be described with *P/M* chirality, with a C_2 -axis passing through the carbon of the bridge between the nitrogens. In the present case, the original benzene moieties of the core are substituted by naphthalimide groups with larger π -surfaces and electron-poor character.^[7] The ligand employed is derived from a previous analog bearing a *para*-pyridine^[7] and presents a peculiar ribbon structure that should offer a more enclosed cavity, and create so-called capsules, as opposed to the more porous character of cages. Such capsules possess large aromatic walls favoring both hydrophobic effect and stabilizing host-guest interactions. They have proven to be suitable hosts for numerous neutral guests but also for polyaromatic hydrocarbons such as fullerene C_{60} .^[8–17] It was therefore anticipated that a chiral capsule could be obtained from this Tröger base ligand. Among the multiple hosts reported for fullerene binding,^[18] very few examples have combined it with chirality and chiral induction on pristine fullerenes remains a very rare phenomenon.^[19–21]

The first two chapters of this thesis have established a new type of self-sorting where multiple complex assemblies can coexist orthogonally in solution. It gives rise to the notion of cage populations, then developed to be capable of first “functions” such as guest segregation. However, this remained a “static” behavior. Even in the second chapter, while the guests alter or control the self-sorting, only the final state of the system represents a defined population. In this second chapter, I took advantage of a capsule and of its strong affinity for fullerene C_{60} to drive the formation of the population. The final part of this dissertation will now discuss dynamic cage populations and the emergence of complex behavior and take another step into systems chemistry. For this, competitive fullerene binding between several capsules and their competition for the formation of heteroleptic species will be exploited. Leveraging the difference in kinetics of these two competitive processes, the first hints at the formation of an out-of-equilibrium system will, eventually, be highlighted.

1. Träger base ligand for chiral fullerene receptors

The ligand (**B^{P/M}**) was synthesized by Dr. Helen O'Connor from a 1,8-naphthalimide Träger base functionalized with two pyridyl donor groups. It was produced as a racemic mixture of the *P* and *M* enantiomers. When the racemic ligand **B^{P/M}** was mixed with a Pd(II) source in a 1:1 ratio and heated at 70 °C overnight in CD₃CN, a mixture of Pd₂L₄ isomers was obtained (Figure 1a). ESI-MS analysis revealed prominent peaks corresponding to [Pd₂**B^{P/M}**₄+*n* BARF]^{(4-*n*)⁺ (or other anions when employed). Under these conditions, there is no driving force for a fully selective chiral self-sorting to occur despite the main species identified corresponding to the homochiral cage. On the other hand, when certain polyaromatic hydrocarbons (PAH) were introduced, the ¹H NMR spectra became clearer. In the presence of fullerene C₆₀ or corannulene, a unique set of signals could be observed indicating the chiral self-sorting of the host-guests complexes into **G**@Pd₂**B^P**₄/Pd₂**B^M**₄ (Figure 1b). In the case of fullerene C₇₀, changes were also observed. The ¹H NMR spectrum, however, remained very complex which was attributed to either the formation of several isomers of the host-guest complex (in terms of composition of enantiomeric ligands) or the desymmetrization of the host-guest complexes by conformationally locked, non-spherical C₇₀, or a combination of both. Interestingly, crystallization also led to a chiral narcissistic self-sorting and the cage crystallized into a racemic 1:1 mixture of Pd₂**B^P**₄/Pd₂**B^M**₄.}

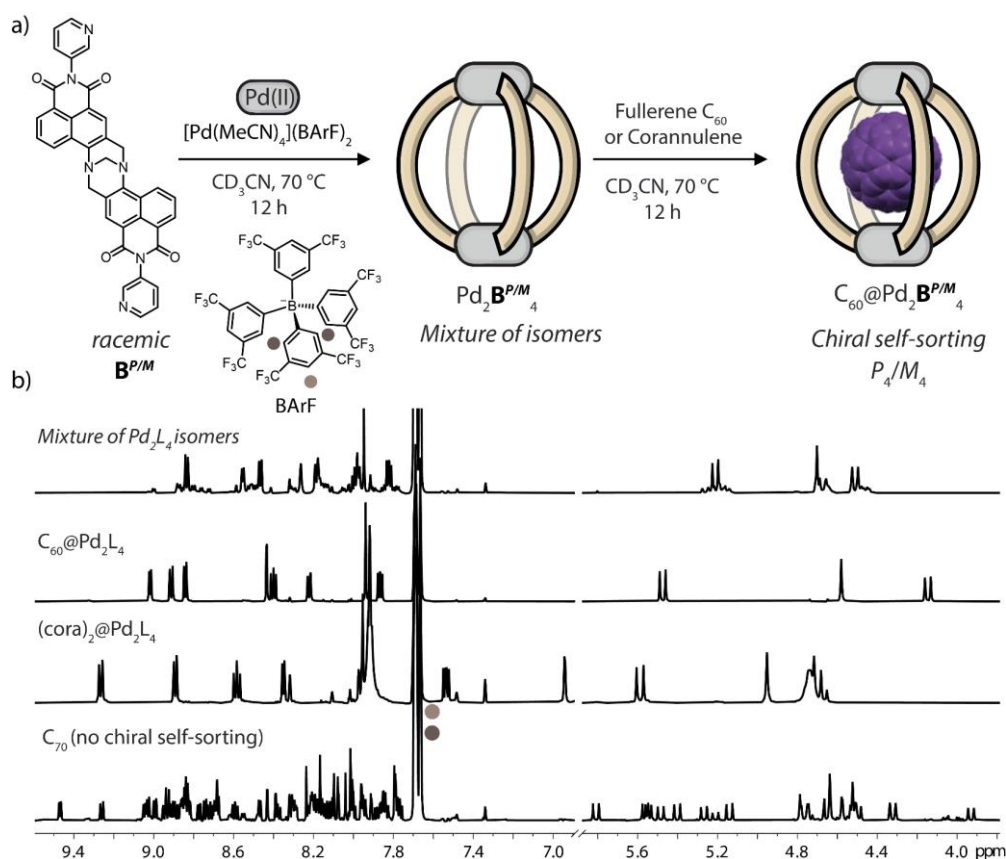


Figure 1: Formation of a mixture of Pd₂L₄ isomers from the racemic ligand **B^{P/M}** and chiral self-sorting upon guest encapsulation. b) ¹H-NMR (CD₃CN, 500 MHz) stack of the mixture of Pd₂L₄ isomers from the addition of Pd(II) to a solution of **B^{P/M}** and the outcome upon uptake of fullerene C₆₀, corannulene or fullerene C₇₀.

The two ligand enantiomers were separated by chiral HPLC (IA Chiralpak column) using a mixture of DCM and MeOH (97.5/2.5) as eluent. ¹H NMR in CD₃CN of the two separated fractions were identical to that of the racemic mixture in the same solvent and displayed perfect mirror images in CD spectroscopy (Figure 2a,c and e). By comparing the sign of their cotton effects with literature for similar derivatives of the same core structure their chirality could be empirically assigned. This assignment was further confirmed by X-ray crystallography of the

cages formed from the different enantiomers and analyzing their Flack parameters (Figure 2b). Consequently, the first eluted fraction corresponds to the M enantiomer, while the second is attributed to the P enantiomer.

When mixed in CD_3CN with a Pd(II) source, enantiomerically pure ligands $\mathbf{B}^P$ or $\mathbf{B}^M$ yielded the anticipated $\text{Pd}_2\mathbf{B}^P_4$ or $\text{Pd}_2\mathbf{B}^M_4$ (Figure 2a-b). From this point forward, I will use a single enantiomer notation unless their behaviors are being compared. The resulting cages displayed a single set of signals in ^1H NMR spectrum, matching the major set of signals of the aforementioned mixture resulting from the racemic ligand. Proton *Ha* undergoes a downfield shift while other protons, mostly of the pyridine donor group, are also affected. This shift is typically indicative of the coordination to the metal center. The stoichiometry was confirmed by ESI-MS analysis as well as by DOSY NMR which revealed a hydrodynamic radius of $r_h = 12.8 \text{ \AA}$ typical for this type of dinuclear assembly. Finally, crystals of both $\text{Pd}_2\mathbf{B}^P_4$ and $\text{Pd}_2\mathbf{B}^M_4$ were obtained by slow vapor diffusion of diverse solvents into acetonitrile solution of the cages (Figure 2b).

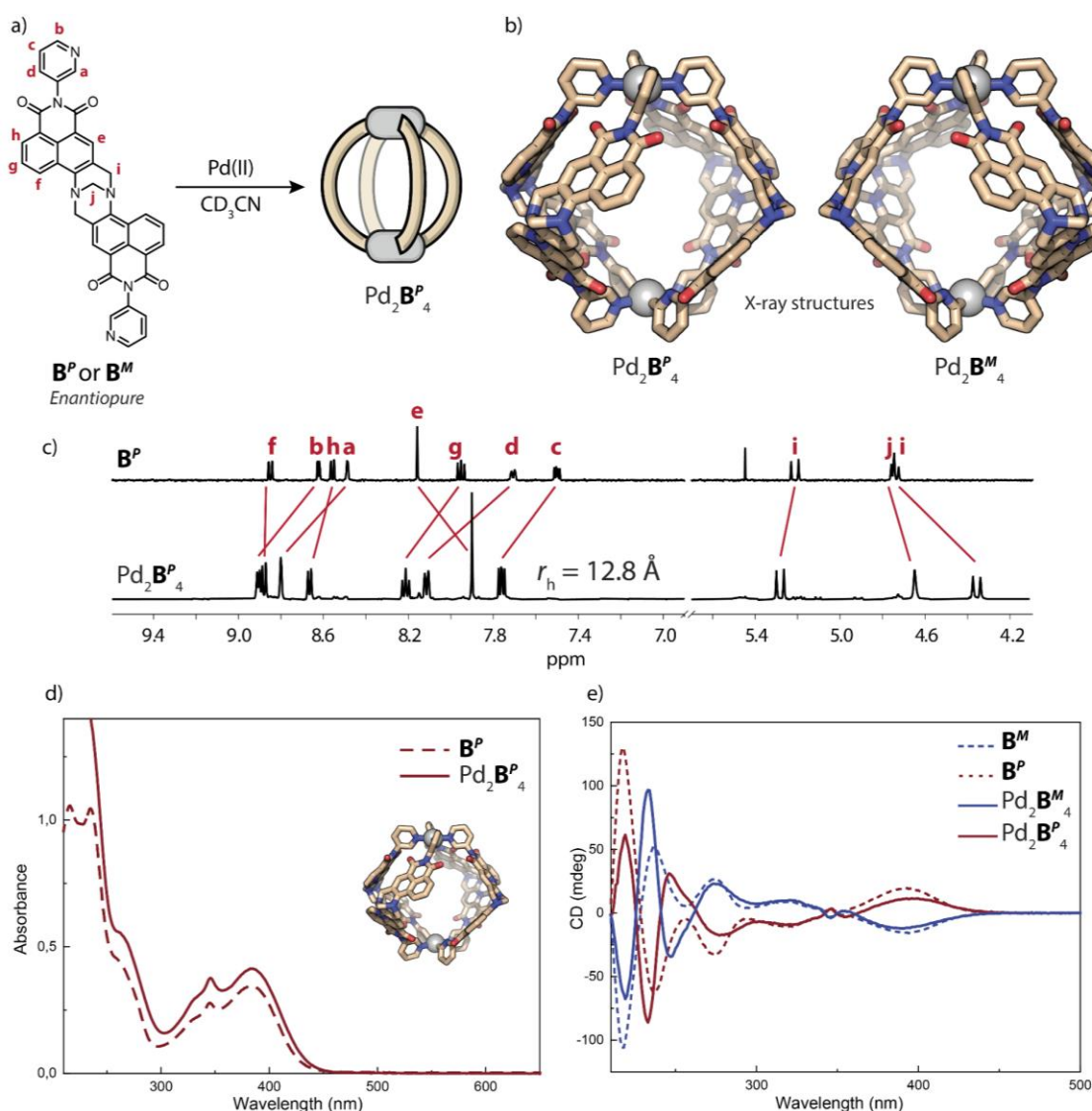


Figure 2: a) Self-assembly of enantiopure $\text{Pd}_2\mathbf{B}^P_4$. b) X-ray structures of $\text{Pd}_2\mathbf{B}^P_4$ and $\text{Pd}_2\mathbf{B}^M_4$. c) ^1H -NMR (CD_3CN , 500 MHz) stack of $\mathbf{B}^P$ and $\text{Pd}_2\mathbf{B}^P_4$. d) UV-Vis and e) CD of $\mathbf{B}^P$ and $\text{Pd}_2\mathbf{B}^P_4$ in acetonitrile, 2 mm cuvette, 0.12 mM concentration in ligand.

In accordance with the previously reported derivative bearing a *para*-pyridine donor group,^[7] the ligand presented an absorption band in the UV region at 346 nm, which corresponds to π - π^* transition, as well as a broader band at 385 nm attributed to an intramolecular charge transfer (ICT) transition of the 4-amino-1,8-naphthalimide unit (Figure 2d). Following its coordination with Pd(II), the absorbance properties remained nearly

identical to those of the free ligand with no significant shifts of the bands despite slight changes in intensity. The addition of a small excess of Pd(II) did not further alter this spectrum. Additionally, both the ligand and the cage exhibited a shoulder in the far-UV region, clearly observable at 265 nm. The similarities between ligand and cage were also reflected in their CD spectroscopy profiles (Figure 2e).

The host-guest properties of the enantiopure assemblies were then further investigated (Figure 3). As with the racemic cage, the homochiral $\text{Pd}_2\text{B}^{\text{P}}_4$ was capable of taking up fullerene C_{60} and two molecules of corannulene (cora). Additionally, when a solution of the cage was stirred at 70 °C in the presence of an excess of C_{70} powder, the ^1H NMR signals of the assembly shifted significantly with the inward-pointing proton H_a being notably affected (Figure 3a). This change in the chemical environment, similar to observations with other guests and numerous reported systems, indicates the encapsulation of fullerene within the available inner space of the cage. These binding events were further corroborated using ^{13}C NMR by the observation of signals corresponding to the respective encapsulated guests, otherwise insoluble in organic solvent. For example, a prominent signal at 141.2 ppm corresponding to fullerene C_{60} within the cavity of the cage $\text{Pd}_2\text{B}^{\text{P}}_4$ could be observed in the ^{13}C NMR of the host-guest complex. The encapsulation of the three guests was eventually confirmed by ESI-MS analysis where prominent peaks for $[\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4]^{4+}$, $[\text{C}_{70}@\text{Pd}_2\text{B}^{\text{P}}_4]^{4+}$ or $[(\text{cora})_2@\text{Pd}_2\text{B}^{\text{P}}_4]^{4+}$ could be identified on the respective spectra (Figure 3b). We attempted the encapsulation of several other planar aromatic guests as well as fullerene derivatives but these efforts were unsuccessful. However, this cage was found to encapsulate numerous other neutral molecules such as testosterone or Mirex though these results will not be discussed further in this dissertation. In the three discussed examples, a large excess of guests was necessary to observe the full conversion into the host-guest complexes which we solely attribute to the solubility of those guests in organic solvent.

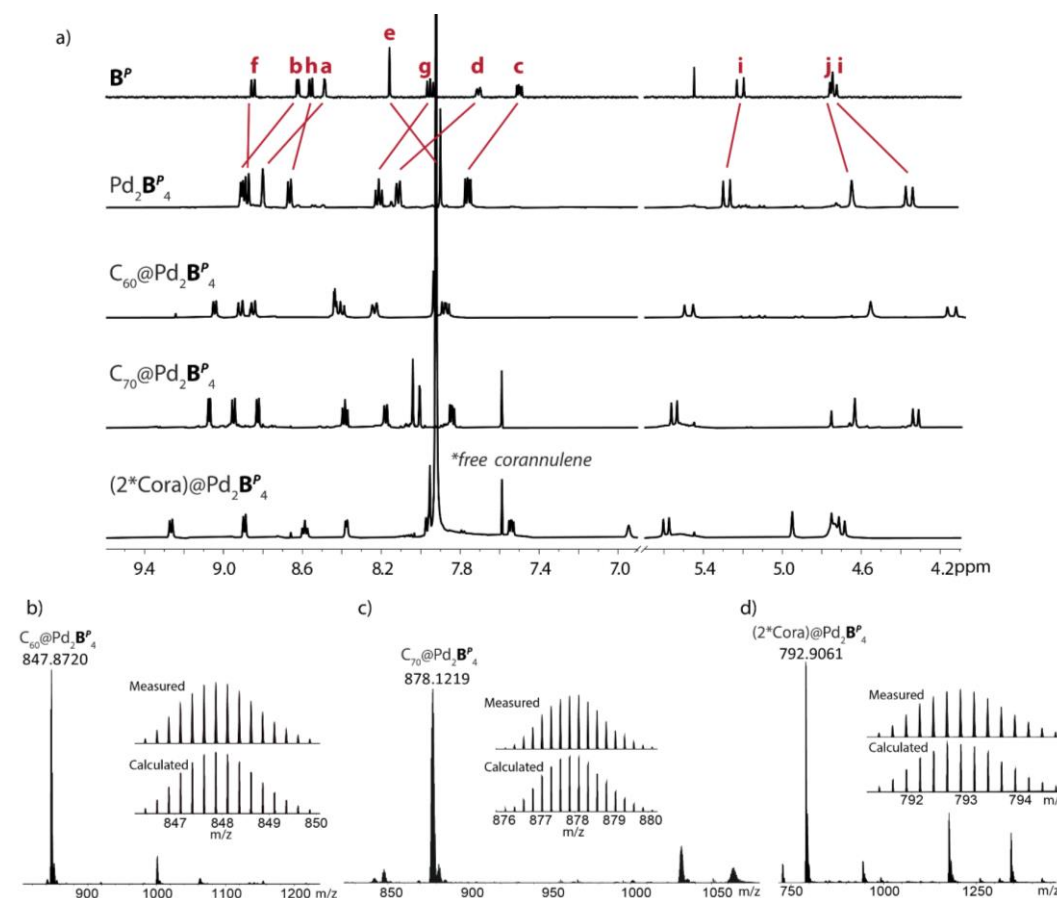


Figure 3: a) Stacked ^1H -NMR (CD₃CN, 500 MHz) stack of enantiopure ligand B^{P} and $\text{Pd}_2\text{B}^{\text{P}}_4$, $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$, $\text{C}_{70}@\text{Pd}_2\text{B}^{\text{P}}_4$ and $(\text{Cora})_2@\text{Pd}_2\text{B}^{\text{P}}_4$. b)-d) HR-ESI-MS of the host-guest complexes $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$, $\text{C}_{70}@\text{Pd}_2\text{B}^{\text{P}}_4$ and $(\text{Cora})_2@\text{Pd}_2\text{B}^{\text{P}}_4$ respectively. Isotopic patterns are highlighted.

As the solubility of fullerene is dramatically low in CD_3CN , a binding constant in this solvent could not be directly determined. However, competition experiments enabled to establish a ranking of the binding strength between the three guests as follows: $\text{C}_{60} > \text{C}_{70} > \text{cora}$ (Figure 4). When a preformed solution of $(\text{cora})_2@ \text{Pd}_2\text{B}^{\text{P}}_4$ (still with corannulene excess as it is slightly soluble in acetonitrile) was stirred at 70°C in the presence of C_{60} or C_{70} , the gradual replacement of corannulene from the cavity was observed in a slow exchange fashion (Figure 4a-b). After 72 h the guest exchanges were complete and only the signals corresponding to $\text{C}_{60}@ \text{Pd}_2\text{B}^{\text{P}}_4$ or $\text{C}_{70}@ \text{Pd}_2\text{B}^{\text{P}}_4$ could be observed in the respective NMR spectra. On the other hand, when a solution of empty $\text{Pd}_2\text{B}^{\text{P}}_4$ was stirred at 70°C in presence of C_{60} and C_{70} , the recorded ^1H NMR spectra after 24 h showed only the trace corresponding to $\text{C}_{60}@ \text{Pd}_2\text{B}^{\text{P}}_4$ (Figure 4c). Further heating did not lead to any changes, thus it was concluded that this represented the thermodynamic minimum of the system and not a kinetically trapped state. Selective extraction and purification of C_{60} from a mixture containing several PAHs or from carbon soot was also demonstrated. When those mixtures were stirred with an acetonitrile solution of $\text{Pd}_2\text{B}^{\text{P}}_4$, C_{60} was the only PAH taken up by the assembly. Following this, the mixing of toluene and centrifugation resulted in the host-guest precipitation and the solubilization of the other PAHs. Therefore, this species was selectively separated and recovered. More intriguingly, when $\text{C}_{60}@ \text{Pd}_2\text{B}^{\text{P}}_4$ was stirred in a biphasic system with carbon disulfide CS_2 , no fullerene release was observed attesting to an extremely tight affinity of the cage for guest which is often released and solubilized in such solvent.

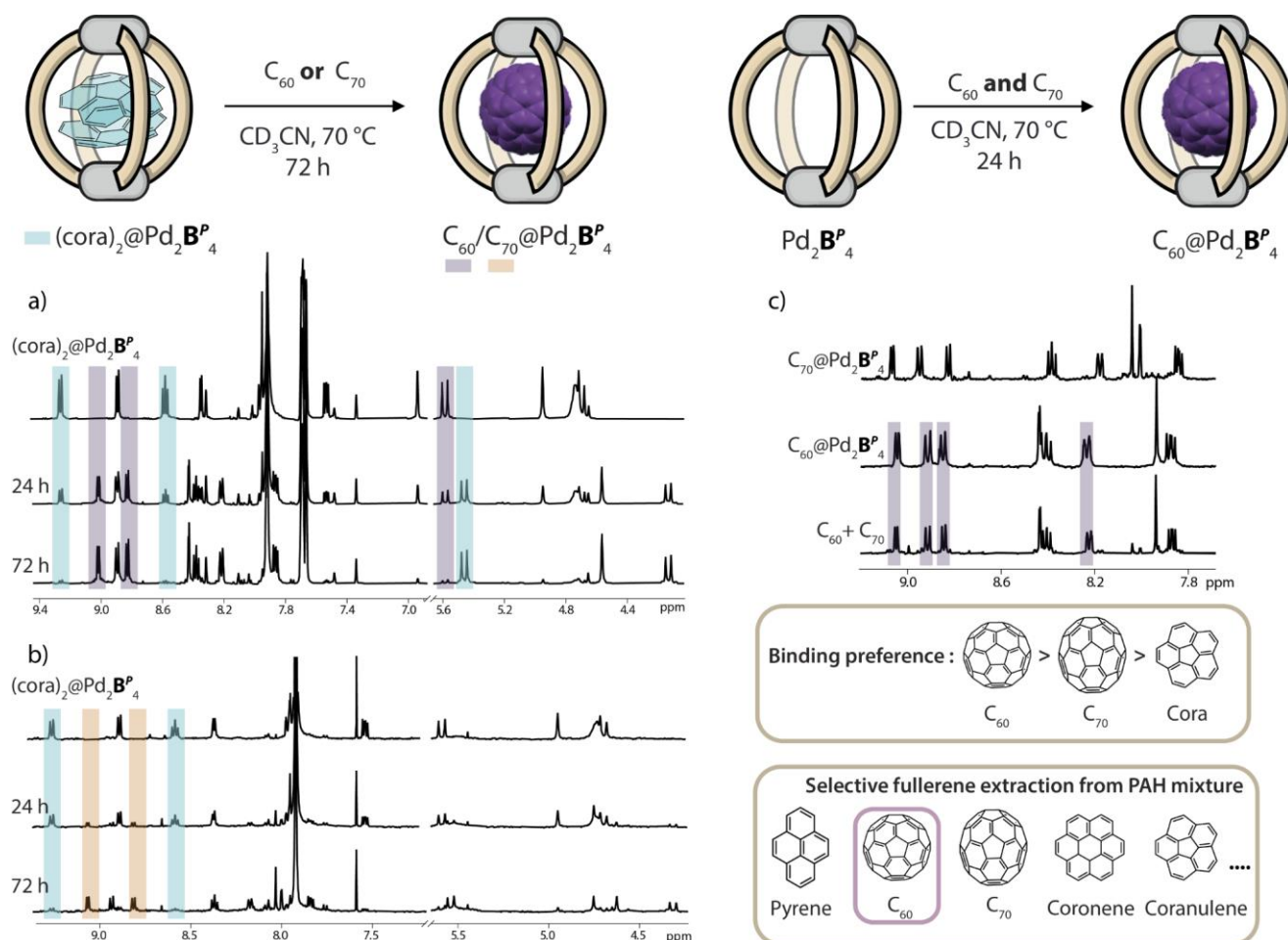


Figure 4: a) ^1H -NMR (CD_3CN , 500 MHz) starting from $(\text{Cora})_2@ \text{Pd}_2\text{B}^{\text{P}}_4$ and following its displacement by C_{60} over 72 hours. b) ^1H -NMR (CD_3CN , 500 MHz) starting from $(\text{Cora})_2@ \text{Pd}_2\text{B}^{\text{P}}_4$ and following its displacement by C_{70} over 72 hours. c) ^1H -NMR (CD_3CN , 500 MHz) of the competition experiment for the uptake of fullerene C_{60} and C_{70} .

The replacement of corannulene is most likely driven by both entropy, as one fullerene releases two molecules of corannulene, and enthalpy with an increase in favorable π - π interactions between host and guest owing to the larger aromatic surfaces of fullerenes. On the other hand, the selective binding of C_{60} over C_{70} is attributed to a better fit between the spherical cavity of $Pd_2B^P_4$ and the likewise shape of C_{60} . These arguments were confirmed by obtaining suitable crystals of $(cora)_2@Pd_2B^P_4$ and $C_{60}@Pd_2B^M_4$ for synchrotron analysis, as well as by using DFT modeling ($\omega B97X-D/def2-SVP$) for $C_{70}@Pd_2B^P_4$ (Figure 5). Comparing the crystal structure of the empty host with those of the host-guest highlighted an induced fit phenomenon, often referred to as “breathing” mechanism (Figure 5a-b). Indeed, the Pd-Pd distance in the empty cage was 14.0 Å but we also measured an average N-N distance of 17.1 Å for the atoms situated on the Tröger base core of the ligand (see Figure 5). The same distances in the $C_{60}@Pd_2B^P_4$ host-guest were respectively 15.3 Å and 15.5 Å, as well as 14.8 Å and 16.3 Å for $(cora)_2@Pd_2B^P_4$. The host, therefore, undergoes a lateral contraction accompanied by an increase in Pd-Pd distance in order to maximize the host-guest interactions. The perfect fit of fullerene C_{60} within the cavity of $Pd_2B^P_4$ was emphasized by visualizing the Conolly surface (also named accessible surface area) representation of the guest and showed a near-fully filled inner space (Figure 5b).

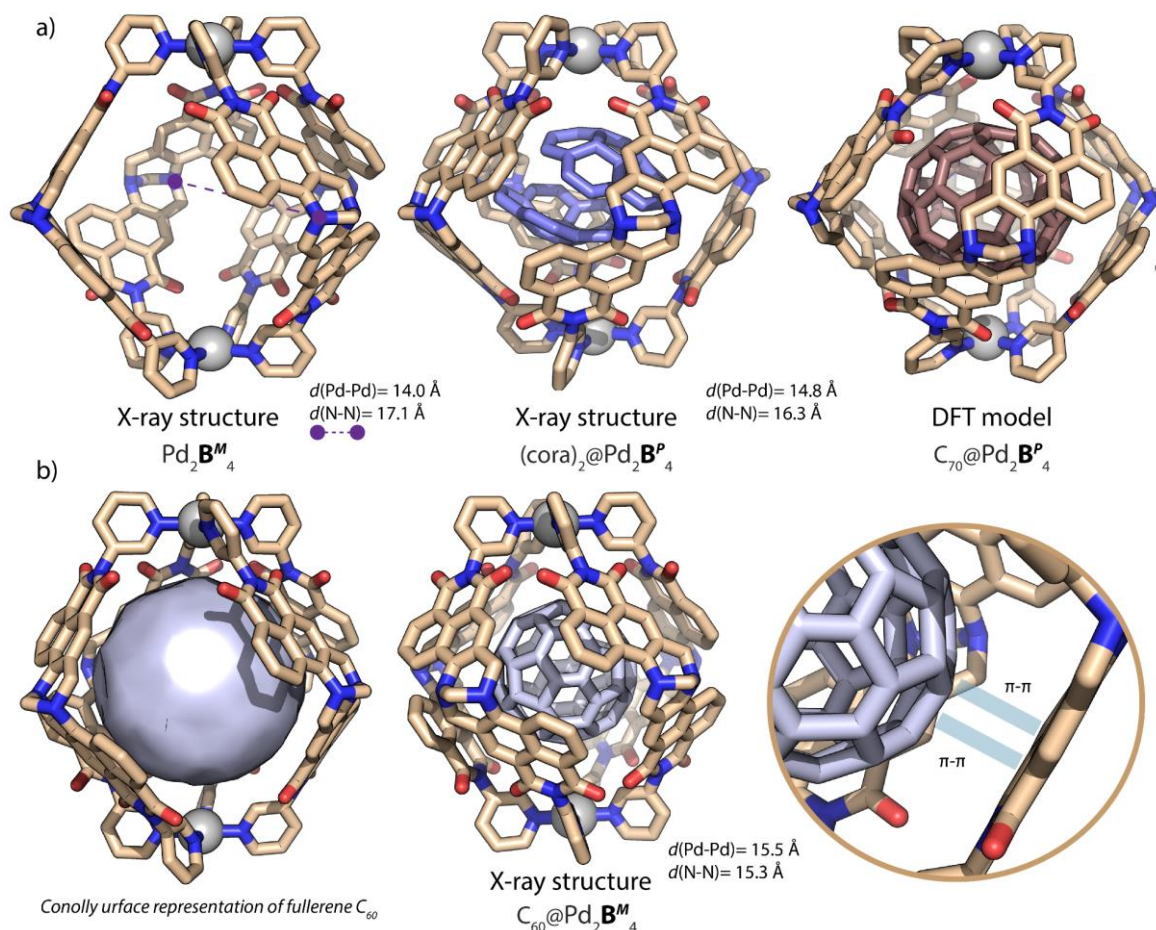


Figure 5: X-ray structures of (left) $Pd_2B^M_4$ (center) and $(Cora)_2@Pd_2B^P_4$, and (right) DFT model ($\omega B97X-D/def2-SVP$) of $C_{70}@Pd_2B^P_4$. b) X-ray structures $C_{60}@Pd_2B^M_4$ with (left) the Conolly surface representation of the fullerene to visualize the occupied space within the cavity. (right) highlighted host-guest π - π interactions with the naphthyl panels of the cage.

These strong interactions between the chiral host and the guests prompted me to dig deeper into the photophysical characterization of these systems. The UV-Vis analysis on the fullerenes host-guest complexes brought new observations as compared to the empty cage (Figure 6). Encapsulation of fullerene C_{60} in a 1:1 manner resulted in a clear increase of the far-UV contribution, with the shoulder initially located at 265 nm becoming a clear band centered at the same wavelength. This effect was, however, moderate for C_{70} . C_{60} binding

also led to a broadening of the following band previously centered at 346 nm and two maxima could be observed at 338 nm and 348 nm. Eventually, the band at 385 nm underwent a decrease in intensity as well as a more pronounced tailing observable up to 500 nm at this concentration. While C_{70} led to similar modifications for the first aforementioned band at 346 nm, the effect was significantly stronger for the second one. Indeed, not only the band initially located at 390 nm shows a clear tailing to higher wavelength but the rise of a new band around 500-550 nm was observable (Figure 6). Comparison of the UV-Vis spectra at a higher chromophore concentration of 1.4 mM, in the assemblies, further strengthened our previous observations. The empty cage absorption band completely disappears at 475 nm while the one for the cage with C_{60} is prolonged until 650 nm. On the other hand, the host-guest complex of C_{70} presents a new band at 485 nm with a shoulder at 565 nm and is still visible at 750 nm at this concentration (Figure 6). The strong π - π interactions between the naphthyl moieties of the ligands, amplified by the curved shape of the latter, and the fullerenes within the cavity result in an aromatic electron-poor electron-rich host-guest complex.

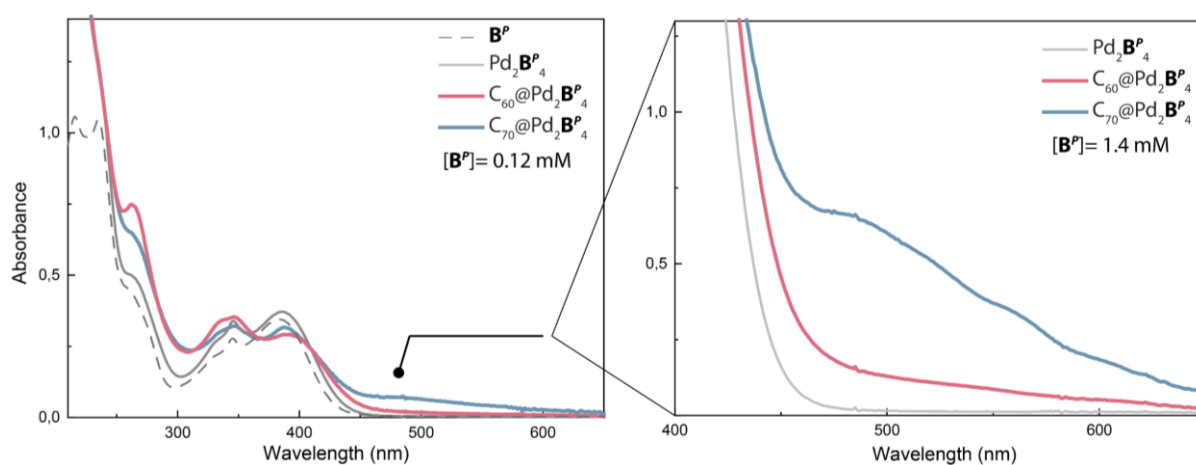


Figure 6: UV-Vis spectra overlap of B^P , $Pd_2B^P_4$, $C_{60}@Pd_2B^P_4$, $C_{70}@Pd_2B^P_4$ in acetonitrile, 2 mm cuvette, 0.12 mM (left) and 1.4 mM (right) concentration in ligand.

The fluorescence of the ligand B^P as well as both of the empty cage $Pd_2B^M_4$ and of host-guest complexes $C_{60}@Pd_2B^M_4$ and $C_{70}@Pd_2B^M_4$ was measured (Figure 7a). When excited at 350 nm, B^P presented a broad emission band centered at 560 nm and tailing up to more than 700 nm, while also displaying a shoulder in the blue region at 430 nm. Interestingly, coordination to Pd(II) led to an increase in the luminescence intensity of the main band and the shoulder disappeared. The emission remained overall broad (400 nm to >700 nm). This increase in emission is likely triggered by a restriction of motion of the ligand in the rather tight cage assembly which results in a suppression or decrease of nonradiative pathways. Excitation at higher wavelengths such as 450 nm drastically decreased the intensity of emission and blue-shifted the band to 520 nm. Furthermore, the binding of C_{60} or C_{70} caused a severe quenching of the fluorescence of the assembly and the intensity decreased by a factor of five (Figure 7a). A conceivable explanation for this phenomenon would be the photo-induced electron transfer from the excited state of the ligand to fullerene which becomes competitive to the emission pathway (*i.e.* dark state(s) being populated). This would not be surprising as fullerenes are commonly known to be electron acceptors. However, this can not be proven from the presented data.

Further DFT calculations (geometry optimizations ω B97X-D/def2-SVP and single point energy calculations ω B97X-D/def2-TZVP) for both $C_{60}@Pd_2B^M_4$ (Figure 7b) and $C_{70}@Pd_2B^M_4$ also enabled the visualization the orbitals of the species. The HOMOs are fully (for C_{60}) or mostly (for C_{70}) located on the ligand(s) while in both cases the LUMOs are located on the fullerene guest which hints at one electron richer moiety and one electron poorer one.

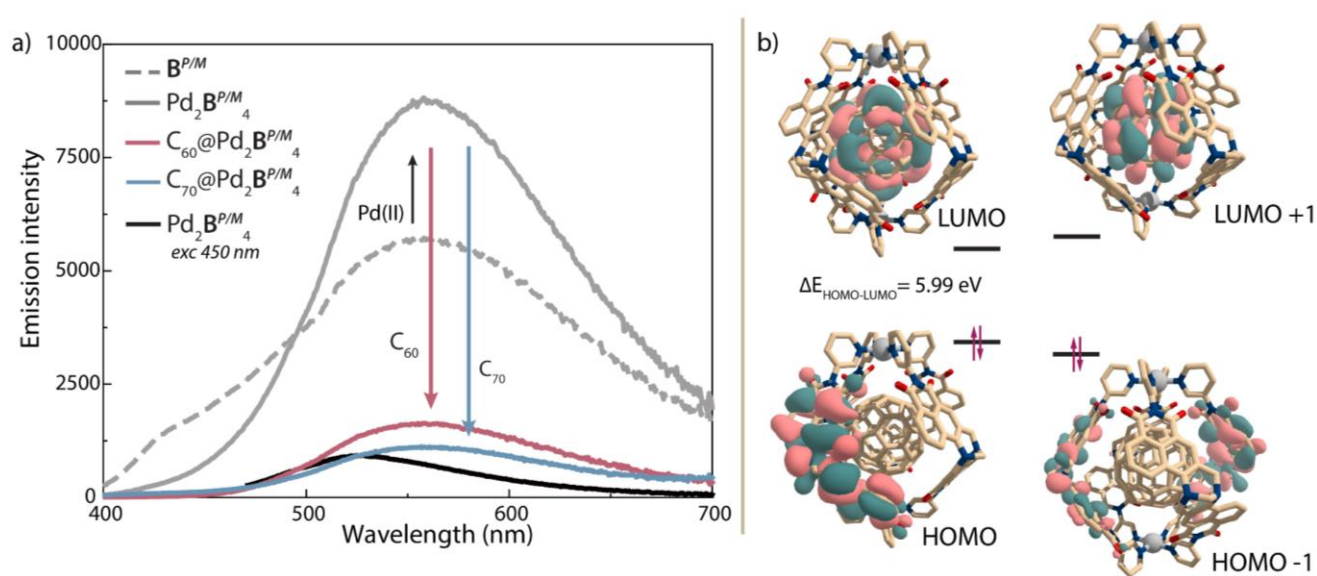


Figure 7: a) Fluorescence spectra overlap of B^P , Pd_2B^P/M_4 , $C_{60}@Pd_2B^P/M_4$ and $C_{70}@Pd_2B^P/M_4$ in acetonitrile, 2 mm cuvette, 0.012mM concentration in ligand, excitation at 350 nm. b) Frontier orbitals diagram of the $C_{60}@Pd_2B^P/M_4$ host-guest complex with highlighted HOMO-LUMO gap energy. Representation of the orbitals shows their localization on the host (HOMO) or the guest (LUMO).

More interestingly here, the systems were further characterized using CD spectroscopy (Figure 8). Effects arose upon encapsulation of fullerenes as observed before in the absorption study. At 0.12 mM in chromophore (within the assembly), encapsulation of C_{60} and C_{70} led to the disappearance of the small Cotton Effects at 342 nm, 349 nm and 362 nm as well as the emergence of a new change in the CD signal sign at 329 nm (Figure 8). The CD band of the empty cage located at 390 nm underwent a redshift, especially for C_{70} , reaching 404 nm. Eventually, even at this concentration, a new CD band with very low intensity could be seen at 530 nm for the C_{70} host-guest complex. Increasing the concentration to 1.4 mM unambiguously confirmed these new CD bands (Figure 8). For the C_{60} host-guest complex, the previously described absorbance tail was also observable in the CD and small fluctuations were observable after 600 nm with a more pronounced CD band at 687 nm. The effect arising from the C_{70} HG complex was even more consequent. Stronger CD bands could be observed centered at 530 nm, 590 as well as 645 nm. Moreover, a positive Cotton effect at 485 nm was followed by a negative one at 563 nm.

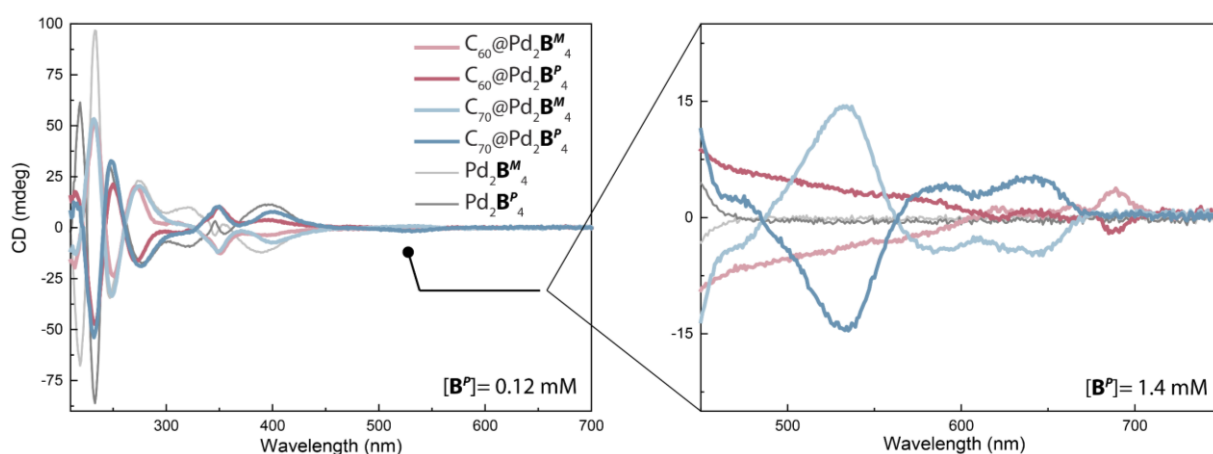


Figure 8: CD spectra overlap of Pd_2B^P/M_4 , $C_{60}@Pd_2B^P/M_4$, $C_{70}@Pd_2B^P/M_4$ in acetonitrile, 2 mm cuvette, 0.12 mM (left) and 1.4 mM (right) concentration in ligand.

All these effects emerge in a region (450-700 nm) in which neither the organic ligand nor the empty cage absorbs and therefore could be attributed to the fullerenes' forbidden electronic transitions within the host-guest system, also explaining their weak intensity. Note that, in the host-guest system, the total concentration of fullerene is four times lower than the one of the chromophores (ligands) which also results in lower intensity.

In order to confirm that those absorption and CD bands were the consequence of fullerene-centered transitions, the UV-Vis spectra of C_{60} and C_{70} and the host-guest complexes were recorded in benzene and in a 1:1 acetonitrile/benzene mixture, where they are all soluble (Figure 9). This absorption region (450-700 nm) corresponds to the typical window for symmetry-forbidden $t_{1u} \leftarrow h_u$ transitions in fullerenes (Figure 9a). A detailed analysis of the fullerene electronic situation and DFT calculations (geometry optimizations ω B97X-D/def2-SVP and single point energy calculations ω B97X-D/def2-TZVP) of both the free fullerene C_{60} and C_{70} guests and their corresponding host-guest complexes can be found in the experimental section of this chapter. Comparing the spectra of free and encapsulated C_{70} (Figure 9b) or C_{60} (Figure 9c) in the previously mentioned absorption region unambiguously confirmed their similar origin as they can be accurately matched. Moreover, the wavelengths of these bands are also in adequation with those observed in circular dichroism (Figure 8). Thus we can assume that the effects observed in the CD experiments are emerging from a host-to-guest chiral induction of the chiral $Pd_2B^{P/M}_4$ capsule onto the pristine fullerene guest within its cavity.

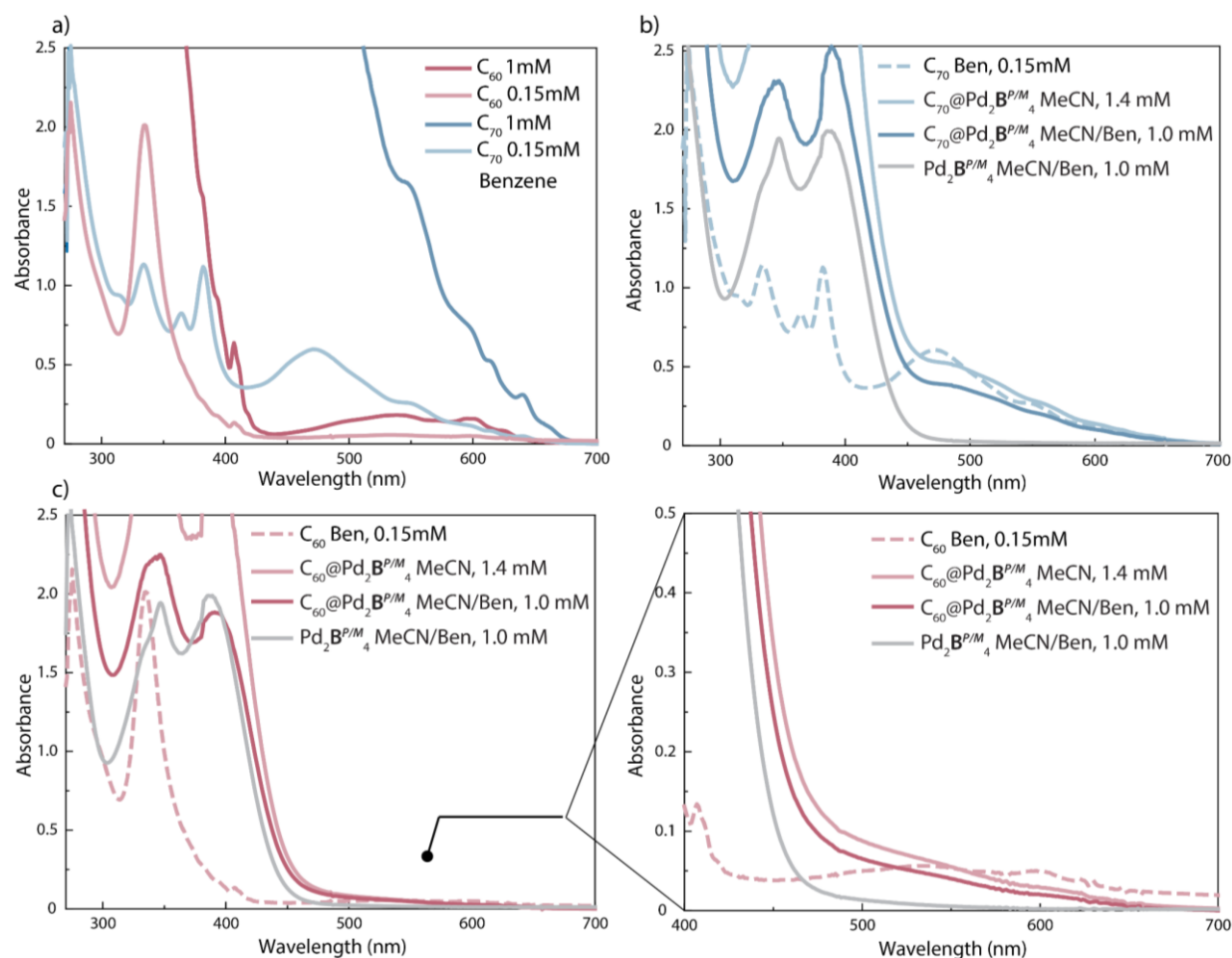


Figure 9: a) UV-Vis spectra of fullerene C_{60} and C_{70} in benzene. b) Stack of UV-Vis spectra of C_{70} in benzene, $C_{70}@Pd_2B^{P/M}_4$ in acetonitrile and acetonitrile/benzene mixture and empty cage $Pd_2B^{P/M}_4$ in acetonitrile/benzene mixture. The bands can be matched by comparing the 450-700 nm window. c) Stack of UV-Vis spectra of C_{60} in benzene, $C_{60}@Pd_2B^{P/M}_4$ in acetonitrile and acetonitrile/benzene mixture and empty cage $Pd_2B^{P/M}_4$ in acetonitrile/benzene mixture. The bands can be matched by comparing the 450-700 nm window. Inset displays a zoom on this region for better clarity. 2 mM cuvette, concentration in ligand, or fullerene directly indicated.

Changing the polarity of the solvent, using 1:1 mixtures of MeCN/Ben, MeCN/Diox, MeCN/DCM or MeCN/Water, and recording UV-Vis spectra of $C_{70}@Pd_2B^M_4$, in which the effect is more strongly marked, also highlighted no significant shift of these bands and allowed us to exclude those bands as originating from a ground state charge transfer interaction. It also shows the strong shielding effect provided by the cage walls to the fullerenes as these $t_{1u} \leftarrow h_u$ transitions are also known to be sensitive to solvent modifications.

These results all together present a chiral host-guest complex in which pristine fullerene C_{60} (or C_{70}) undergoes chiral induction, leading to new absorption and CD bands in the visible region (Figure 8). We proceeded to a control experiment in which free ligand at a concentration of 1.4 mM was mixed with fullerene C_{60} or C_{70} in acetonitrile, sonicated and heated to favor potential fullerene solubilization. Recording of CD spectra does not show the previously described band witnessing the importance of the cage environment both for solubilization of the fullerene and for the chiral information transfer. Introducing chirality into fullerene has attracted considerable attention over the last few years and only a few reports have described chirality transfer from a chiral host molecule onto an encapsulated achiral fullerene entity via supramolecular interactions.^[19–23] This phenomenon has been referred to as chirogenesis. With the emergent interest in the CISS effect,^[24] the growth of research on spintronics,^[25] and other fullerene-based materials,^[26] this sort of chiral induction process will hopefully find broader application in the near future. Eventually, we also showed that one can generate a long-lived C_{60} radical anion within the cavity of a Pd_2L_4 capsule.^[27] Further studies will now explore the possibility of generating and stabilizing such species within the cavity of our chiral host and therefore obtaining radicals in a chiral environment.

2. Homochiral figure-of-eight cage

It is straightforward to observe that ligand **B^{P/M}** shares several analogies with previously reported nanoribbon ligand **B3** (also noted **L3** in **Chapter II**).^[16] Both ligands exhibit a curved, three-dimensional structure, with the pyridine moiety oriented perpendicular to the curved core. They also possess aromatic surfaces that facilitate the binding of polycyclic aromatic hydrocarbons (PAHs) such as fullerene C₆₀. The homoleptic species formed from these ligands can be described as capsules, as they possess more enclosed cavities compared to the classical Pd₂L₄ assemblies. This observation led to the investigation of the potential association of **B^{P/M}** with diketopyrrolopyrrole (DPP) ligand **A**. A previously undiscussed aspect of the heteroleptic figure-eight cages such as Pd₂**A₂B3₂** is their intrinsic chirality. Indeed, the interlaced arrangement of the two ligands **A** into this “8” shape gives rise to two enantiomers noted *P* or *M* (Figure 10a). While **B3** is not chiral, the formation of *P* or *M* was not preferentially biased, thus both enantiomers were obtained as a racemate in solution.

When combined in a 1:1:1 ratio in CD₃CN, enantiopure **B^{P/M}**, **A** and Pd(II) produced a single set of ¹H signals by NMR (Figure 10b-d). None of the signals from this trace corresponded to the free ligands in solution or the homoleptic species, attesting to a new species formed quantitatively in solution. DOSY NMR confirmed the formation of a unique assembly with a hydrodynamic radius of *r_h* = 11.8 Å. This was consistent with the formation of a dinuclear assembly Pd₂**A₂B^P₂**, an assumption further supported by ESI-MS analysis (Figure 10c). We could identify the peaks corresponding to [Pd₂**A₂B^P₂ + nBF₄]⁽⁴⁻ⁿ⁾⁺, with isotopic patterns perfectly matching the sum formula. Due to the two chiral configurations of the 8, the introduction of a second chiral component can lead to the formation of a pair of diastereoisomers. Starting from enantiopure **B^P** could thus result in the formation of the **B^PMB^P** or **B^PPB^P** species (herein the central letter denotes the chirality of the 8 and Pd(II) are omitted for simplicity, see figure for visual explanation). The single set of signals, however, suggested the formation of a unique diastereoisomer of the heteroleptic cage. The likelihood of the two isomers having identical ¹H NMR was dismissed due to their significantly different chemical environments. Using the other enantiomers **B^M** led to the exact same NMR spectra confirming the formation of the second enantiomer of the heteroleptic cage. Using VT NMR, we could assign all the proton signals of the species (Figure 10d, inset). Thus, it appears that the chirality of the outer ligand dictates the chirality of the central moiety, likely driven by a preferential arrangement of ligands to minimize steric clashes. As suitable crystals for X-ray diffraction analysis could not be obtained, DFT calculations were employed to decipher which isomer was formed in each case. Two models of diastereoisomers **B^MMB^M** and **B^MPB^M** were geometry-optimized (ωB97X-D/def2-SVP), and their respective energies were extracted from the calculations (Figure 10e). The **B^MMB^M** isomer was found to be more stable than **B^MPB^M** by 17.9 kJmol⁻¹. The structures also showed fewer distortions in the case of **B^MMB^M**, and this arrangement of the ligands likely prevented a steric hindrance between the phenyl moieties of **A** and the outer part of the naphthyl groups present in **B^M**. From these calculations, it was thus concluded that the enantiomer **B^M** enforced the *M* isomer of the 8 while **B^P** led to the *P* one (Figure 10e).**

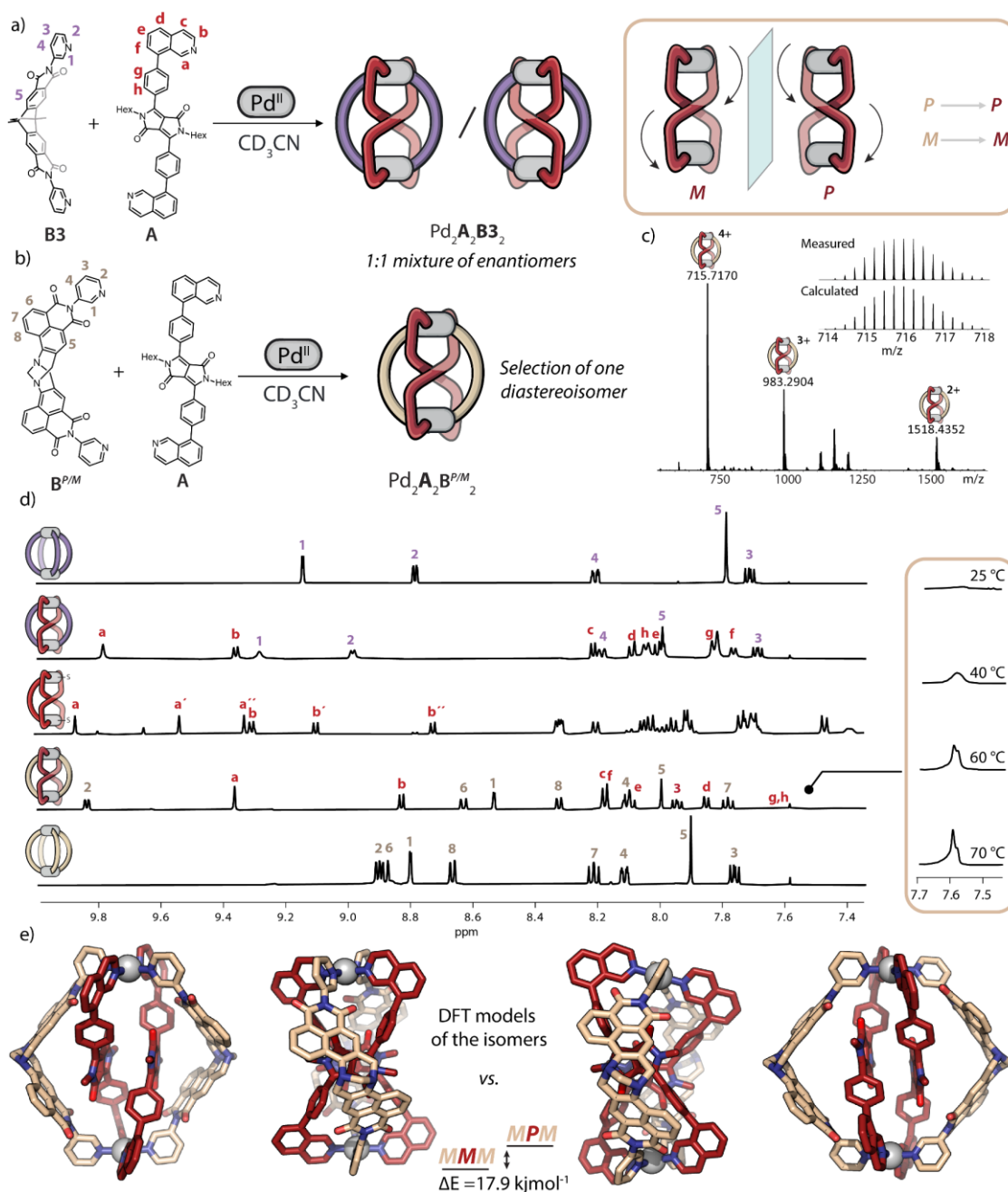


Figure 10: a) Formation of the achiral $\text{Pd}_2\text{A}_2\text{B}_3_2$ or b) homochiral $\text{Pd}_2\text{A}_2\text{B}^{\text{P/M}}_2$ figure-eight. c) HR-ESI-MS of the $\text{Pd}_2\text{A}_2\text{B}^{\text{P/M}}_2$ assembly with isotopic pattern highlighted. d) $^1\text{H-NMR}$ (CD_3CN , 500 MHz) of the different homoleptic and heteroleptic assemblies with assignment. e) Structures and energies comparison between the two possible diastereoisomers of the chiral figure-eight. The outer ligand chirality dictates the δ chirality with B^{M} giving M and B^{P} giving P .

In the present study, it appears that both ribbon-like ligands exhibit similar behaviors in the presence of **A**. However, ligand $\text{B}^{\text{P/M}}$ induced the formation of homochiral species. Consequently, I proceeded to investigate the photophysical properties of this cage (Figure 11), as the figure-eight topology of the DPP ligand has been shown to confer unique luminescence characteristics as described in **Chapter I**. Upon irradiation at 354 nm, the sample exhibited intense luminescence, consistent with observations for the cages discussed in **Chapter I**. All the spectra were recorded using solutions with a total concentration in chromophore ligand of 0.12 mM in acetonitrile. The UV-Vis spectrum showed overlapping contributions from both ligands (Figure 11a), with a prominent absorption band in the UV region around 350 nm, corresponding to the $\pi\text{-}\pi^*$ transition of $\text{B}^{\text{P/M}}$ and overlaying with the contribution of **A**. The ICT transition band (around 390 nm) of $\text{B}^{\text{P/M}}$ can also be partially observed overlaying with

the previously described one. The characteristic absorption band of the DPP moiety, spanning 450 nm to 550 nm, was also observed. These absorption features are reflected in the CD spectra, where the two enantiomers display mirror-image Cotton effects between 200 nm and 350 nm (Figure 11b). The positive Cotton effect observed around 500 nm for $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ (and its corresponding negative effect for $\text{Pd}_2\text{A}_2\text{B}^{\text{M}}_2$) clearly indicated the presence of **A** in a chiral environment. This specific contribution will be utilized later to probe the chiral state of the system. We also studied the emission properties of these two species. Both enantiomers exhibited strong luminescence with a broad band in the 520–620 nm region, specifically corresponding to the emission of the DPP ligand **A**. The main emission band was centered at 555 nm with a shoulder at 600 nm (Figure 11c). These are the typical features of the assemblies obtained from this ligand **A** (see last subsection of **Chapter I**). Furthermore, circularly polarized luminescence (CPL) measurements revealed that the two isomers produced mirror-image CPL emission with a reasonable dissymmetry factor of $1.7 \cdot 10^{-3}$ for Pd (II)-based assemblies (Figure 11c). This observation further confirmed the presence of **A** in a chiral environment, making it another useful tool for probing chirality. Interestingly, exciting the samples at 350 nm or 450 nm resulted in the same CPL emission. While both ligands absorb at 350 nm, only **A** is excited by photons at the latter wavelength. This suggested a possible energy transfer between the two ligands, a phenomenon discussed for similar assemblies in **Chapter I**. I will not delve further into this in the present case. This also implies that observing a CPL emission for a $\text{Pd}_2\text{A}_2\text{B}_2$ figure-of-eight upon excitation at 450 nm allows us to exclude the possibility of a chiral FRET phenomenon. Eventually, we did try to optimize the dissymmetry factors by varying solvents and anions employed for the cage but no significant changes were observed.

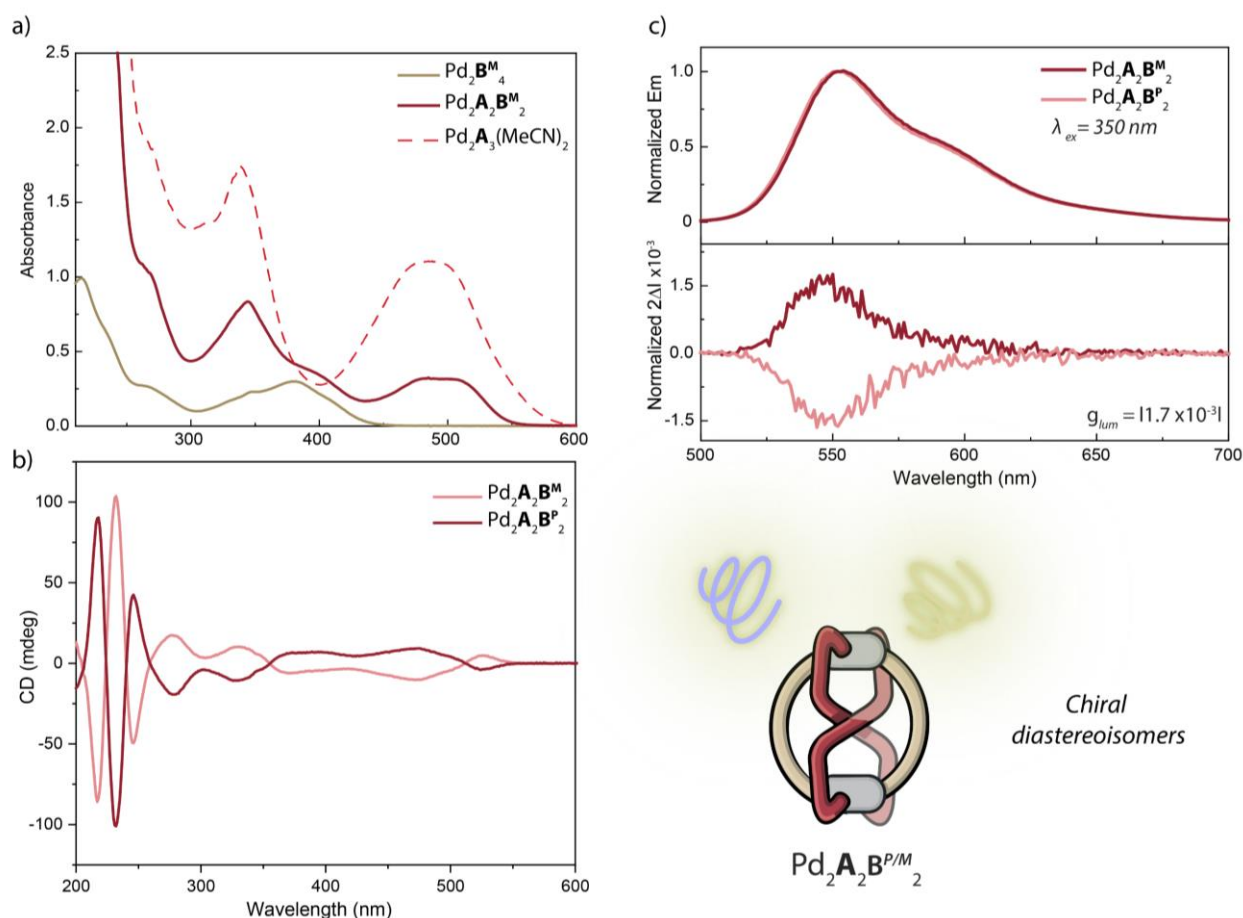


Figure 11: a) UV-Vis spectra of Pd_2B_4 , $\text{Pd}_2\text{A}_2\text{B}_2^{\text{M}}$ and $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ in acetonitrile, 2 mm cuvette, 0.12 mM concentration in ligand. b) CD spectra of $\text{Pd}_2\text{A}_2\text{B}_2^{\text{M}}$ and $\text{Pd}_2\text{A}_2\text{B}_2^{\text{P}}$. c) Fluorescence and CPL spectra of $\text{Pd}_2\text{A}_2\text{B}_2^{\text{M}}$ and $\text{Pd}_2\text{A}_2\text{B}_2^{\text{P}}$.

The creation of this chiral figure-eight structure represents a personal achievement. As indicated in the first chapter of this dissertation, this motif is central to the ideas I developed throughout the years. Although this topology for cages was discovered serendipitously a few years ago,^[28] we soon realized that incorporating quinolines as donor groups on our ligands could further rationalize the design of such heteroleptic assemblies.^[29] The utilization of the DPP backbone also allowed the synthesis of a purely homoleptic figure-eight structure from pyridine donor groups, wherein four DPP moieties are stacked, providing strong stabilization to the assembly.^[29] Additionally, the homoleptic cage derived from **A** constitutes what can be considered another "incomplete" figure-eight topology. In this case, three ligands **A** assemble in a $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ species, where one ligand **A** adopts the *cisoid* conformation and two adopt the S-shaped one and intertwine forming the 8. It is incomplete because a fourth ligand **A** can not coordinate to the final coordination sites of the Pd(II) cations leaving two molecules of solvent occupying those instead. The application of this ligand in the synthesis of heteroleptic structures has demonstrated its versatility. Beyond its structural significance, this ligand has been used to control and fine-tune photophysical properties, and we can now manage the chirality emerging from its pairwise arrangement.

3. Self-sorting and first steps into dynamic cage populations

As mentioned earlier, the similarities between $\text{B}^{\text{P/M}}$ and **B3** led us to draw parallels in their potential properties. Given that this thesis addresses multi-cage systems and self-sorting, the logical next step was to mix these ligands and/or their homoleptic assemblies to observe potential interesting outcomes.

When enantiopure $\text{B}^{\text{P/M}}$ and **B3** were mixed in a 1:1 ratio in the presence of an equimolar amount of Pd(II) in CD_3CN , they did not lead to a discrete species but rather a mixture of assemblies. This outcome aligned with our observations for previous ligands with very similar geometrical parameters.^[30] Further introduction of 2 equivalents of **A** effectively drove the complex mixture towards heteromeric complete self-sorting, resulting in the coexistence of the two heteroleptic cages $\text{Pd}_2\text{A}_2\text{B}^{\text{P}_2}$ and $\text{Pd}_2\text{A}_2\text{B3}_2$ (Figure 12). The ^1H NMR spectrum nicely overlaps the respective trace of the two cages synthesized separately. Thus, in this scenario, we obtained a homochiral assembly and a racemic mixture in solution. More interestingly, we found that the chiral heteroleptic structure was the favored species when competing for Pd(II). Specifically, mixing the ligands **A**, **B3** and B^{P} in a 1:1:1 with a sub-stoichiometric amount of Pd(II) led to the sole formation of the $\text{Pd}_2\text{A}_2\text{B}^{\text{P}_2}$ assembly (Figure 12). Another level of competition could be established in the system when both homoleptic Pd_2L_4 capsules were mixed in presence of one equivalent of fullerene C_{60} , as $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}_4}$ was preferentially formed. We observed that the binding of C_{60} within the cavity of this cage was significantly stronger compared to other aromatic guests because the cavity possesses the ability to adapt and optimize host-guest interactions through paneling π - π interactions. Although a similar feature was observed for $\text{Pd}_2\text{B3}_4$, the smaller cavity and aromatic surfaces offered by ligand **B3** are likely to be responsible for a lower binding strength. Therefore, assemblies containing B^{P} were consistently favored when competing for a resource (**A** or C_{60}) with **B3**. This platform was ideal for developing further complex processes.

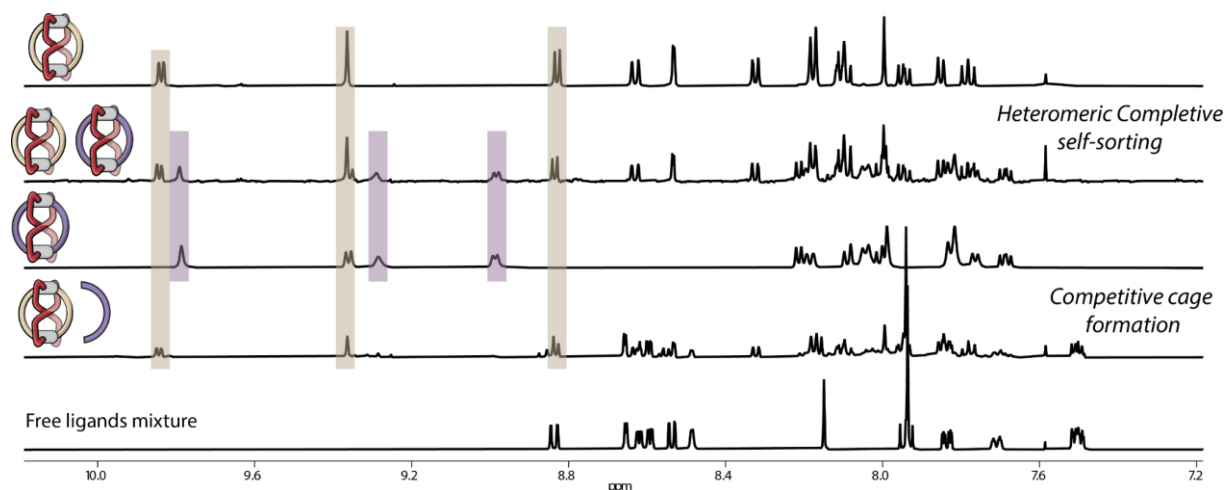


Figure 12: ^1H -NMR (CD_3CN , 500 MHz) stack highlighting the mixture of **B3** and **B^p** (bottom), competitive cage formation leading to the unique formation of $\text{Pd}_2\text{A}_2\text{B}^{\text{p}}_2$, and heteromeric self-sorting with the coexistence of both $\text{Pd}_2\text{A}_2\text{B}^{\text{p}}_2$ and $\text{Pd}_2\text{A}_2\text{B}_3$ (middle).

In the previous chapter, I demonstrated that the introduction of fullerene into cage mixtures can lead to self-sorting with potential ligand recombination. Thus, the question arose whether the host-guest interactions of $\text{Pd}_2\text{B}^{\text{p}}_4$ or Pd_2B_3 with fullerene were strong enough to disrupt their respective heteroleptic $\text{Pd}_2\text{A}_2\text{B}^{\text{p}}_2$ and $\text{Pd}_2\text{A}_2\text{B}_3$ derivatives. One sample of each cage in CD_3CN was prepared and stirred at 70°C for 24 hours in the presence of an excess of solid C_{60} . No changes were observed for $\text{Pd}_2\text{A}_2\text{B}_3$ even after longer heating times. The absence of reactivity of $\text{Pd}_2\text{A}_2\text{B}_3$ to the presence of fullerene underlined the stability of this heteroleptic assembly. To confirm this and exploit its potential, the reverse reaction was then conducted. When $\text{C}_{60}@\text{Pd}_2\text{B}_3$ was mixed and heated at 70°C with $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ (ensuring that the ligands are at the same concentration in solution) the formation of $\text{Pd}_2\text{A}_2\text{B}_3$ was observed accompanied by the release and precipitation of fullerene from the homoleptic capsule (Figure 13a). This result is significant from both a purification and detection standpoint. Indeed, our group had previously demonstrated that Pd_2B_3 could selectively extract C_{60} from carbon soot in acetonitrile.^[15,16] The fullerene could then be released by stirring the filtered liquid with carbon disulfide CS_2 , a well-known solvent allowing fullerene solubilization. However, CS_2 (as most of the solvents capable of solubilizing PAHs) is highly toxic, prompting a need for fullerene purification methods that do not involve its use. Herein, the process describes a simple method for extracting fullerene C_{60} from carbon soot using only acetonitrile as the organic solvent. This is the first example of such a process via heteroleptic cage formation. Furthermore, this release can be easily monitored by fluorescence, as the formation of the heteroleptic cage results in the interlacing of the two DPP ligands **A**. This not only disrupts the cavity of the homoleptic host but also triggers the luminescence of the final assembly. When conducted at higher concentrations the formation of a black precipitate was also observed at the bottom of the NMR tube corresponding to the released fullerene powder (see picture Figure 13b).

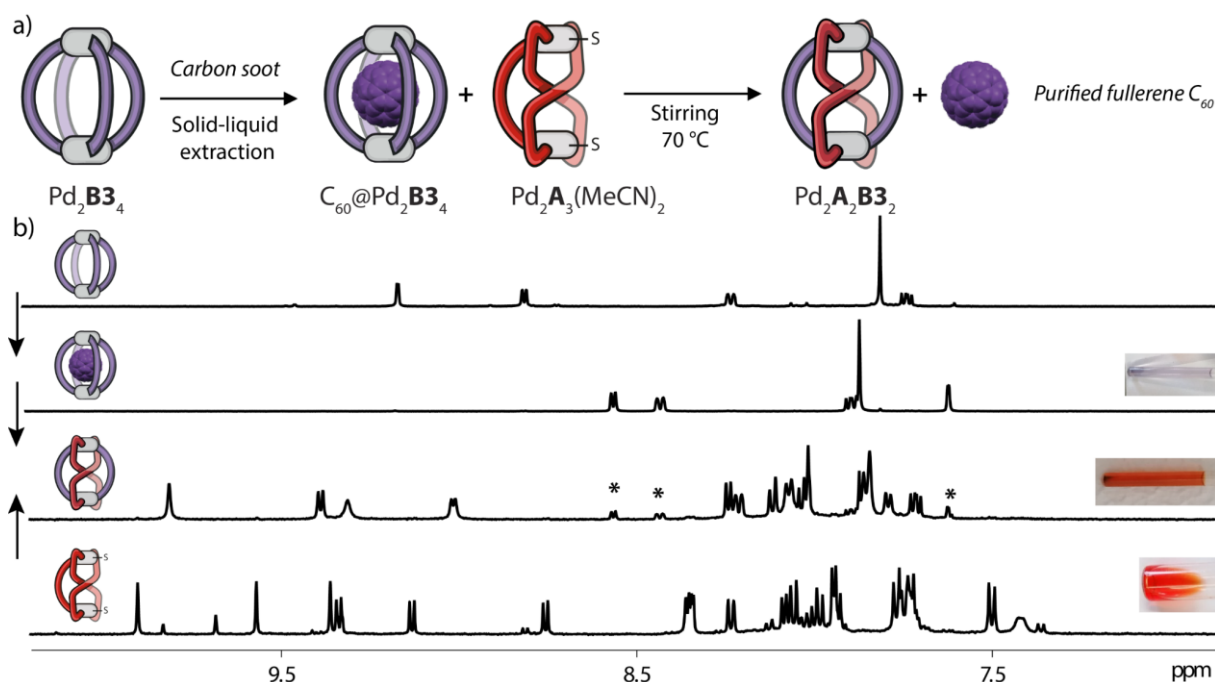


Figure 13: a) Schematic representation of the selective fullerene extraction from carbon soot and its release upon heteroleptic cage formation with **A**. b) ^1H -NMR (CD_3CN , 500 MHz) stack of $\text{Pd}_2\text{B}_3\text{A}_4$, $\text{C}_{60}@\text{Pd}_2\text{B}_3\text{A}_4$ and the outcome of adding an equimolar amount of $\text{Pd}_2\text{A}_3(\text{MeCN})_2$.

On the other hand, when recording the ^1H NMR of the samples containing B^{P} , the signals corresponding to the heteroleptic cage disappeared, while those of the $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$ assembly slowly emerged over time (Figure 14). Surprisingly, however, the signals that would correspond to the homoleptic $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ could not be detected. Repeating this experiment consistently yielded the same results. Since no precipitate was observed other than the residual excess of fullerene powder, and the solution retained the strong red color characteristic of ligand **A**, the exact outcome remained unclear. It is possible that higher-order species templated by fullerene (or other aromatic residues possibly present in the soot) are formed although it was not possible to detect such species by ESI-MS. Nonetheless, it was established that the two heteroleptic cages exhibit opposite transformative behaviors upon interaction with fullerene.

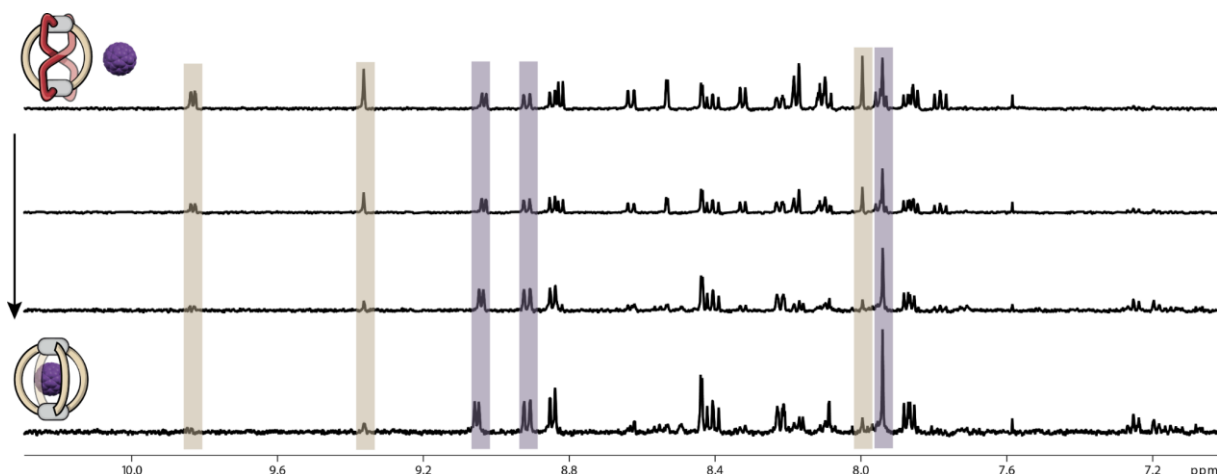


Figure 14: ^1H -NMR (CD_3CN , 500 MHz) stack following the transformation of $\text{Pd}_2\text{A}_2\text{B}_2\text{P}_2$ (beige) in the presence of fullerene C_{60} . While signals of $\text{C}_{60}@\text{Pd}_2\text{B}_2\text{P}_4$ are emerging (purple), those of $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ cannot be identified.

To reach a peak in complexity, I needed to investigate the outcome of combining all components— namely **A**, **B3**, **B^P** and **C₆₀**—in a single experiment. After numerous attempts with various conditions, it was discovered that when **C₆₀@Pd₂B3₄** and **Pd₂A₂B^P₂** were mixed in acetonitrile at room temperature they could coexist stably for an extended period (more than 24 hours) (Figure 15a,b). This is intuitive as the homochiral figure-eight is more stable than its racemic analog **Pd₂A₂B3₂**. ESI-MS analysis also allowed the characterization of this state in which peaks corresponding to $[\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2 + n\text{BF}_4^-]^{(4-n)+}$ and $[\text{C}_{60}\text{@Pd}_2\text{B3}_4 + n\text{BF}_4^-]^{(4-n)+}$ were identified (Figure 15c). However, it was also established that the favored host-gest complex is **C₆₀@Pd₂B^P₄**. Therefore, it seemed that at room temperature, a certain balance was obtained. This state of the system will now be referred to as **State 1**. Upon heating the same sample at 70 °C a slow yet very clean transformation occurred. In fact, the ¹H NMR signals corresponding to the chiral **Pd₂A₂B^P₂** gradually decreased accompanied by those of the **C₆₀@Pd₂B3₄** (Figure 16a). Concomitantly, signals originating from **Pd₂A₂B3₂** as well as **C₆₀@Pd₂B^P₄** started appearing and increased over time. Throughout a day of heating at 70 °C the transformation was completed and the final state of the system consisted of a new cage population composed of **C₆₀@Pd₂B^P₄** and **Pd₂A₂B3₂** (**State 2**) (Figure 16a). Longer heating did not result in further transformations leading to the conclusion that the system had reached its thermodynamic minimum. Gas phase mass analysis was again employed to identify the two species present (Figure 16b).

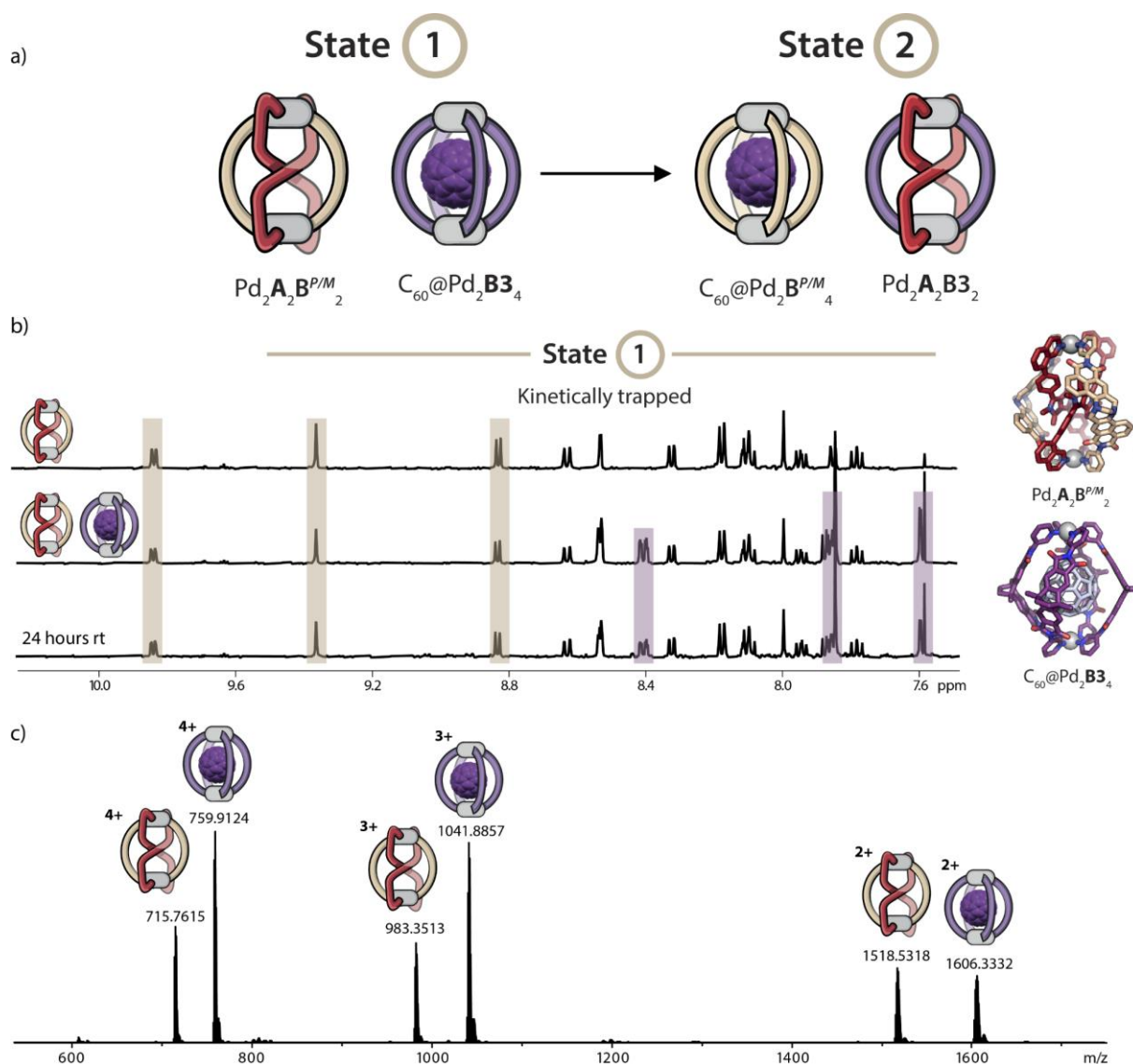


Figure 15: a) Schematic representation of the transformation from **state 1** to **state 2**. b) ¹H-NMR (CD₃CN, 500 MHz) stack of **state 1** and its stability at room temperature over 24 hours. It represents a kinetic trap. c) HR-ESI-MS of **state 1** with peaks corresponding to $[\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2 + n\text{BF}_4^-]^{(4-n)+}$ and $[\text{C}_{60}\text{@Pd}_2\text{B3}_4 + n\text{BF}_4^-]^{(4-n)+}$.

Other experiments in which the ligands were mixed in equimolar amounts with Pd(II) or where the three homoleptic assemblies were combined directly together both in the presence of fullerene C_{60} resulted in the same outcome and converged to the same population. However, the pathway was more challenging to probe as both scenarios resulted in intermediate mixtures containing numerous species more difficult to analyze and quantify. Moreover, when the fullerene was not directly solubilized, *i.e.* encapsulated within $Pd_2B_3_4$, the process occurred at a slower pace, often requiring heating at 70 °C for several days. This can be attributed to the biphasic nature of the fullerene uptake phenomenon. Taking the population $C_{60}@Pd_2B_3_4$ / $Pd_2A_2B^P_2$ as a starting point (Figure 15a) ensured preorganization of the system and facilitated a kinetic of ligand exchange observable by 1H NMR without leading to a more complex mixture of species. Herein, the affinity of the $Pd_2B^P_4$ host for fullerene is the driving force of the transformation process. Simultaneously, the previously established influence of ligand **A** on $C_{60}@Pd_2B_3_4$ facilitates the ligand exchange. From a purely schematic and visual perspective, the outer ligands **B^P** of the figure-eight cage are exchanged for **B3** while the fullerene is effectively “stolen” by the newly assembled $Pd_2B^P_4$ (or vice versa).

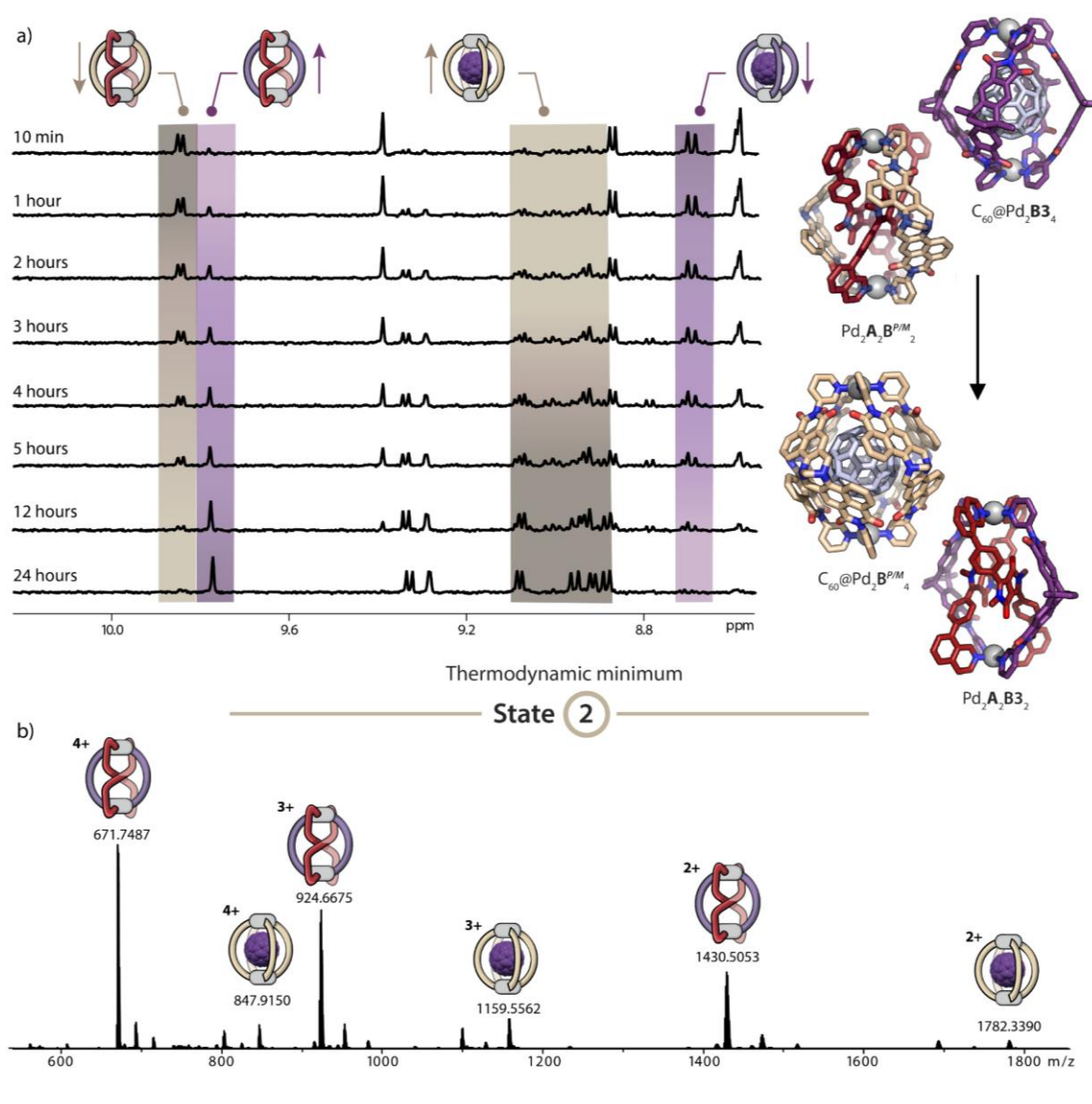


Figure 16: a) 1H -NMR (CD₃CN, 500 MHz) stack of the transformation from **state 1** to **state 2** upon heating at 70 °C over 24 hours. b) HR-ESI-MS of **state 2** with peaks corresponding to $[Pd_2A_2B_3_2+nBF_4^-]^{(4-n)+}$ and $[C_{60}@Pd_2B^P_4+nBF_4^-]^{(4-n)+}$.

The first example of a dynamic population of cages is provided here, therefore advancing further from the systems described in the previous chapters of this dissertation. Although the present case goes from a population of homoleptic host-guest + heteroleptic assembly (**state 1**) to another similar one (**state 2**), under thermodynamic control, we will see later that it can also be extended to more complex populations. However, let's first have a closer look at an emergent property from the transformation described above.

4. Emergence of chiral memory

When describing the transformation, nothing was mentioned about the figure-of-eight formed from the two ligands **A**. In the initial population, the chirality of **B^P** dictates the chirality of the "8" and therefore the conformation is locked in either *P* or *M* conformation. However, whether or not this conformation was affected by the transformation process remained, so far, elusive. In the eventuality of configuration retention, one would obtain a final state where the Pd₂**A₂B₃**₂ assembly is (at least partially) enriched in one enantiomer and not a racemic mixture anymore. This was obviously not yet observable through ¹H NMR spectroscopy as two enantiomers display identical spectra. Such phenomena would also require the kinetic of outer ligand exchange to be faster than the figure-eight racemization one. To determine if chiral memory was emerging from the population transformation I turned to the analysis of the (chiro)optical properties of the two states.

The absorption of C₆₀@Pd₂**B₃**₄ in the visible range is neglectable and only a small band centered at 340 nm was observable in the UV range. As previously mentioned, Pd₂**A₂B^M**₂ presented three noticeable bands respectively centered at 350 nm, 390 nm, and 500 nm. Thus, when measuring the UV Vis spectrum of **State 1**, we could observe these features mainly emerging from Pd₂**A₂B^M**₂ (Figure 17a). On the other hand, **State 2** displayed an overlap of the contributions from Pd₂**A₂B₃**₂ and C₆₀@Pd₂**B^M**₂ (Figure 17b). A few key disparities allowed a clear distinction between the two states by UV-Vis spectroscopy and also confirmed the transformation we had observed by NMR (Figure 17c). In **State 2** the first band was slightly blue-shifted, centered at 345 nm instead of 350 nm, and corresponded mainly to the Pd₂**A₂B₃**₂ species. It also presented a broader shape as compared to the same contribution in Pd₂**A₂B^M**₂. Additionally, the band arising from the sole contribution of **A** in the longer wavelength was again slightly blue-shifted to 490 nm while being sharper for Pd₂**A₂B₃**₂ than for Pd₂**A₂B^M**₂.

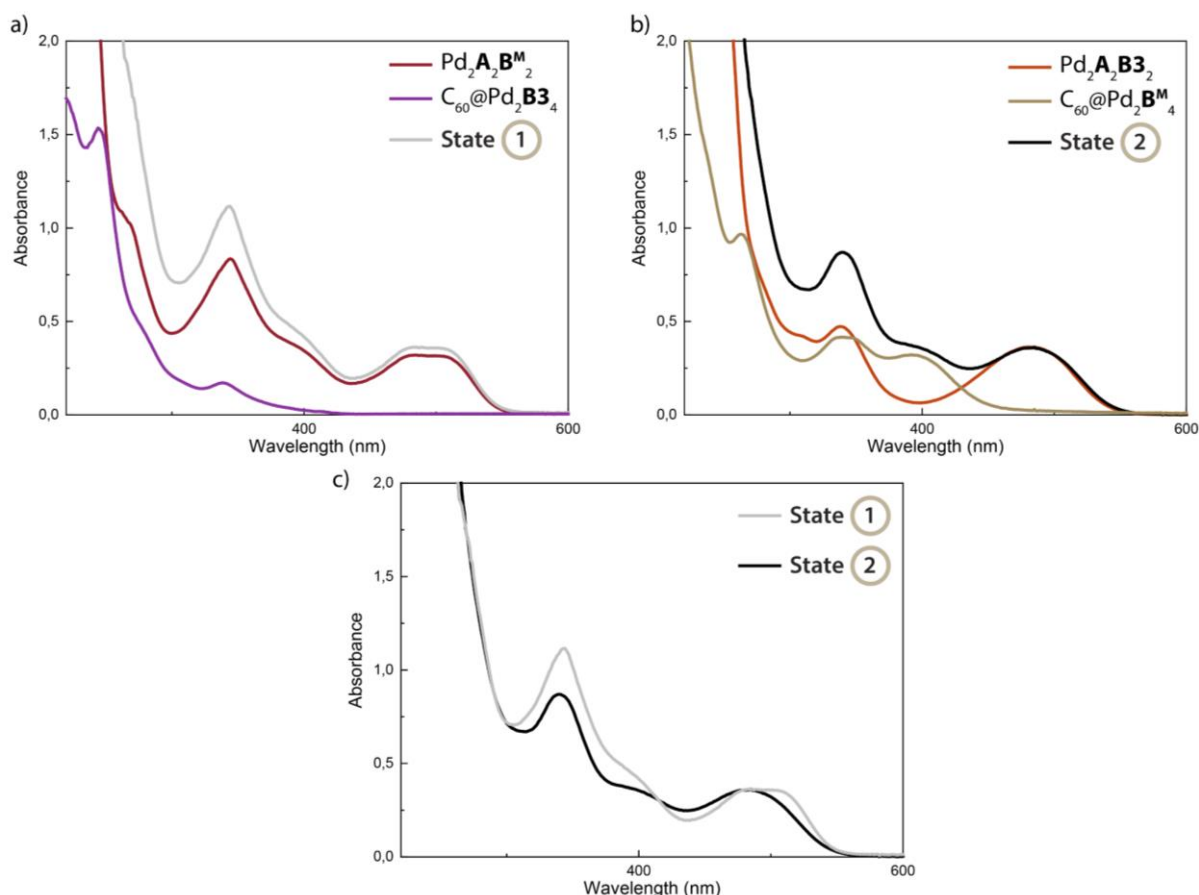


Figure 17: a) UV-Vis spectra overlap of **state 1** and its respective components. b) a) UV-Vis spectra overlap of **state 2** and its respective components. c) Overlap of **state 1** and **state 2** displaying their differences. Solvent= acetonitrile, 2 mm cuvette, 0.12 mM concentration in ligand.

To decipher the emergence of a chiral memory effect circular dichroism as well as circularly polarized luminescence techniques were used. Measuring **state 1** displayed the same spectrum as for the sole $\text{Pd}_2\text{A}_2\text{B}^{\text{M}}_2$ assembly since the $\text{C}_{60}@\text{Pd}_2\text{B}_3_4$ species is achiral (Figure 18a). However, measurements of the sample from **state 2** revealed a Cotton effect at 510 nm, which could only arise from contributions of ligand **A**. It was a first hint indicating that the figure-eight structure did not fully racemize during the outer ligand exchange, retaining partial chirality. This partial retention of chirality was corroborated by CPL measurements. Spectra recorded immediately after the transformation and 24 hours later at room temperature showed CPL emission centered at 550 nm, similar to what was observed for $\text{Pd}_2\text{A}_2\text{B}^{\text{M}}_2$ but accompanied by a lower g_{lum} of $11.1 \cdot 10^{-3}$ (Figure 18b). As a control experiment, the CPL spectra and the emission of (racemic) $\text{Pd}_2\text{A}_2\text{B}_3_2$ were recorded. The emission band matched that of **state 2**, but as anticipated, the sample exhibited no CPL effect. To further verify this assumption, a sample at a higher concentration was prepared so that the transformation could be followed by both NMR and CD. This ensured that traces of $\text{Pd}_2\text{A}_2\text{B}^{\text{M}}_2$ could not be detected. The presence of this species would be responsible for the CD activity in the same region. Upon complete conversion of **state 1** into **state 2** (confirmed by NMR) (Figure 18c, inset), the CD effect persisted, validating that the chiral memory was genuine and not an artifact (Figure 18c). Eventually, we monitored the CD band between 500 nm and 550 nm by prolonged heating at 70 °C of the sample over six days and observed a gradual decrease in intensity indicative of a slow racemization of the figure-eight over time (Figure 18d). These two experiments also highlighted that the kinetics of ligand exchange and racemization were, as anticipated, occurring on a different timescale. This should allow us to dissect further the memory effect and obtain its efficiency by monitoring both processes at different temperatures and concentrations and calculating the respective rate constants and activation energies. From these, we should be able to extrapolate the “maximum” effect upon full ligand exchange.

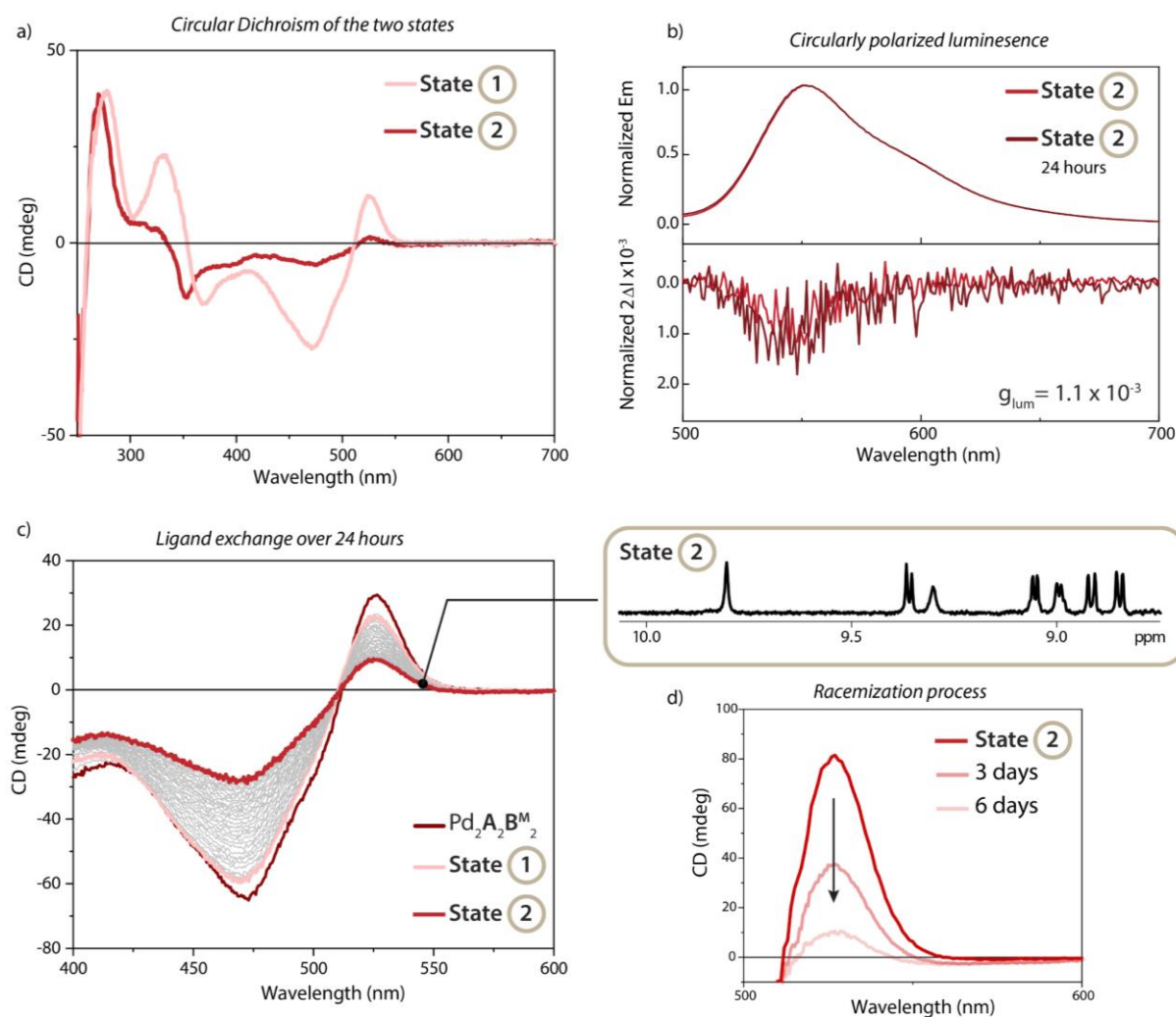


Figure 18: a) CD spectra of *state 1* and the resulting spectra after the conversion into *state 2*. 2 mm cuvette, 0.12 mM chromophore concentration. b) CPL spectra of *state 2* measured after CD and 24 hours resting at room temperature. Excitation at 350 nm. c) CD spectra following the transformation of *state 1* into *state 2*. The $Pd_2A_2B^M_2$ spectrum is given as a reference. The inset highlights the 1H NMR spectra of the system corresponding to the bright red curve where no trace of $Pd_2A_2B^M_2$ can be detected. 2mm cuvette, 0.7 mM chromophore concentration. d) CD spectra of the racemization of the figure-eight over six days. 2 mM cuvette, 1.4 mM chromophore concentration.

The emergence of such properties from cage populations represent a real advancement in terms of complexity. In (systems) chemistry, the notion of emergence is fundamental as it explores how complex chemical behavior and functions arise from the interaction of simpler chemical entities.^[31–34] Herein, not only did we present the first dynamic cage population but we were also able to show that the collective behavior of the population surpasses the one of each of its individuals taken separately. While the system remained under thermodynamic control and drove to its energetic minimum, it showed the potential of exploiting events occurring with distinct kinetics for observing emergent properties.

5. Dissipative nature of the transformation

The system we presented above underlined the preferential formation of $C_{60}@Pd_2B^P_4$ in a mixture of assemblies, further triggering a complex shuffling of ligands into **State 2** under thermodynamic control. However as highlighted by previous experiments, the kinetics of outer ligand exchange and fullerene uptake occurred at distinct rates, the latter being seemingly much slower. In the meantime, it was shown that when competing for the formation of the figure-eight, $Pd_2A_2B^P_2$ is favored in comparison to $Pd_2A_2B_3_2$. I therefore inferred the possibility of driving the system kinetically out of equilibrium by playing with the two competitive processes. I conceived an experiment in which a reservoir of fullerene C_{60} powder was mixed with a solution of $Pd_2A_2B_3_2$. As discussed above, this is a stable state. A solution of $Pd_2B^P_4$ was then introduced in an amount ensuring a 1:1:1 ligand ratio (Figure 19). At room temperature, the system was locked and the two species are observable. In such a system, $Pd_2B^P_4$ acts as a predatory species and is both capable of competing with $Pd_2A_2B_3_2$ for ligand **A** and of uptaking fullerene. By monitoring the 1H NMR of the sample, the disappearance of the signals corresponding to $Pd_2B^P_4$ was first observed after only 20 min and was then accompanied by the rise of signals matching those of $Pd_2A_2B^P_2$. This set appeared after a period of 1 hour and the doublet at 9.85 ppm is easily identifiable. Over time, within a few hours, the relative ratio between $Pd_2A_2B^P_2$ and $Pd_2A_2B_3_2$ changed so that the first one increased slowly while the second decreased (Figure 19, top). The $Pd_2A_2B^P_2$ species reached a maximum in abundance around 8 hours before starting to decrease again until it completely disappeared after 72 hours. The reverse process occurred for the $Pd_2A_2B_3_2$ assembly and its initial concentration was restored at the end of the experiment after 72 hours. Concomitantly, the emergence of signals from $C_{60}@Pd_2B^P_4$ was observable after 8 hours and continuously increased until the end of the experiment. The chiral figure-eight is, therefore, a transient kinetic species and the system is pushed into an out-of-equilibrium state before relaxing to the established thermodynamic sink. To verify this, another cycle was performed starting from the final 1:1 mixture of $C_{60}@Pd_2B^P_4$ and $Pd_2A_2B_3_2$ (Figure 19, bottom). The introduction of $Pd_2B^P_4$ (fuel) led, again, first to the emergence of $Pd_2A_2B^P_2$ (transient species) followed by the formation of $C_{60}@Pd_2B^P_4$ (waste) which built up from the previous cycle. $Pd_2A_2B_3_2$ underwent partial destruction and reformation during the experiment.

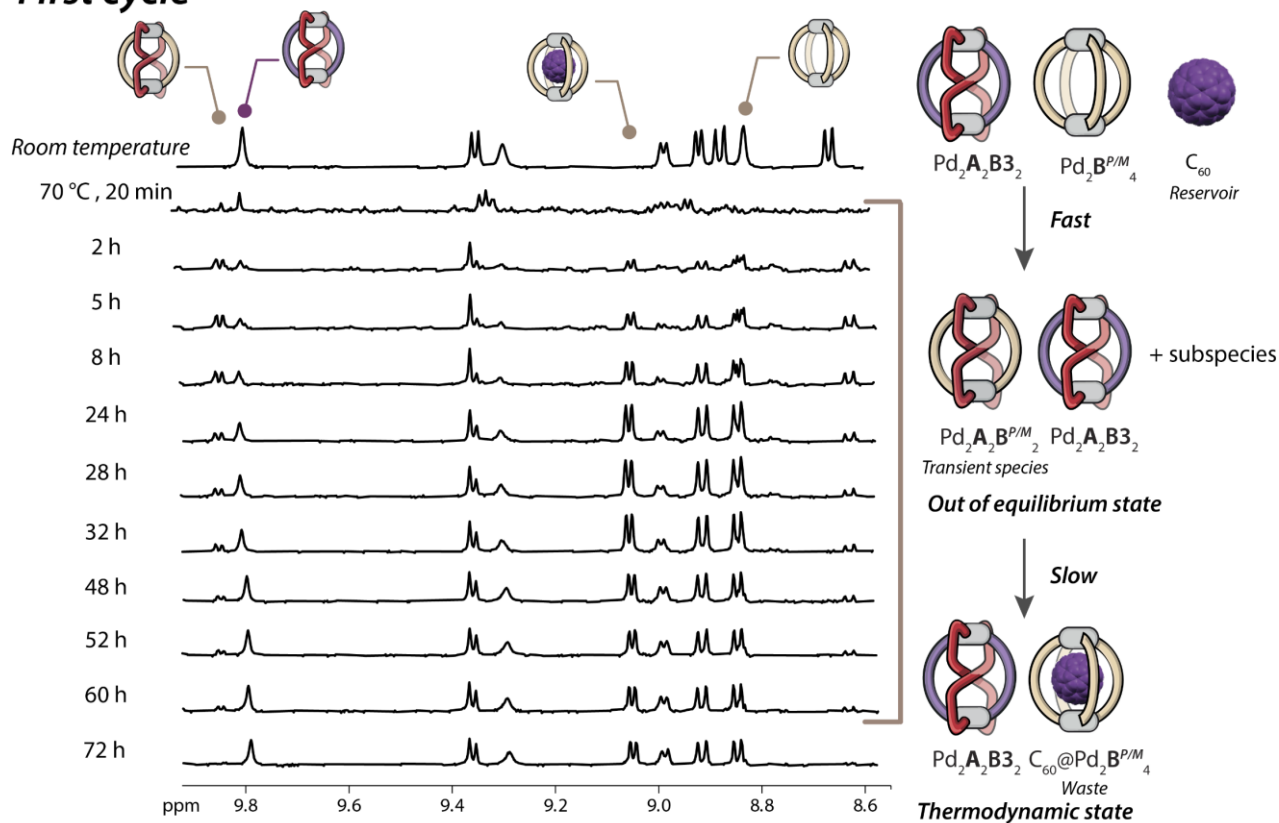
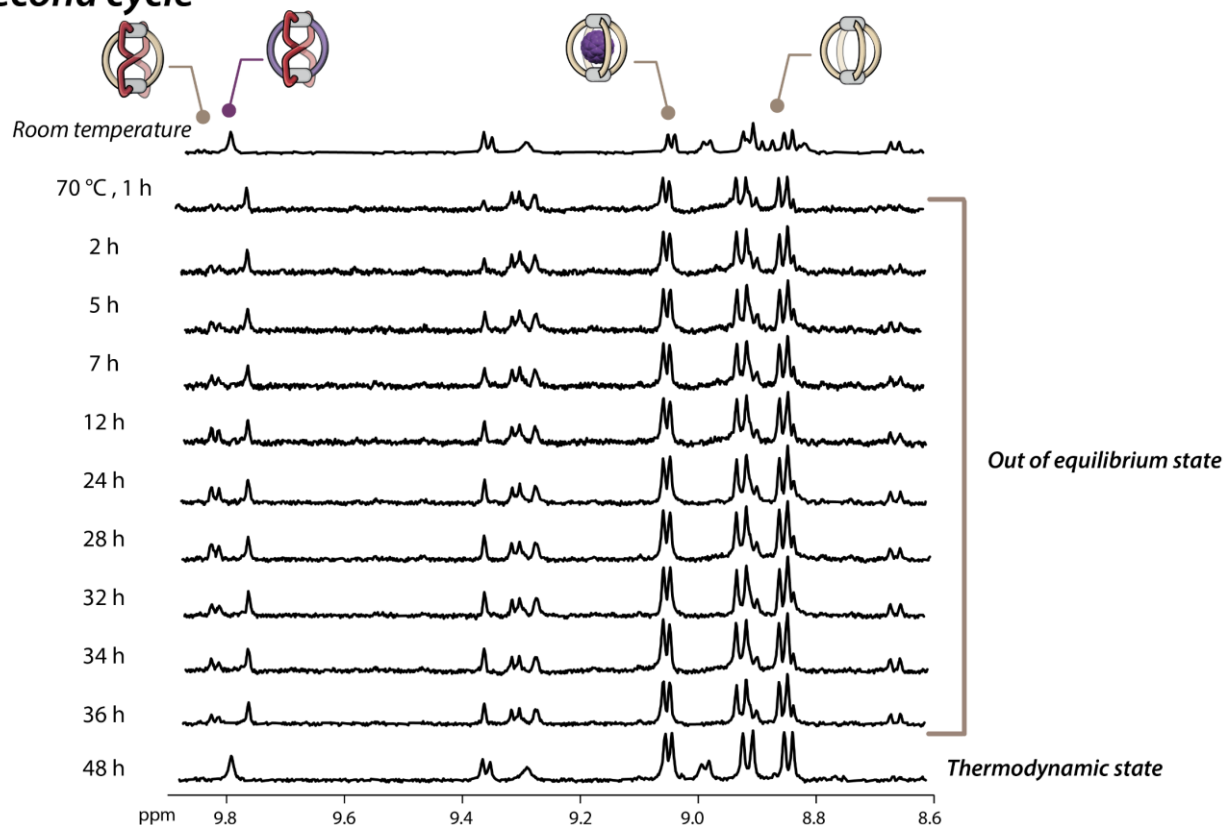
First cycle**Second cycle**

Figure 19: ^1H -NMR (CD₃CN, 500 MHz) stack for the first (up) and second cycle (down) monitoring the state of the system over time when heated at 70 °C. The system goes out of equilibrium upon injection of Pd₂B^P (fuel) and Pd₂A₂B^P₂ forms as a transient species before slowly relaxing and reforming the thermodynamically stable C₆₀@Pd₂A₂B^P₂ (waste).

Quite surprisingly, it was not possible to identify signals corresponding to either $C_{60}@Pd_2B_3_4$ or $Pd_2B_3_4$ which was problematic to characterize properly the transient state of the overall system. The concentration of this ligand remained, as for **A**, constant in the medium and we should thus be able to observe species containing these ligands at all times. The ratio used here is also not ideal as it did not allow the full transient conversion of $Pd_2A_2B_3_2$ into $Pd_2A_2B^P_2$ before observing relaxation (see Figure 20 for a simplified scheme of the relative amounts of each species). In an ideal system (Figure 21), it should be possible to observe this full conversion accompanied by the formation of the homoleptic species or host-guest containing ligand **B3**. Ultimately, since two competitive processes are occurring concomitantly, it is also a possibility that the system can not fully go towards $Pd_2A_2B^P_2$ and that the ligand exchanges happening in the system also facilitate and accelerate the uptake of C_{60} . Likewise, **B3** might form different type of subspecies, polymeric or not, which are in fast exchange as compared to the NMR timescale and will then be hard to identify. HR-ESI-MS analysis of the system over time might be of help here. Eventually, numerous experimental parameters can affect the overall system. Among them is concentration in cages (each cycle leads to dilution as for now) which will influence the kinetics of the different transformation processes separately, but also for example the amount of fullerene reservoir, the stirring of the solutions, and the accumulation of waste. Despite the system still being in its infancy and needing further optimization I unambiguously demonstrated the possibility of driving it out of equilibrium by forming a kinetic state where the chiral figure-of-eight $Pd_2A_2B^P_2$ was transiently observable (Figures 20 and 21). This also means that it foresees the creation of a dynamic cage population showing emergent properties and being capable of out-of-equilibrium behavior, which altogether would make it the most complex cage system reported to date (from the perspective described in the **Introduction** of this dissertation).

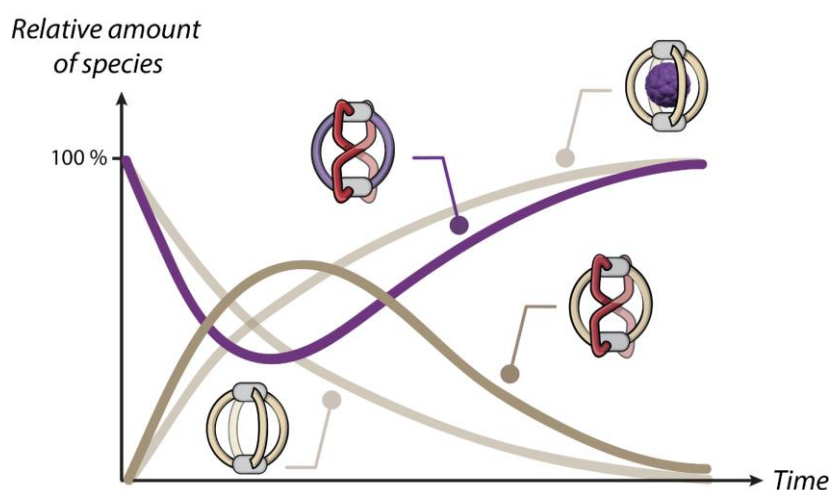


Figure 20: Schematic representation of the relative amount of each species monitored over time during the dissipative transformation. Hypothesis is based on qualitative observations from the NMR data.

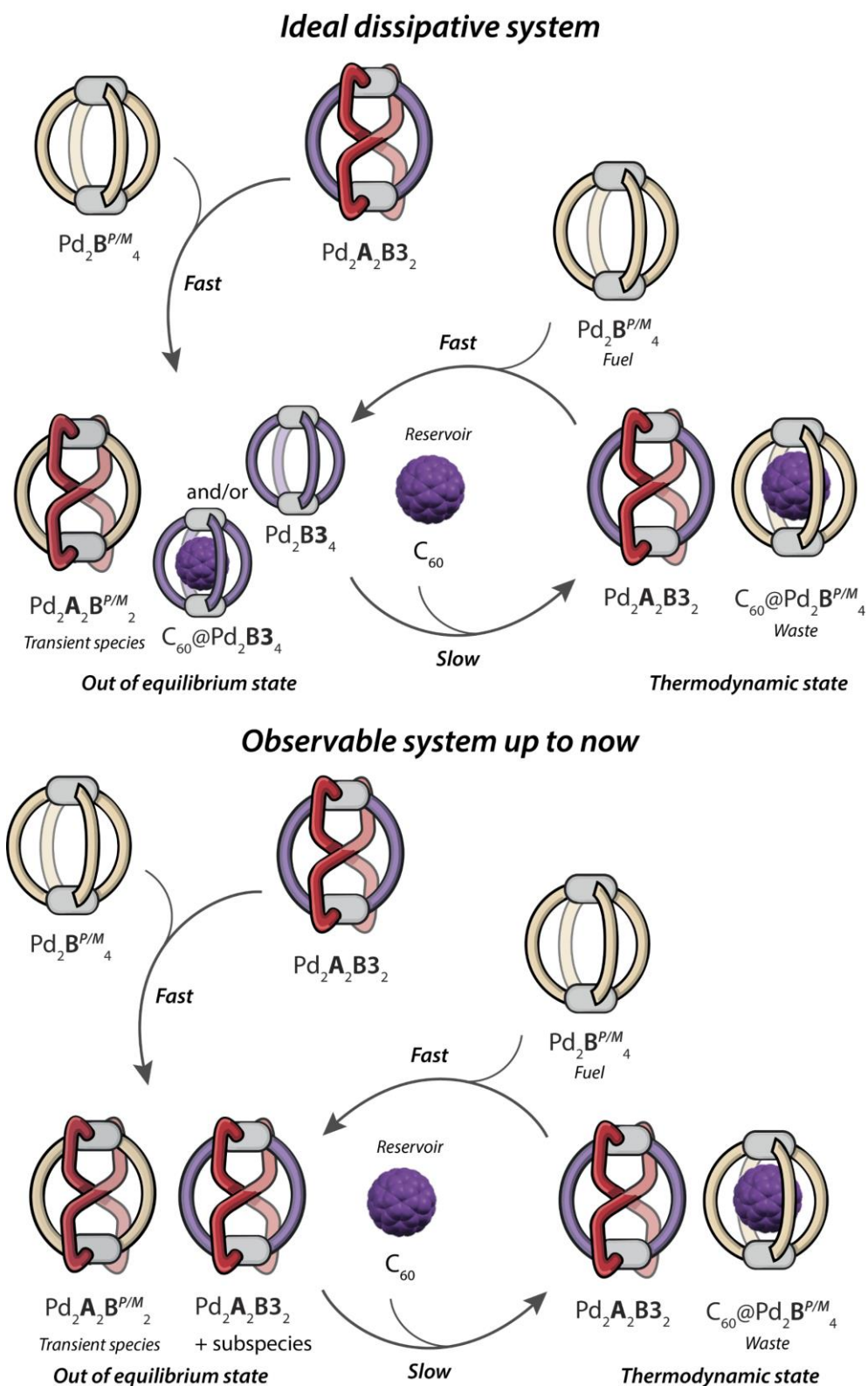


Figure 21: (top) Ideal dissipative system composed of the same components as the observed (bottom) system. In this state, species containing **B3** should be identifiable as the amount of this ligand remains constant in the system.

6. Signal transduction and complex population control

In the previously described transformation, I took advantage of the figure-eight topology and the relatively fast outer ligand exchange between similar assemblies obtained from building blocks **B3** and **B^{P/M}**. However, it was also outlined that this process did not necessitate the direct solubilization of fullerene C₆₀ through its encapsulation within a cage and could proceed in a system where a reservoir of fullerene was present as solid powder. Thus, the possibility of extending the combinations of ligands for such transformations and showing their versatility was envisaged. I was also curious whether or not the chiral memory effect could be reproduced or canceled in a controllable fashion by selecting the ligand associated with **A**. The first chapter of this dissertation has offered a library of possible assemblies created from ligand **A** in combination with **Bx** or **Cx** counterparts. Thus, I used this as a platform for exploring those processes.

Separate samples of Pd₂**A**₂**B^P**₂ and Pd₂**B1**₄ were prepared in deuterated acetonitrile. It was first assessed whether or not the assemblies were stable when mixed in a 1:1 fashion. Mixing equimolar amount of the cages at room temperature did not result in a shuffling of their components and they remained stable for several hours in this state. Changing the Pd₂**A**₂**B^P**₂/Pd₂**B1**₄ from 1:1 to 2:1 in order to create a 1:1:1 ligand's ratio did not alter the mixture, neither did the addition of fullerene powder. Thus, a **State 1** could be reached similar to what was created for the case of **B3** and remaining kinetically trapped at room temperature for several days (Figure 22a-b). Heating the sample at 70 °C triggered a change in the ¹H NMR spectra of the population and signals corresponding to Pd₂**A**₂**B1**₂ and C₆₀@Pd₂**B^P** arose after 24 hours (Figure 22b) accompanied by a decrease in those assigned to Pd₂**A**₂**B^P**₂ and Pd₂**B1**₄. To accelerate the process, the sample was stirred while heating it for a longer period of time. After 48 hours of stirring, the population was fully converted into a mixture of Pd₂**A**₂**B1**₂ and C₆₀@Pd₂**B^P**. The transformation could also be probed by following the ESI-MS of the mixture and the respective starting and ending spectra display the different species contained in **state 1** and **state 2** (Figure 22d). Eventually, measuring circular dichroism of the final state, where no more of the Pd₂**A**₂**B^P**₂ was present, revealed the chiral memory effect by the presence of a Cotton effect around 510 nm characteristic of the **8** in a chiral environment (Figure 22c). While this effect was really small, it is inferred in this case that the prolonged heating of the sample necessary for the full completion of the transformation (Figure 22b) was also responsible for the advanced racemization of the **8** thus resulting in a lower intensity of the signal. This transformation is comparable to the one presented before, and the figure-eight undergoes an outer ligand exchange driven by the propensity of **B^P** to form a cage capable of encapsulating fullerene. The mechanism is likely similar and thus the chiral memory effect arose from a slower kinetic of the racemization of the **8**. Thus, one can generalize the emergence of chiral memory to ligands capable of forming *trans*-Pd₂A₂B₂ heteroleptic assemblies when combined with **A**.

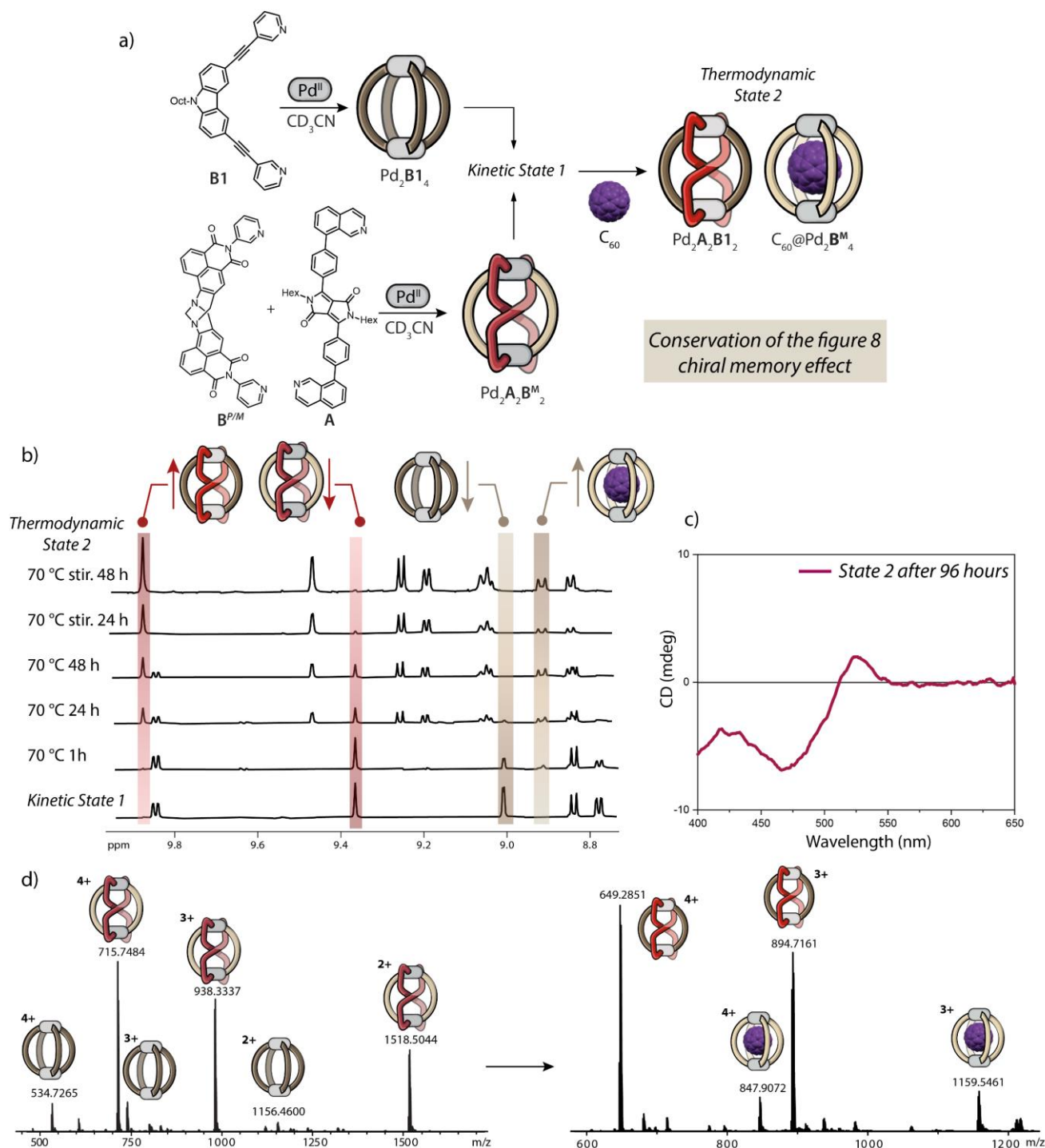


Figure 22: a) Schematic representation of the transformation between $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_2\text{B}^{\text{P}}_{14}$. b) $^1\text{H-NMR}$ (CD₃CN, 500 MHz) stack monitoring the process over time when heating at 70 °C. d) CD spectrum of the final mixture displaying chiral memory. 2 mm cuvette, acetonitrile, 0.12 mM in chromophore. d) HR-ESI-MS of the two states of the transformation with highlighted peaks of the respective species.

I was curious about the possibility of conducting the same transformation in a system where the final assembly containing ligand **A** would not be a *trans* heteroleptic figure-of-eight. This should result in a loss of the chiral information, and thus, no chiral memory effect. Separate samples of $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and the cage mixture $\text{Pd}_3\text{C}^{\text{P}}_{16}/\text{Pd}_4\text{C}^{\text{P}}_{18}$ were prepared (which we will treat as "assembly") (Figure 23). Again, the 1:1 and 2:1 mixtures of assemblies remained stable at room temperature and after the addition of fullerene C_{60} . The ligand exchange proceeded when the mixture was heated at 70 °C and then stirred for a long period of time resulting in a 2:1 population of $\text{Pd}_2\text{A}_2\text{C}^{\text{P}}_{12}$ and $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$ (Figure 23a-b). HR-ESI-MS displayed the two population states as the two species of

each state could respectively be identified in the gas phase (Figure 23d). Since $\text{Pd}_2\text{A}_2\text{C1}_2$ possesses a *cis* arrangement of ligands **A** and **C1**, the chiral information implemented by **B^P** was, as anticipated, lost through the cage transformation with the $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ to $\text{Pd}_2\text{A}_2\text{C1}_2$ topology change. This was shown by the disappearance of the CD bands at 475 nm and 525 nm (Figure 23c). In this case, the mechanism differs as it can not be referred to it as “outer ligand exchange”. The figure-of-eight motif formed by the two ligands **A** must disassemble in order for **A** to adopt its *C* conformation and associate with **C1** by shape complementary assembly.

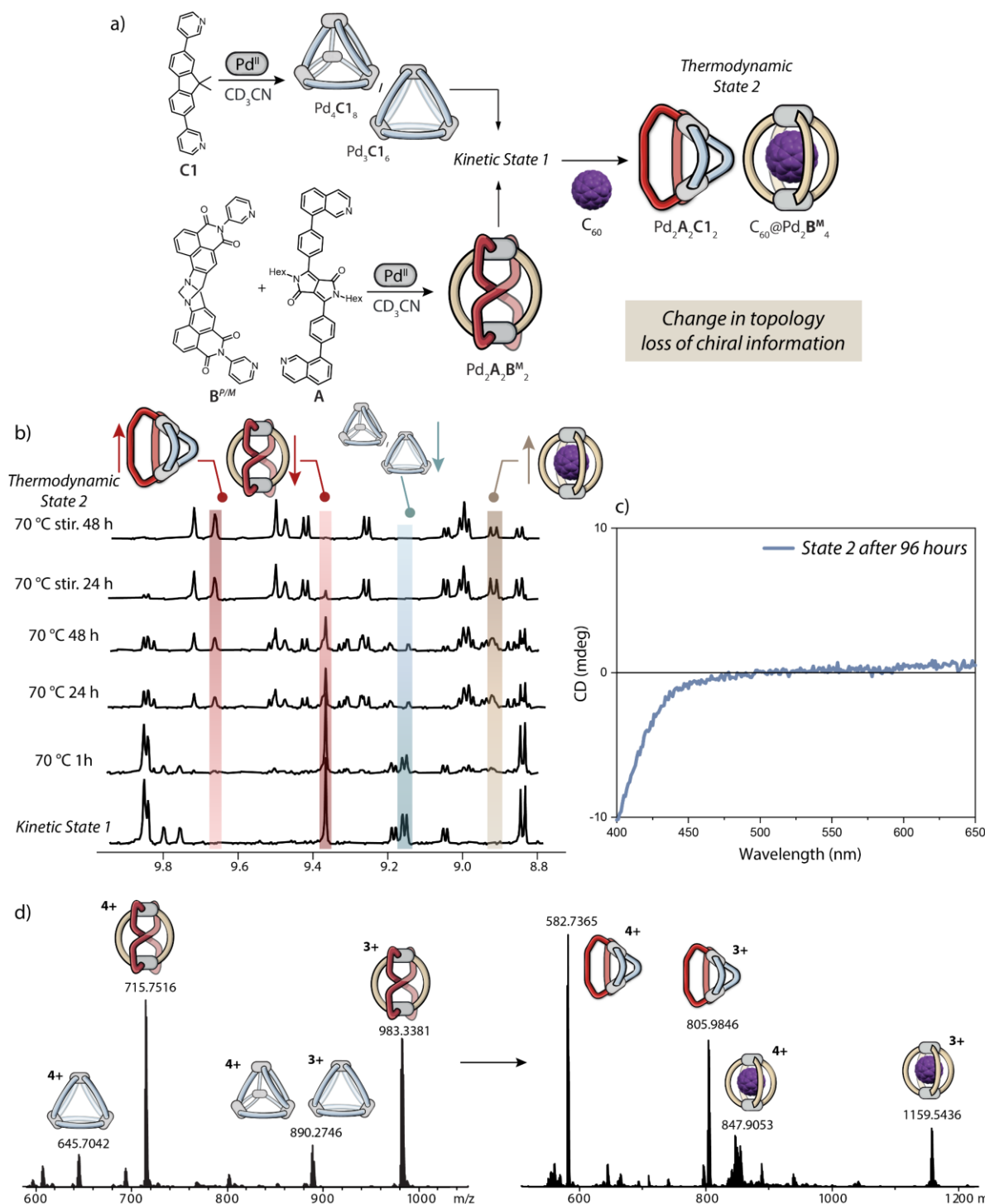


Figure 23: a) Schematic representation of the transformation between $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_3\text{C1}_6/\text{Pd}_4\text{C1}_8$. b) $^1\text{H-NMR}$ (CD_3CN , 500 MHz) stack monitoring the process over time when heating at 70 °C. d) CD spectrum of the final mixture displaying chiral memory. 2 mm cuvette, acetonitrile, 0.12 mM in chromophore. d) HR-ESI-MS of the two states of the transformation with highlighted peaks of the respective species.

This strongly emphasizes the binding of fullerene by $\text{Pd}_2\text{B}^{\text{P}}_4$ as the driving force in these transformation processes. This also shows that any third ligand present in the system and capable of combining with **A** would lead to the associated heteroleptic cage. Additionally, I could also verify that this was not restricted to systems containing ligand **A** (Figure 24). Pre-forming $\text{Pd}_2\text{B}^{\text{P}}_2\text{C1}_2$ and $\text{Pd}_2\text{B1}_4$ and mixing them in a 2:1 ratio resulted again in a stable kinetically trapped mixture. Subsequent heating and stirring triggered the anticipated population-to-population transformation and we observed the rise in signals from $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$ and $\text{Pd}_2\text{B1}_2\text{C1}_2$ in ^1H NMR (Figure 24b). Several small signals in the same aromatic region showed that this transformation was not as clean as the previous ones, yet the two sets of $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$ and $\text{Pd}_2\text{B1}_2\text{C1}_2$ were unambiguously identified and dominated the mixture. $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$ can be considered the “thermodynamic product species” in the sense that it will form no matter what as long as the components are present.

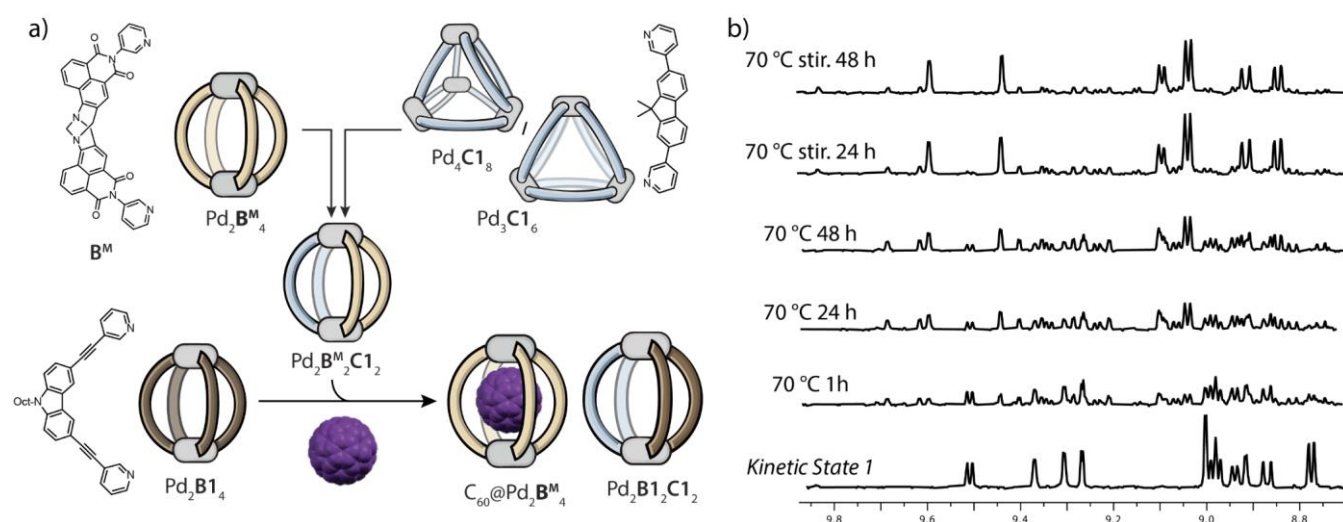


Figure 24: a) Schematic representation of the transformation between $\text{Pd}_2\text{C1}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_2\text{B1}_4$. b) ^1H -NMR (CD_3CN , 500 MHz) stack monitoring the process over time when heating at 70 °C.

Eventually, by combining the knowledge established from these previous experiments and **Chapter I**, I designed a system of transformable cage populations of higher complexity and reached the climax of this dissertation (Figure 25). Both $\text{Pd}_2\text{B1}_2\text{C1}_2$ and $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ could kinetically coexist when mixed in 1:2 ratio at room temperature over a period of several days (Figure 25a). In the present case, **State 1** resembled the outcome of *heteromeric complete self-sorting* where two heteroleptic coexisted orthogonally. Taken separately, the introduction of C_{60} in a sample of $\text{Pd}_2\text{B1}_2\text{C1}_2$ does not trigger any transformation as none of the possible assemblies can uptake the fullerene. On the other hand, fullerene destroys the $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ assembly, leading to a ‘release’ of ligand **A**. Introducing fullerene in the previously described mixture thus led to a more complex population transformation (Figure 25b) in which the formation of $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$ is accompanied by the formation of the two separate $\text{Pd}_2\text{A}_2\text{B1}_2$ *trans*-figure-of-eight and $\text{Pd}_2\text{A}_2\text{C1}_2$ *cis*-cage. The two states of the transformation could be analyzed by HR-ESI-MS highlighting peaks of the respective species (Figure 25c). The process can be broken down by analyzing what happens for each component of the system (Figure 25d-e). This description is, however, a simplified schematic one, and those processes were not directly observed (thus far) during the experiment. Regarding ligand B^{P} , the presence of fullerene pushes the formation of its homoleptic capsule $\text{Pd}_2\text{B}^{\text{P}}_4$ which ensures the fullerene uptake. This results in the “release” of ligand **A**, initially contained in the heteroleptic $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ structure. The presence of this ligand in solution leads to two different processes both triggering the disassembly of $\text{Pd}_2\text{B1}_2\text{C1}_2$. On the one hand, half of the amount of ligand, **A** initially in its *S* conformation forming the δ , conserves this topology and undergoes an outer ligand exchange with ligand **B1** occupying this position on the newly formed $\text{Pd}_2\text{A}_2\text{B1}_2$. The other half must change its conformation and the δ is disassembled to obtain two ligands in the *C* shape, which associate with **C1** to form $\text{Pd}_2\text{A}_2\text{C1}_2$. All these phenomena occur in a cascade fashion (Figure 25d), comparable to

signal transduction, in which the C_{60} acts as a trigger and is followed by the preferential formation of a cage population in the presence of **A** (see **Chapter I**).

Herein, the switching did not occur anymore between populations formed of one heteroleptic assembly and one homoleptic. Indeed, the system went from heteromeric self-sorting where two heteroleptic cages already coexisted to a population made of two distinct heteroleptic cages and an additional homoleptic host-guest complex. The final population thus contained three orthogonally existing coordination cages, as in **Chapter II**, although with a composition that differs again from what was presented earlier. Eventually, it is worth noting that this system was composed of four different ligands resonating with the recently reported study on Pd_2ABCD cages.^[30] I demonstrated that using multiple building blocks (three in **Chapter I** and now four in **Chapter III**) could therefore not only lead to a statistical mess or precise integrative self-sorting but also to defined cage populations where distinct heteroleptic cages are present in solution.

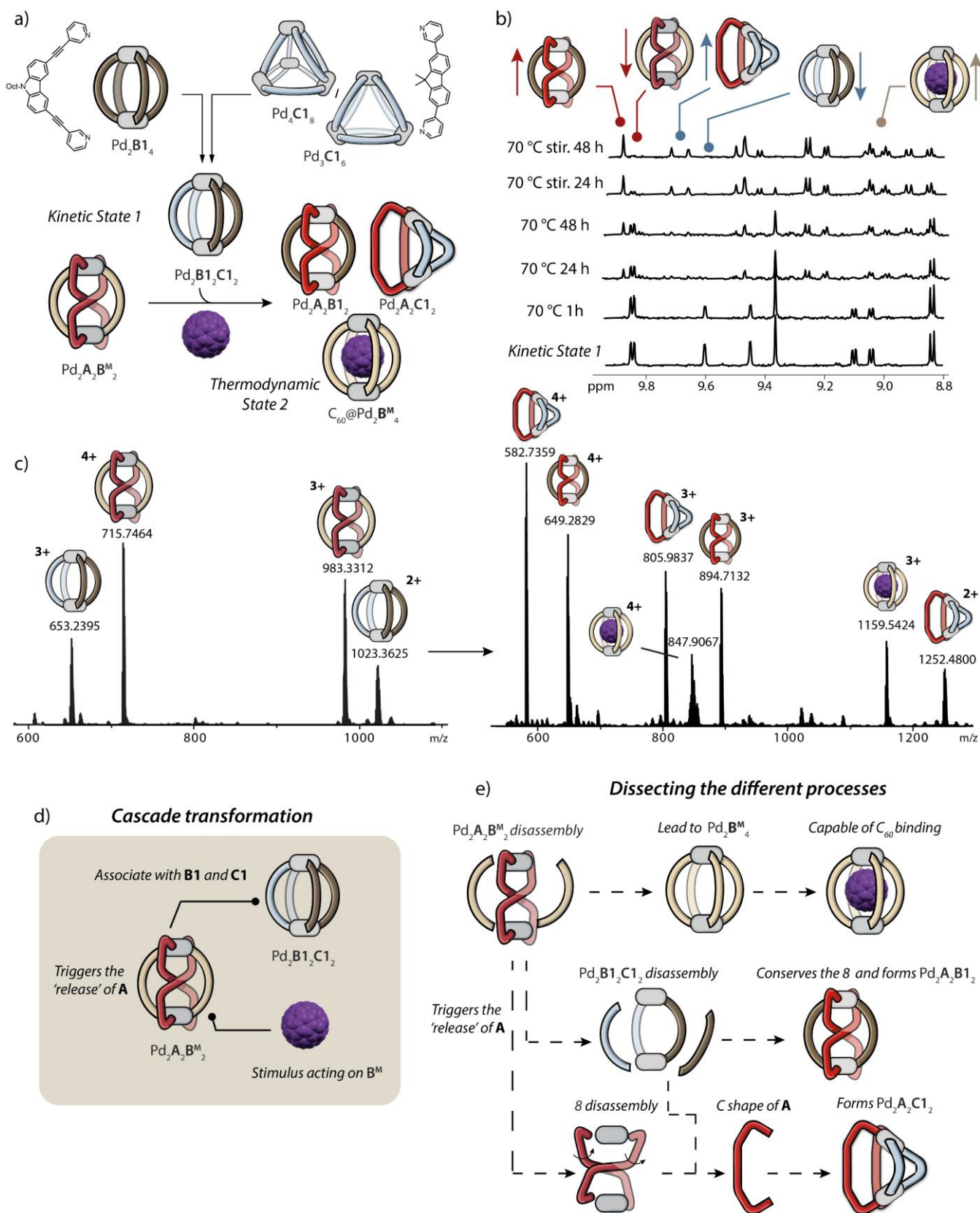


Figure 25: a) Schematic representation of the transformation between $\text{Pd}_2\text{A}_2\text{B}^{\text{M}}_2$ and $\text{Pd}_2\text{B}_1\text{A}_1\text{C}_1_2$. b) $^1\text{H-NMR}$ (CD₃CN, 500 MHz) stack monitoring the process over time when heating at 70 °C. d) CD spectrum of the final mixture displaying chiral memory. 2 mm cuvette, acetonitrile, 0.12 mM in chromophore. d) HR-ESI-MS of the two states of the transformation with highlighted peaks of the respective species.

Conclusion and outlook

In **Chapter III**, I studied several processes all emerging from the use of a singular ribbon-like chiral ligand **B^{P/M}**.

The homoleptic capsule formed from this ligand showed outstanding host-guest properties with the notable encapsulation of fullerene C₆₀ and C₇₀. The strong interactions between the host and the guest in the inner void allowed the selective separation of C₆₀ from a mixture of PAHs but also led to interesting optical properties and notably to the demonstration of chiral information transfer from the host to pristine fullerenes which remain a phenomenon scarcely reported in the literature. Further hints at the possibility of generating a photoinduced charge-transfer state or a fullerene radical anion within the host-guest complex were observed and might lead to exciting follow-up studies.

The similarity of this ligand with the ribbon-like one of **Chapter I** prompted me to investigate its use for the formation of *trans*-Pd₂A₂B₂ figure-of-eight assemblies and I demonstrated the possibility of forming chiral diastereoisomers. The chirality of the outer ligand dictated the chirality of the figure-eight formed by the two ligands **A**, which was reflected by CD and CPL signals in the specific region corresponding to the diketopyrrolopyrrole moiety.

Eventually, I took advantage of both of these properties and the knowledge acquired in **Chapter I** and **Chapter II** to develop dynamic cage populations presenting emerging chiral memory effects and was well as out of equilibrium behavior. Competition between **B^{P/M}** and **B3** (or other ligands) for resources such as counter ligand **A** and/or fullerene guest created a population system in which two figure-of-eight assemblies Pd₂A₂B^P₂ and Pd₂A₂B3₂ underwent outer ligands shuffling with partial retention of chirality. The process was driven by the strong “will” of the system to form C₆₀@Pd₂B^P₄ as the thermodynamic driving force. The characterizations of this process are not finished and will necessitate a deeper investigation and quantification. Additionally, a subtle balance between the kinetics of ligands exchange and fullerene uptake allowed to push a system, containing Pd₂A₂B3₂ and fullerene, transiently toward a kinetic state made partially of Pd₂A₂B^P₂ which would then relax to its thermodynamic minimum. The system, although still in its infancy, presents all the characteristics of a chemically fueled dissipative system. To conclude, I extended the population transformations to a broader range of ligands by using the combinations introduced in **Chapter I**. We could obtain a population of three orthogonally coexisting cages (two heteroleptic cages and one homoleptic host-guest) from the use of four distinct organic ligands therefore demonstrating that the population strategy can be mirrored to the most complex Pd₂ABCD cage obtained through integrative self-sorting.

7. Experimental section

General Method

NMR

NMR spectroscopic data was measured on the spectrometers Bruker AV 500 Avance NEO and AV 600 Avance III HD. For ^1H and ^{13}C NMR spectra, chemical shifts were calibrated to the solvent lock signal. Chemical shifts δ are given in ppm, coupling constants J in Hz. The following abbreviations are used to describe signal multiplicity for ^1H NMR spectra: s: singlet, d: doublet, t: triplet, dd: doublet of doublets; dt: doublet of triplets; m: multiplet, br: broad. All proton signals were assigned with the aid of 2D NMR spectra. All spectra were recorded in standard 5 mm NMR tubes at the indicated temperature.

Mass Spectrometry

Mass spectra were measured on Bruker ESI-timsTOF (electrospray ionization-trapped ion mobility-time of flight) and Bruker compact high-resolution LC mass spectrometers (positive mode). For calibration of the TIMS and TOF devices, Agilent ESI-Low Concentration Tuning Mix was used.

Computational analysis

Models of the structures were constructed using Wavefunction SPARTAN '18.1 The MMFF-optimized model was then optimized on semi-empirical PM6 level of theory without constraints. Structures were then further refined by DFT optimization on the $\omega\text{B97X-D/def2-SVP}$ level.

UV-Vis absorption and emission spectroscopy

UV-vis spectra were recorded on a DAD HP-8453 UV-Vis spectrometer; wavelength: 240 nm – 700 nm, step size: 1 nm. Emission spectra were recorded on a Jasco FP-8300 fluorimeter. Cuvette path length 0.2 cm in absorption and 1 cm in emission.

CD and CPL spectroscopy

Circular dichroism spectra were recorded in CD_3CN with an Applied Photophysics Chirascan qCD Spectrometer with a temperature-controlled cuvette holder. The spectra were background-corrected and smoothed with a window size of 5. Circularly polarized luminescence measurements were performed using a JASCO CPL-300 spectrophotometer equipped with a (150 W) Xe lamp as light source.

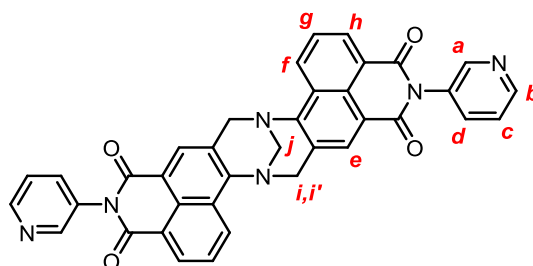
Experimental procedures

Ligands **A**, **B1**, **B3**, and **C1** were synthesized following procedures described in the literature.

The results compiled here have benefited from the help of PhD colleague Björn Schmidt.

Subsection 1

Synthesis of the assemblies

Synthesis of $B^{P/M}$ (by Dr. Helen O'Connor)Figure S1: Representation of the ligand $B^{P/M}$.

N-(3-Pyridyl)-4-amino-1,8-naphthalimide (400 mg, 1.38 mmol) and paraformaldehyde (63 mg, 2.07 mmol) were placed into trifluoroacetic acid (5 mL). A drying tube containing calcium chloride was attached and the mixture was stirred in the absence of light for 3 days before it was transferred onto ice (25 cm³). Water (5 mL) was added, and the mixture was basified to pH 10 using a 6 M aqueous sodium hydroxide solution. Saturated aqueous sodium chloride (100 mL) was added before the organics were extracted with chloroform (3 x 200 mL). The organics were combined and washed with saturated aqueous sodium bicarbonate, water, and saturated aqueous sodium chloride. The organics were dried over magnesium sulfate and the solvent was removed *in vacuo*. Acetone was added, and the mix sonicated for 20 minutes to help remove the solid from the walls of the flask. The precipitate was collected under vacuum and washed with acetone (3 x 5 mL) and diethyl ether (3 x 5 mL), leaving *N*-(3-pyridyl)-4-amino-1,8-naphthalimide Tröger's Base, $B^{P/M}$, as a bright yellow solid. The solid was recrystallised by dissolving the solid in the minimum amount of chloroform and layering with diethyl ether (302 mg, 0.49 mmol, 71%).

¹H NMR (600 MHz, DMSO-*d*₆) δ 8.79 (2H, d, *J* = 8.3 Hz, H_f), 8.62 (2H, d, *J* = 4.2 Hz, H_b), 8.49 (4H, m, H_a and H_h), 8.15 (2H, s, H_e), 7.99 (2H, t, *J* = 8.0 Hz, H_g), 7.79 (2H, d, 7.7 Hz, H_d), 7.55 (2H, dd, *J* = 12.5, 7.95, 4.5 Hz, H_c), 5.20 (2H, d, *J* = 17.4 Hz, H_{i/i'}), 4.78 (2H, s, H_j), 4.70 (2H, d, *J* = 17.4 Hz, H_{i/i'}) ppm.

¹³C NMR (151 MHz, DMSO-*d*₆) δ 163.7, 163.1, 149.8, 149.3, 149.0, 137.0, 132.7, 130.8, 130.4, 129.4, 128.0, 127.2, 126.8, 126.2, 123.9, 122.8, 118.0, 66.4, 56.9 ppm.

HR-ESI-MS *m/z* calculated for C₃₇H₂₂N₆O₄[−] [M-H][−] 614.1708; found 614.1701.

The ligand enantiomers (*P/M*) were separated by chiral HPLC methods with an eluent of dichloromethane/methanol (97.5:2.5). The absorbance was set at 280 nm with a flow rate of 2 mL/min. Retention times: *M* enantiomer, L^M (10 minutes); *P* enantiomer, L^P (13 minutes).

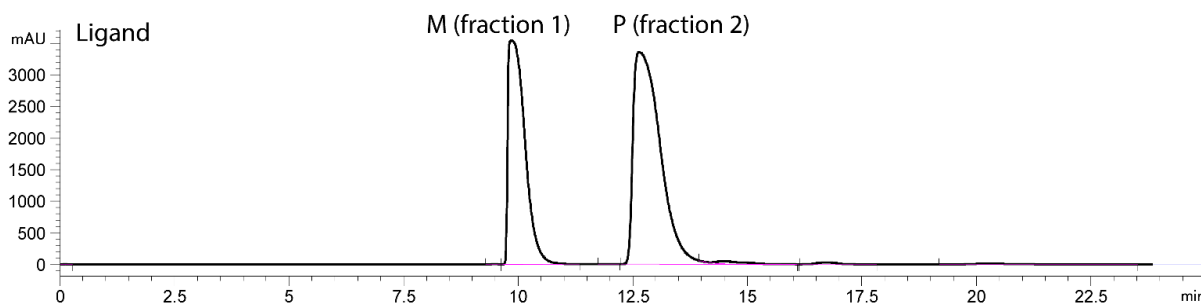


Figure S2: Chromatogram of the separation of enantiomers of ligand through chiral HPLC methods. Conditions: dichloromethane/methanol (97.5:2.5); abs. = 280 nm, flow rate = 2 mL/min.

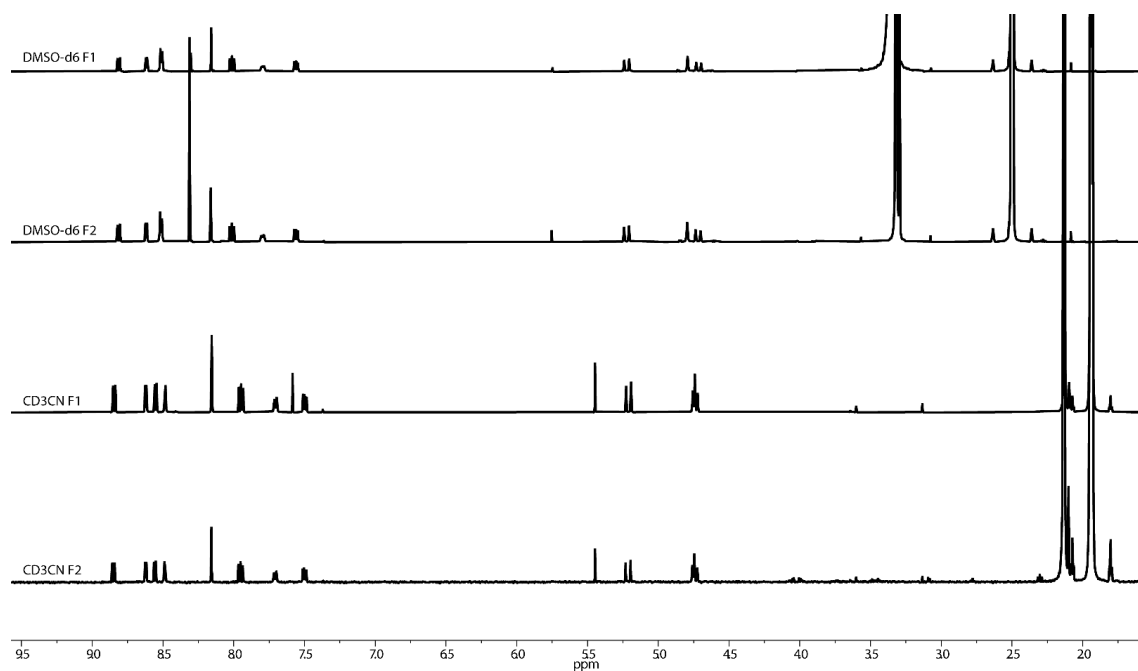


Figure S3: ^1H NMR spectrum (500 MHz, 298K, CD_3CN or DMSO-d_6) of the two fractions after chiral HPLC separation.

Racemic ligand and self-sorting upon guest encapsulation

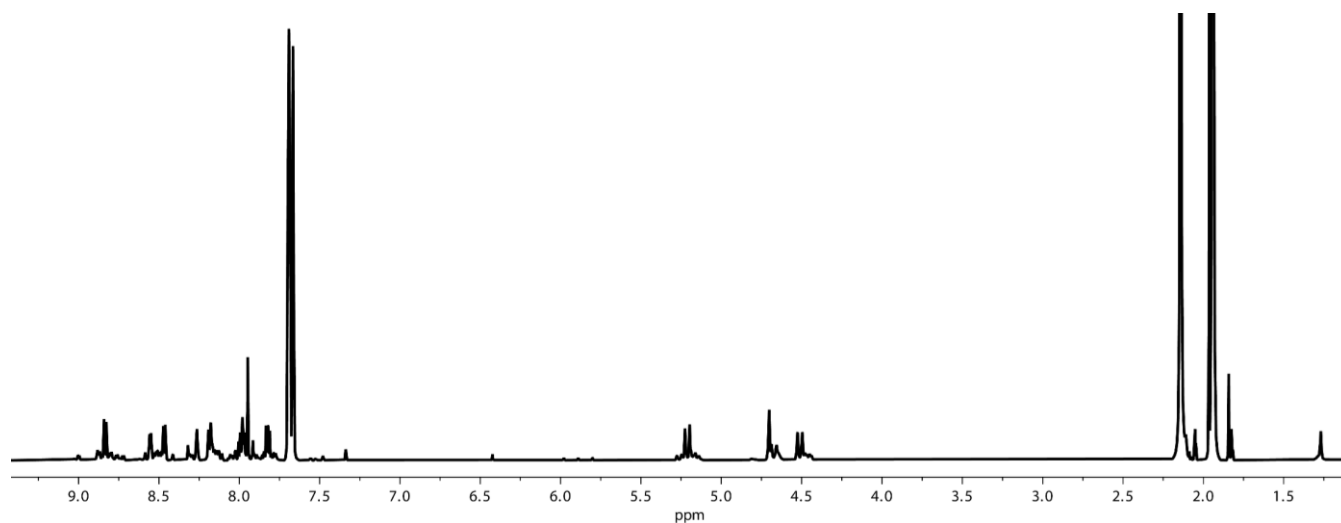


Figure S4: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of the addition of 0.5 equivalent of $[\text{Pd}(\text{MeCN})_4](\text{BARf})_2$ to a solution of racemic ligand $\text{B}^{\text{P/M}}$. A mixture of isomers of the $\text{Pd}_2\text{B}^{\text{P/M}}_4$ cage is obtained.

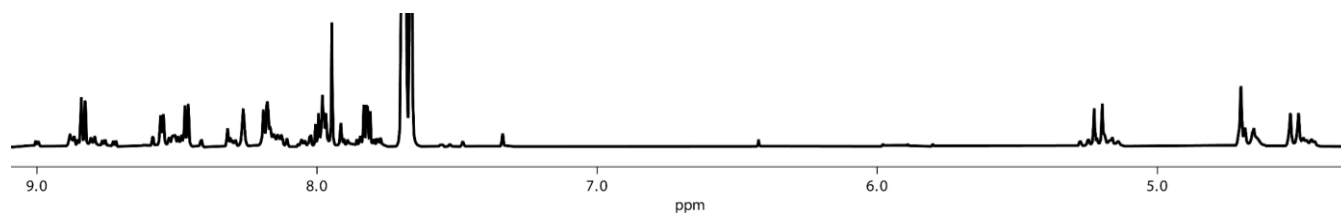


Figure S5: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the addition of 0.5 equivalent of $[\text{Pd}(\text{MeCN})_4](\text{BARf})_2$ to a solution of racemic ligand $\mathbf{B}^{P/M}$. A mixture of isomers of the $\text{Pd}_2\mathbf{B}^{P/M}_4$ cage is obtained.

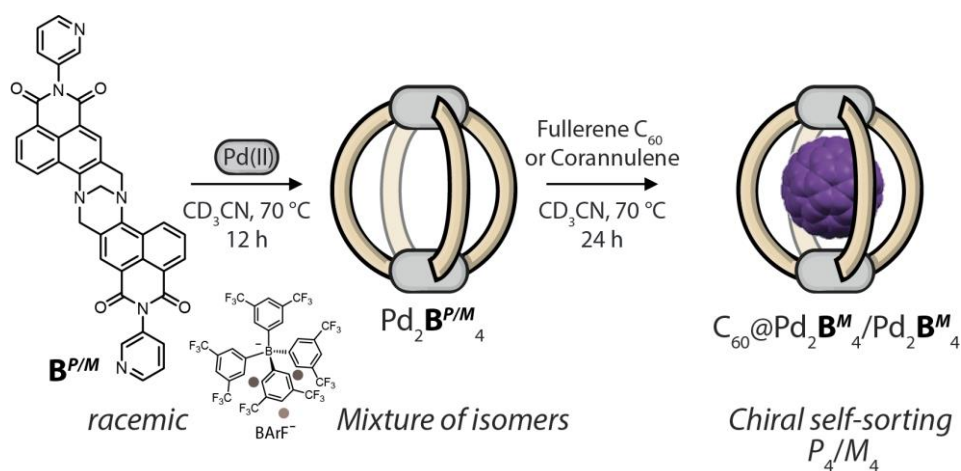


Figure S6: Self-sorting upon addition of guests in the mixture of isomers of the cage

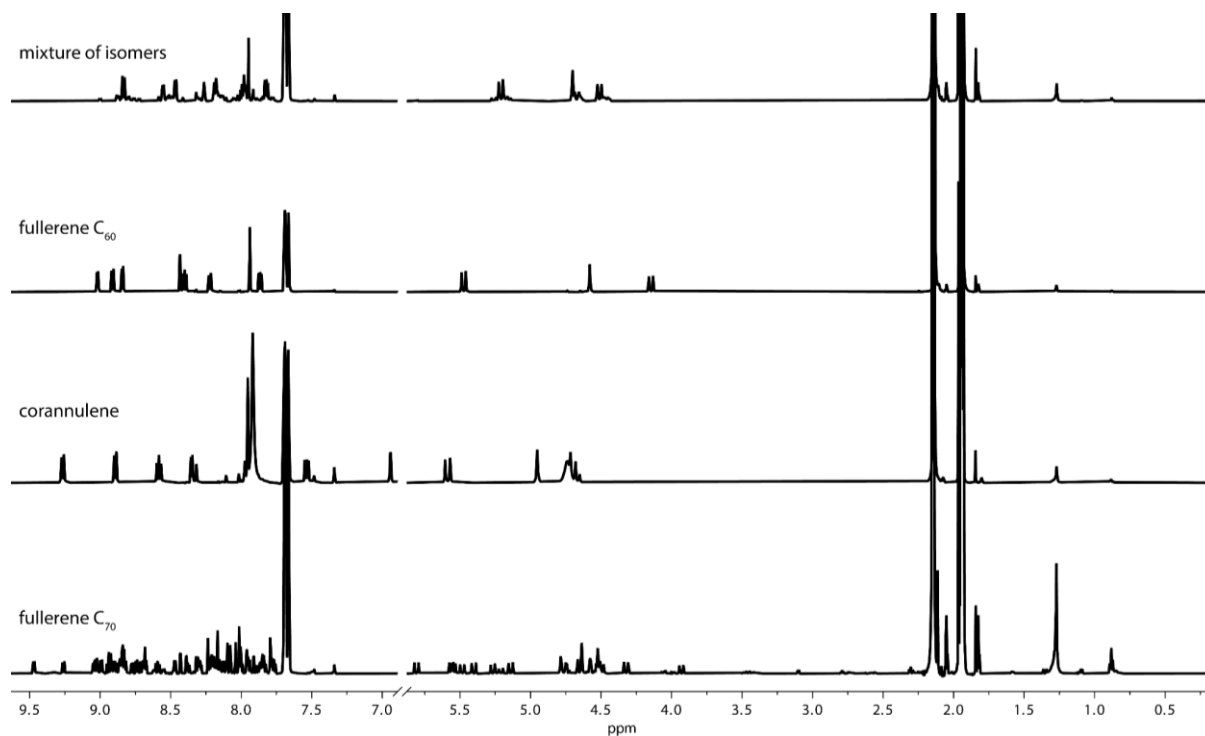


Figure S7: ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the mixture of isomers and the outcome in the presence of guests.

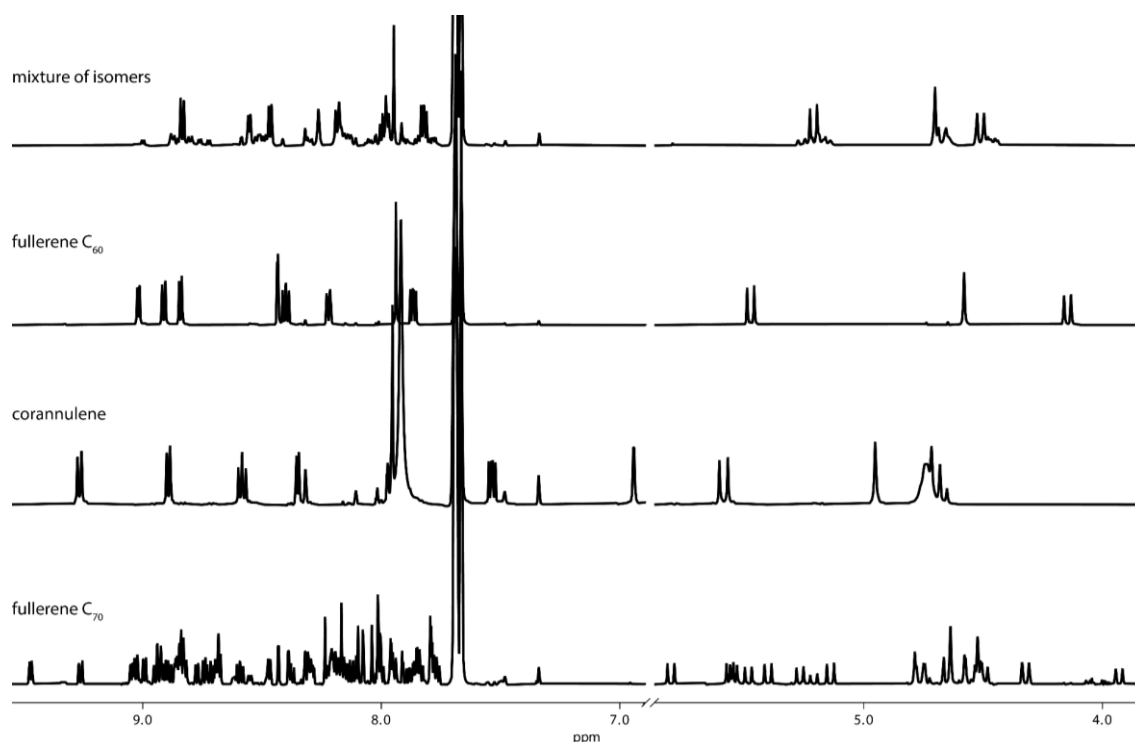


Figure S8: ^1H NMR spectra (500 MHz, 298 K, CD_3CN) enlarged on the aromatic region of the mixture of isomers and the outcome in the presence of guests.

Synthesis of $\text{Pd}_2\text{B}^{\text{P}}_4$ / $\text{Pd}_2\text{B}^{\text{M}}_4$

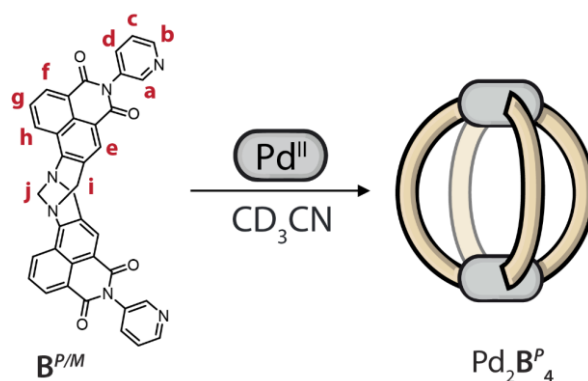


Figure S9: Formation of heteroleptic cage $\text{Pd}_2\text{B}^{\text{P}}_4$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of both ligands.

450 μL of a 3.11 mM solution of B^{P} in CD_3CN (or DMSO-d_6) and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN (or DMSO-d_6) were mixed in an NMR tube and shaken vigorously to afford $\text{Pd}_2\text{B}^{\text{P}}_4$ in the equilibrated solution.

^1H NMR (500 MHz, 298 K, DMSO-d_6) δ 9.38 (dd, $J = 5.75$ Hz, $J = 0.80$ Hz, 8H), 9.07 (d, $J = 1.25$ Hz, 8H), 8.91 (d, $J = 8.70$ Hz, 8H), 8.70 (d, $J = 7.25$ Hz, 8H), 8.38 (t, $J = 7.65$ Hz, 8H), 8.22 (m, 8H), 7.94 (dd, $J = 5.80$ Hz, $J = 8.15$ Hz, 8H), 7.83 (s, 8H), 5.39 (d, $J = 17.30$ Hz, 4H), 4.70 (s, 8H), 4.29 (d, $J = 17.90$ Hz, 24H).

^1H NMR (500 MHz, 298 K, CD_3CN) δ 8.90 (dd, $J = 5.75$ Hz, $J = 0.80$ Hz, 8H), 8.88 (dd, $J = 0.88$ Hz, $J = 8.50$ Hz, 8H), 8.80 (d, $J = 1.15$ Hz, 8H), 8.66 (d, $J = 7.30$ Hz, 8H), 8.21 (t, $J = 8.05$ Hz, 8H), 8.11 (m, 8H), 7.90 (s, 8H), 7.76 (dd, $J = 5.80$ Hz, $J = 8.3$ Hz, 8H), 5.28 (d, $J = 17.45$ Hz, 4H), 4.65 (s, 8H), 4.35 (d, $J = 17.55$ Hz, 24H).

^{13}C NMR (151 MHz, DMSO- d_6) δ 162.4, 161.8, 151.3, 149.9, 149.7, 149.7, 141.7, 134.0, 130.6, 130.4, 130.0, 129.9, 128.0, 127.7, 127.2, 127.1, 122.6, 65.6, 56.4 ppm

ESI-HRMS ($[\text{C}_{148}\text{H}_{88}\text{N}_{24}\text{O}_{16}\text{Pd}_2]^{4+}$):

found: 667.6220

calculated: 667.6229

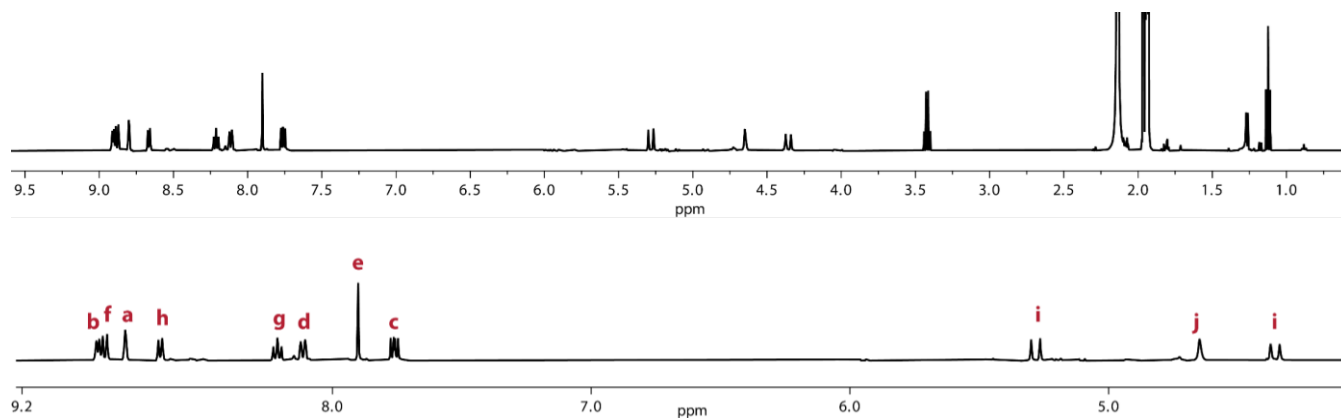


Figure S10: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of the homoleptic assembly Pd_2Bp_4 .

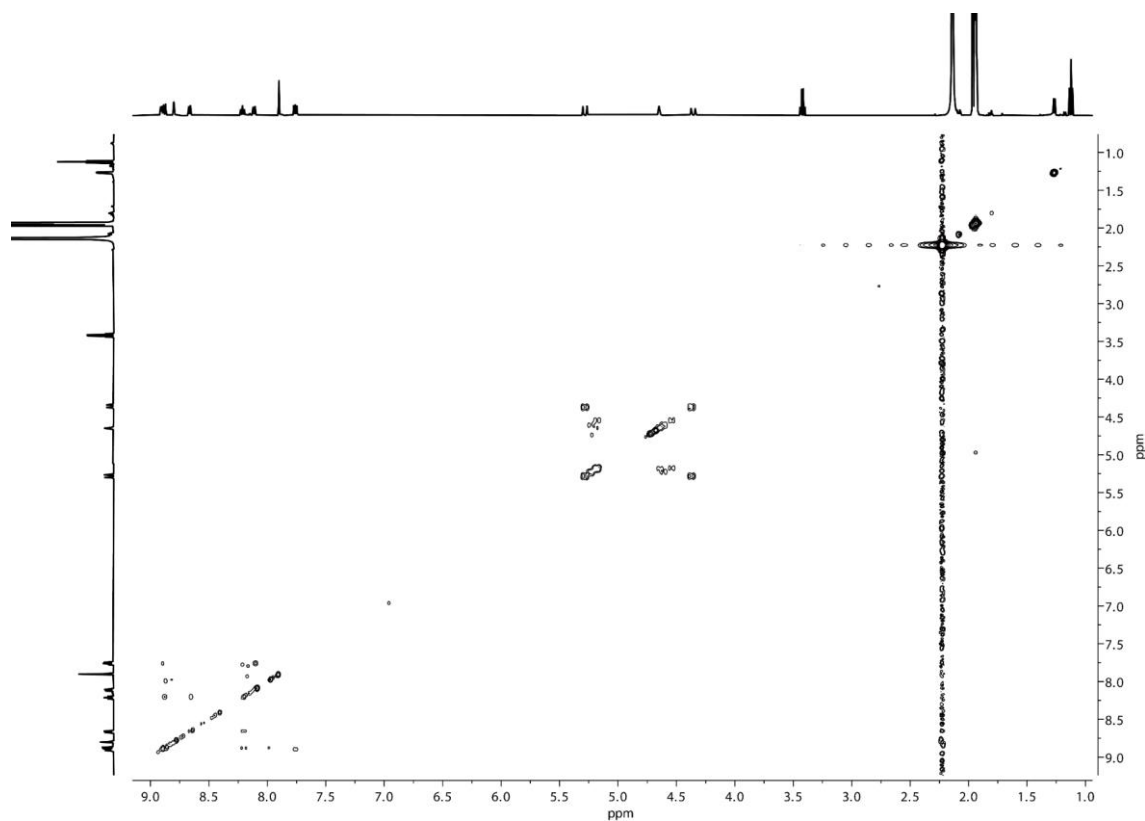


Figure S11: ^1H COSY spectrum (500 MHz, 298K, CD_3CN) of the homoleptic assembly Pd_2Bp_4 .

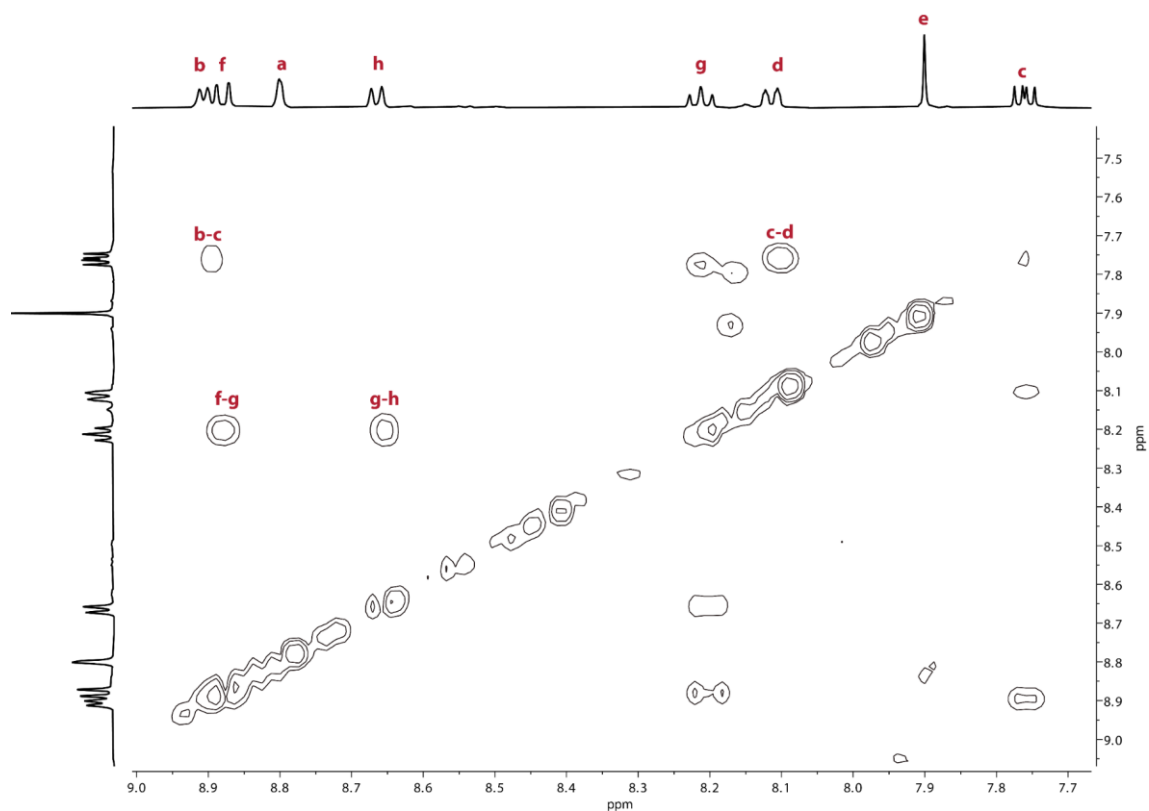


Figure S12: ^1H COSY spectrum (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the of homoleptic assembly $\text{Pd}_2\text{B}^{\text{p}}_4$.

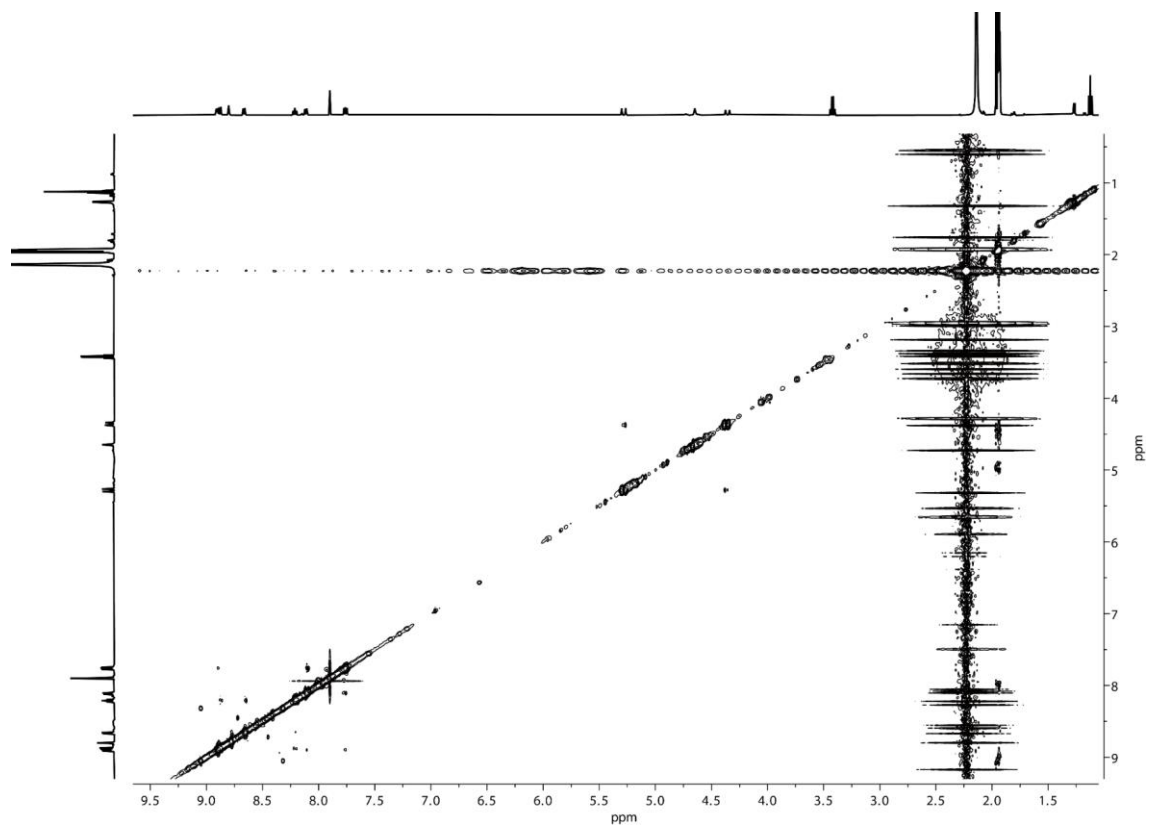


Figure S13: ^1H NOESY spectrum (500 MHz, 298K, CD_3CN) of the of homoleptic assembly $\text{Pd}_2\text{B}^{\text{p}}_4$.

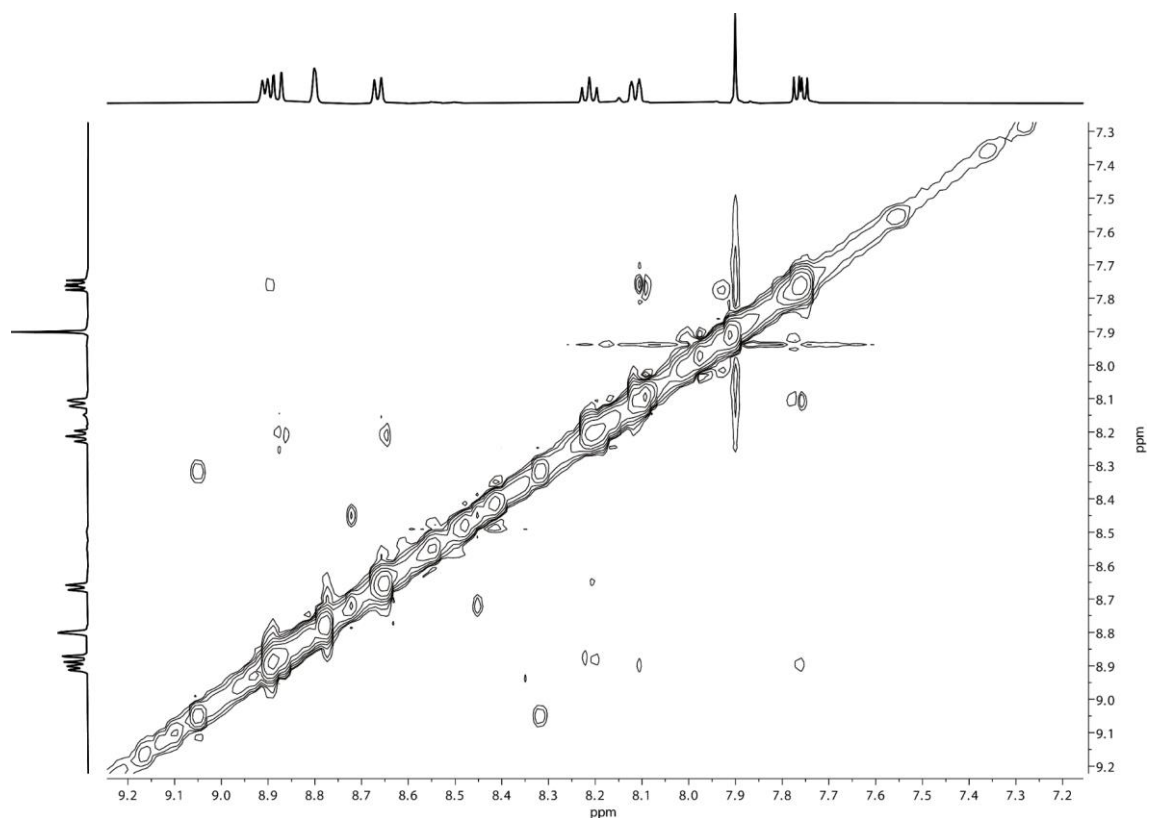


Figure S14: ^1H NOESY spectrum (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the homoleptic assembly $\text{Pd}_2\text{B}^{\text{P}}_4$.

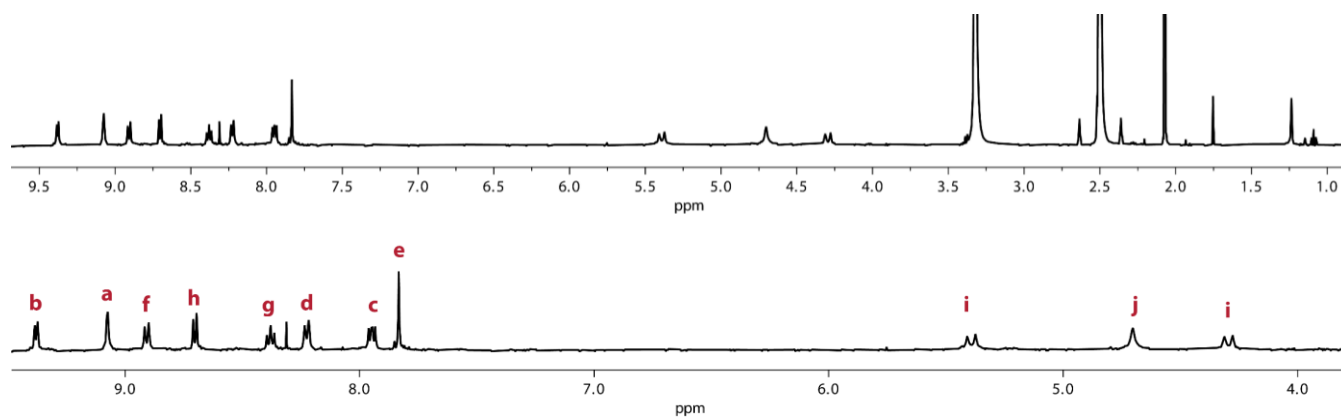


Figure S15: ^1H spectrum (500 MHz, 298K, DMSO-d_6) of the homoleptic assembly $\text{Pd}_2\text{B}^{\text{P}}_4$.

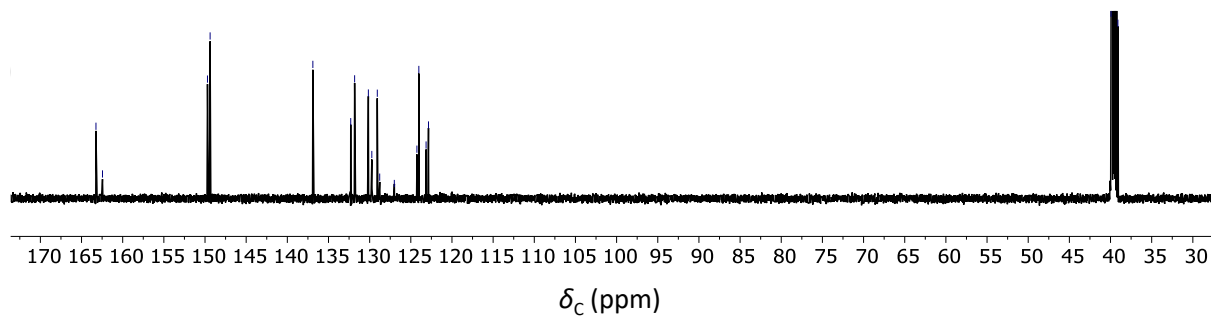


Figure S16: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of $\text{Pd}_2\text{B}^{\text{P}}_4$.

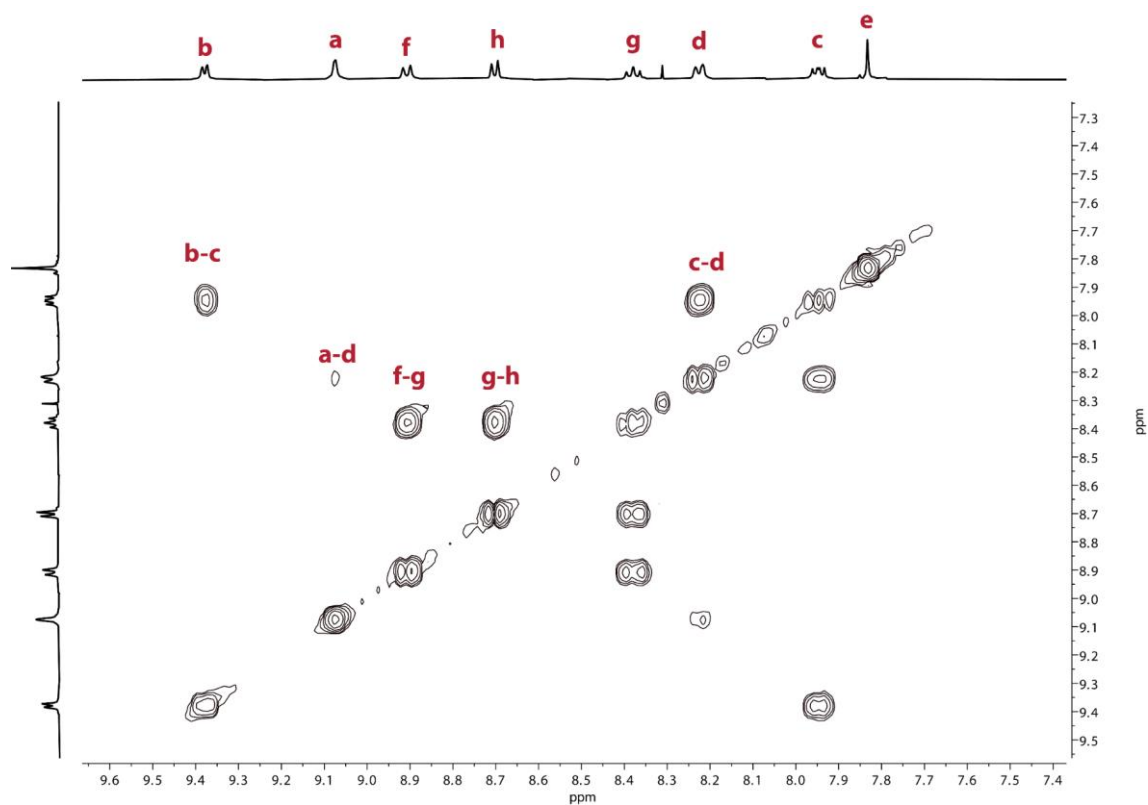


Figure S17: ^1H COSY spectrum (500 MHz, 298K, DMSO-d_6) enlarged on the aromatic region of the homoleptic assembly Pd_2BP_4 .

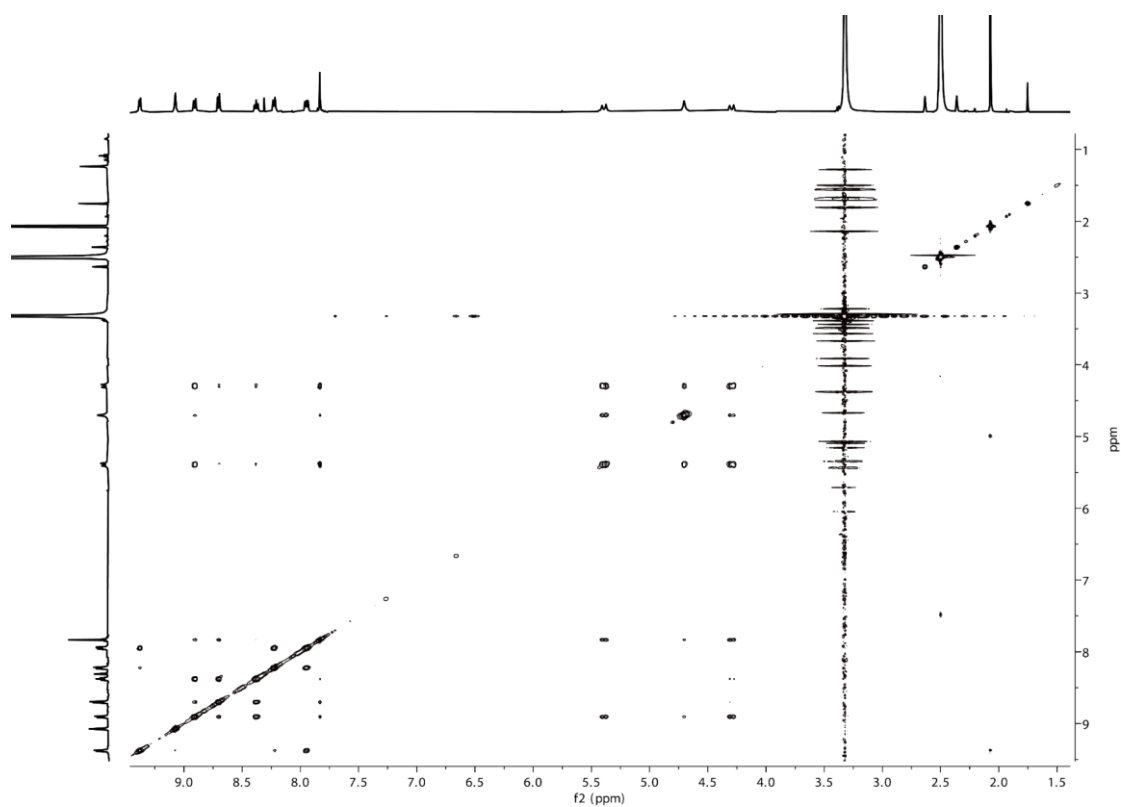


Figure S18: ^1H NOESY spectrum (500 MHz, 298K, DMSO-d_6) of the homoleptic assembly Pd_2BP_4 .

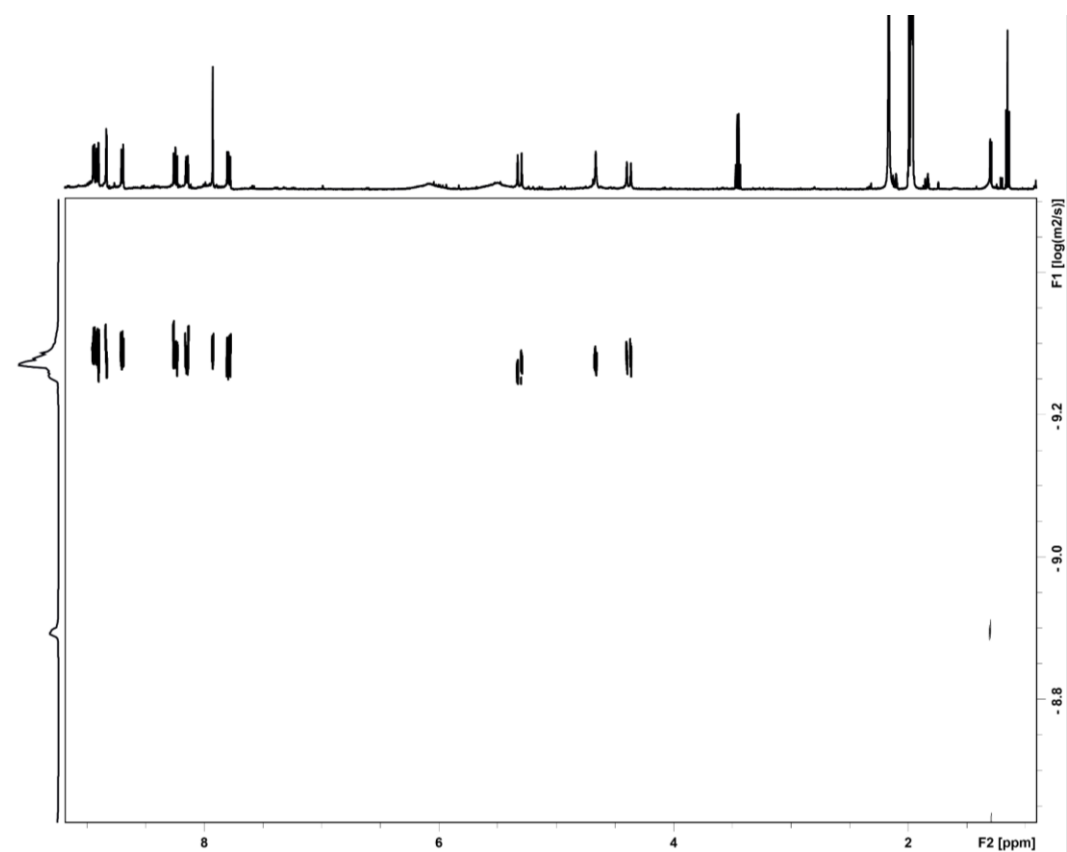


Figure S19: ^1H DOSY spectrum (500 MHz, 298K, CD_3CN) of the of homoleptic assembly Pd_2BP_4 .

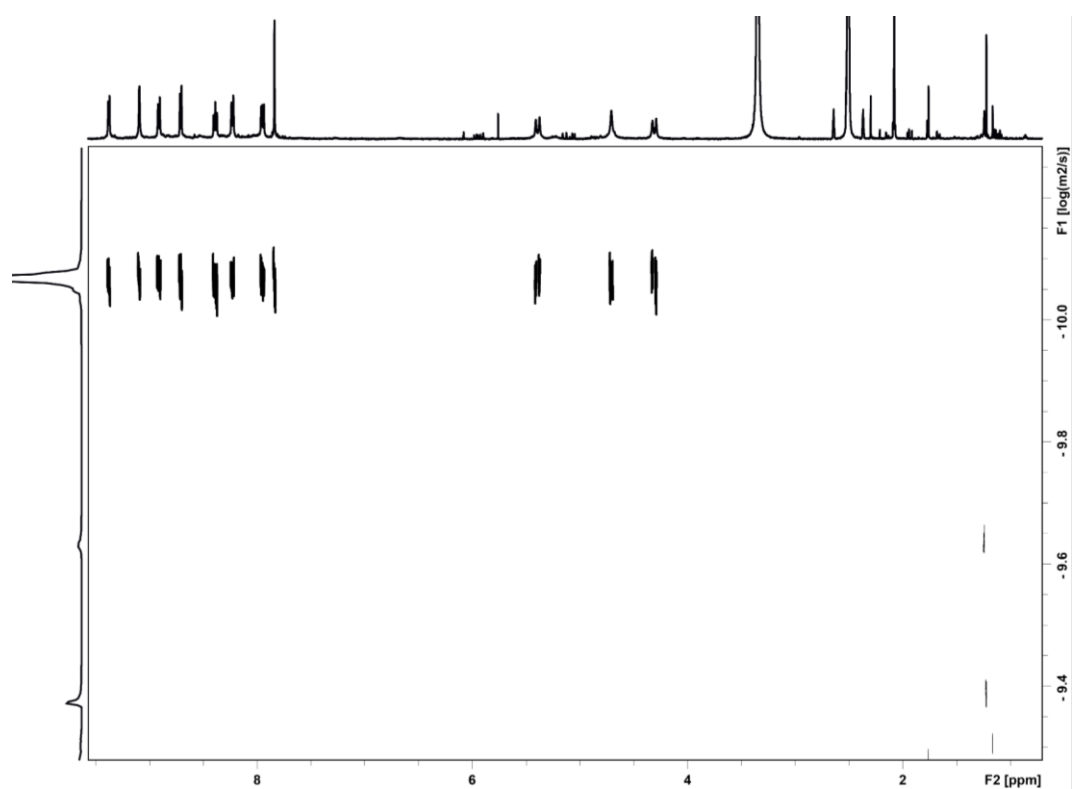


Figure S20: ^1H DOSY spectrum (500 MHz, 298K, DMSO-d_6) of the of homoleptic assembly Pd_2BP_4 .

The hydrodynamic radii were calculated using the Stokes-Einstein equation:

$$r = \frac{k \times T}{6 \times \pi \times \eta \times D}$$

With r = radius, k = Boltzmann const., T = Temp., η = dynamic viscosity of solvent and D = Diffusion values estimated by the DOSY experiment.

- $r_h(\text{CD}_3\text{CN}) = 12.75 \text{ \AA}$
- $r_h(\text{DMSO-}d_6) = 12.88 \text{ \AA}$

Host Guest Chemistry with enantiopure $\text{Pd}_2\text{B}^{\text{P}}_4$

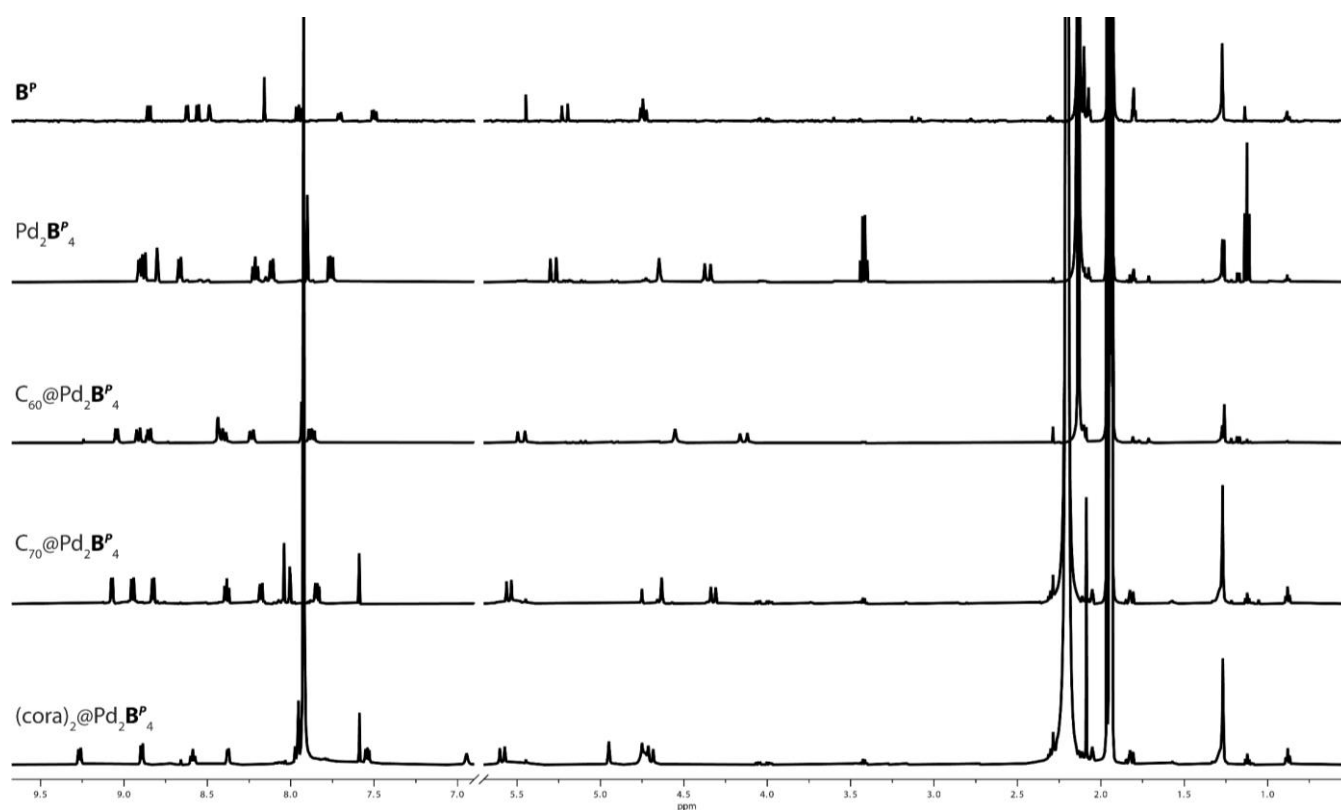


Figure S21: ^1H NMR (CD_3CN , 500 MHz) stack enlarged on the aromatic region of B^{P} and $\text{Pd}_2\text{B}^{\text{P}}_4$, $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$, $\text{C}_{70}@\text{Pd}_2\text{B}^{\text{P}}_4$ and $(\text{Cora})_2@\text{Pd}_2\text{B}^{\text{P}}_4$.

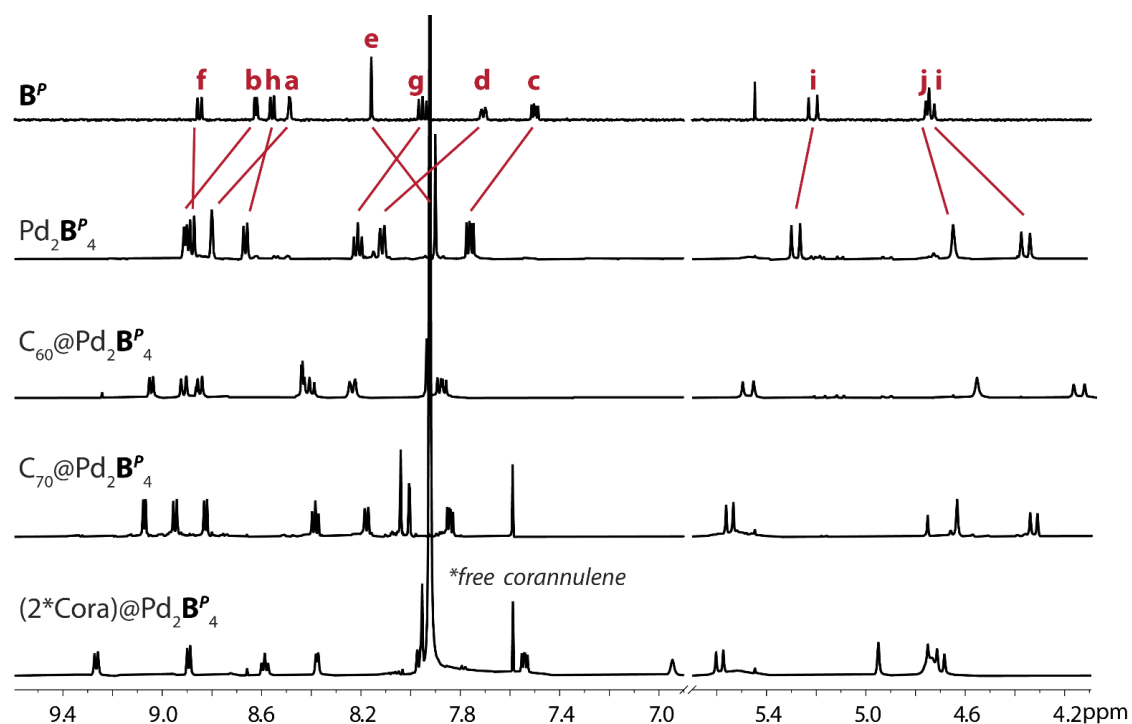


Figure S22: ^1H NMR (CD₃CN, 500 MHz) stack enlarged on the aromatic region of B^{P} and $\text{Pd}_2\text{B}^{\text{P}}_4$, $\text{C}_{60}\text{@Pd}_2\text{B}^{\text{P}}_4$, $\text{C}_{70}\text{@Pd}_2\text{B}^{\text{P}}_4$ and $(\text{Cora})_2\text{@Pd}_2\text{B}^{\text{P}}_4$.

$\text{C}_{60}\text{@Pd}_2\text{A}_2\text{B}^{\text{P}}_2$

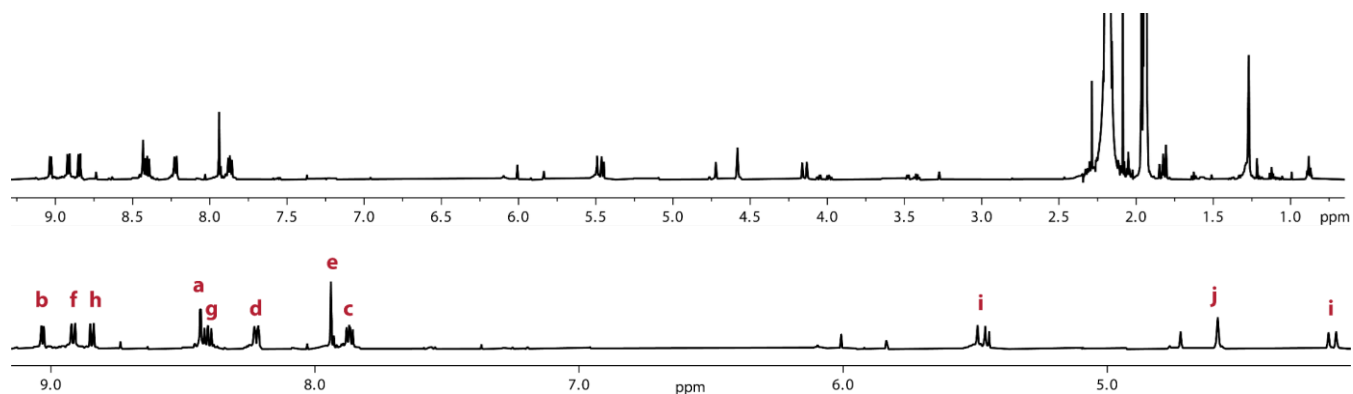
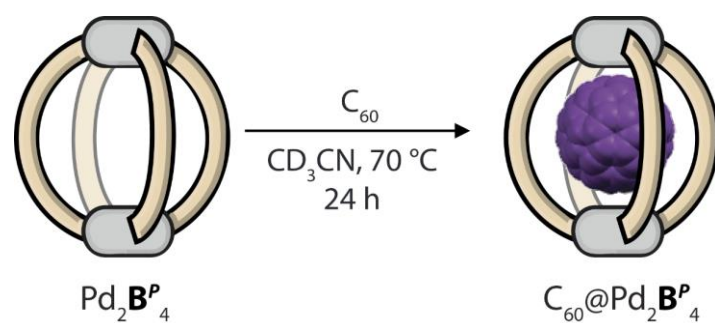


Figure S23: ^1H NMR spectrum (CD₃CN, 500 MHz, 298K) of $\text{C}_{60}\text{@Pd}_2\text{B}^{\text{P}}_4$.

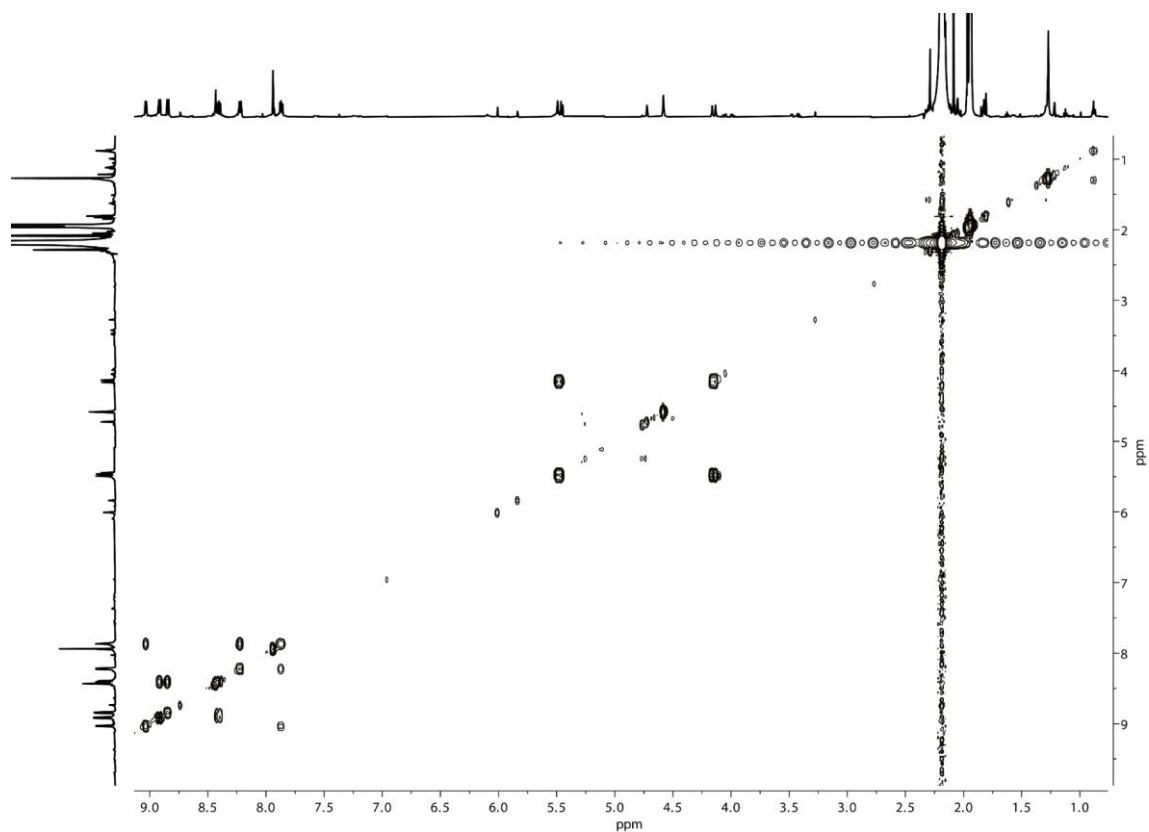


Figure S24: ^1H COSY NMR spectrum (CD_3CN , 500 MHz, 298K) of $\text{C}_{60}\text{@Pd}_2\text{B}^{\text{P}}_4$.

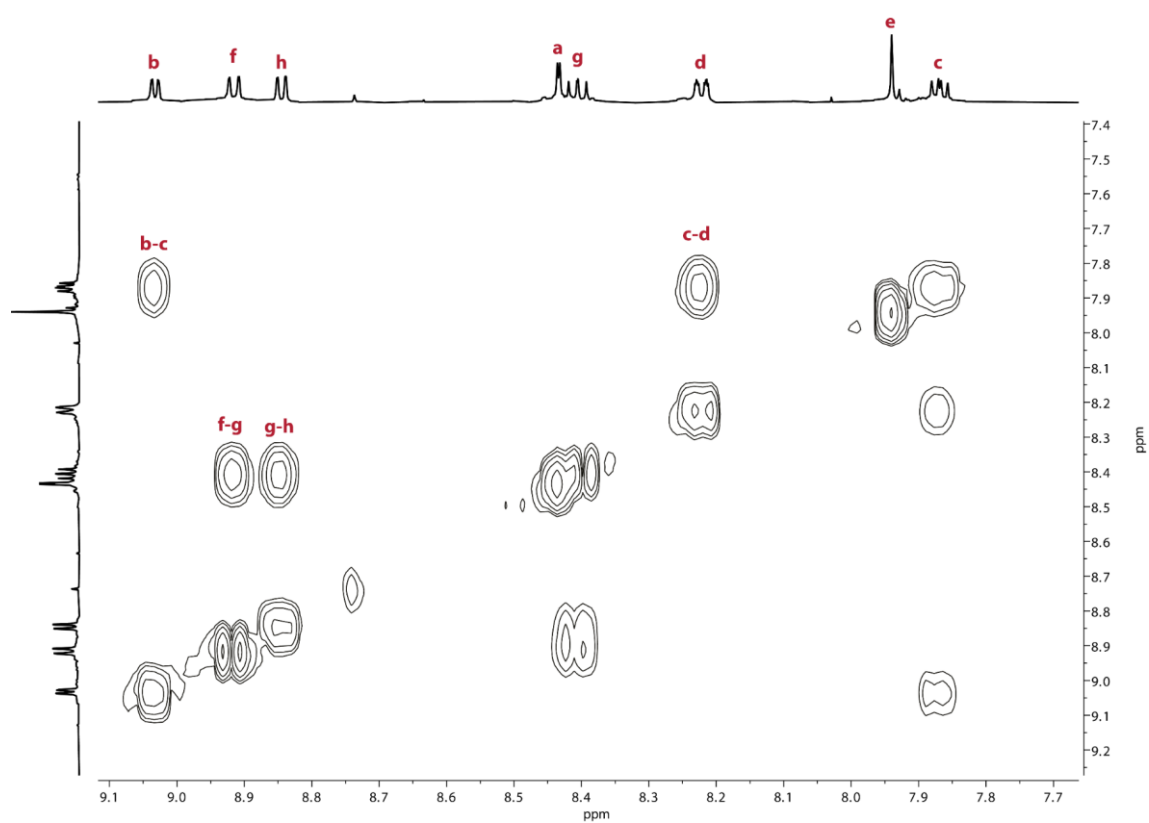


Figure S25: ^1H COSY NMR spectrum (CD_3CN , 500 MHz, 298K) enlarged on the aromatic region of $\text{C}_{60}\text{@Pd}_2\text{B}^{\text{P}}_4$.

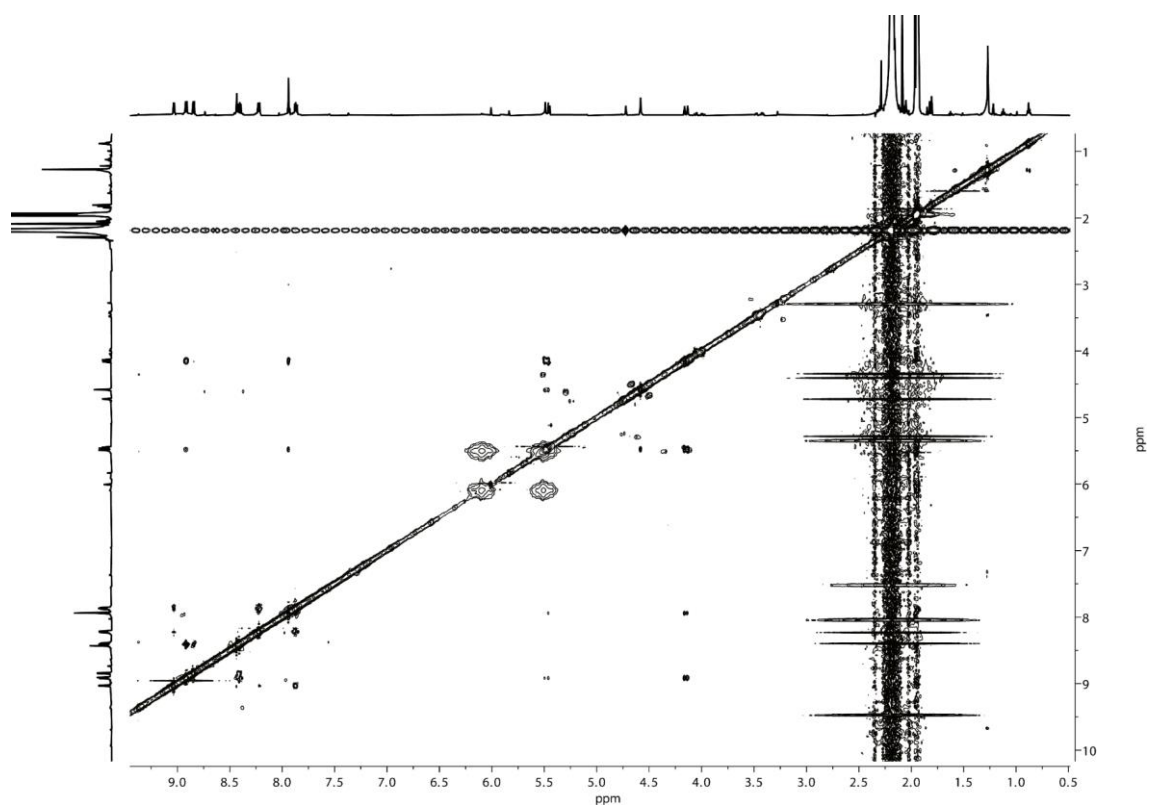


Figure S26: ^1H NOESY NMR spectrum (CD_3CN , 500 MHz, 298K) of $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$.

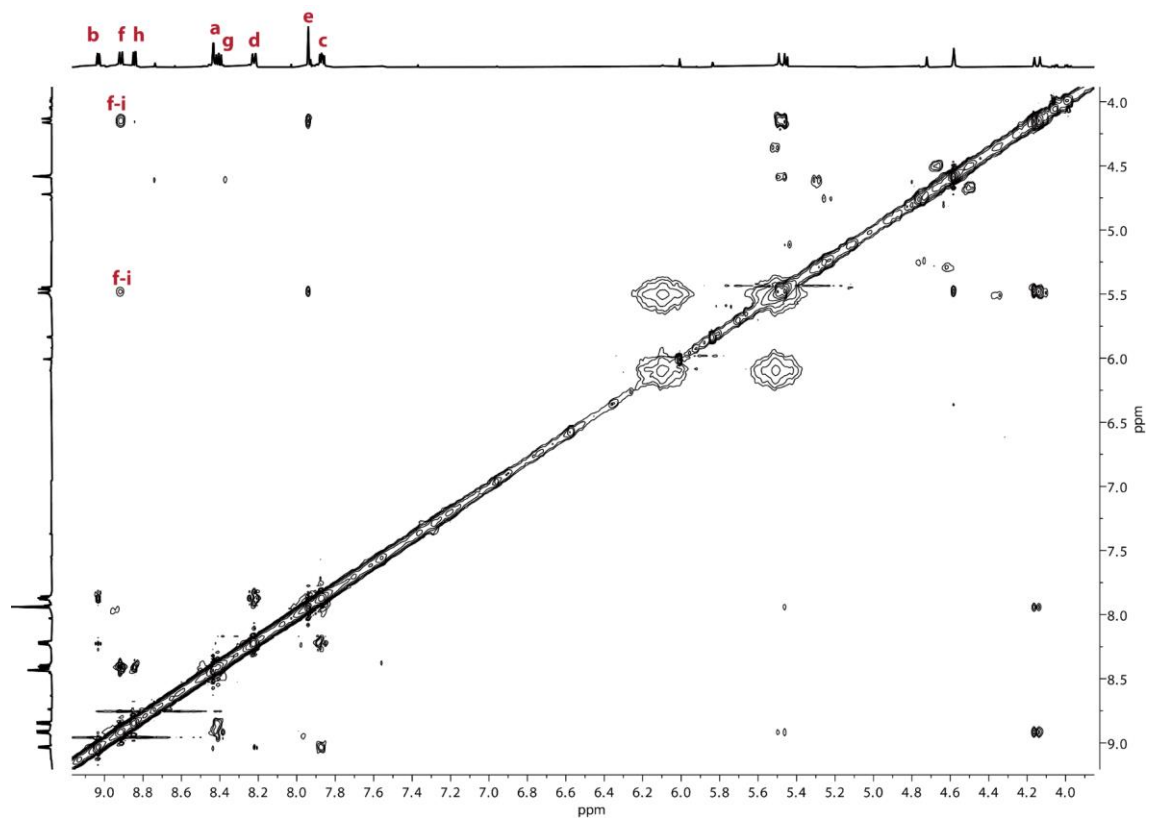


Figure S27: ^1H NOESY NMR spectrum (CD_3CN , 500 MHz, 298K) enlarged on the aromatic region of $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$.

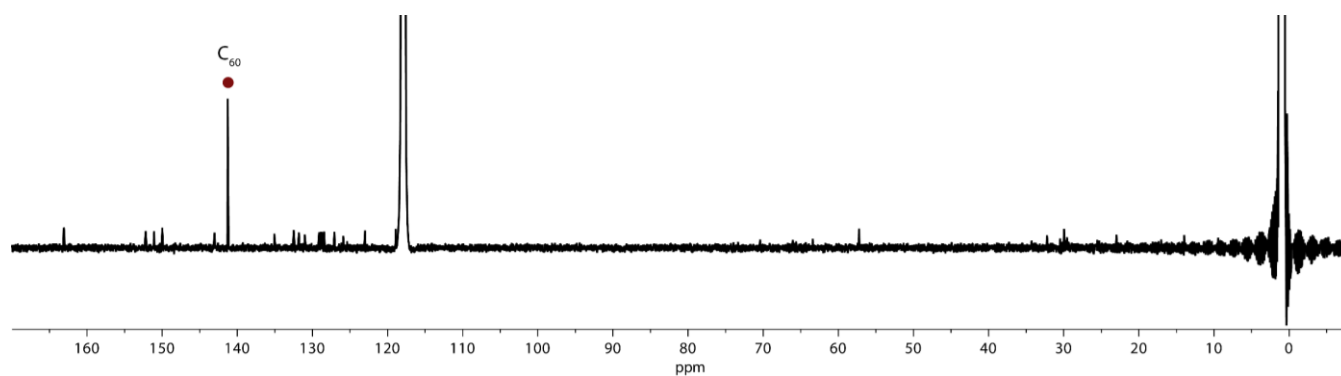


Figure S28: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of $\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4$.

$\text{C}_{70}@\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$

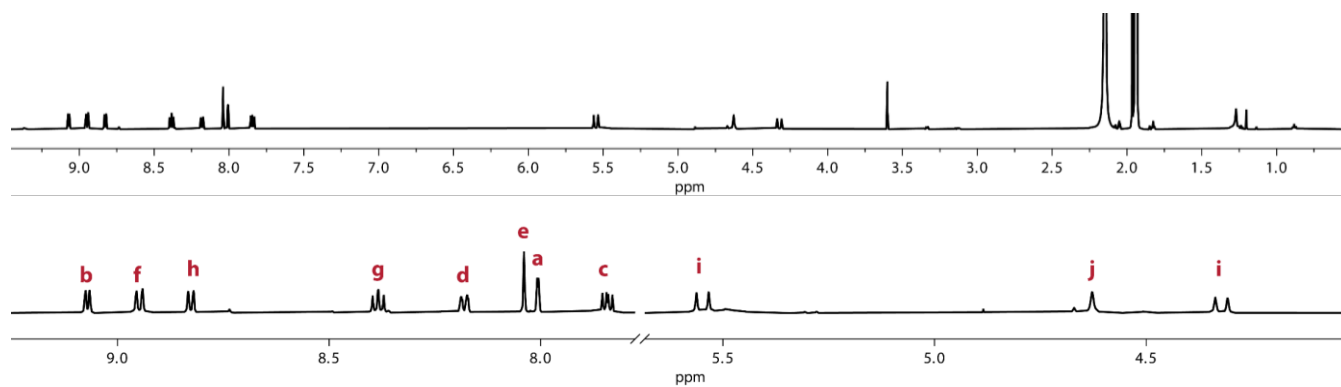
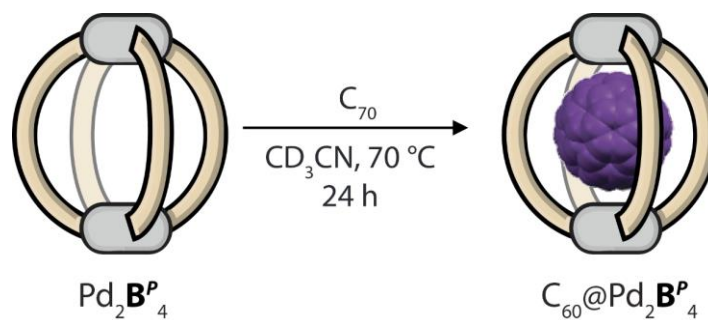


Figure S29: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of $\text{C}_{70}@\text{Pd}_2\text{B}^{\text{P}}_4$.

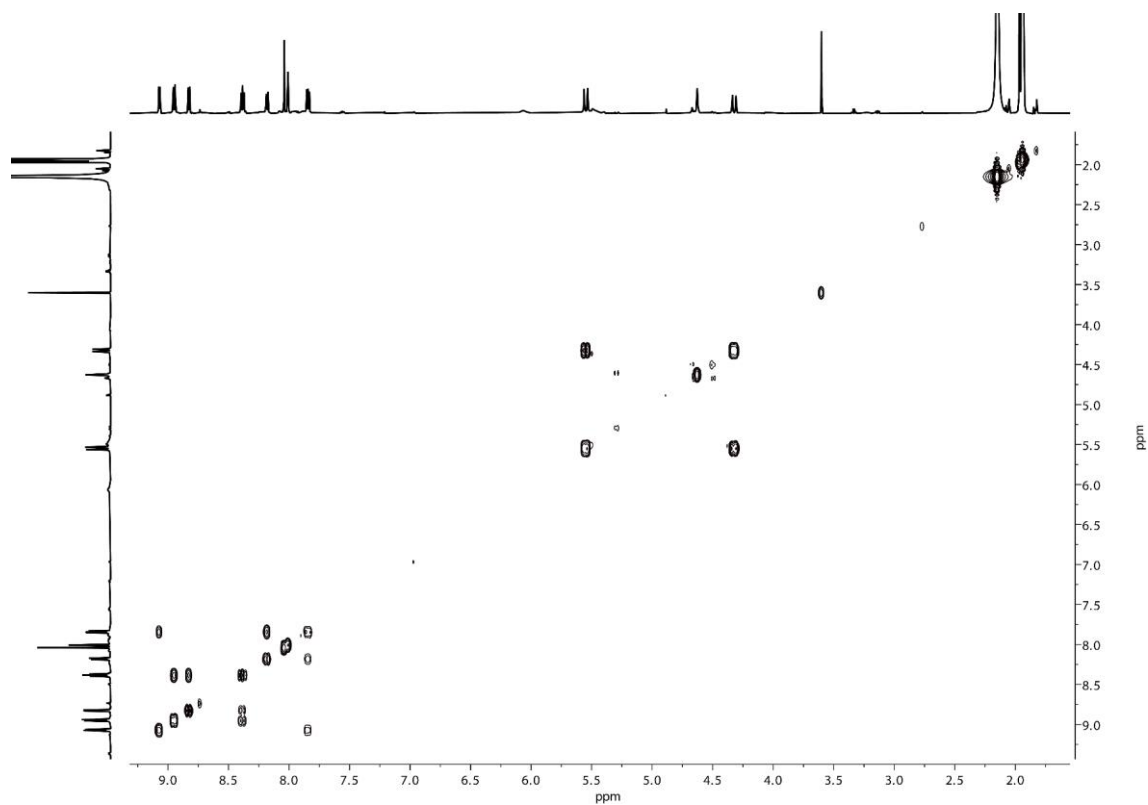


Figure S30: ^1H COSY NMR spectrum (500 MHz, 298K, CD_3CN) of $\text{C}_{70}\text{@Pd}_2\text{Bp}_4$.

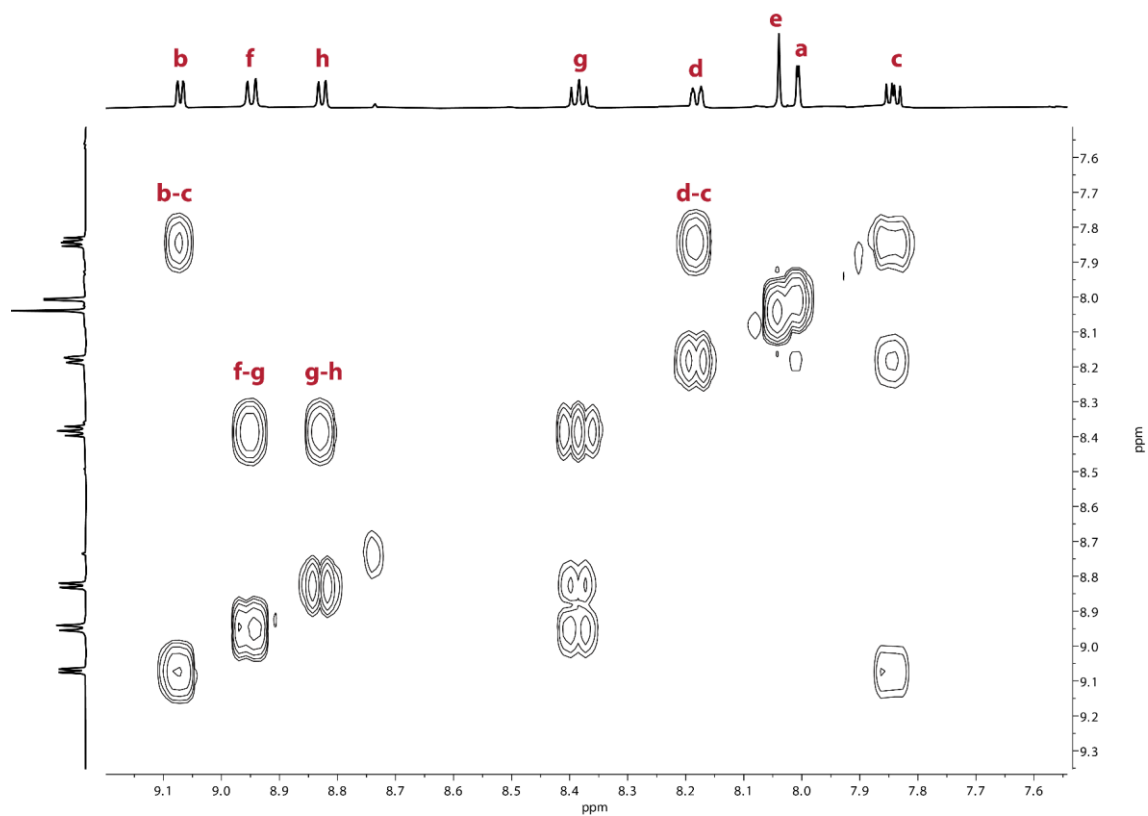


Figure S31: ^1H COSY NMR spectrum (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of $\text{C}_{70}\text{@Pd}_2\text{Bp}_4$.

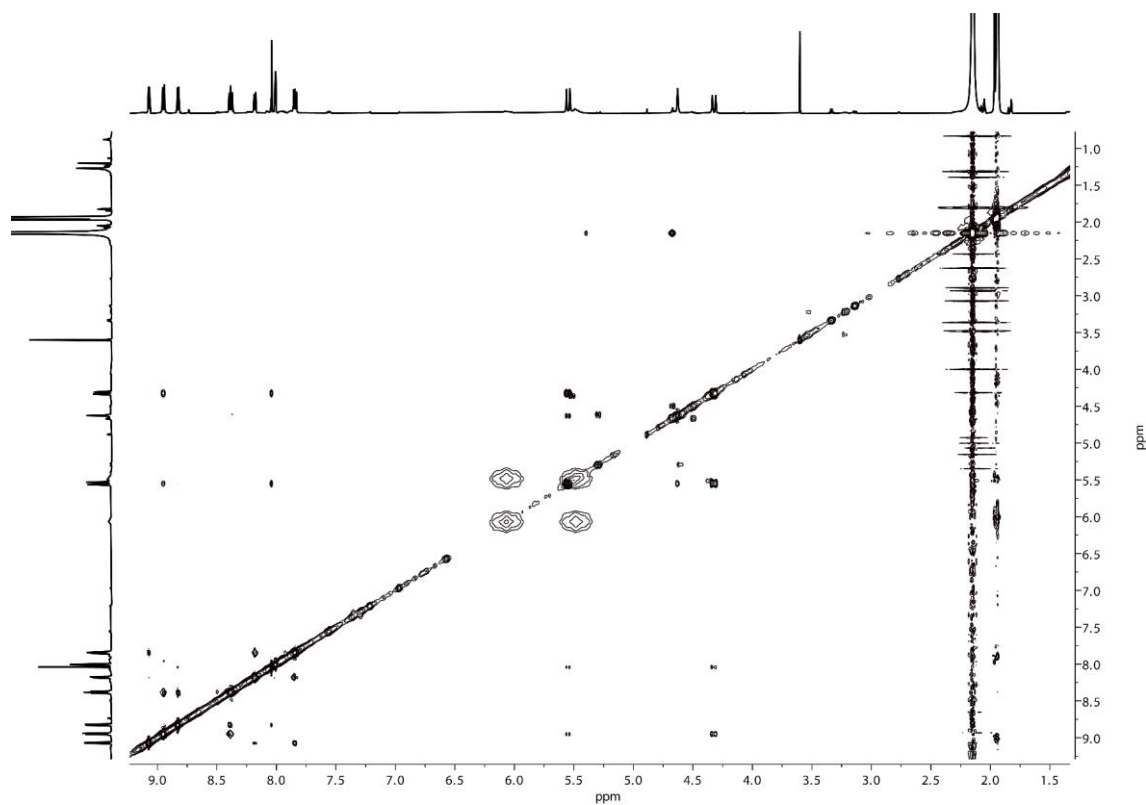


Figure S32: ^1H NOESY NMR spectrum (500 MHz, 298K, CD_3CN) of $\text{C}_{70}@\text{Pd}_2\text{BP}_4$.

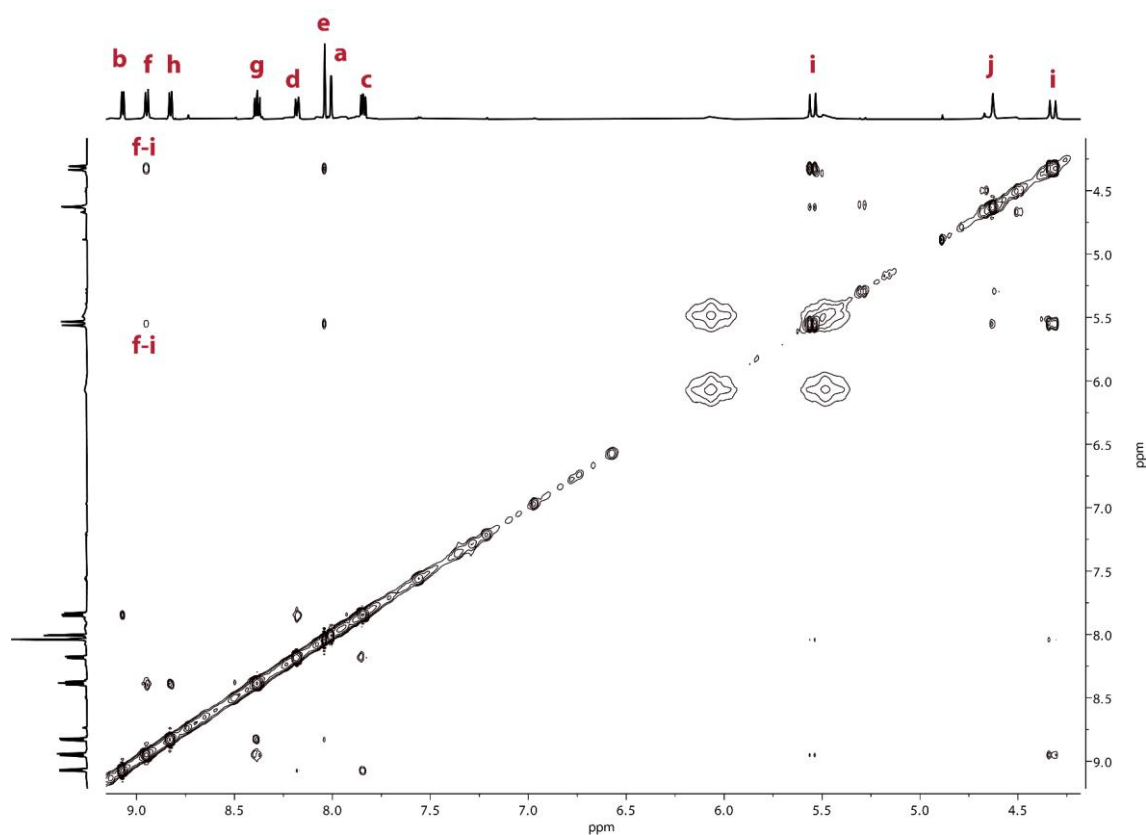


Figure S33: ^1H NOESY NMR spectrum (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of $\text{C}_{70}@\text{Pd}_2\text{BP}_4$.

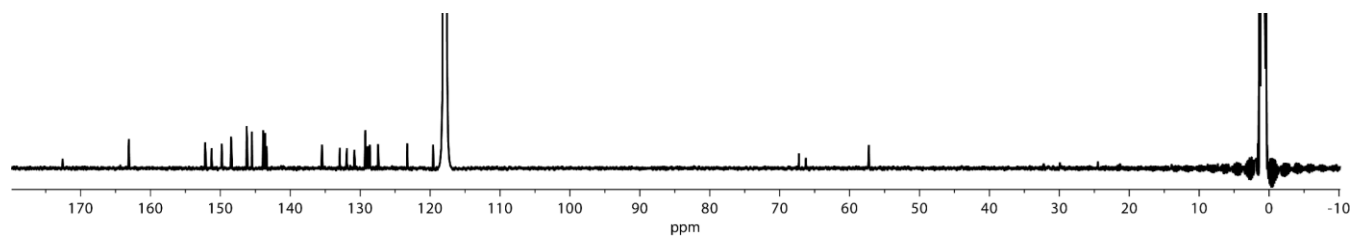


Figure S34: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of the of $\text{C}_{70}@\text{Pd}_2\text{B}^{\text{P}}_4$.

$(\text{cora})_2@\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$

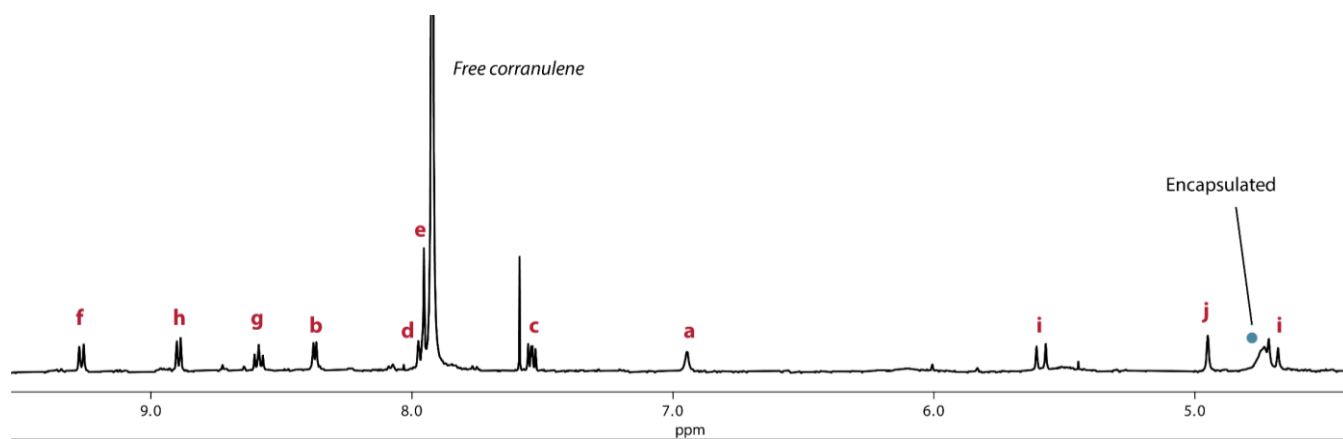
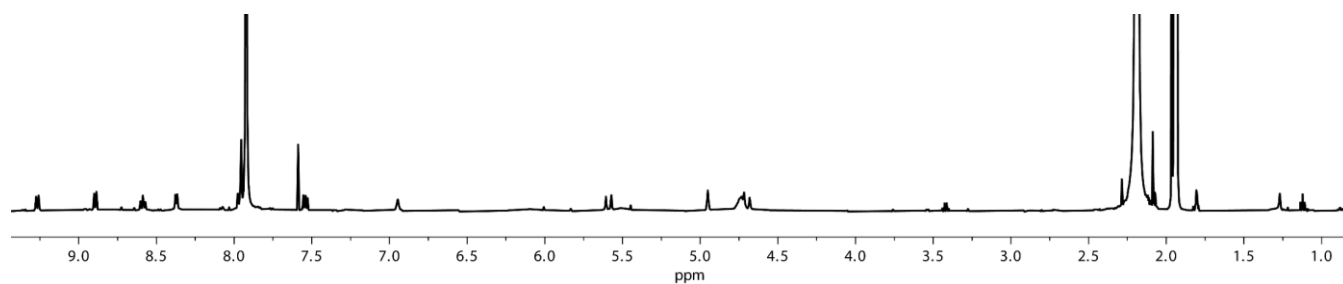
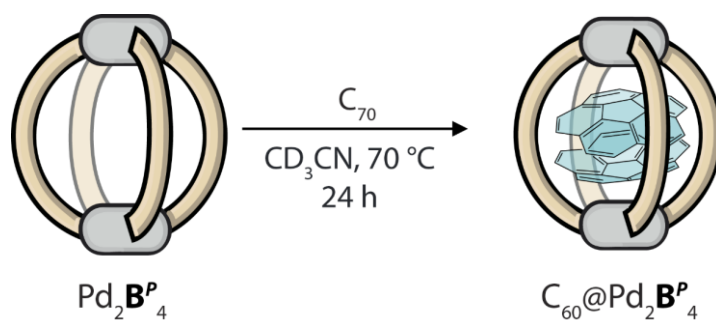


Figure S35: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of $(\text{cora})_2@\text{Pd}_2\text{B}^{\text{P}}_4$.

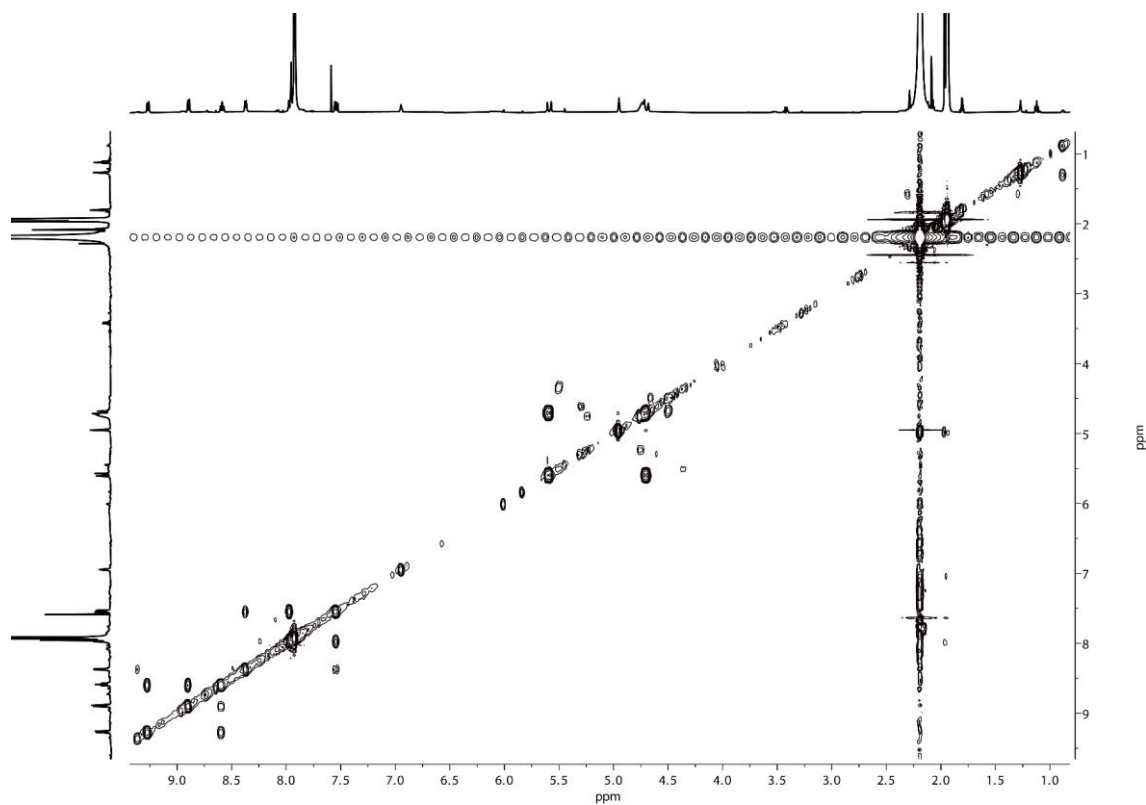


Figure S36: ^1H COSY NMR spectrum (500 MHz, 298K, CD_3CN) of $(\text{cora})_2@Pd_2B_4$.

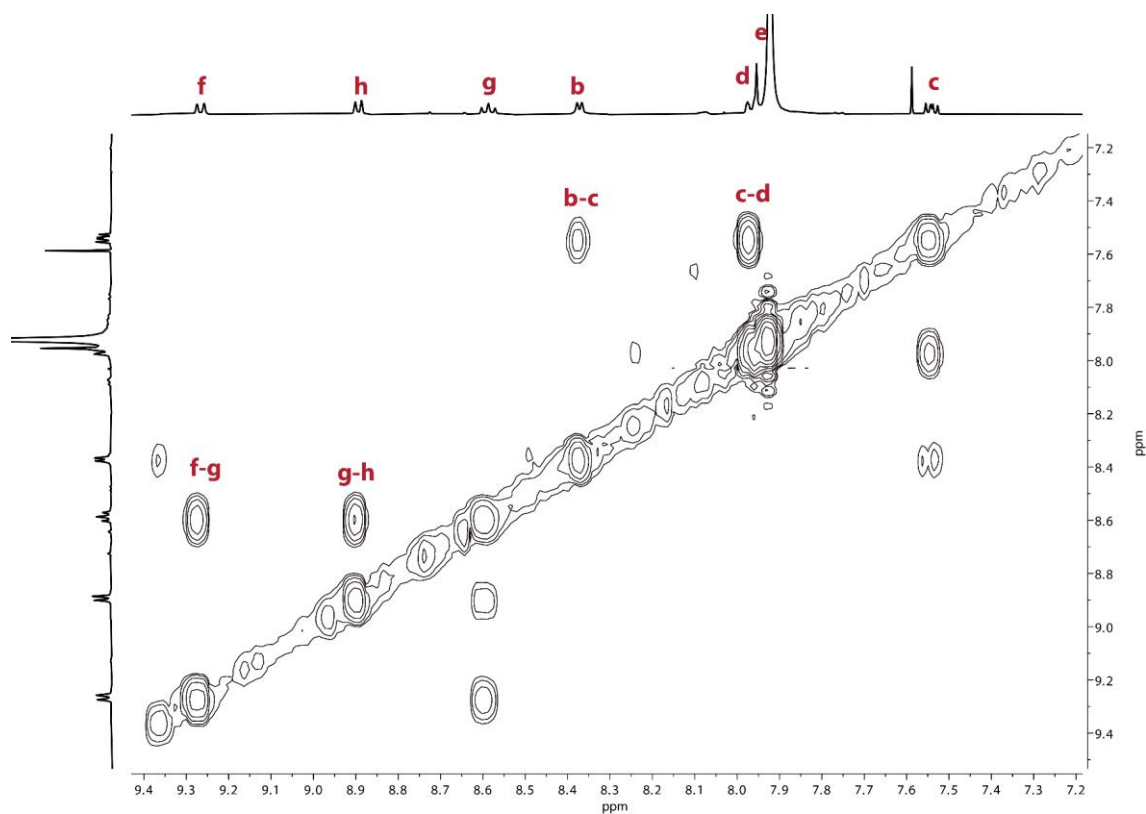


Figure S37: ^1H COSY NMR spectrum (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of $(\text{cora})_2@Pd_2B_4$.

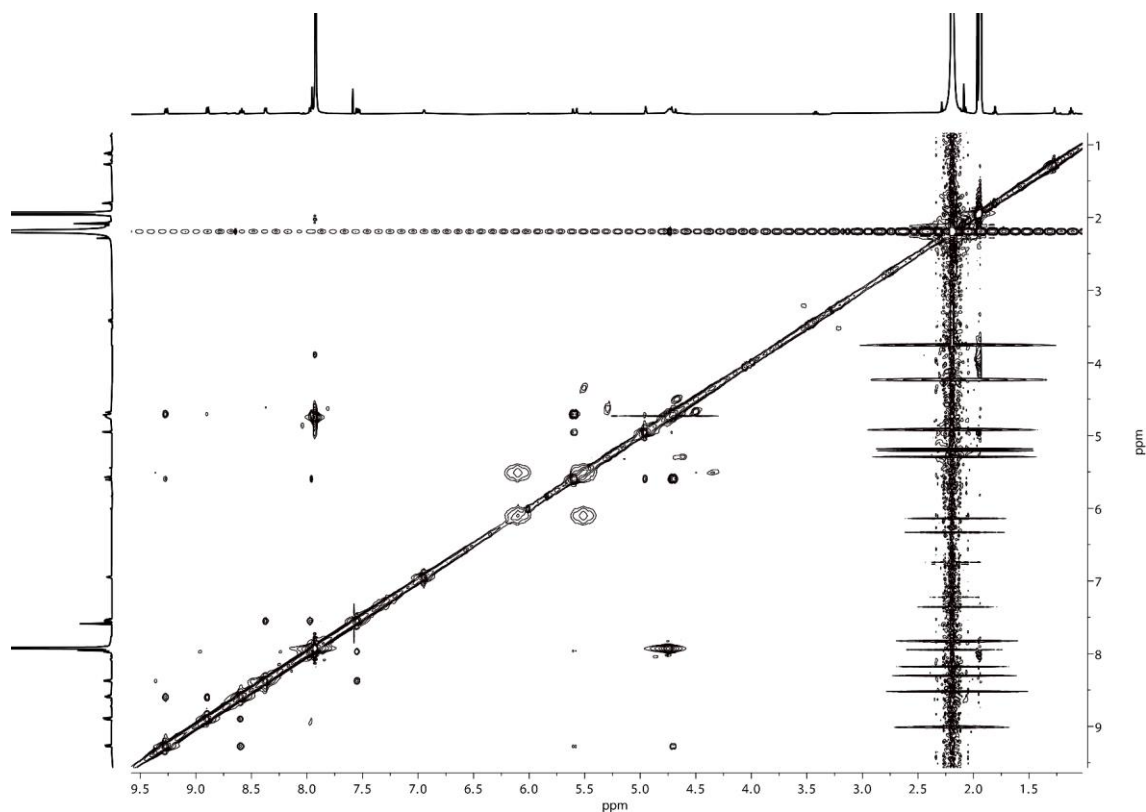


Figure S38: ^1H NOESY NMR spectrum (500 MHz, 298K, CD_3CN) of $(\text{cora})_2@Pd_2B^P_4$.

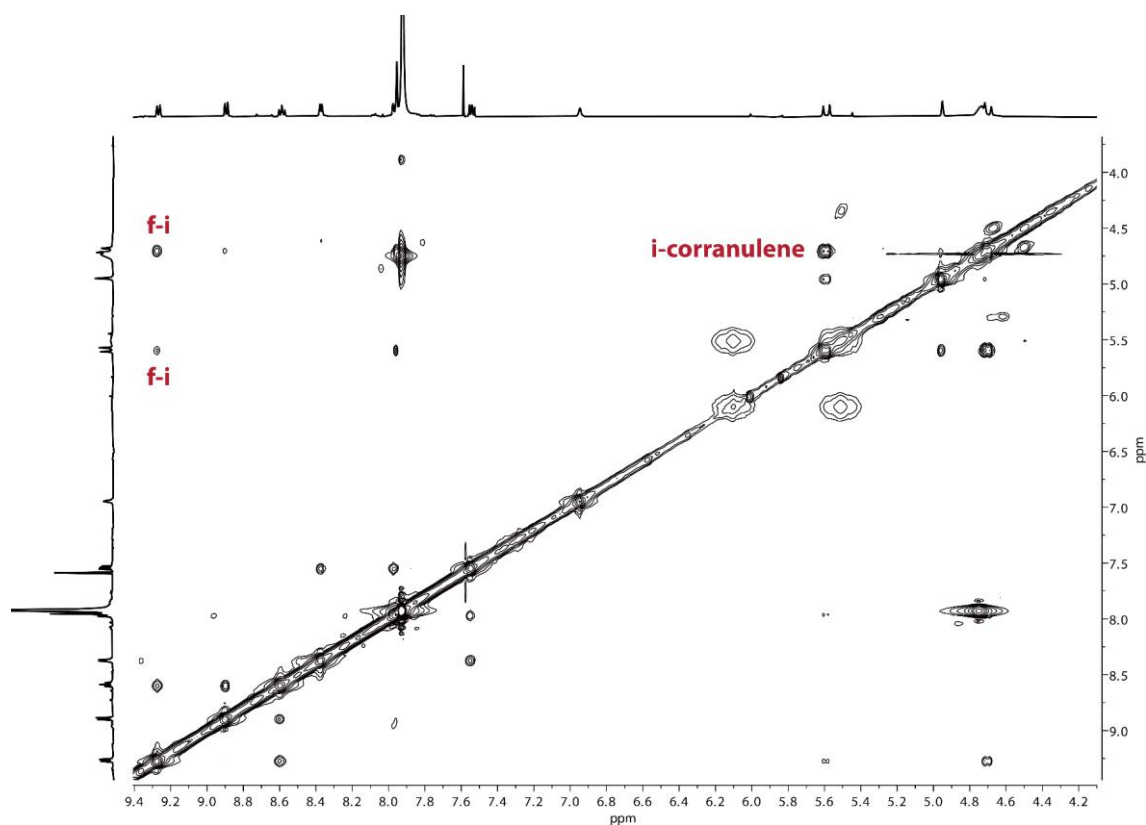


Figure S39: ^1H NOESY NMR spectrum (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of $(\text{cora})_2@Pd_2B^P_4$.

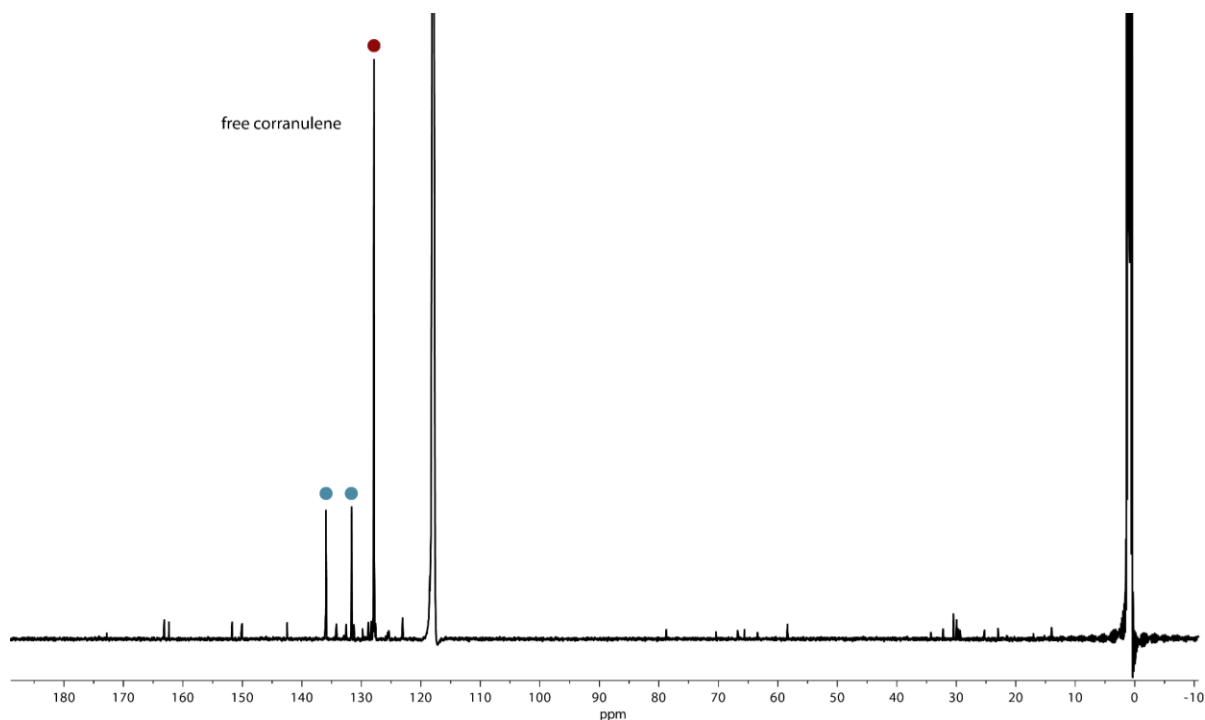


Figure S40: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of the of $(\text{cora})_2@Pd_2Bp_4$.

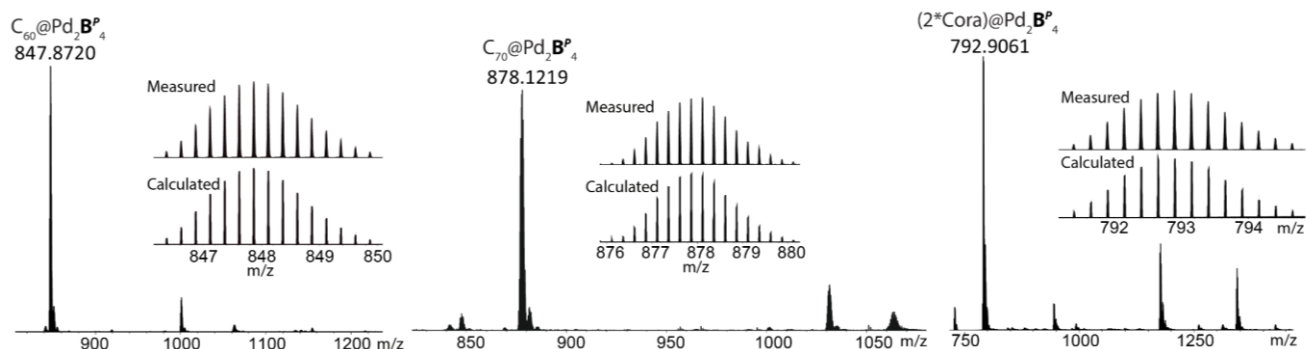
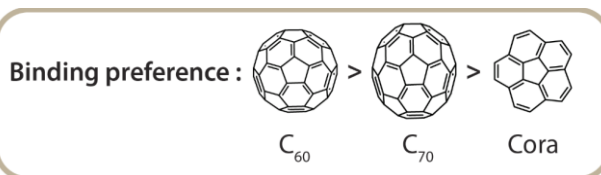


Figure S41: ESI-MS spectrum of a MeCN solution B^P with 0.5 equiv. Pd(II) with the respective guest encapsulated. The observed peaks correspond to $[\text{G}@Pd_2Bp_4+nBF_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[\text{G}@Pd_2Bp_4]^{4+}$ are shown in the inset. $\text{G} = \text{C}_{60}$, C_{70} or corannulene.

Competition experiments



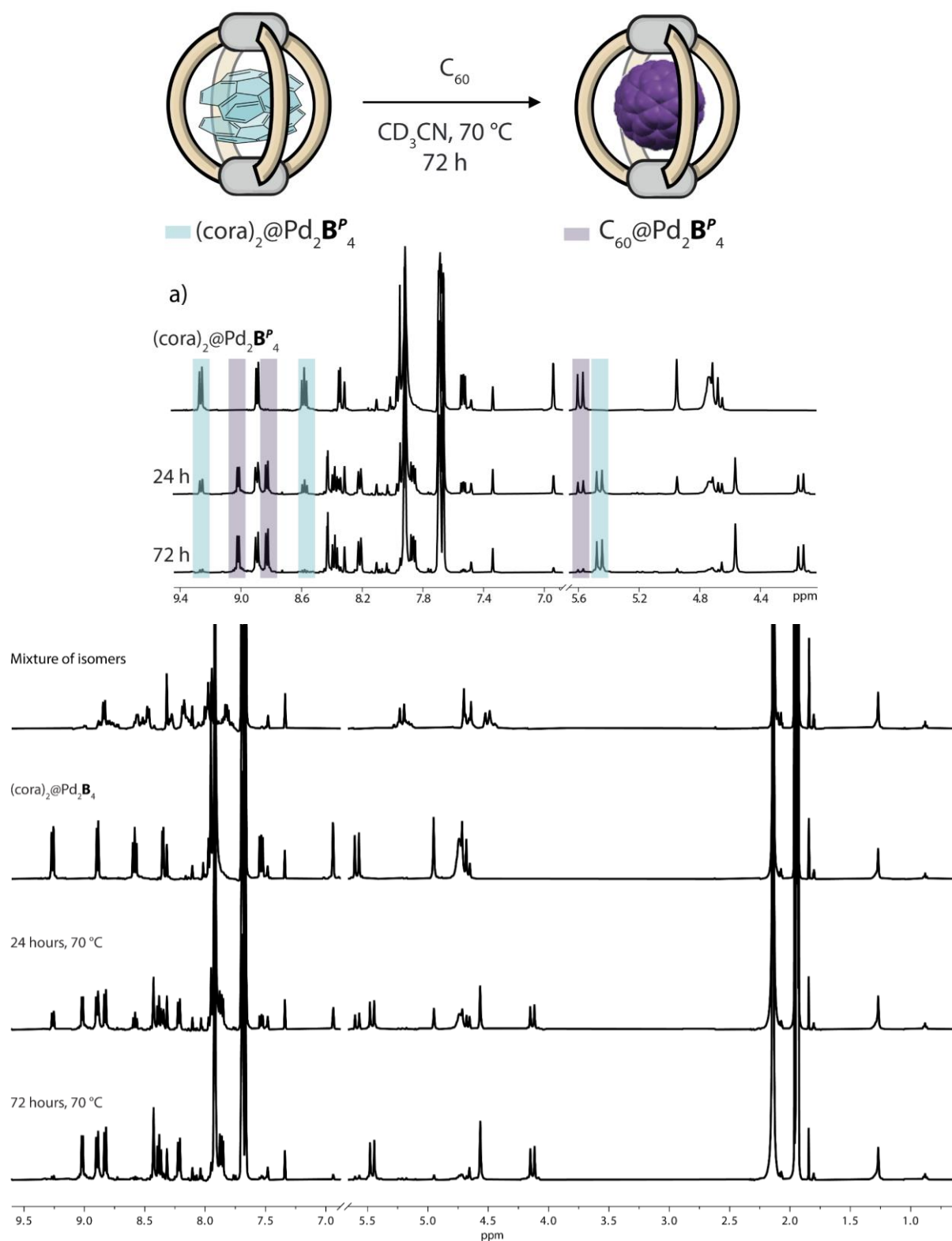


Figure S42: ¹H NMR (CD₃CN, 500 MHz) stack of starting point (cora)₂@cage and slow replacement by C₆₀ after a solution of (cora)₂@cage at 0.7 mM is heated at 70 °C for 24 hours in the presence of C₆₀ fullerene powder and final state, after 72 hours at 70 °C, where corannulene is fully replaced by C₆₀ in the cage. Here, the counter anions of the cage are BArF⁻ and give rise to the signal at 7.7 ppm.

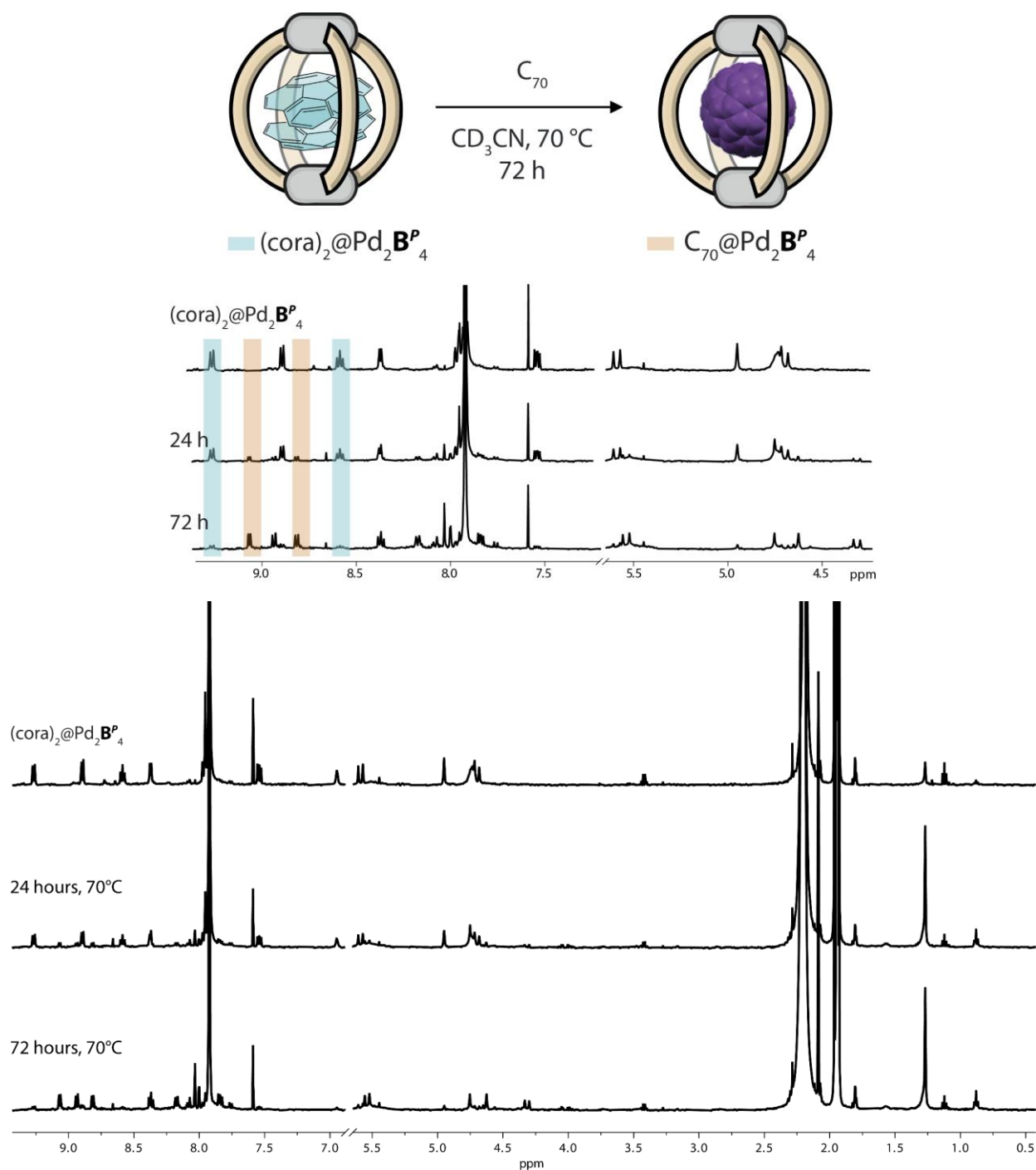


Figure S43: ¹H NMR (CD₃CN, 500 MHz) stack of starting point (cora)₂@cage and slow replacement by C₇₀ after a solution of (cora)₂@cage at 0.7 mM is heated at 70 °C for 24 hours in presence of C₇₀ fullerene powder and final state, after 72 hours at 70 °C, where corannulene is fully replaced by C₇₀ in the cage.

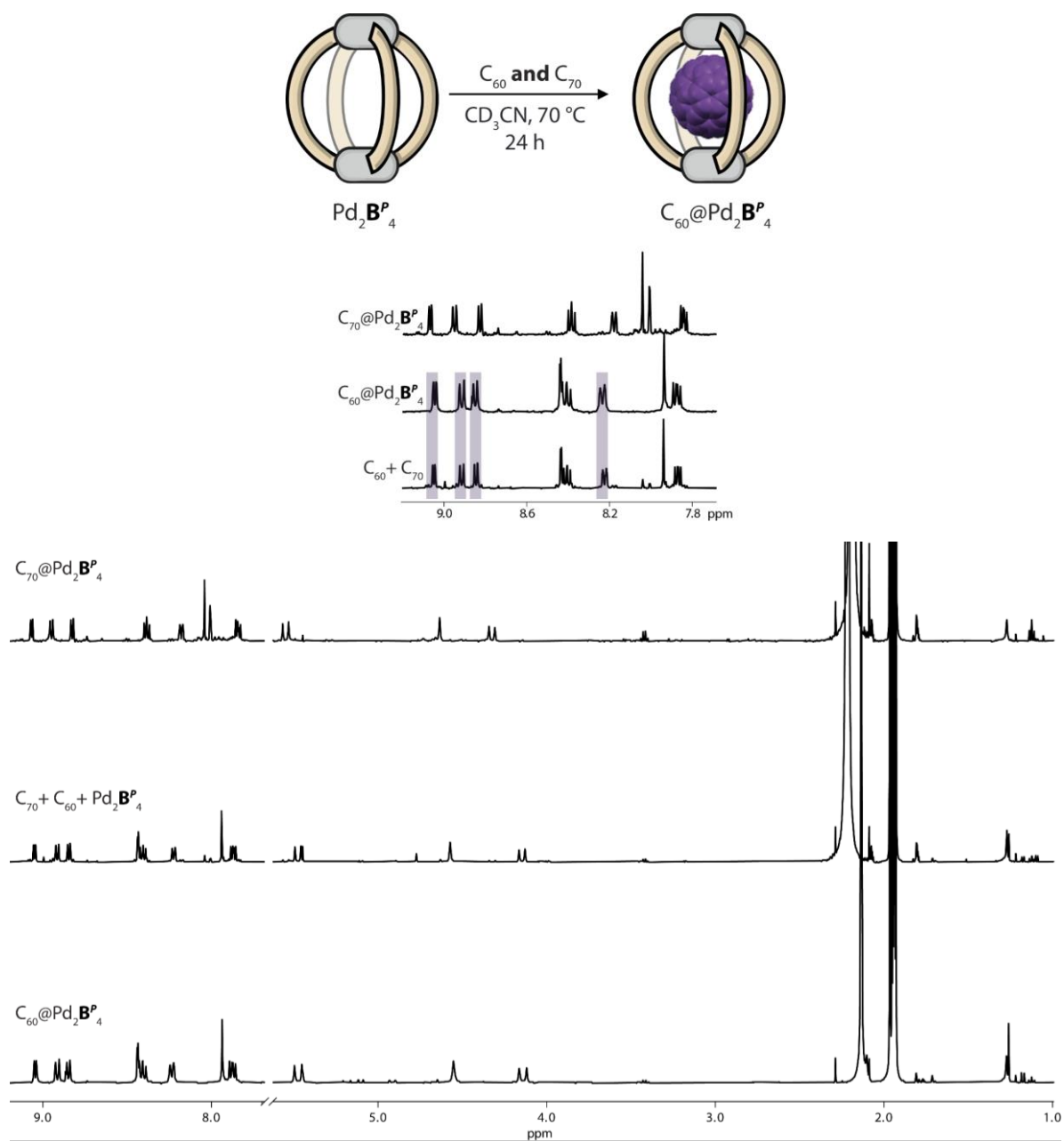


Figure S44: ¹H NMR (CD₃CN, 500 MHz) of (top) reference C₇₀@cage, (middle) reference C₆₀@cage (bottom) competition experiment where a solution of cage at 0.7 mM is heated at 70 °C for 48 hours in the presence of both C₆₀ and C₇₀ fullerene powders. Here, the counter anions of the cage are tetrafluoroborate.

Selective fullerene extraction

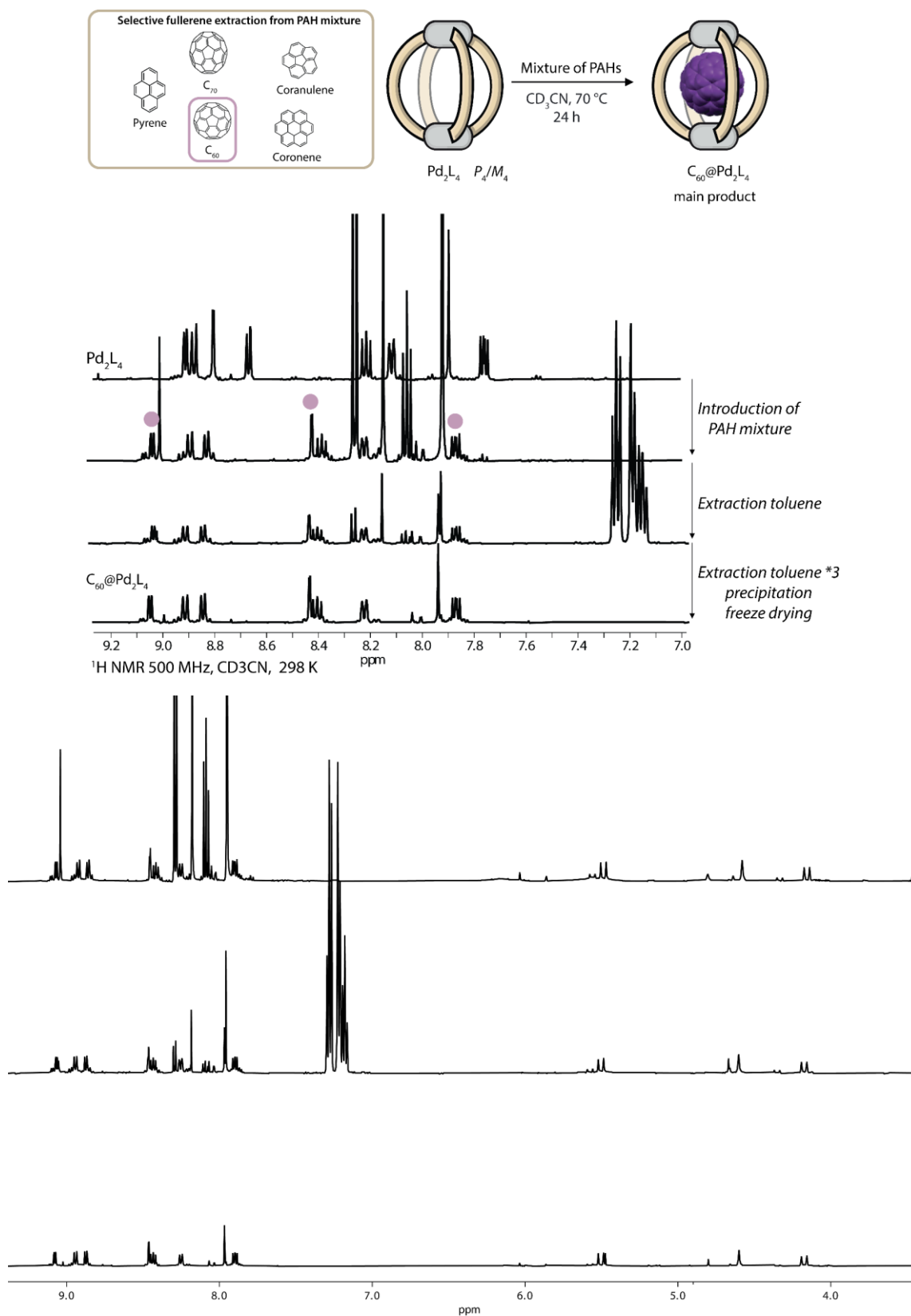


Figure S45: ¹H NMR (CD₃CN, 500 MHz) of fullerene extraction from a mixture of PAHs. In presence of the PAHs mixture the cage favors an encapsulation of fullerene C₆₀ showing a high selectivity. After extraction with toluene, in which the PAHs have a higher solubility but where the cage precipitate, the solid is dissolved in acetonitrile. Upon consecutive extractions and freeze drying to eliminate toluene traces the cage is dissolved in acetonitrile and the ¹H NMR displays a near quantitative obtention of the host-guest complex with fullerene C₆₀.

Photophysical properties

Ligand's enantiomers and homoleptic cage

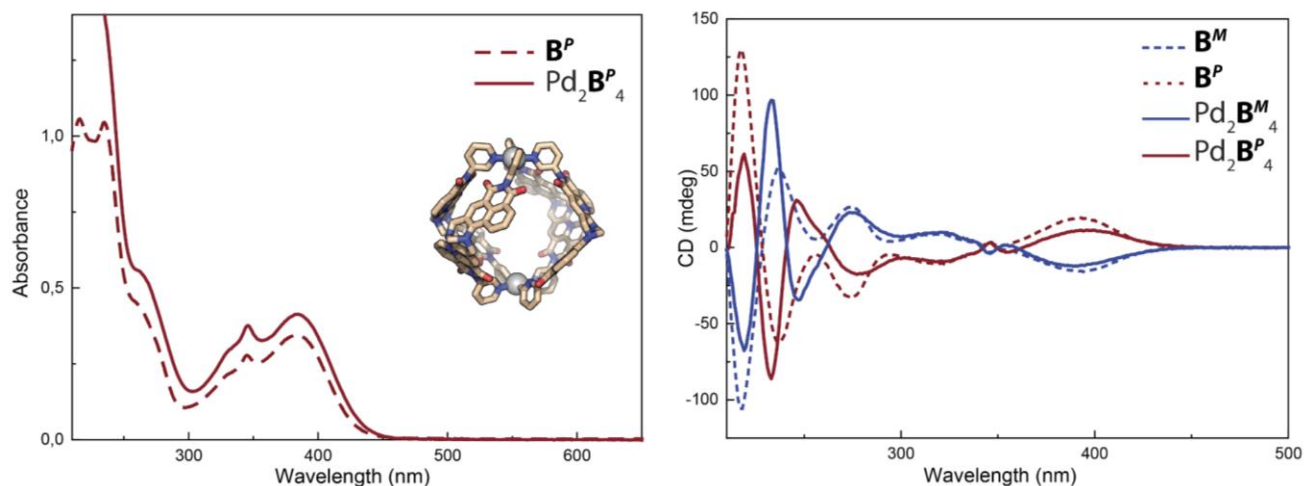


Figure S46: (Left) UV-Vis spectra of ligand B^P and cage $Pd_2B^P_4$ after enantiomer separation and (right) CD spectra of both separated ligand enantiomers B^P/B^M and corresponding cages formed by addition of 0.5 equivalent of Pd(II). Acetonitrile, 0.12 mM chromophore concentration, 2 mm cuvette, 298 K.

Host-guest complexes

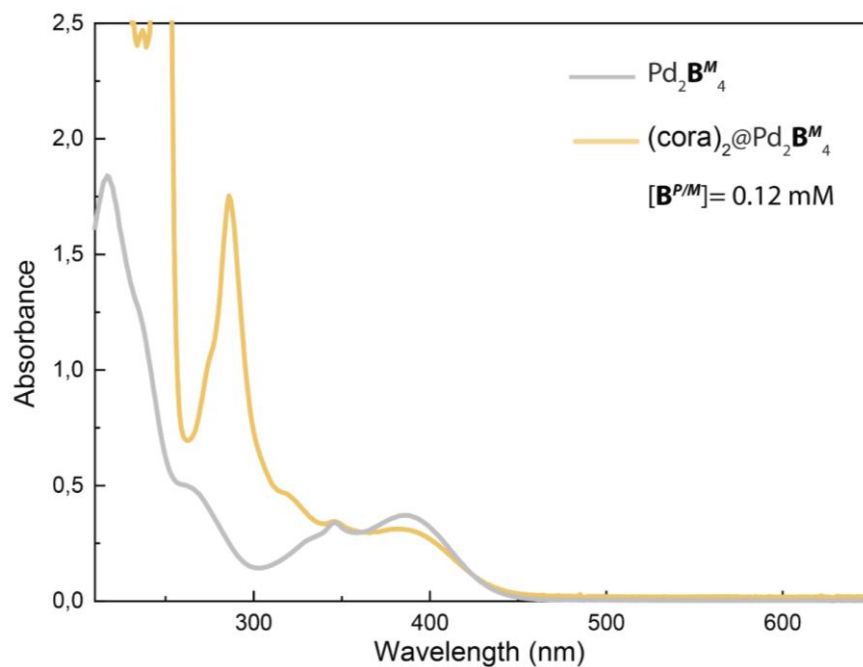


Figure S47: UV-Vis spectra of empty cage $Pd_2B^P_4$ and host-guest complex $(cora)_2@Pd_2B^M_4$. Acetonitrile, 0.12 mM chromophore concentration, 2 mm cuvette, 298 K.

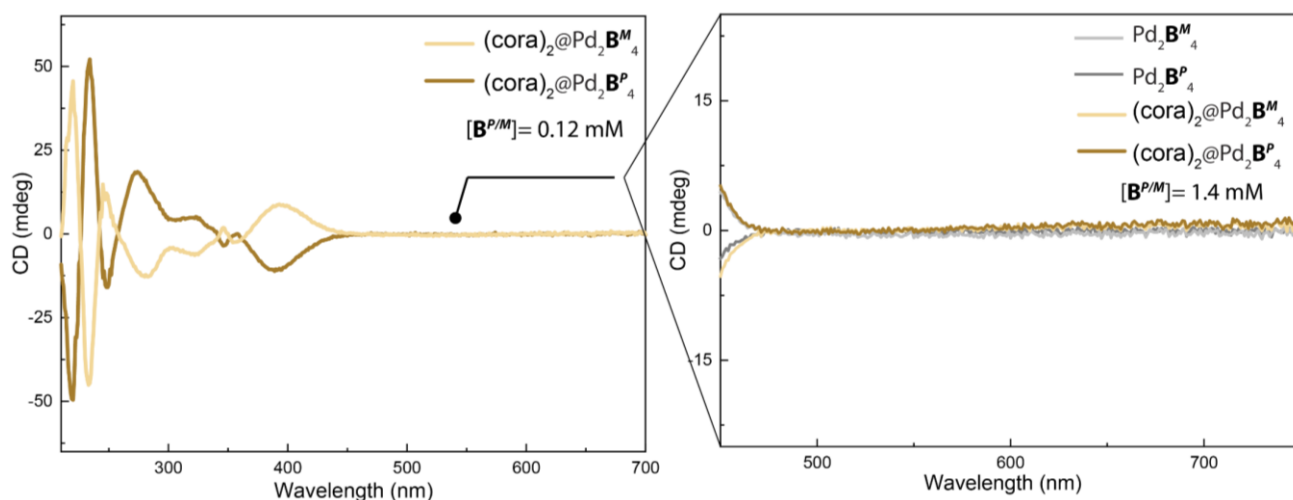


Figure S48: CD spectra of host-guest complex $(cora)_2@Pd_2B_4^P$ and $(cora)_2@Pd_2B_4^M$. Acetonitrile, 0.12 mM (left) or 1.4 mM (right) chromophore concentration, 2 mm cuvette, 298 K.

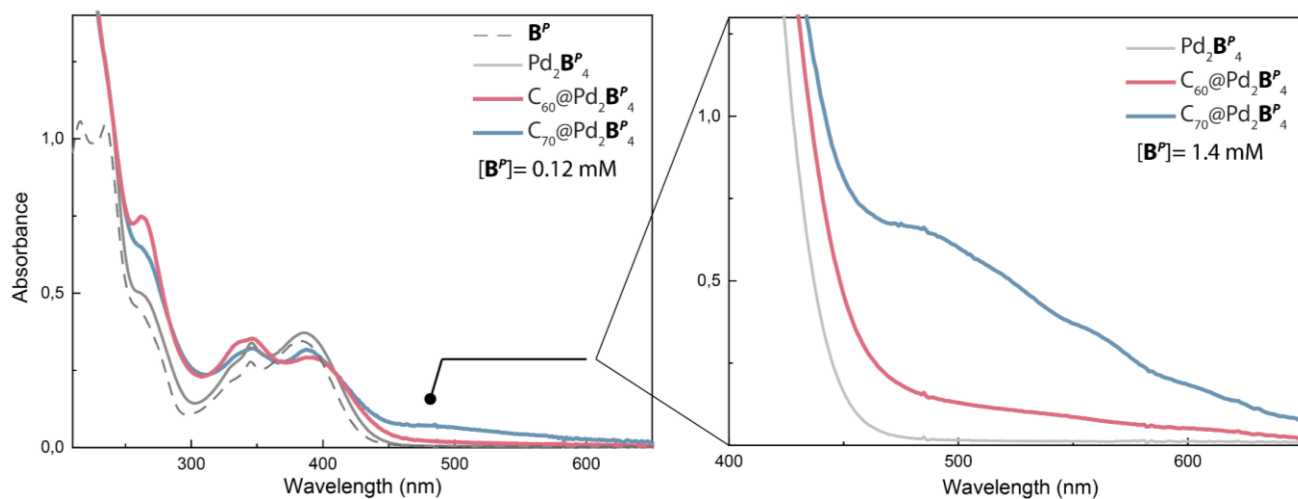


Figure S49: UV-Vis spectra overlap of B^P , $Pd_2B_4^P$, $C_{60}@Pd_2B_4^P$, $C_{70}@Pd_2B_4^P$ in acetonitrile, 2 mm cuvette, 0.12 mM (left) and 1.4 mM (right) concentration in ligand.

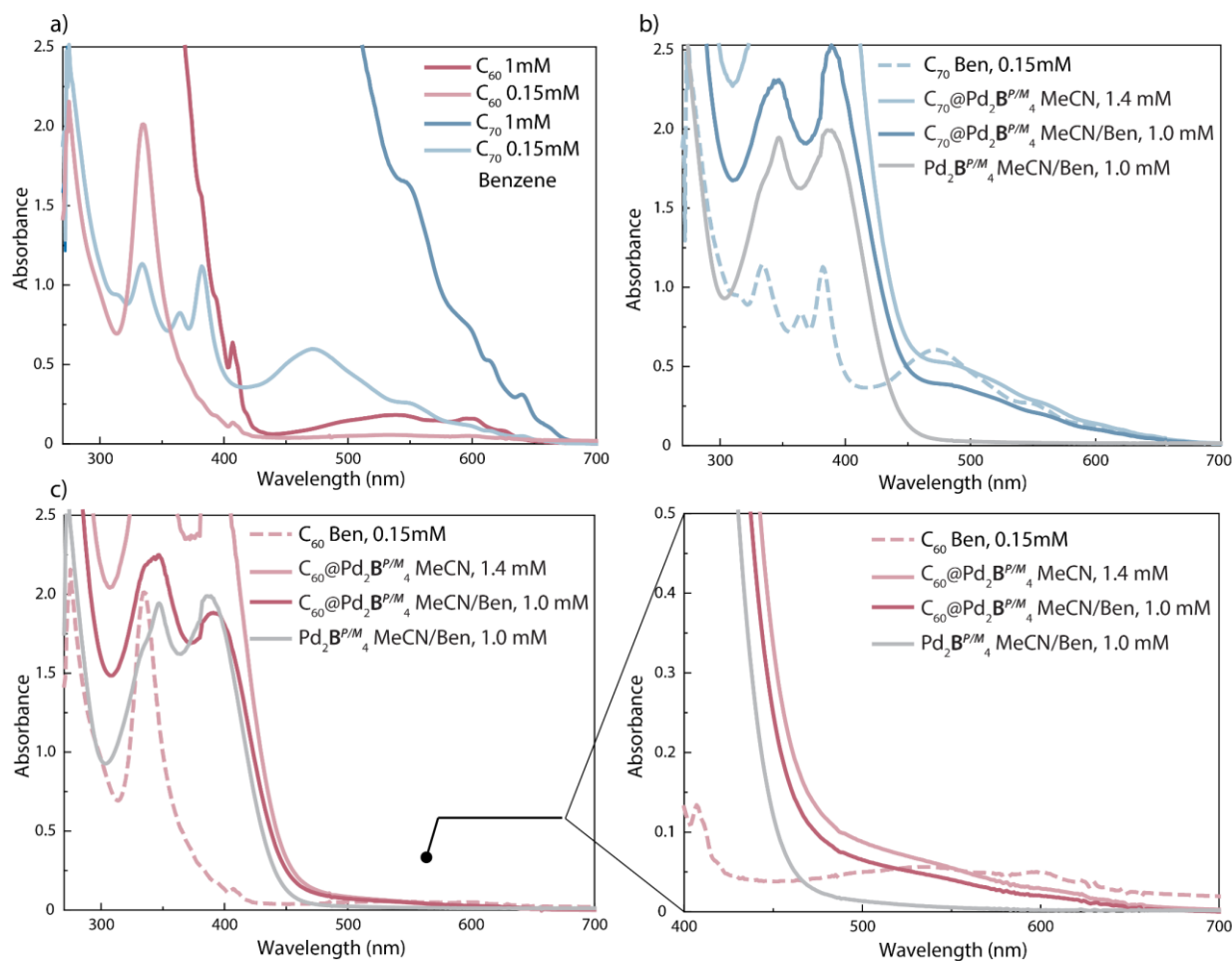


Figure S50: a) UV-Vis spectra of fullerene C₆₀ and C₇₀ in benzene. b) Stack of UV-Vis spectra of C₇₀ in benzene, C₇₀@Pd₂B^{P/M}₄ in acetonitrile and acetonitrile/benzene mixture and empty cage Pd₂B^{P/M}₄ in acetonitrile/benzene mixture. The bands can be matched by comparing the 450-700 nm window. c) Stack of UV-Vis spectra of C₆₀ in benzene, C₆₀@Pd₂B^{P/M}₄ in acetonitrile and acetonitrile/benzene mixture and empty cage Pd₂B^{P/M}₄ in acetonitrile/benzene mixture. The bands can be matched by comparing the 450-700 nm window. Inset displays a zoom on this region for better clarity. 2 mM cuvette, concentration in ligand, or fullerene directly indicated.

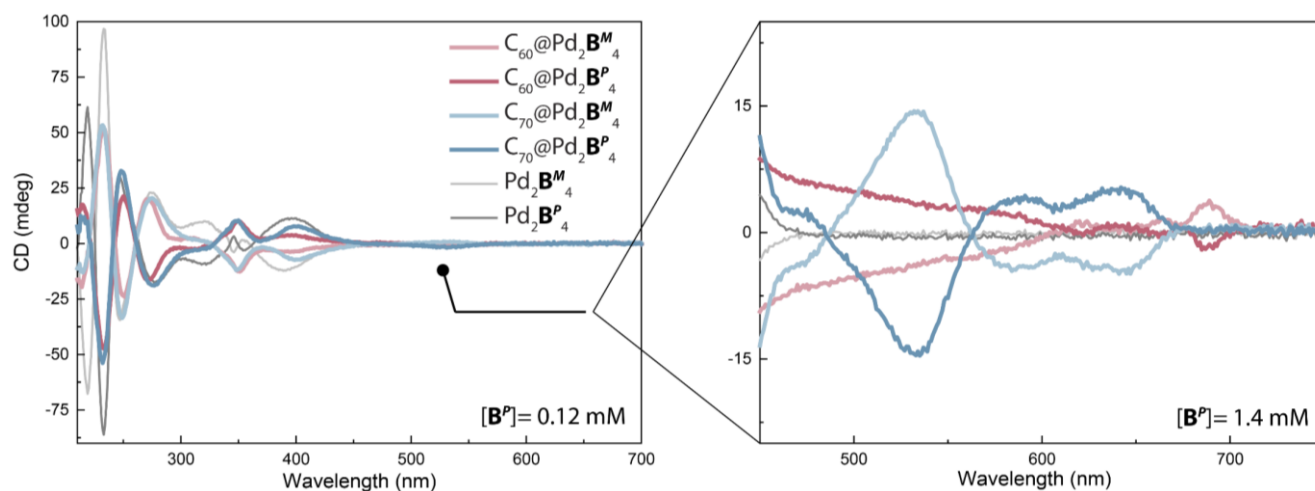


Figure S51: CD spectra overlap of Pd₂B^{P/M}₄, C₆₀@Pd₂B^{P/M}₄, C₇₀@Pd₂B^{P/M}₄ in acetonitrile, 2 mm cuvette, 0.12 mM (left) and 1.4 mM (right) concentration in ligand.

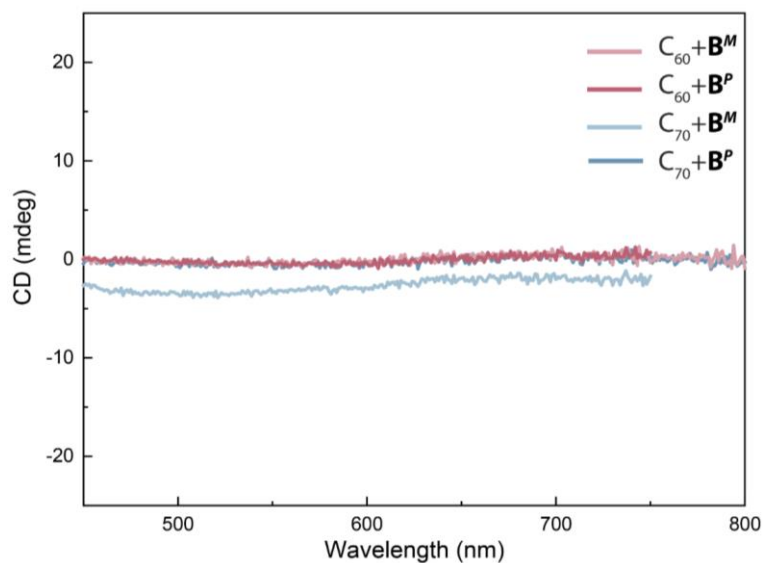


Figure S52: Control experiment. CD spectra overlap of $C_{60}+B^{P/M}_4$, $C_{70}+B^{P/M}_4$ in acetonitrile, 2 mm cuvette 1.4 mM concentration in ligand.

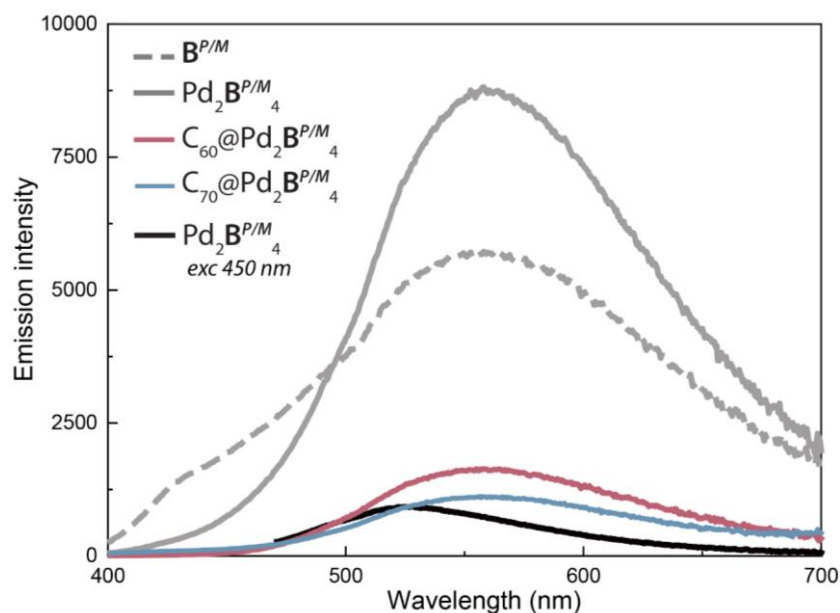


Figure S53: Fluorescence spectra overlap of B^P , $Pd_2B^P_4$, $C_{70}@Pd_2B^P_4$ and $C_{60}@Pd_2B^P_4$ in acetonitrile, 2 mm cuvette, 0.012mM concentration in ligand, excitation at 350 nm if not indicated differently.

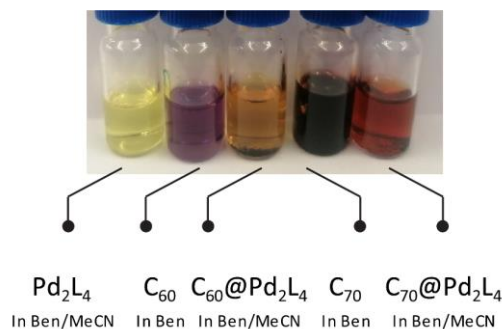


Figure S54: Picture of the empty cage and fullerenes with respective host-guest complexes. 1 mM concentration.

Computational Studies Subsection 1

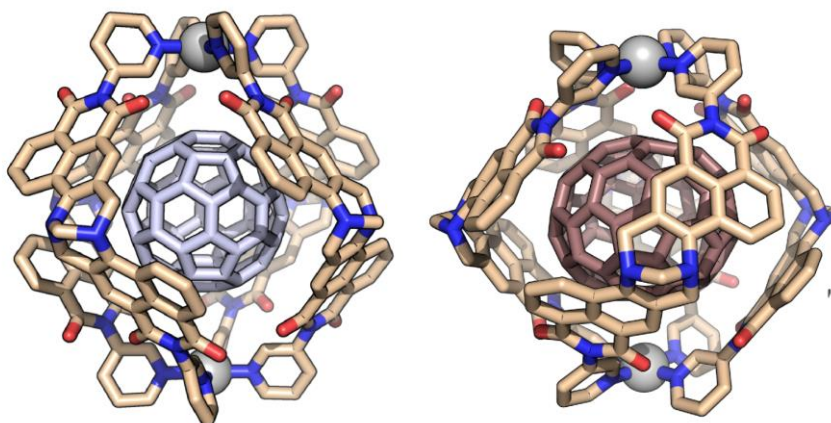


Figure S55: Geometry-optimized structure of $C_{70}@Pd_2Bp_4$ and $C_{60}@Pd_2Bp_4$, DFT level ($\omega B97X-D/def2-SVP$).

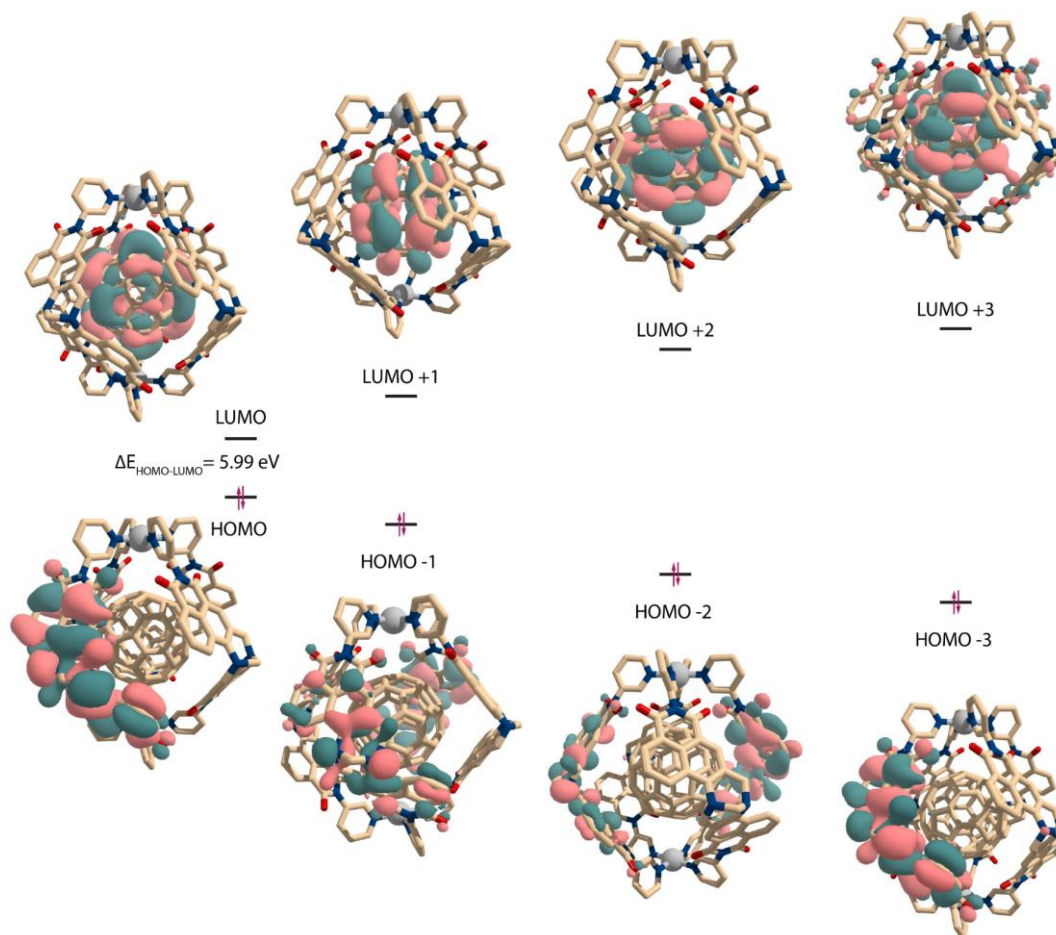


Figure S56: Representation of the frontier orbitals of $C_{60}@Pd_2Bp_4$. From single point energy calculation DFT level ($\omega B97X-D/def2-TZVP$).

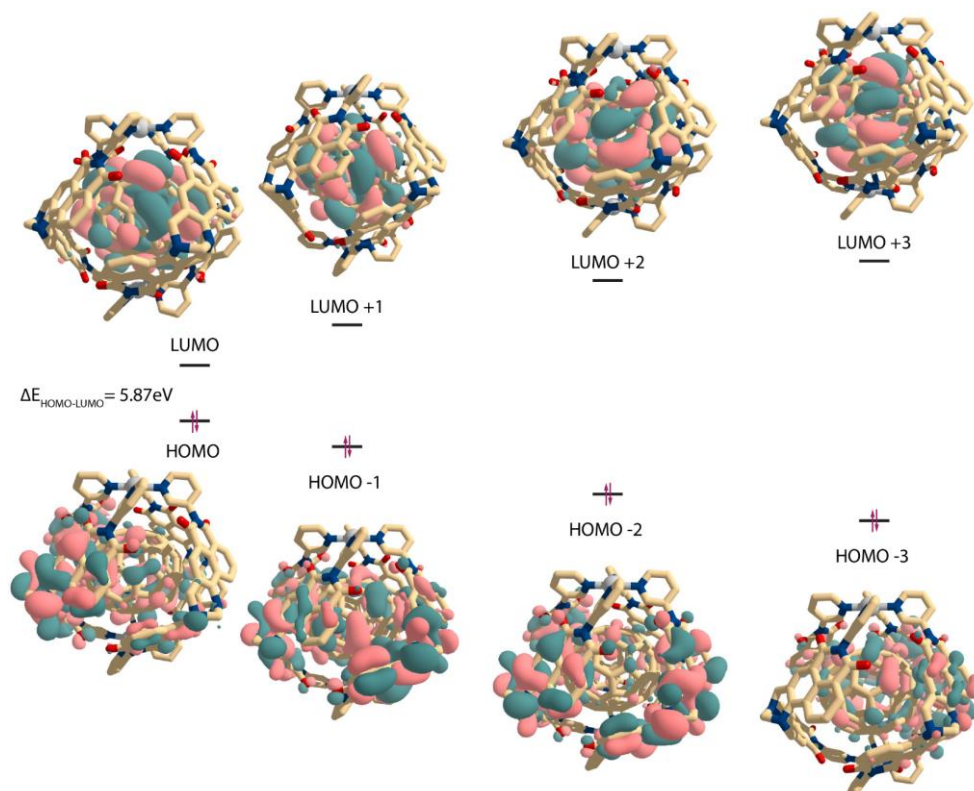


Figure S57: Representation of the frontier orbitals of $C_{70}@Pd_2B^P_4$. From single point energy calculation DFT level ($\omega B97X-D/def2-TZVP$).



1 carbon linked to 3 carbon with 3 σ and 1 π
 60 e^- , so one πe^- assigned per carbon
 Each angular moment (s, p, d...) get $2(2l+1) e^-$ and l_{max} correspond to the HOMO

Electronic configuration: $s^2p^6d^{10}f^{14}g^{18}h^{10}$

Applying solving as a sphere and applying Hund and Pauli exclusion principle:

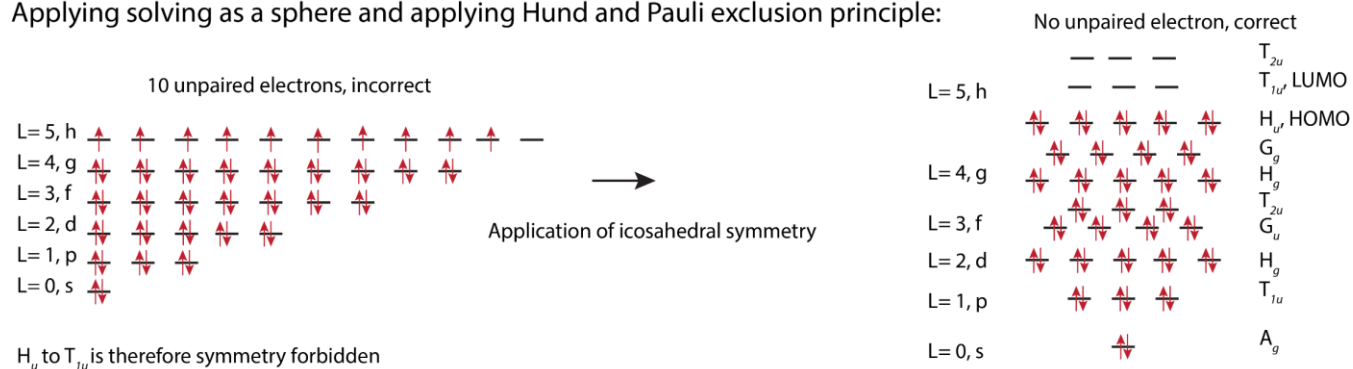


Figure S58: Short description of the electronic situation of fullerene C₆₀. The HOMO-LUMO transition is symmetry forbidden which explains why its intensity is low and its shape broad.

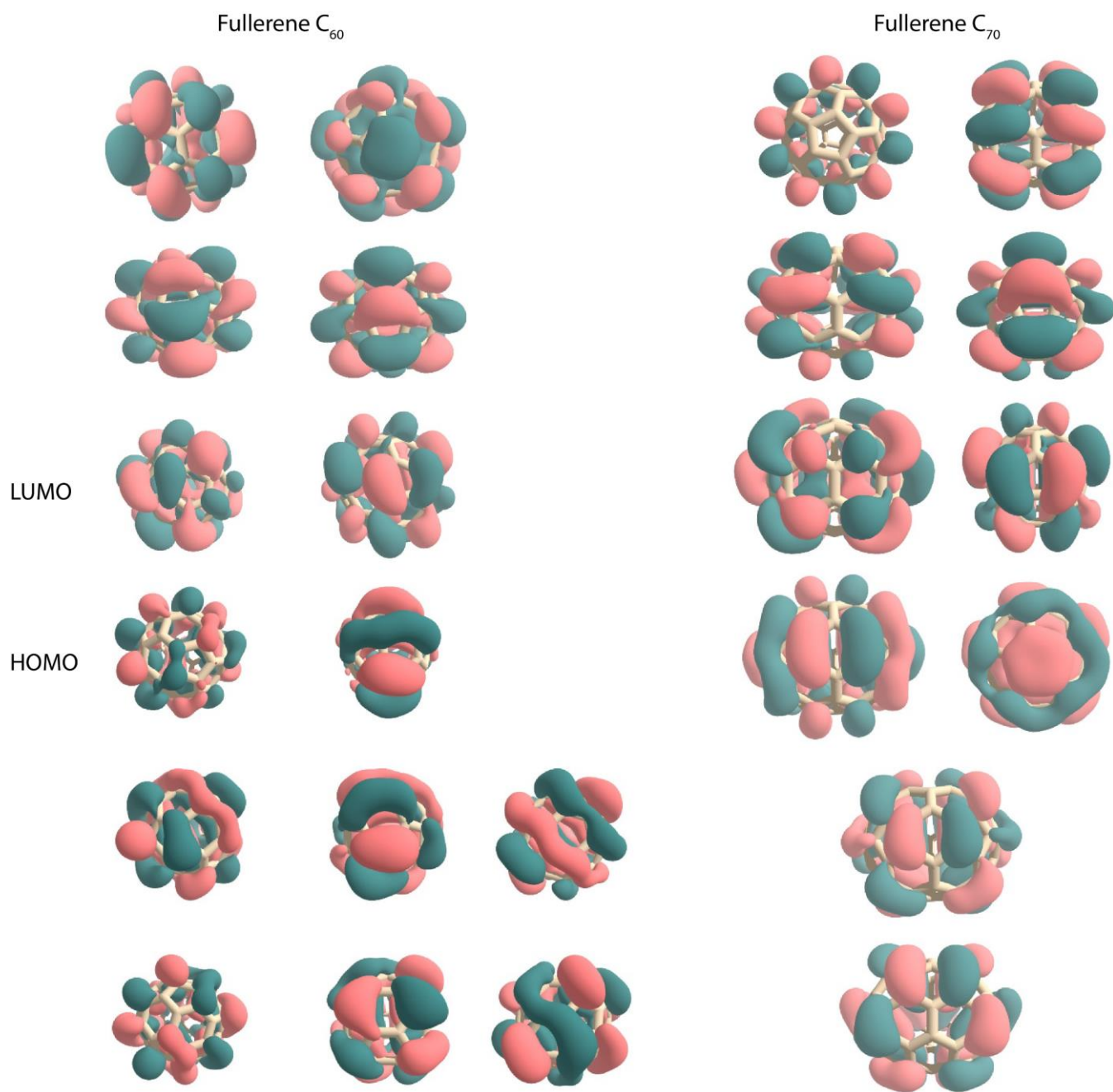


Figure S59: Representation of the frontier orbitals of C₆₀ and C₇₀. From single point energy calculation DFT level (ω B97X-D/def2-TZVP).

X-ray crystallography

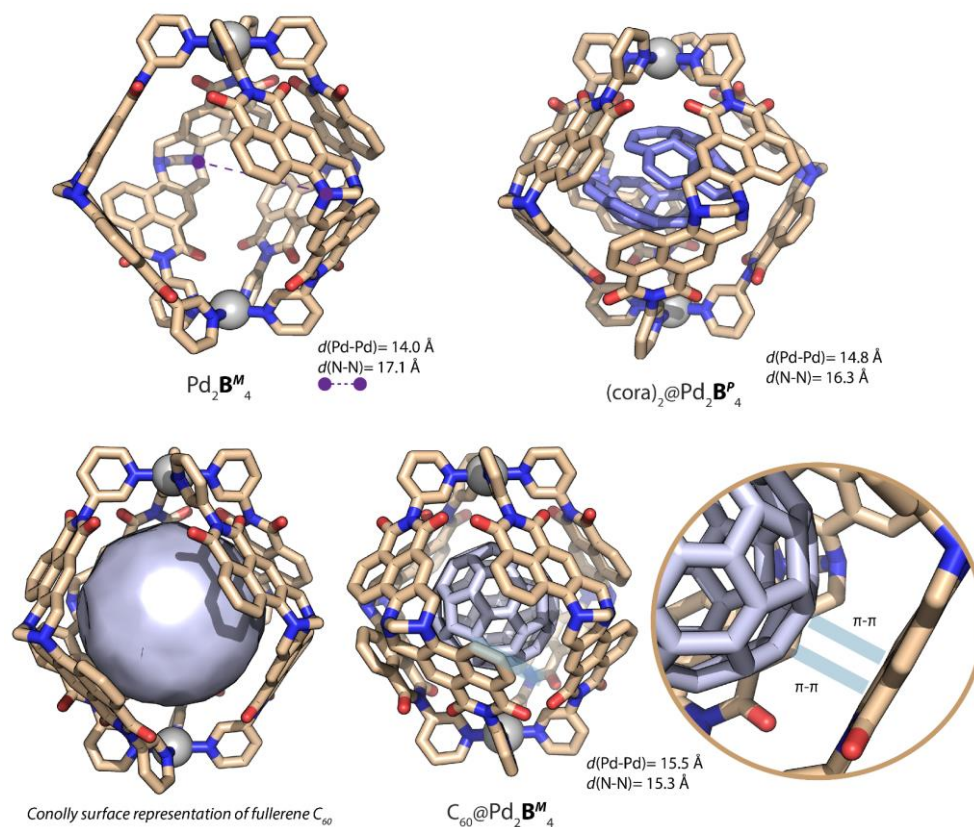
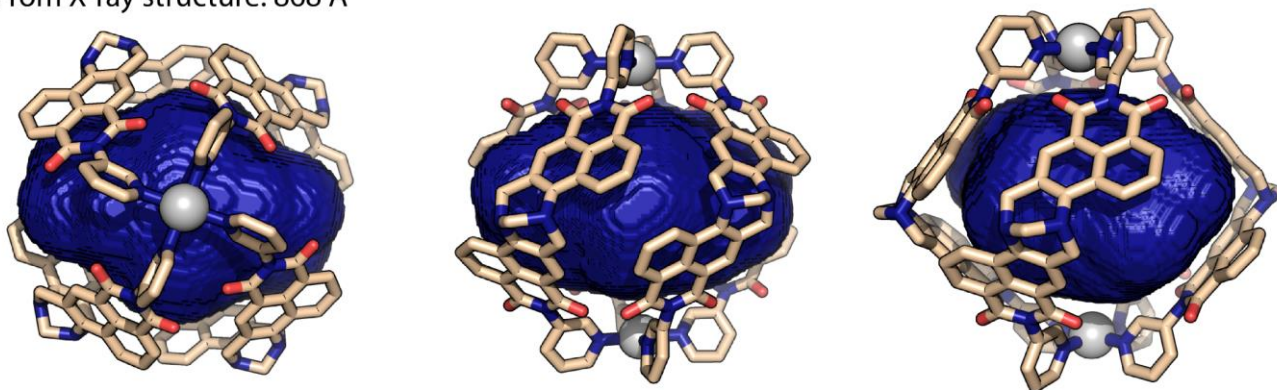


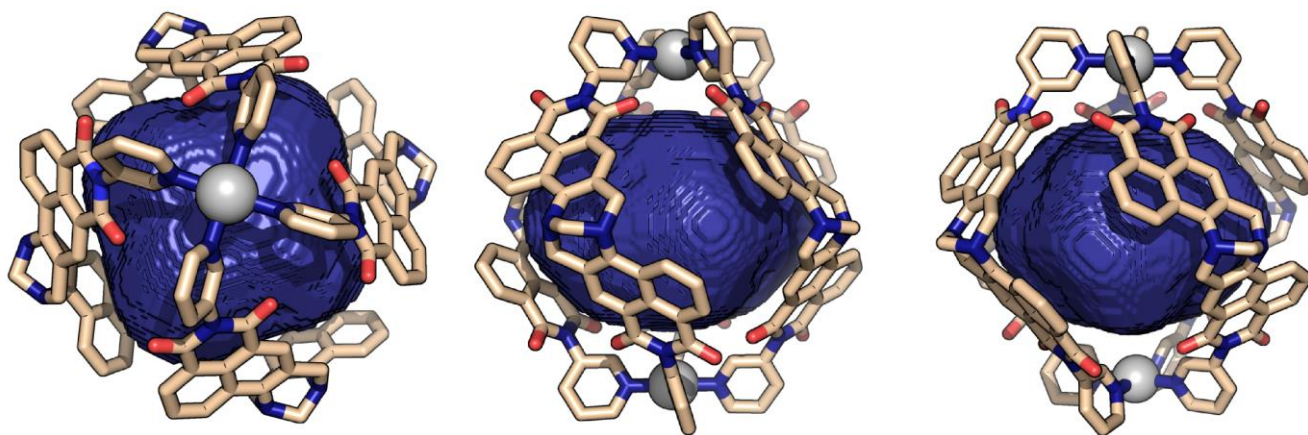
Figure S60: X-ray structures of Pd_2B_4 , $(\text{Cora})_2@ \text{Pd}_2\text{B}_4$ and $\text{C}_{60}@ \text{Pd}_2\text{B}_4$ with the Conolly surface representation of the fullerene to visualize the occupied space within the cavity. Highlighted host-guest $\pi-\pi$ interactions with the naphthyl panels of the cage.

Cavity volume representation

From X-ray structure: 868 Å³



From DFT optimized structure: 723 Å³



Small probe head 2.8 Å
Big probe head 6 Å

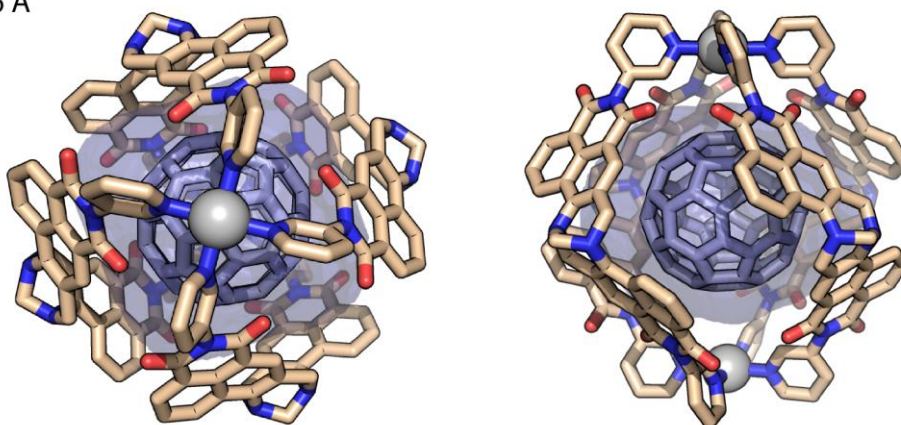


Figure S61: Cavity surface representations using MolVol. The probe head radii are given. In the top part is displayed the cavity obtained from the crystal structure of the empty cage in which the high symmetry is lost because of packing effects. The middle part represents the same cavity from the DFT model of the empty cage, showing higher symmetry. To compare with this at the bottom, the known molecular volume of fullerene C₆₀ is 546 Å³. This also highlights that the Rebek rule of 55 % is violated in the presented case because of the favored host-guest interactions and the cavity/guest shape match.

Subsection 2

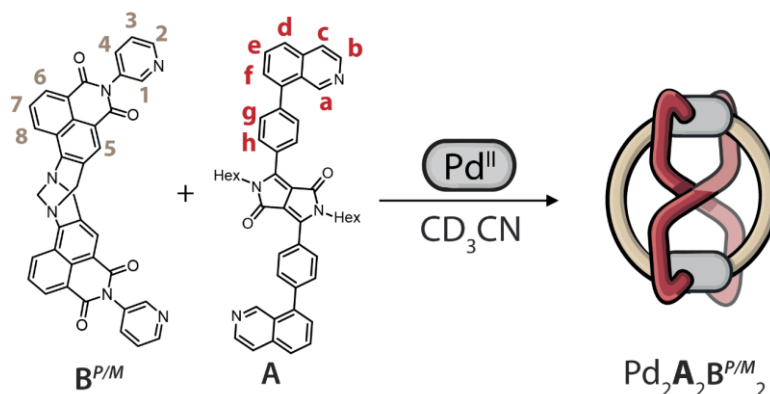
Synthesis of $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ / $\text{Pd}_2\text{A}_2\text{B}^{\text{M}}_2$ 

Figure S62: Formation of heteroleptic cage $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ upon addition of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in an acetonitrile solution of both ligands.

224 μL of a 3.11 mM solution of B^{P} , 224 μL of a 3.11 mM solution of A in CD_3CN and 50 μL of a 15 mM solution of $[\text{Pd}(\text{CH}_3\text{CN})_4](\text{BF}_4)_2$ in CD_3CN were mixed in an NMR tube and shaken vigorously. The mixture was then heated to 70 $^\circ\text{C}$ for 4 h to afford $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ in the equilibrated solution.

^1H NMR (hexyl chains omitted) (500 MHz, CD_3CN) δ 9.85 (dd, $J = 6.1, 1.4$ Hz, 1H), 9.37 (s, 1H), 8.85 (d, $J = 6.3$ Hz, 1H), 8.63 (dd, $J = 8.4, 1.2$ Hz, 1H), 8.53 (d, $J = 2.1$ Hz, 1H), 8.33 (dd, $J = 7.3, 1.2$ Hz, 1H), 8.20 – 8.14 (m, 2H), 8.12 – 8.07 (m, 2H), 8.00 (s, 1H), 7.95 (dd, $J = 8.2, 6.1$ Hz, 1H), 7.85 (dd, $J = 7.1, 1.1$ Hz, 1H), 7.78 (dd, $J = 8.5, 7.3$ Hz, 1H), 7.61 (br, 2H) 5.06 (d, $J = 17.1$ Hz, 1H), 4.43 (s, 1H), 4.36 (d, $J = 17.2$ Hz, 1H).

^{13}C NMR (151 MHz, CD_3CN) δ 165.18, 164.41, 162.20, 153.60, 152.99, 150.77, 150.55, 148.62, 143.60, 142.03, 141.01, 140.03, 137.82, 137.78, 134.88, 131.11, 131.07, 130.65, 130.52, 129.12, 128.99, 128.17, 127.95, 127.69, 127.62, 127.23, 126.44, 126.21, 123.92, 110.45, 66.15, 57.00, 43.72, 31.10, 29.21, 26.63, 22.98, 13.65.

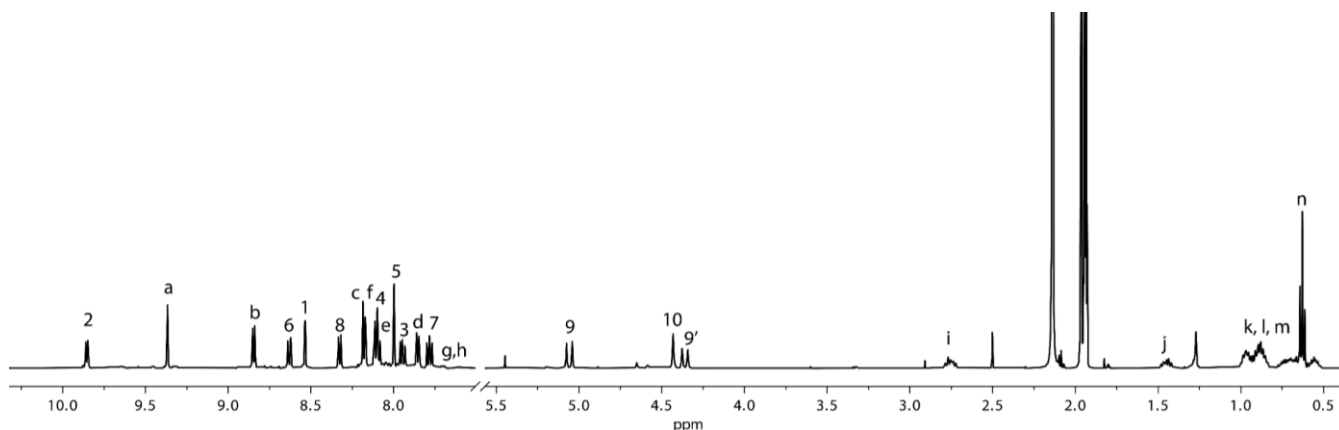


Figure S63: ^1H NMR spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$.

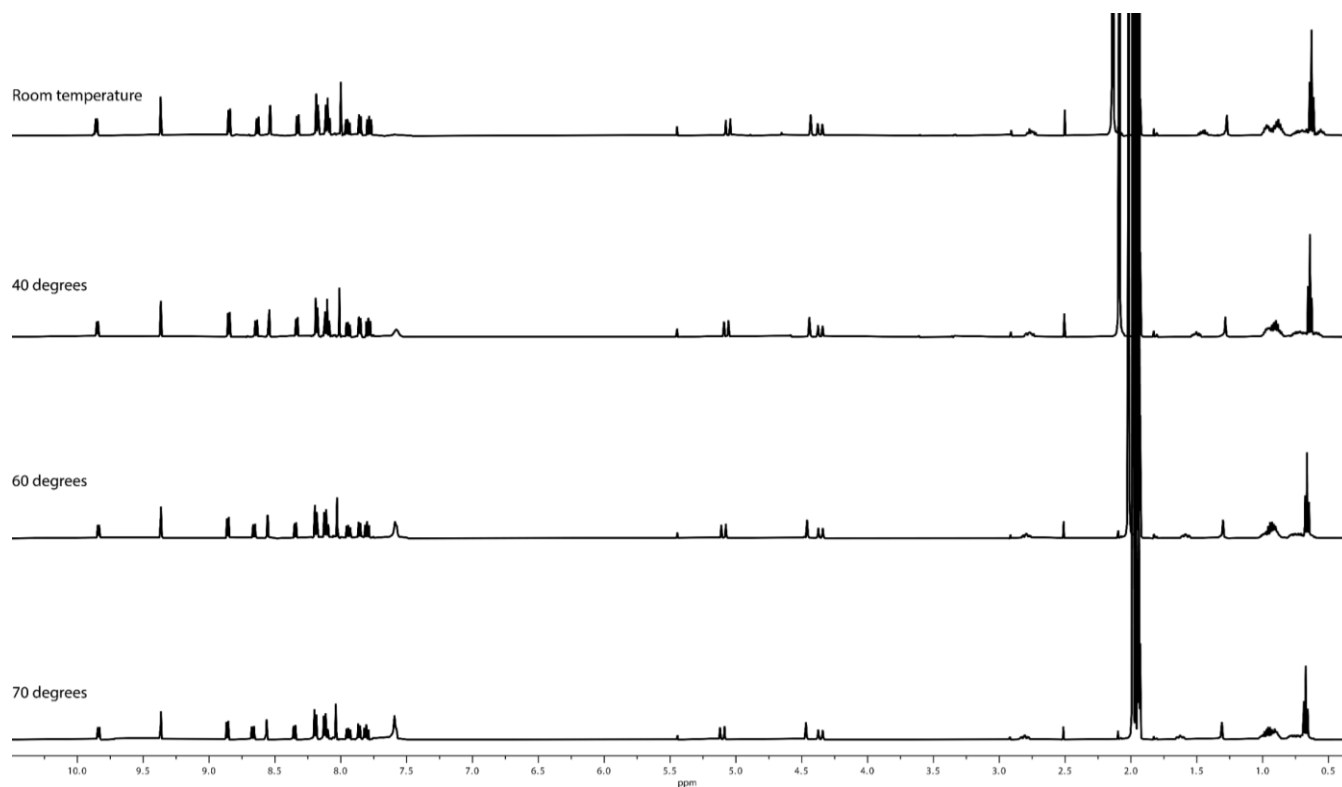


Figure S64: Variable temperature ^1H NMR spectra (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{A}_2\text{B}'_2$. This allows the visualization of proton Hg and Hh otherwise broad at room temperature.

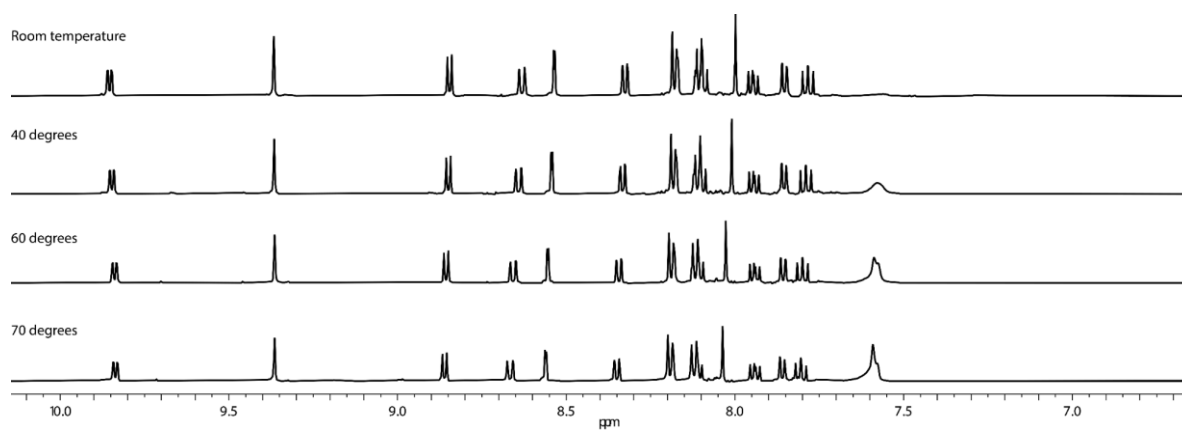


Figure S65: Variable temperature ^1H NMR spectra (500 MHz, 298K, CD_3CN), zoomed aromatic region, of heteroleptic cage $\text{Pd}_2\text{A}_2\text{B}'_2$. This allows the visualization of proton Hg and Hh otherwise broad at room temperature.

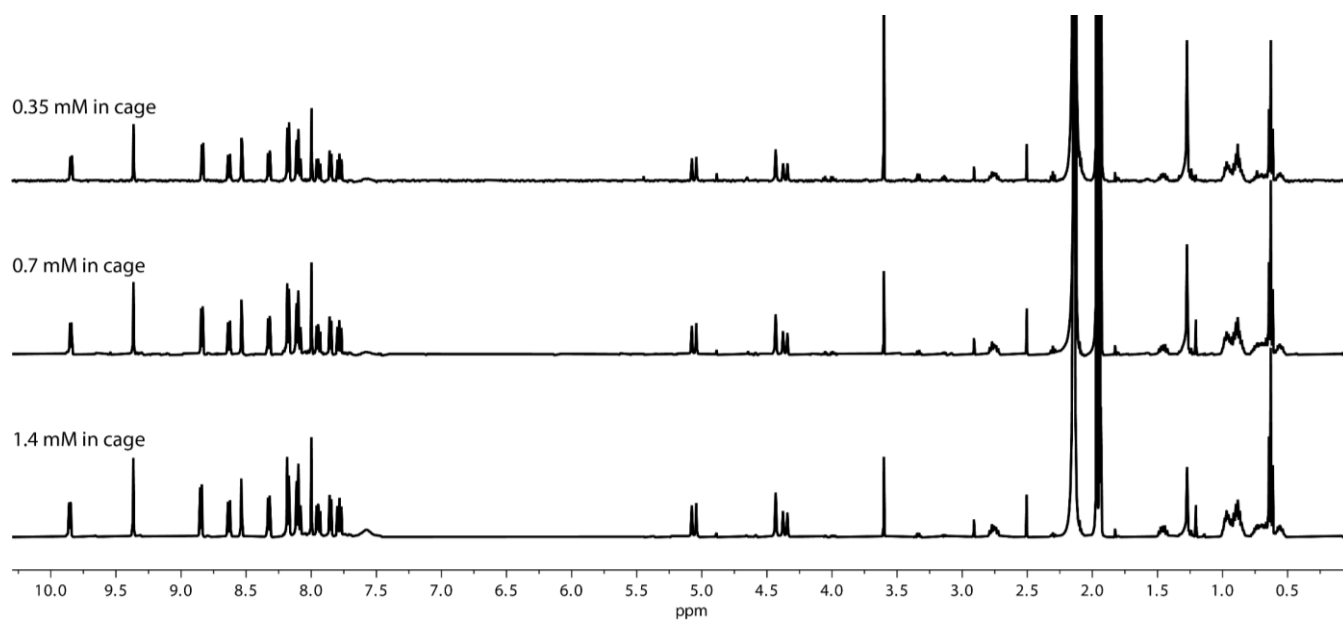


Figure S66: ^1H NMR spectra (500 MHz, 298 K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{A}_2\text{B}'_2$ at different concentrations.

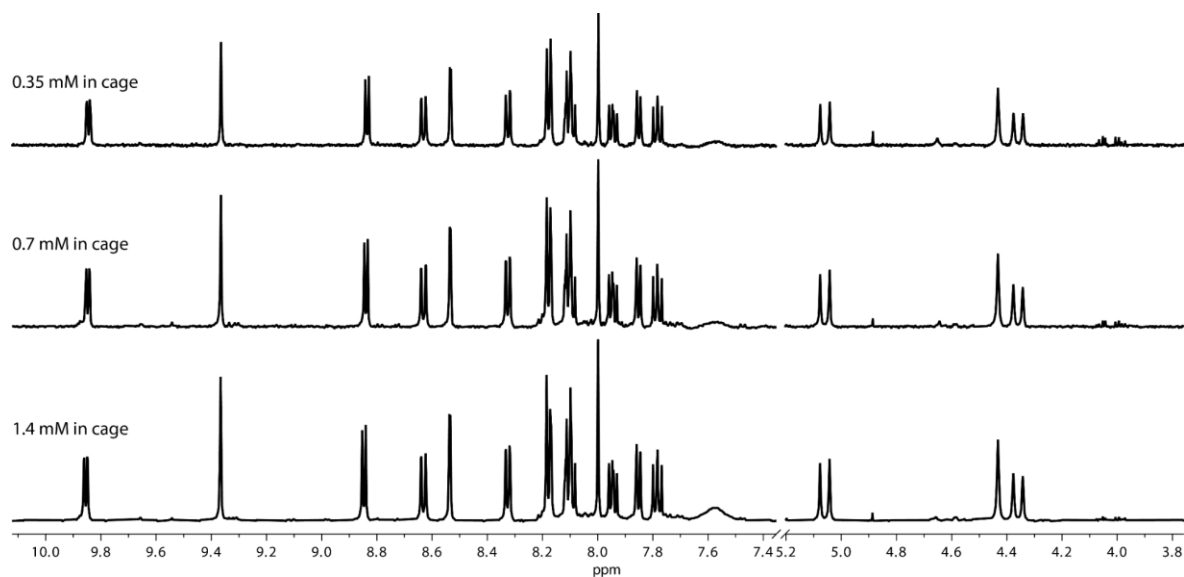


Figure S67: ^1H NMR spectra (500 MHz, 298 K, CD_3CN), zoomed aromatic region, of heteroleptic cage $\text{Pd}_2\text{A}_2\text{B}'_2$ at different concentrations.

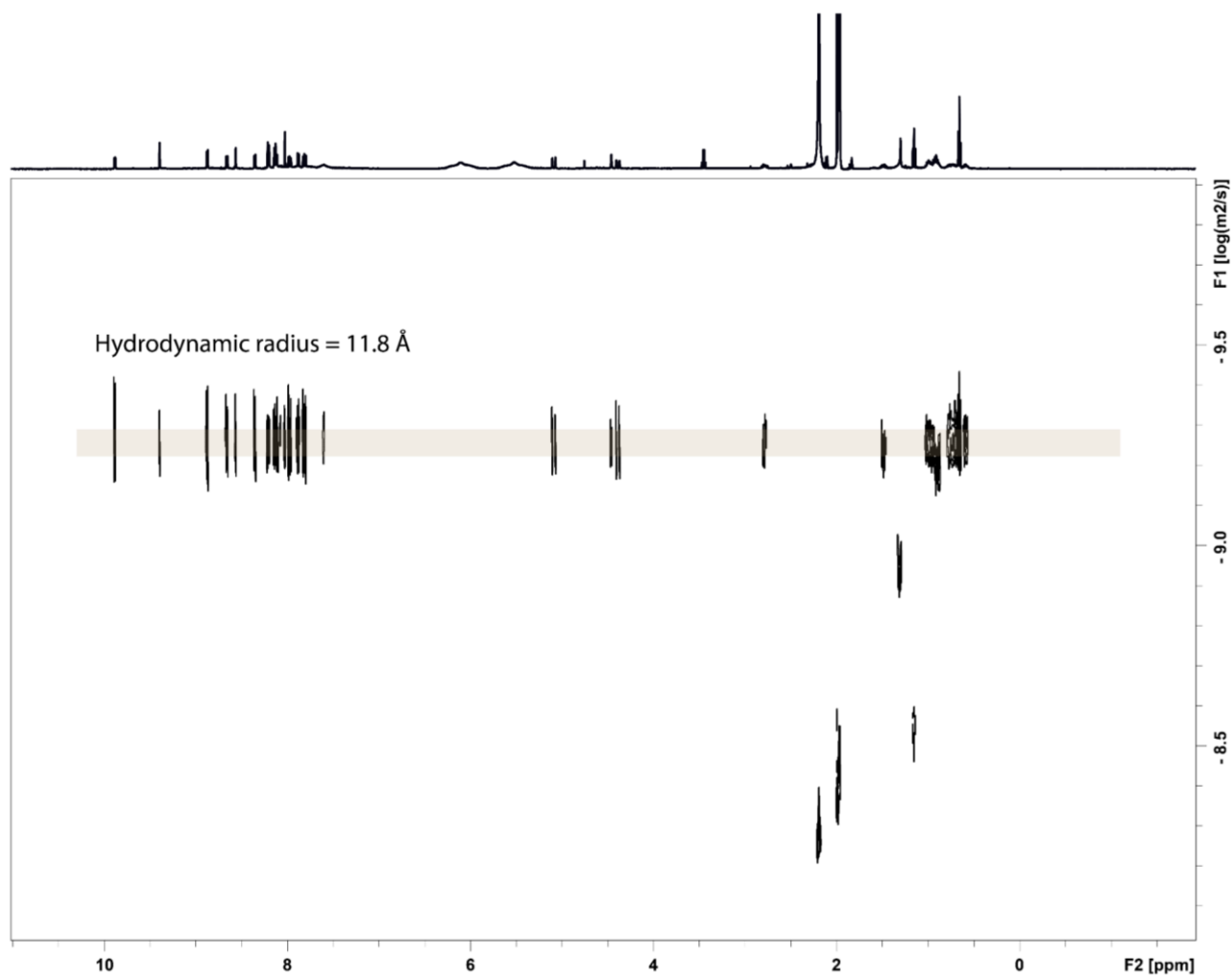


Figure S68: ^1H DOSY spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{A}_2\text{B}^{\text{p}}_2$, the hydrodynamic radius of the species is highlighted.

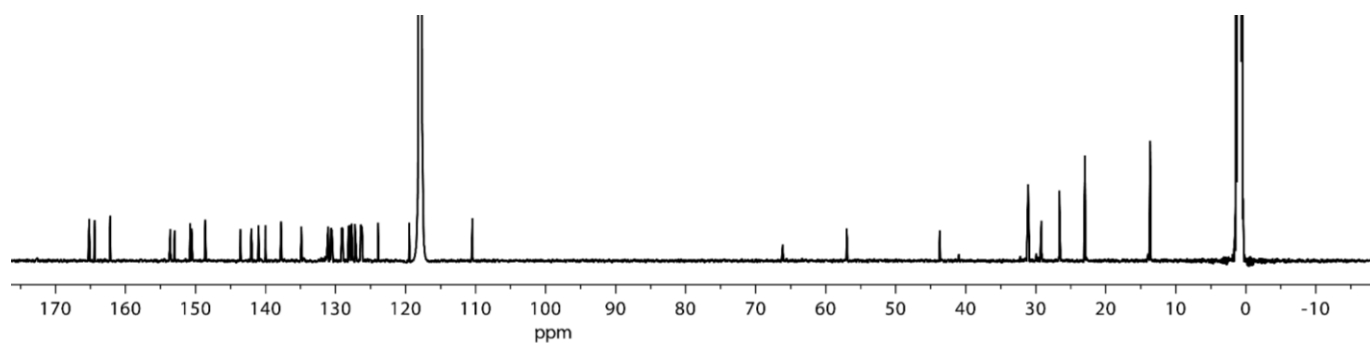


Figure S69: ^{13}C NMR spectrum (176 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{A}_2\text{B}^{\text{p}}_2$.

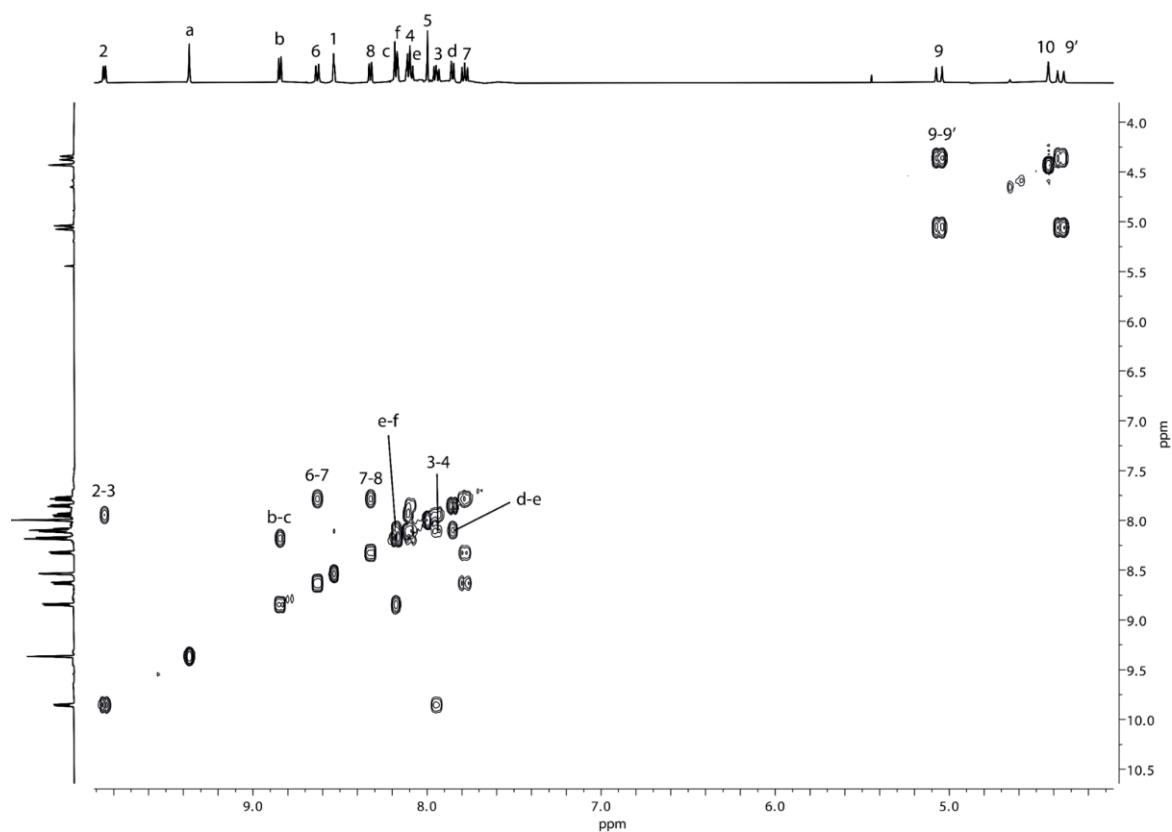


Figure S70: ^1H ^1H COSY spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{A}_2\text{BP}_2$,

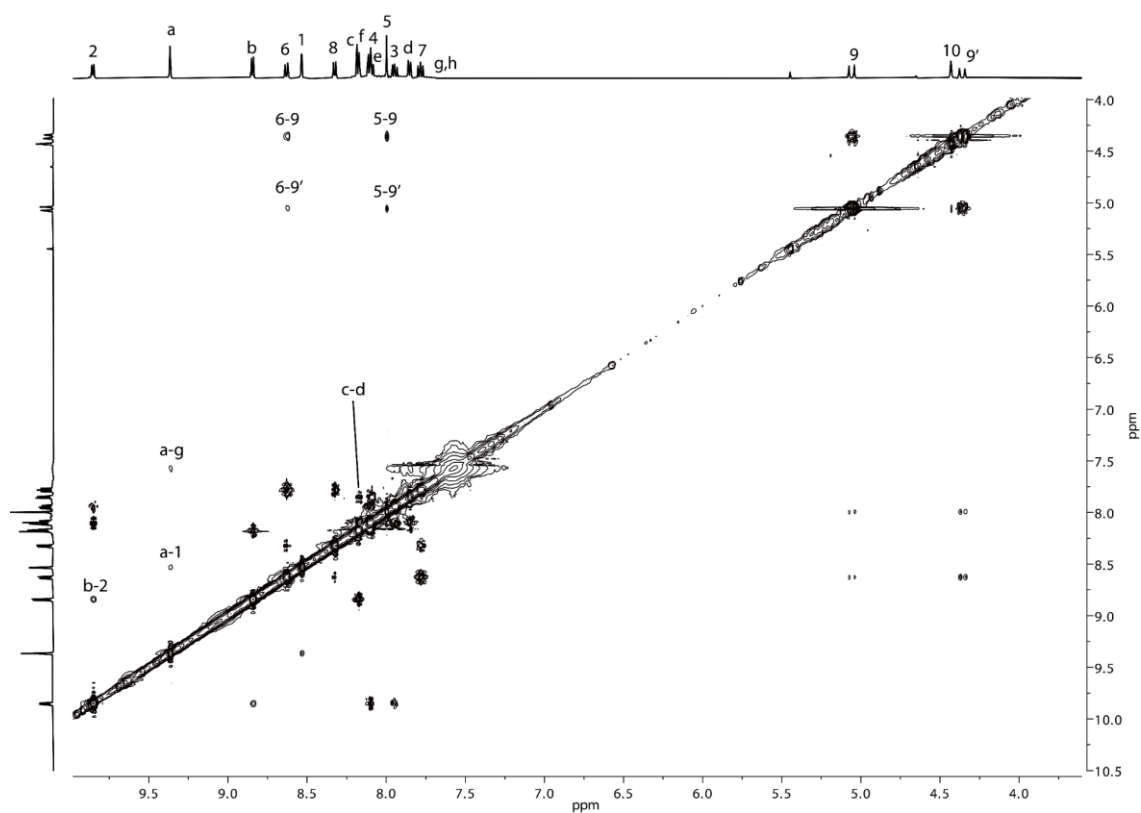


Figure S71: ^1H ^1H NOESY spectrum (500 MHz, 298K, CD_3CN) of heteroleptic cage $\text{Pd}_2\text{A}_2\text{BP}_2$,

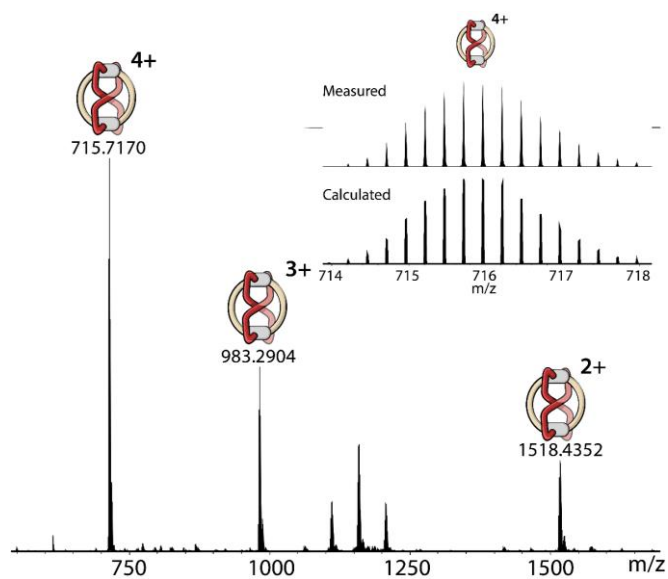


Figure S72: ESI-MS spectrum of a MeCN solution of **A** and **B1** with 0.5 equiv. Pd(II). The observed peaks correspond to $[Pd_2A_2B^p_2+nBF_4]^{(4-n)+}$ with $n=0-2$. The observed and calculated isotopic patterns of $[Pd_2A_2B^p_2]^{4+}$ are shown in the inset.

Self-sorting and dynamic cage population

Statistical mixture between B3 and B^{P/M}

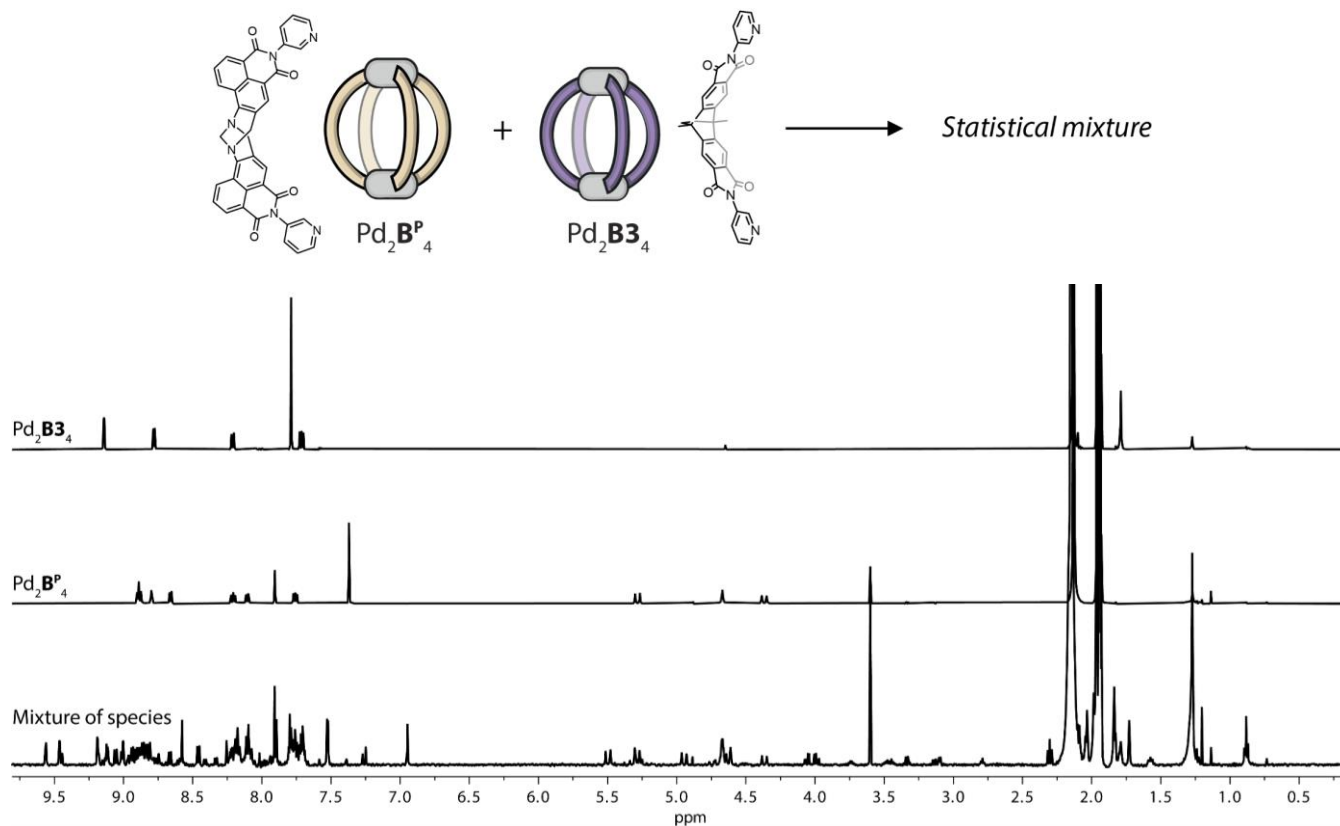


Figure S73: 1H NMR spectra (500 MHz, 298K, CD_3CN) of the outcome of mixing the two homoleptic cages together in solution.

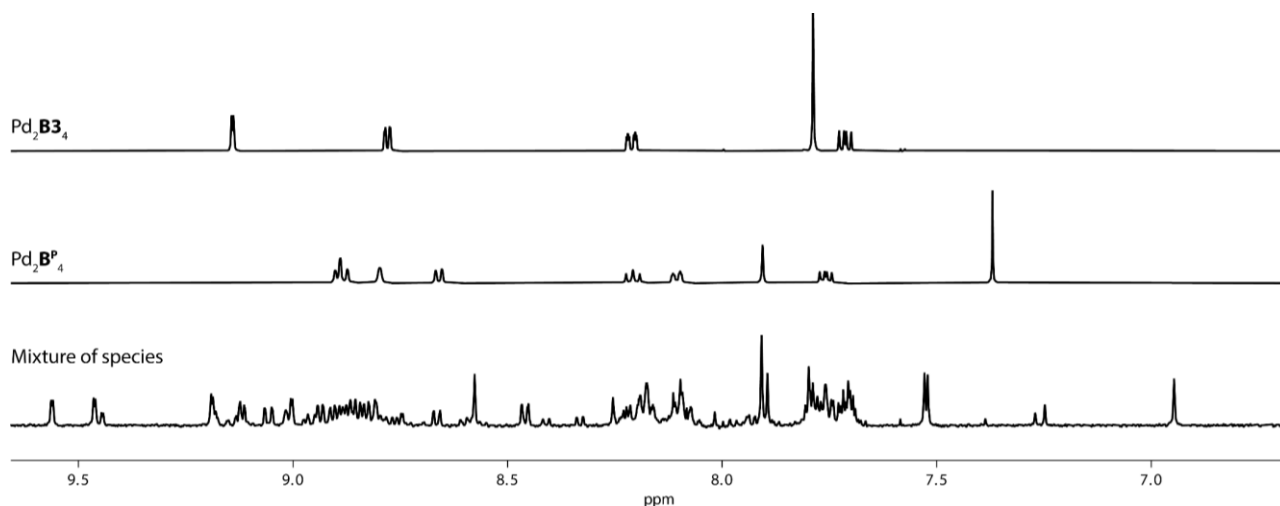


Figure S74: ^1H NMR spectra (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the outcome of mixing the two homoleptic cages together in solution.

Competition for the formation of figure-eight

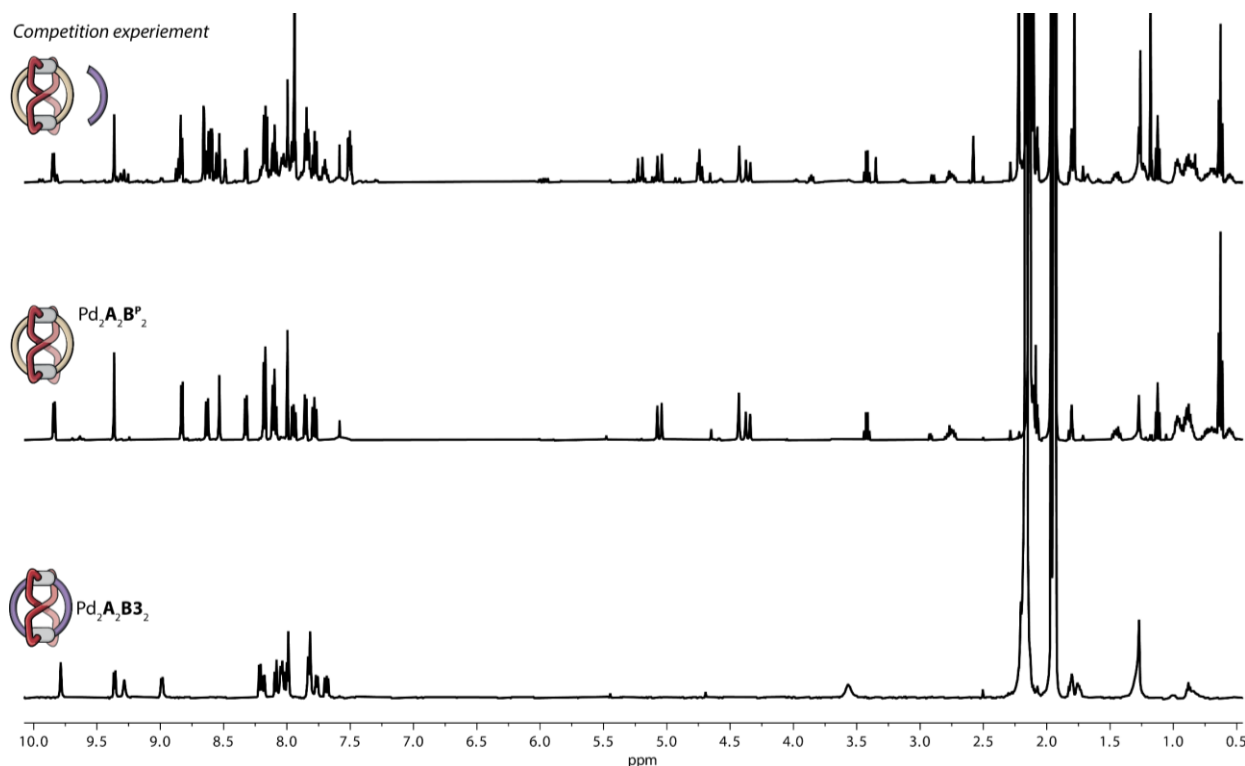


Figure S75: ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the competition experiment in which ligands **A**, **B3** and **B^p** are mixed in an equimolar ratio in the presence of a substoichiometric amount of Pd(II). The outcome is the formation of the $\text{Pd}_2\text{A}_2\text{B}^p_2$ species.

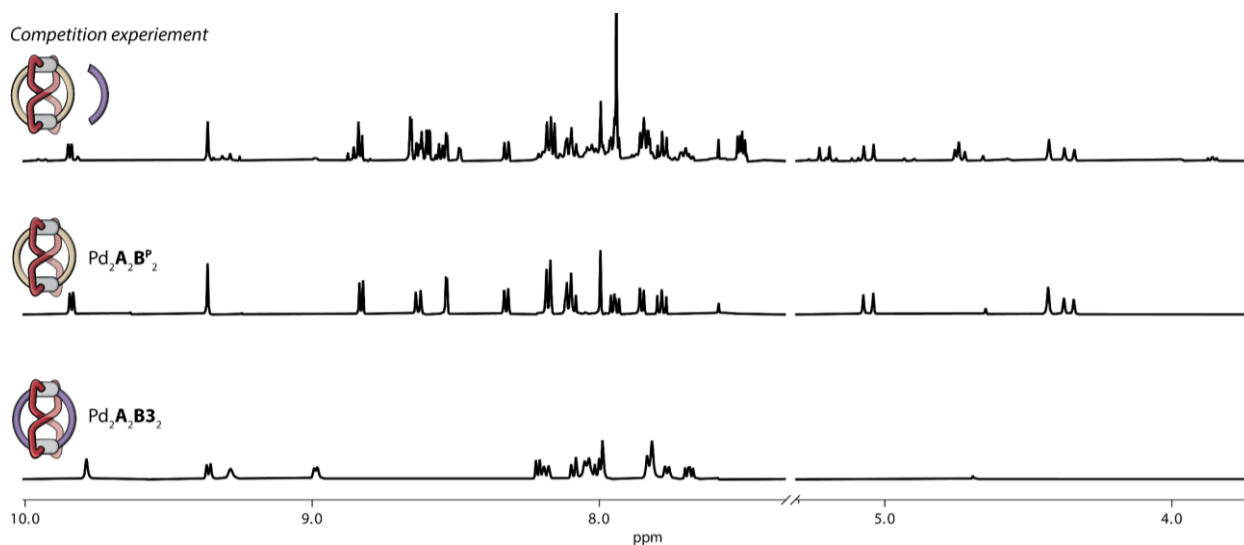


Figure S76: ^1H NMR spectra (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the competition experiment in which ligands **A**, **B3** and **B^p** are mixed in an equimolar ratio in the presence of a substoichiometric amount of Pd(II). The outcome is the formation of the $\text{Pd}_2\text{A}_2\text{B}^{\text{p}}_2$ species.

Heteromeric complete self-sorting between the two figure-eight

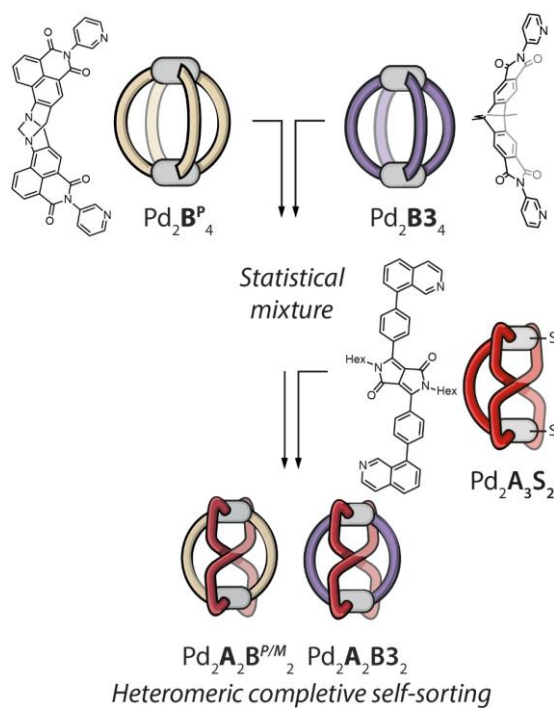


Figure S77: Schematic representation of the heteromeric complete self-sorting between the two figure-eight species.

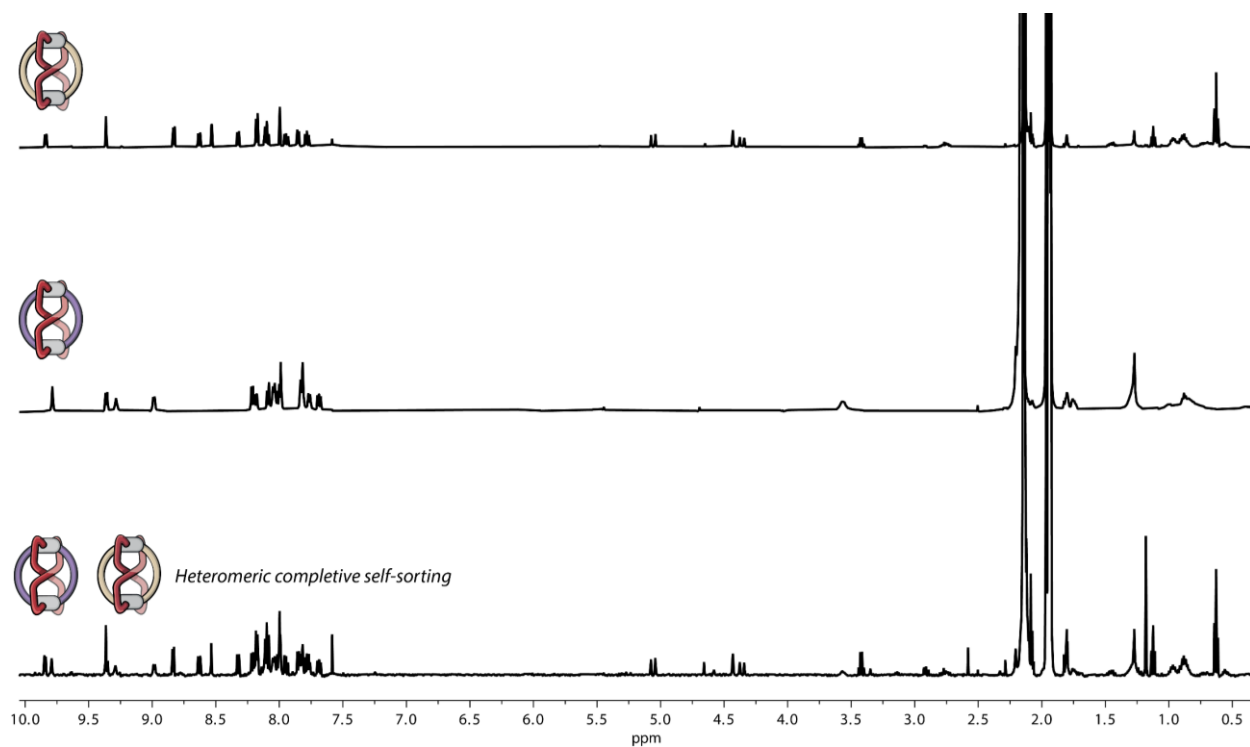


Figure S78: ^1H NMR spectra (500 MHz, 298K, CD_3CN) of the heteromeric complete self-sorting between the two species.

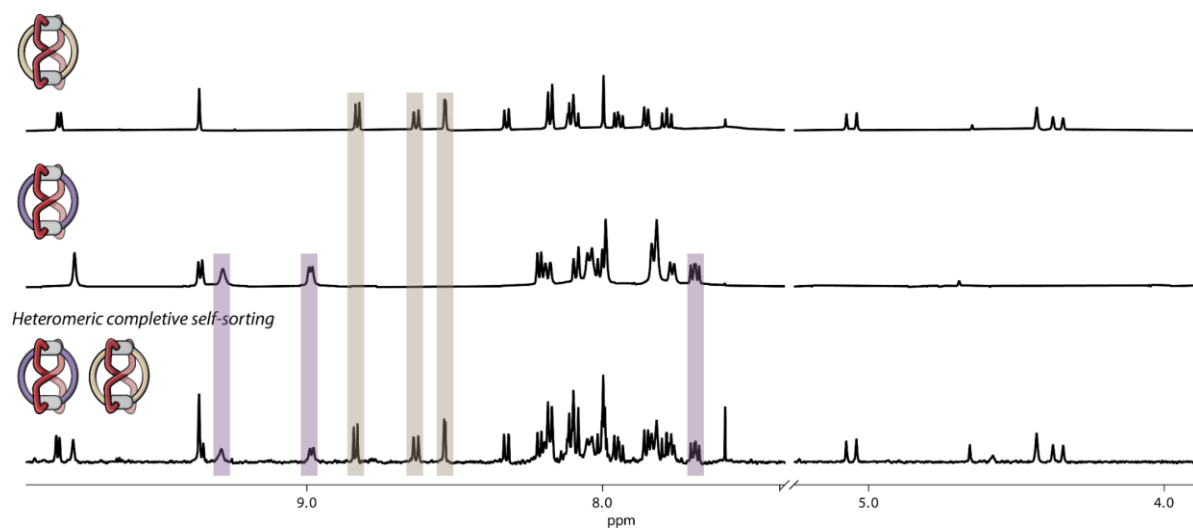
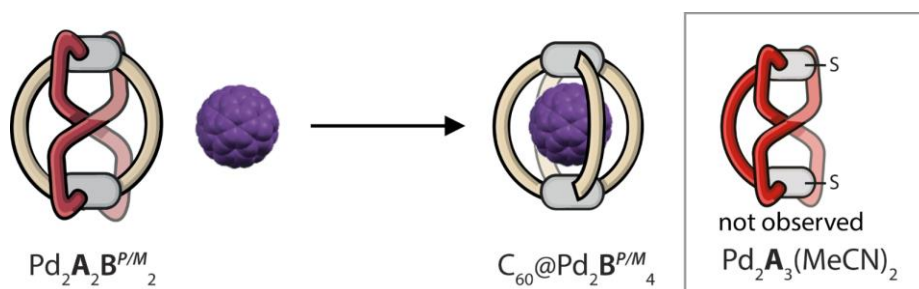


Figure S79: ^1H NMR spectra (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the heteromeric complete self-sorting between the two species.

Transformation between $\text{Pd}_2\text{A}_2\text{B}_2^{\text{P/M}}$ and fullerene C_{60}



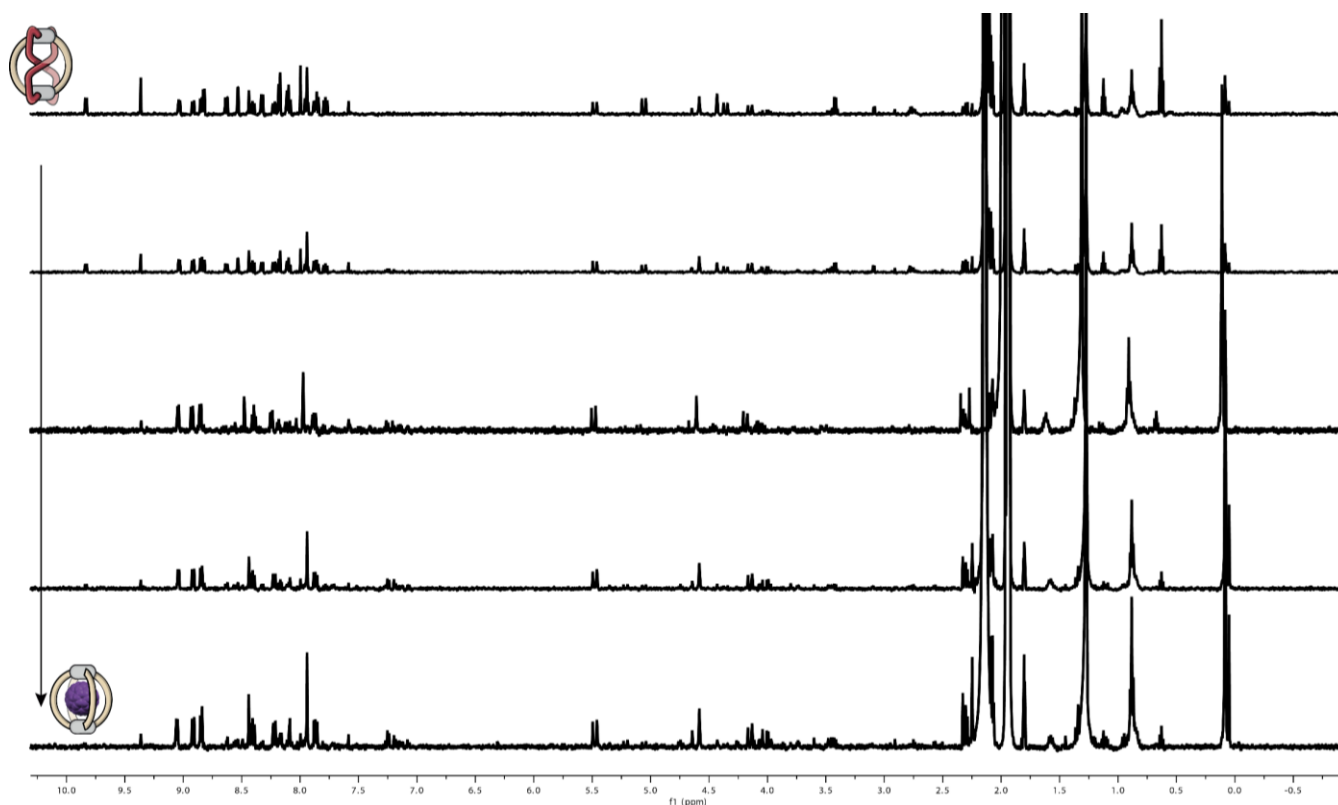


Figure S80: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation from $\text{Pd}_2\text{A}_2\text{B}_2\text{P}_2$ to $\text{C}_{60}@\text{Pd}_2\text{B}_4\text{P}_4$. The signals corresponding to the homoleptic species of **A** can not be identified.

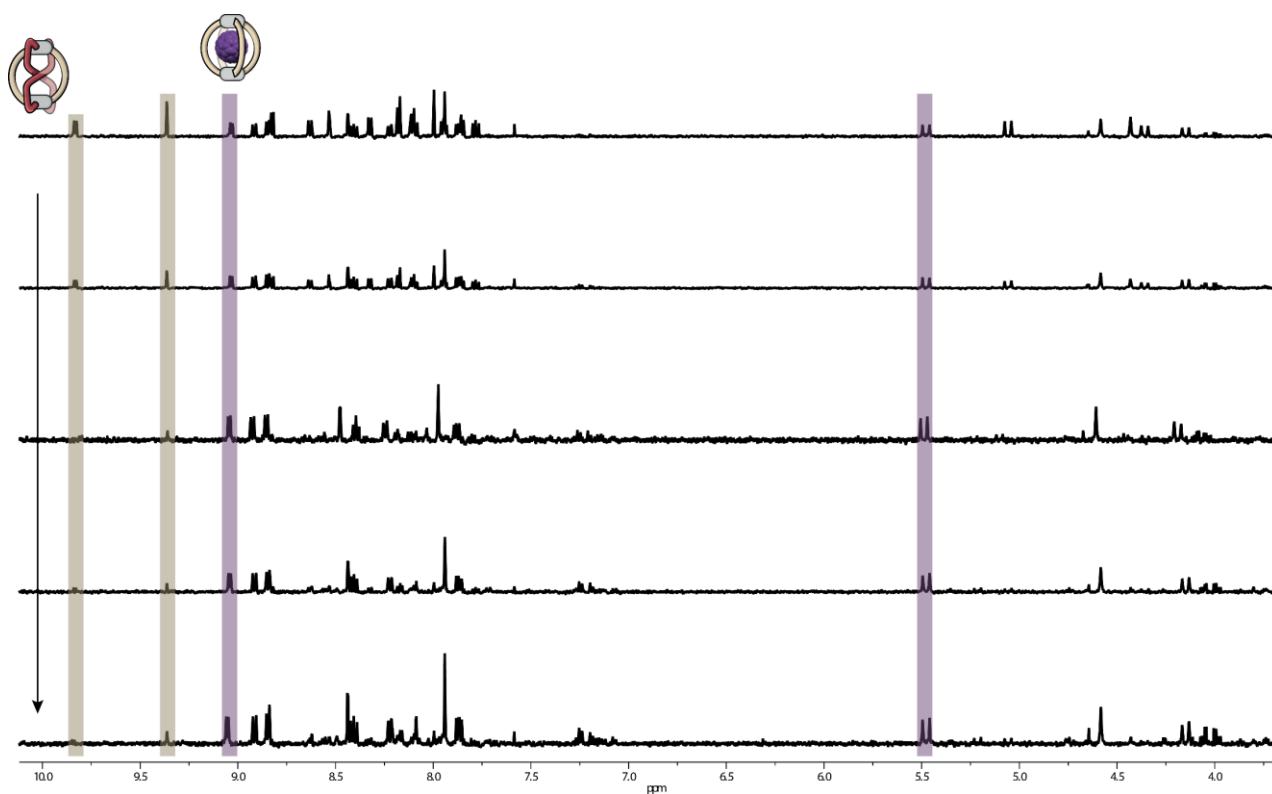


Figure S81: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN), enlarged on the aromatic region, following the transformation from $\text{Pd}_2\text{A}_2\text{B}_2\text{P}_2$ to $\text{C}_{60}@\text{Pd}_2\text{B}_4\text{P}_4$. The signals corresponding to the homoleptic species of **A** can not be identified.

Controlled fullerene extraction and release upon heteroleptic cage formation

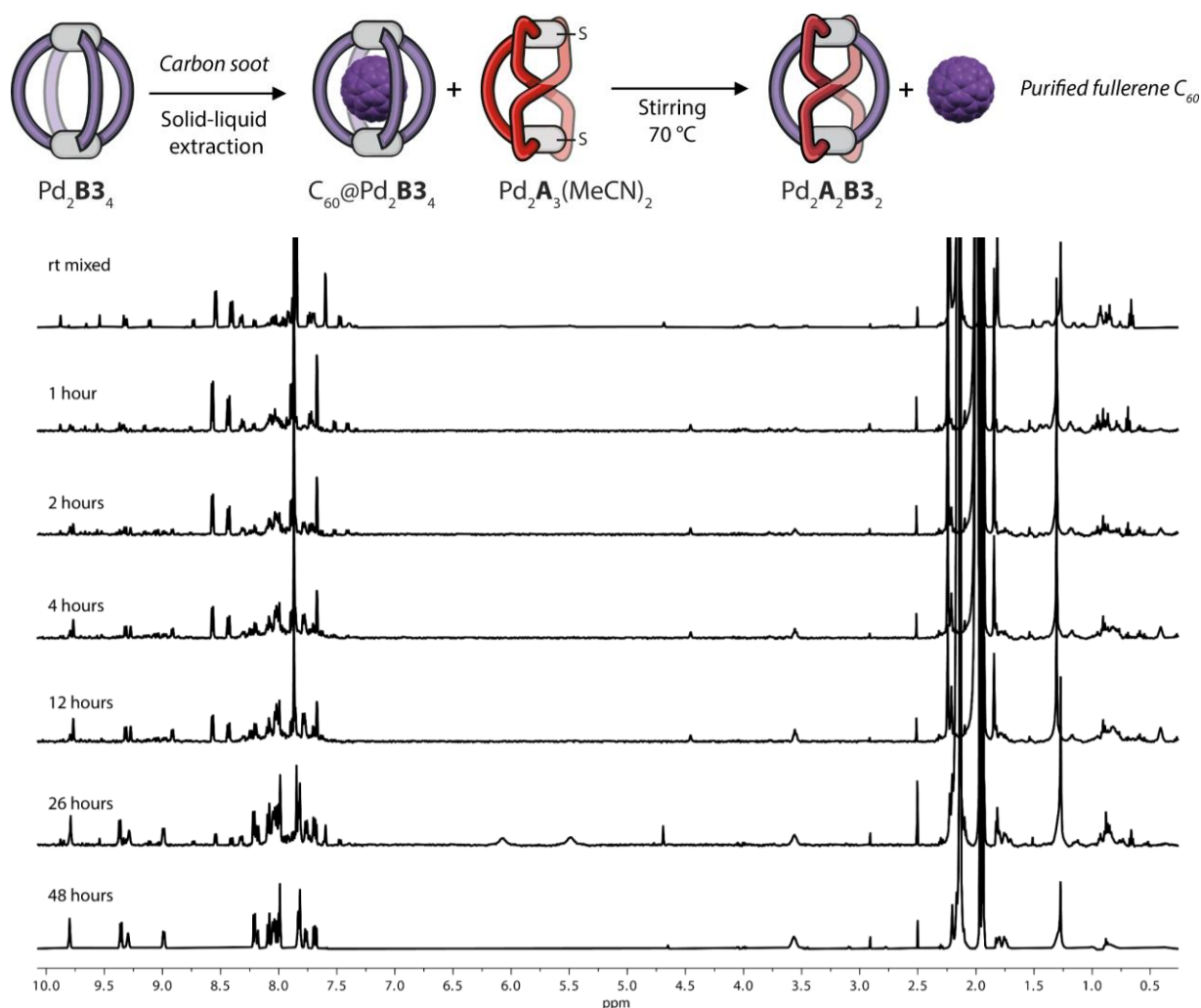


Figure S82: 1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation of $C_{60}@Pd_2B_3$ into heteroleptic Pd_2AB_3 upon addition of $Pd_2A_3(MeCN)_2$. The fullerene is selectively released from the cavity and can be recovered.

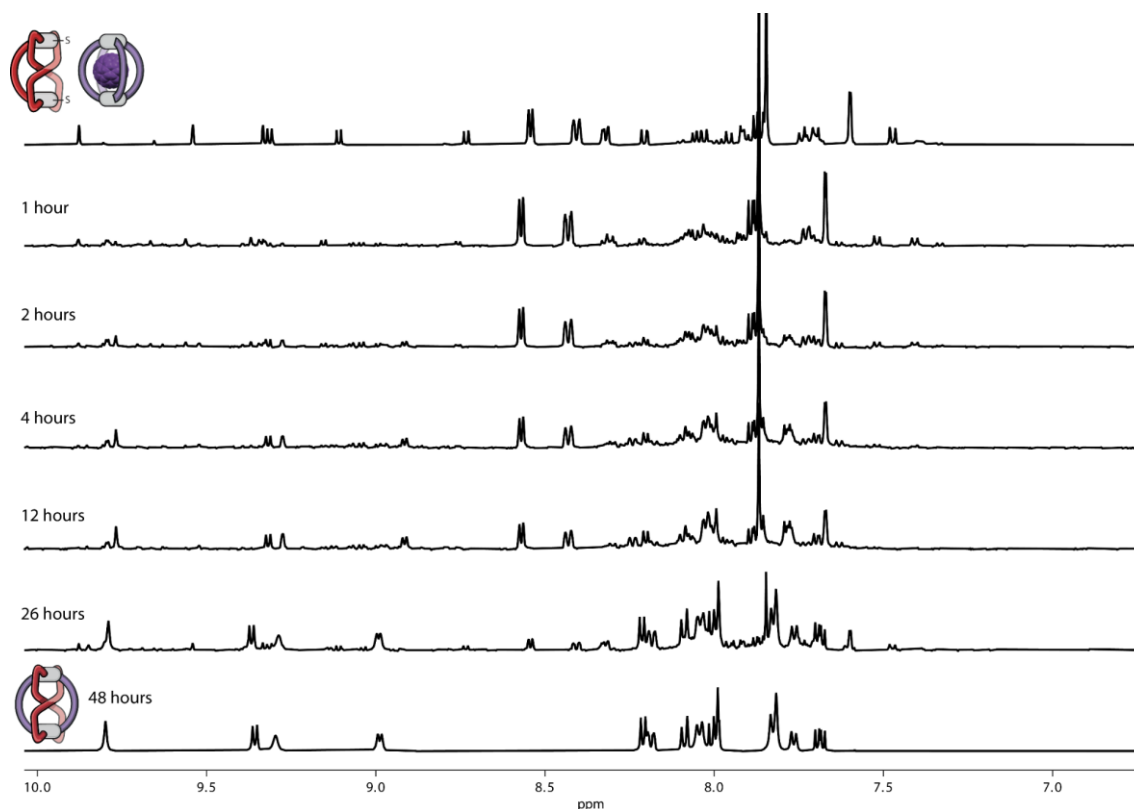


Figure S83: ^1H NMR spectra stack (500 MHz, 298 K, CD_3CN), aromatic region, following the transformation of $\text{C}_{60}@\text{Pd}_2\text{B}_3$ into heteroleptic $\text{Pd}_2\text{A}_2\text{B}_3$ upon addition of $\text{Pd}_2\text{A}_3(\text{MeCN})_2$. The fullerene is selectively released from the cavity and can be recovered.

From the competition experiment

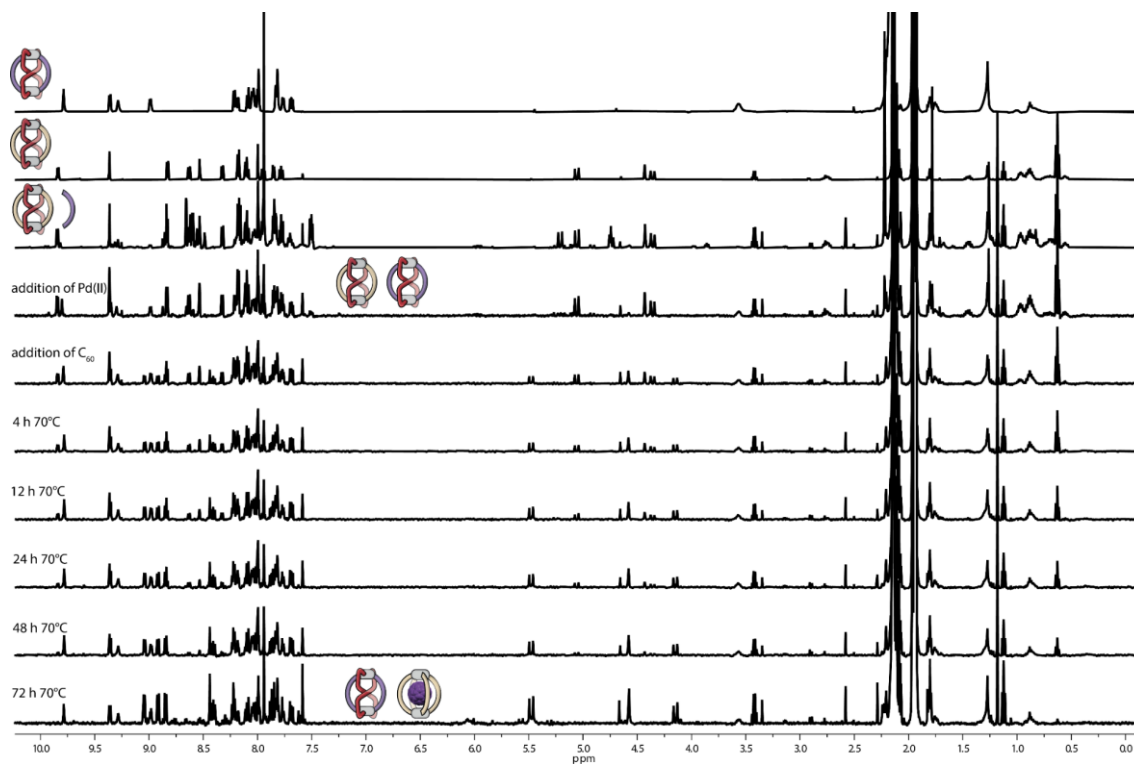


Figure S84: ^1H NMR spectra stack (500 MHz, 298 K, CD_3CN), following the transformation of the mixture obtained from the competition experiment upon addition of fullerene and prolonged heating.

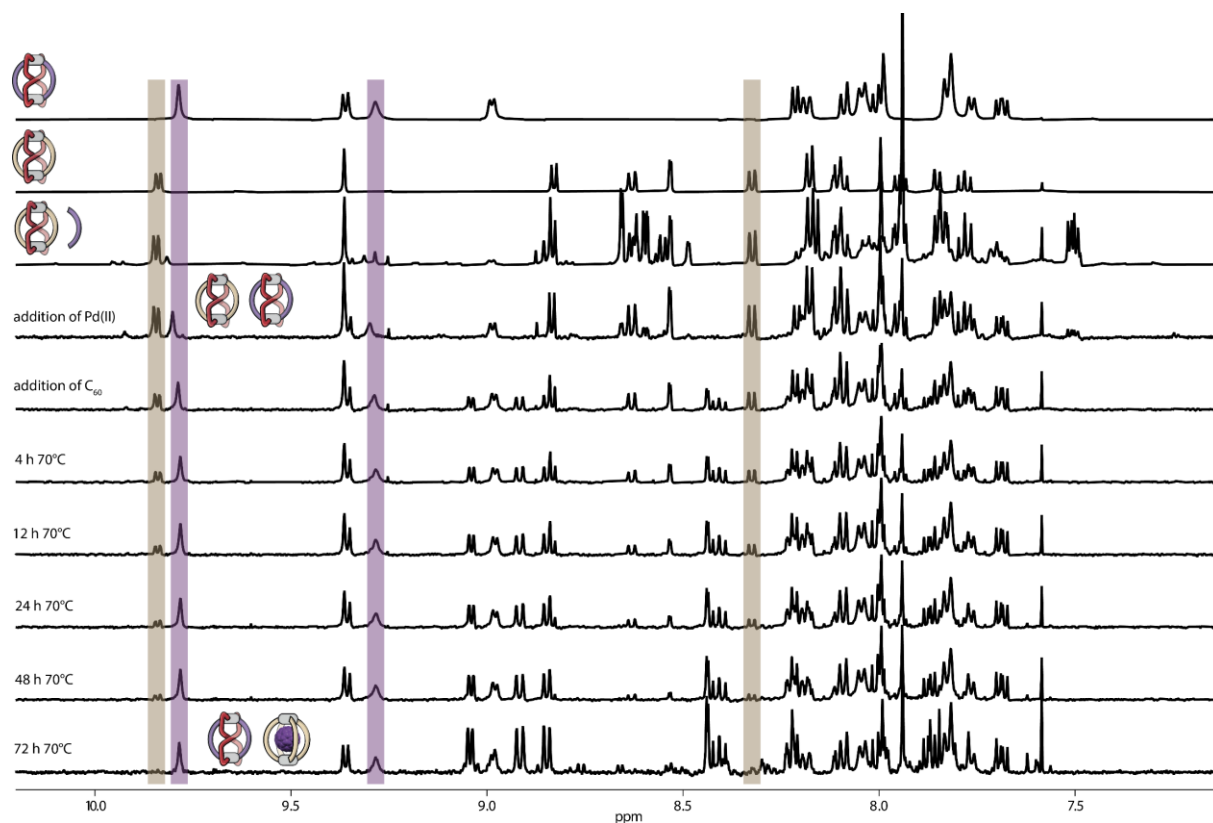


Figure S85: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN), zoomed aromatic region, following the transformation of the mixture obtained from the competition experiment upon addition of fullerene and prolonged heating.

From heteromeric complete self-sorting

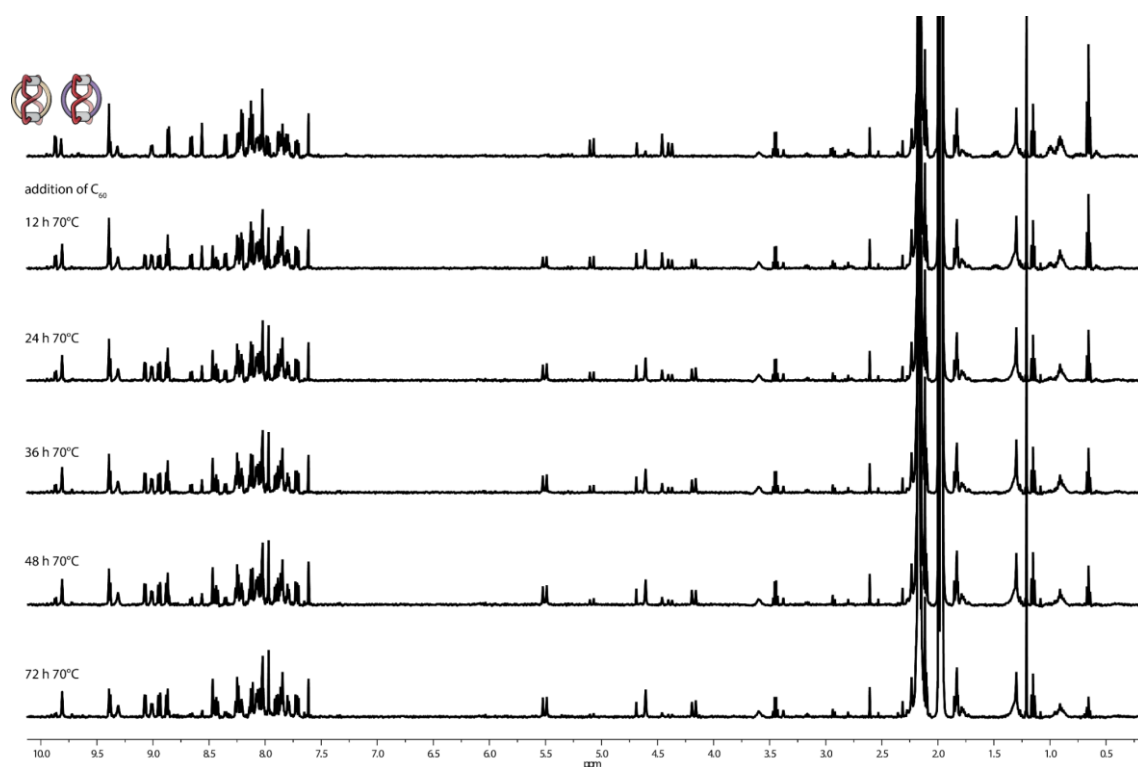


Figure S86: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation of the mixture obtained from heteromeric complete self-sorting upon addition of fullerene and prolonged heating.

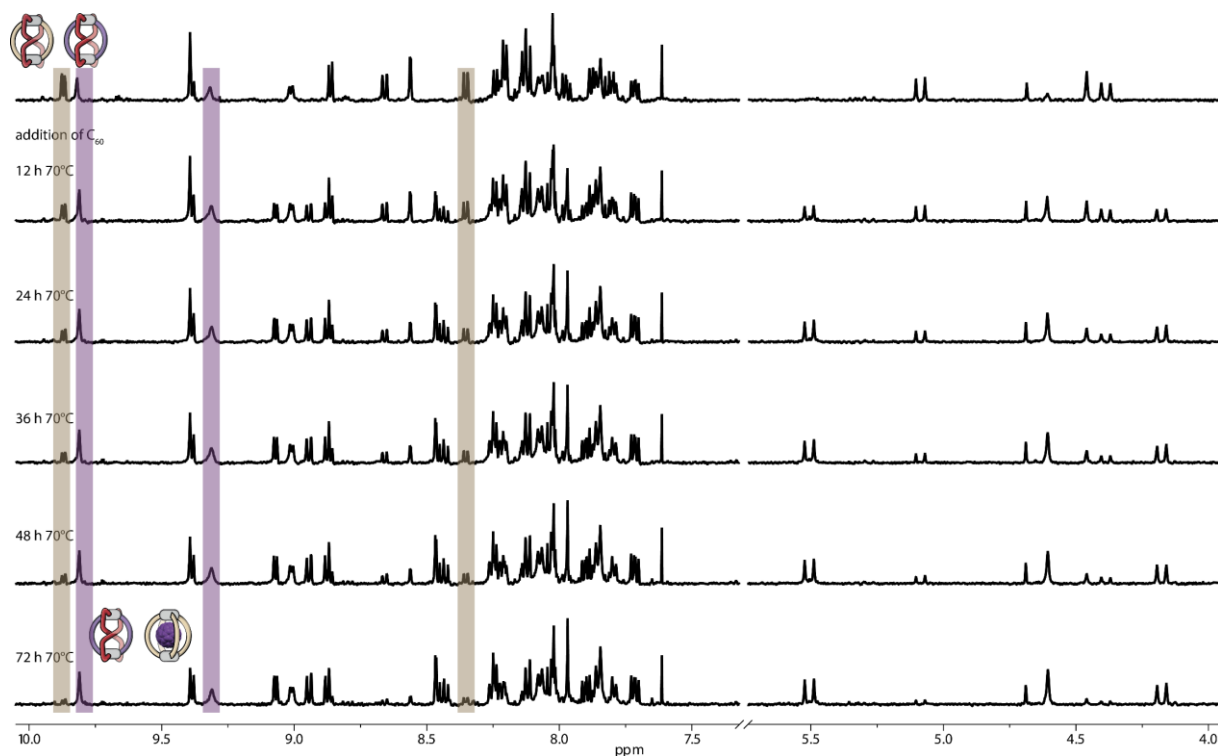


Figure S87: ^1H NMR spectra stack (500 MHz, 298 K, CD_3CN), zoomed aromatic region, following the transformation of the mixture obtained from heteromeric complete self-sorting upon addition of fullerene and prolonged heating.

Controlled population transformation

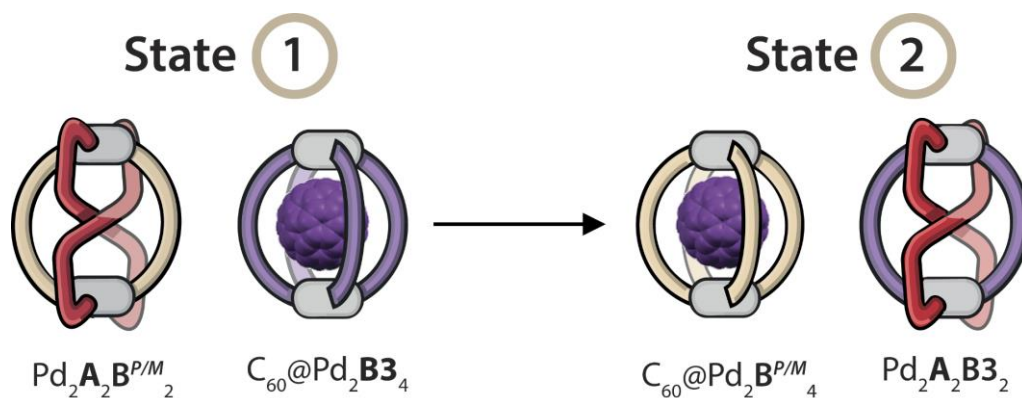


Figure S88: Schematic representation of the transformable population of cages upon guest and ligand exchange

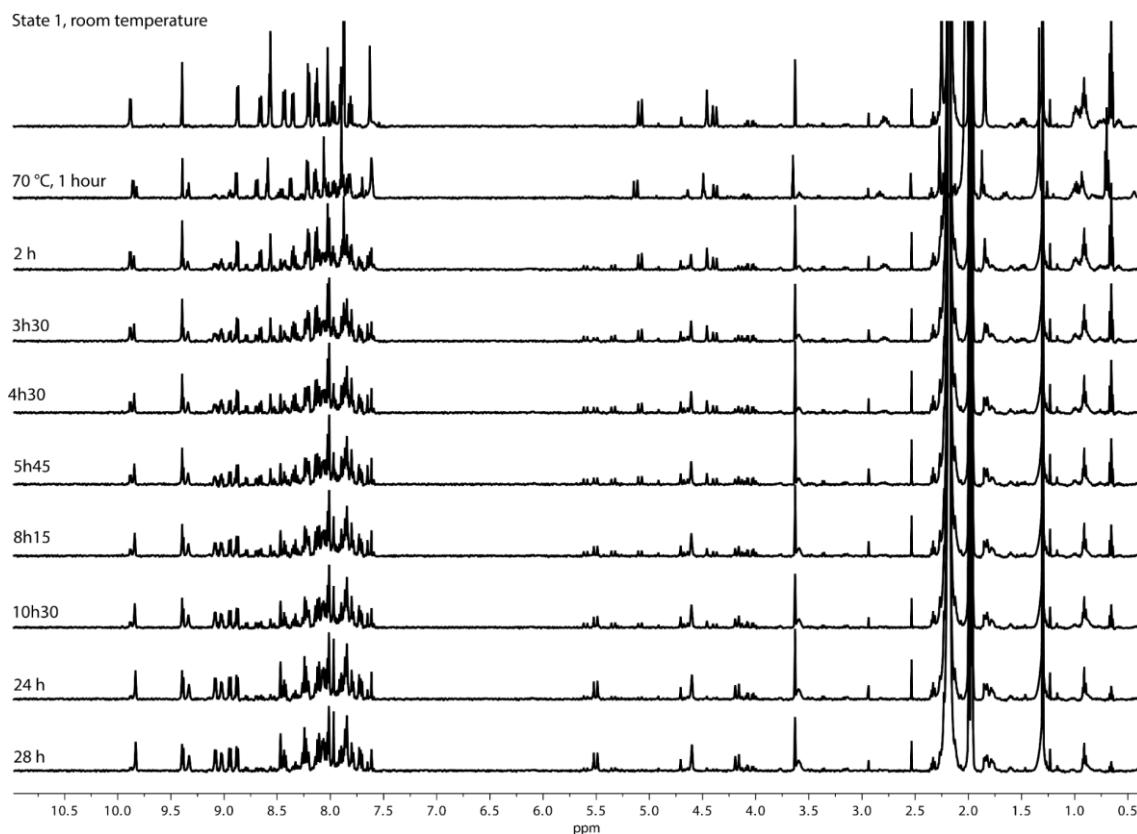


Figure S89: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation from **State 1** to **State 2** upon heating at 70 °C.

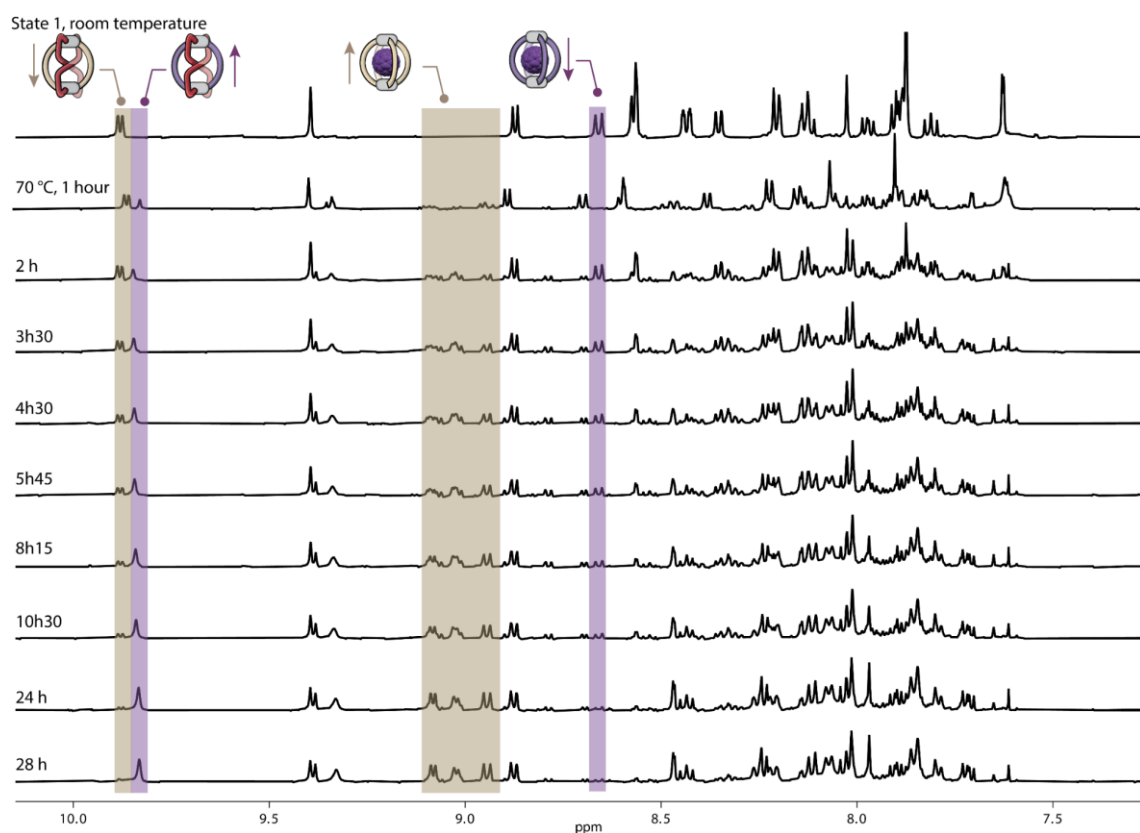


Figure S90: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN), zoomed aromatic region, following the transformation from **State 1** to **State 2** upon heating at 70 °C.

Temperature-dependent transformation

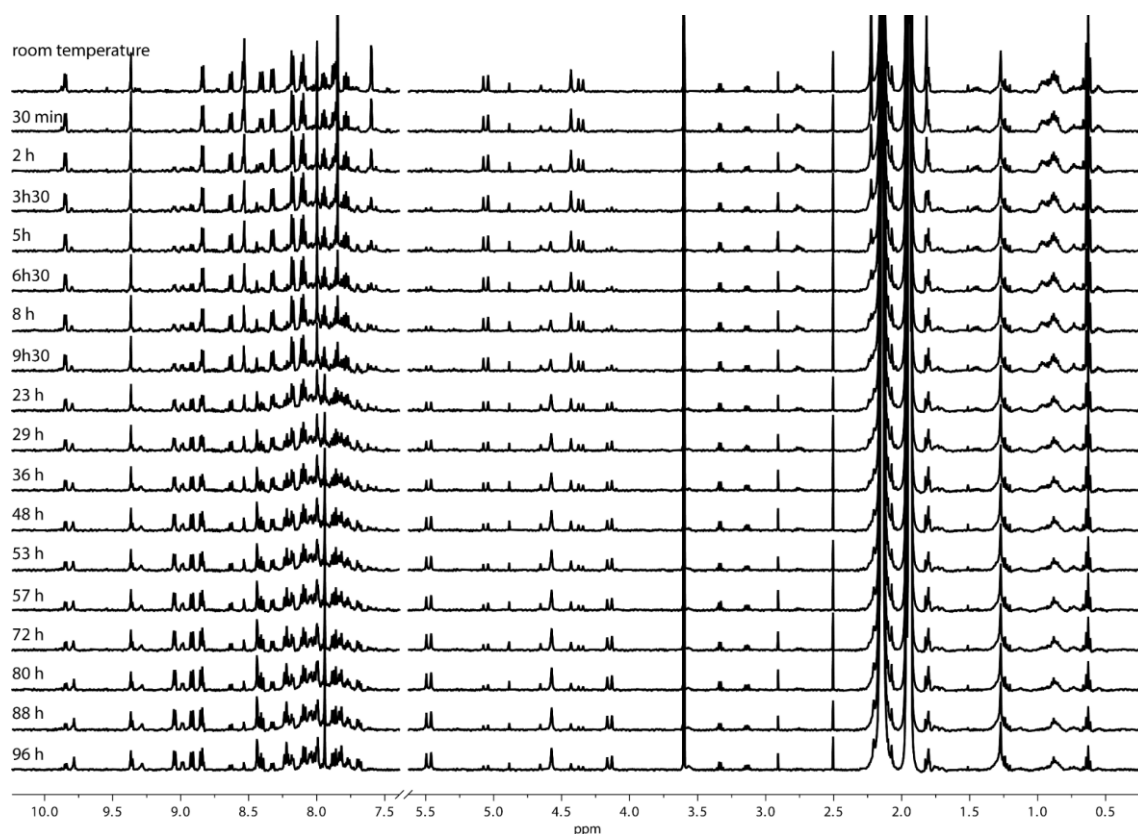


Figure S91: ¹H NMR spectra stack (500 MHz, 298K, CD₃CN) following the transformation from *State 1* to *State 2* upon heating at 50 °C.

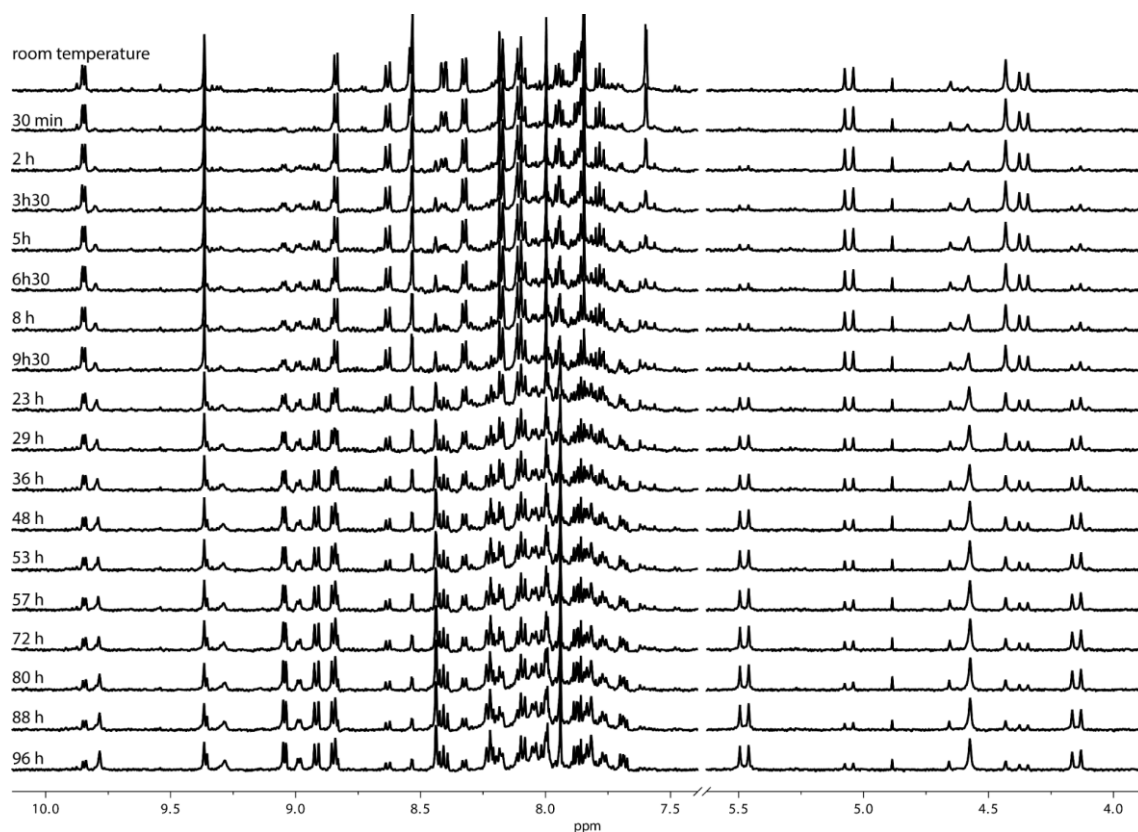


Figure S92: ¹H NMR spectra stack (500 MHz, 298K, CD₃CN) following the transformation from *State 1* to *State 2* upon heating at 50 °C.

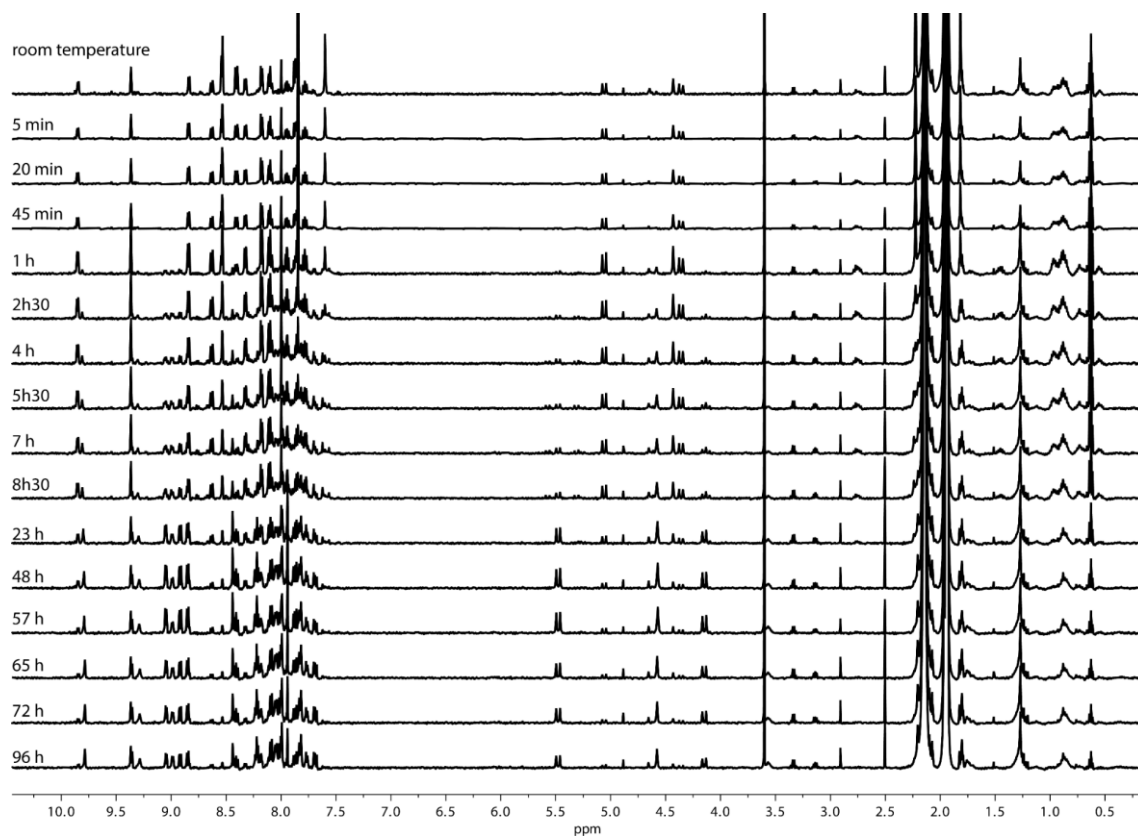


Figure S93: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation from **State 1** to **State 2** upon heating at 60 °C.

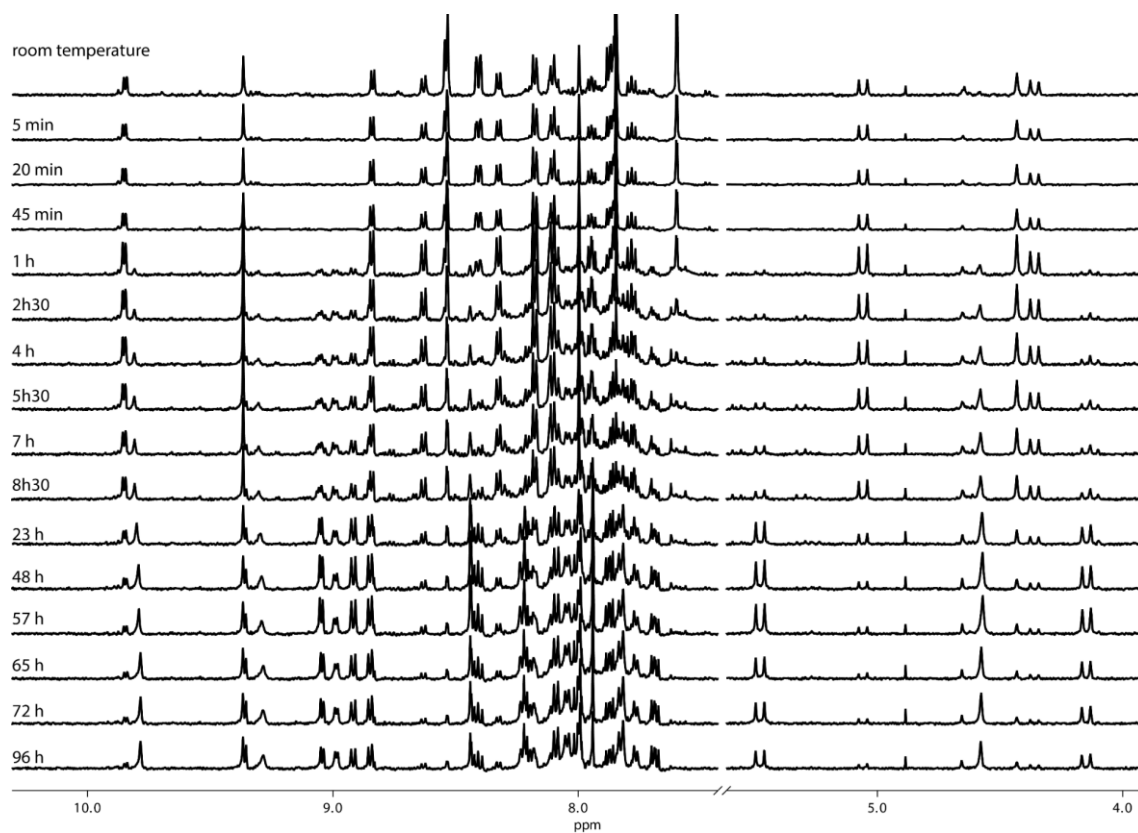


Figure S94: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation from **State 1** to **State 2** upon heating at 60 °C.

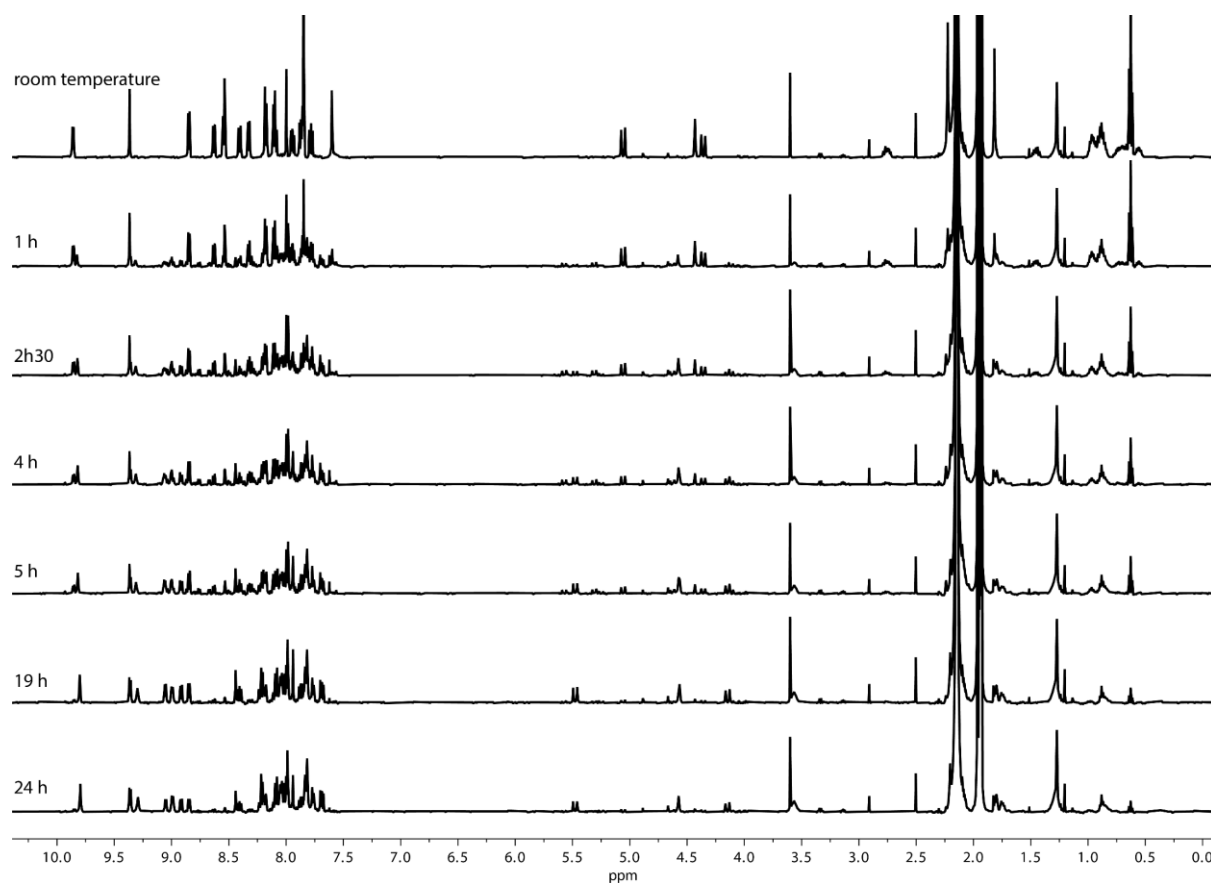


Figure S95: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation from **State 1** to **State 2** upon heating at 80 °C.

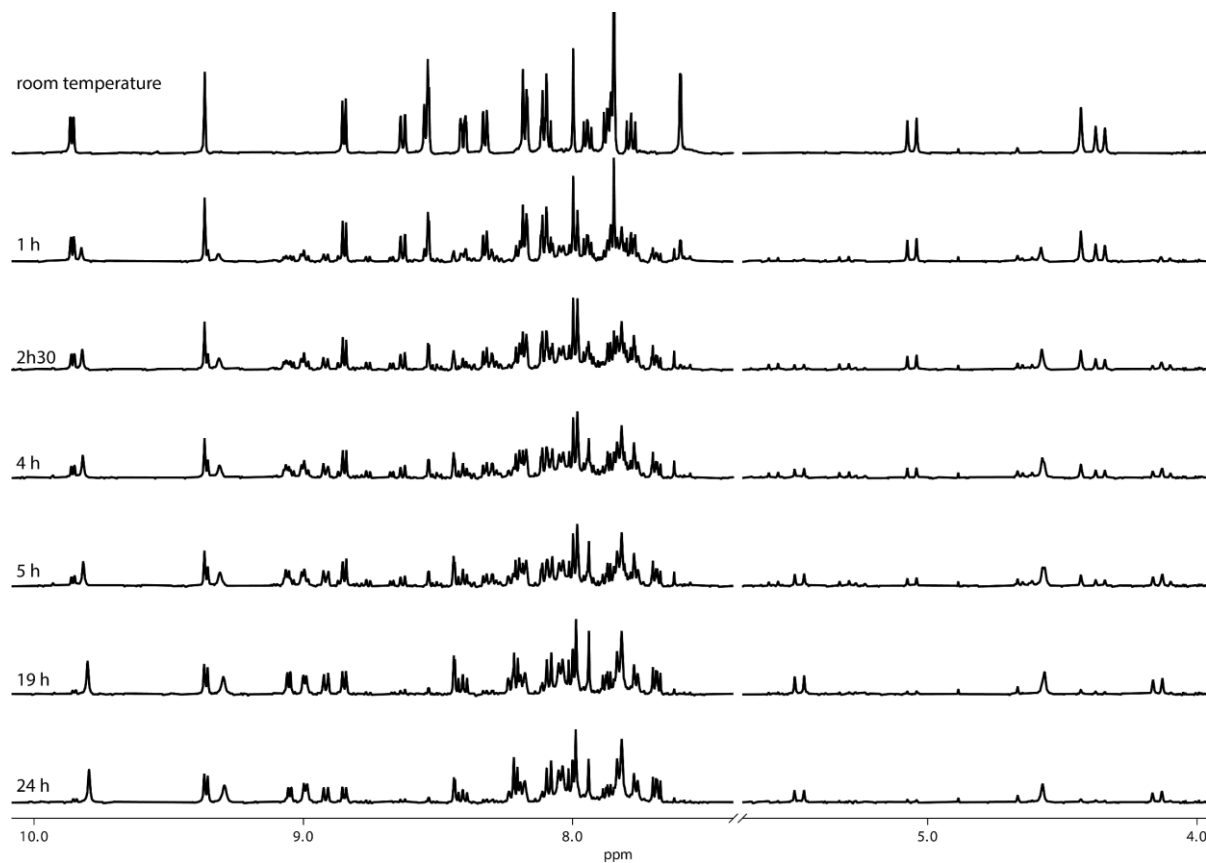


Figure S96: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation from **State 1** to **State 2** upon heating at 80 °C.

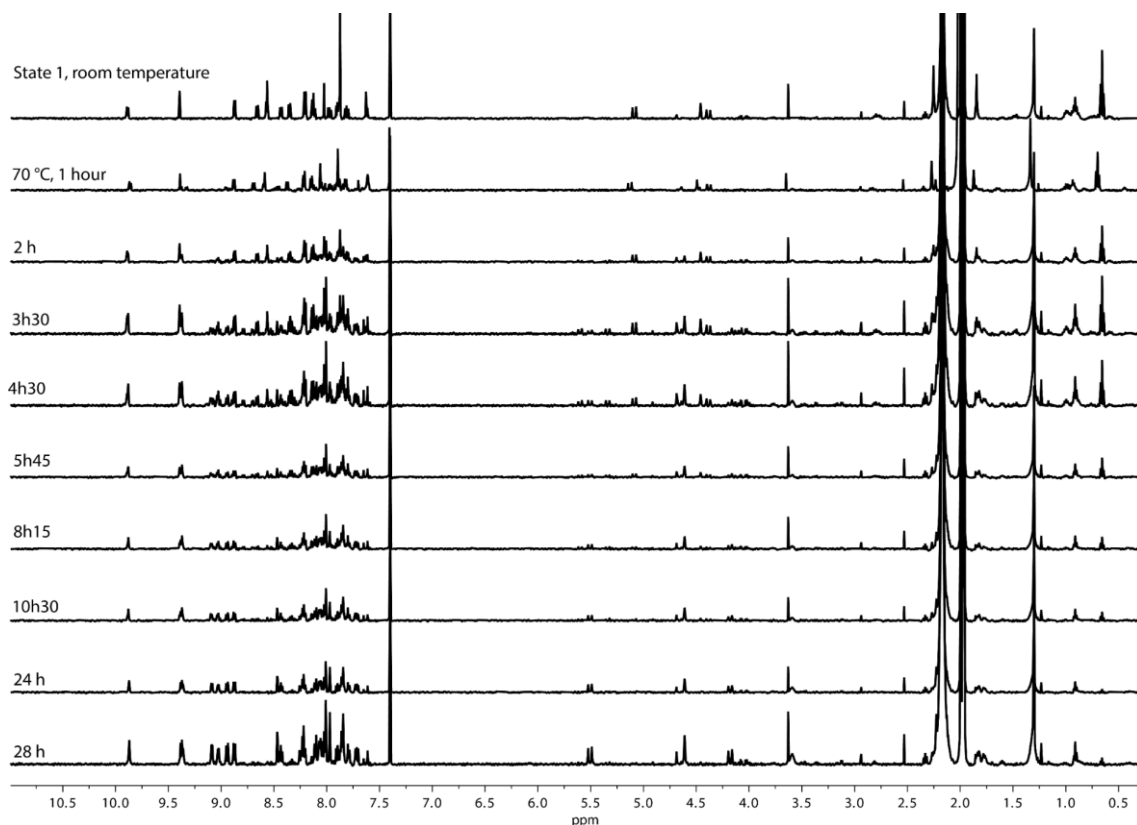


Figure S97: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation from **State 1** to **State 2** upon heating at 70 °C, lower concentration.

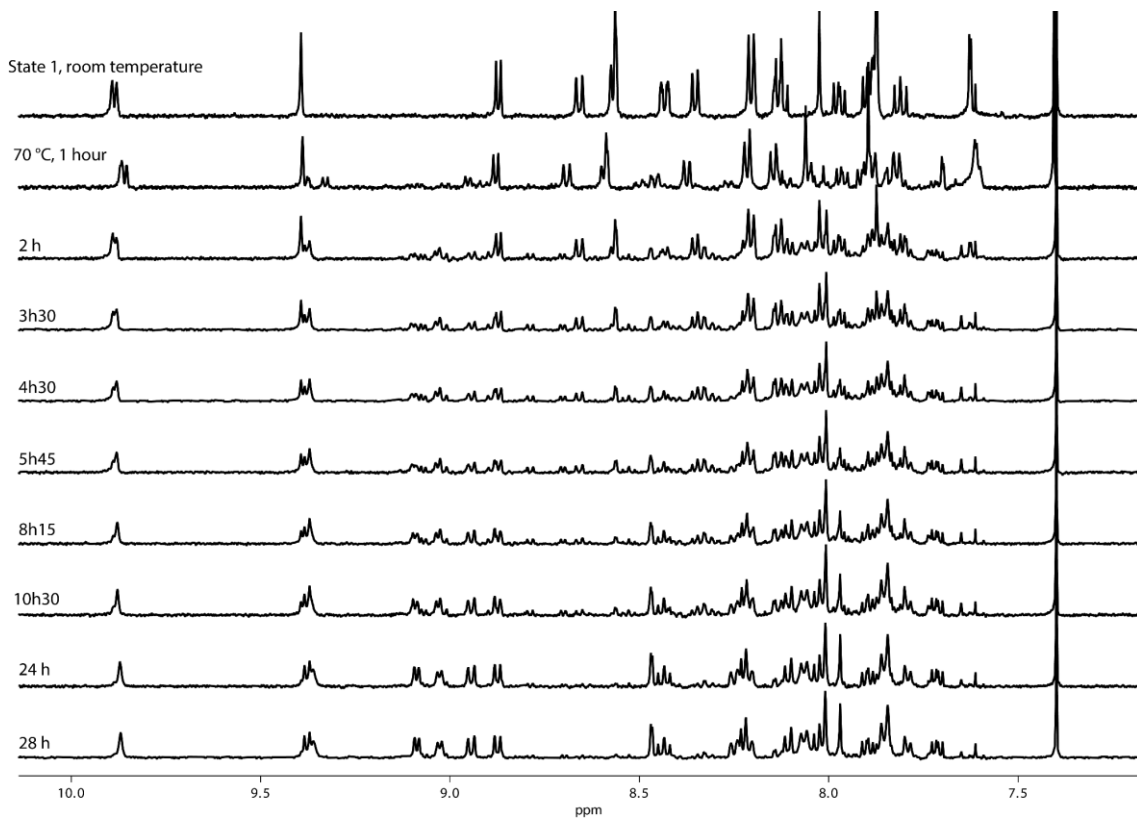


Figure S98: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation from **State 1** to **State 2** upon heating at 70 °C, lower concentration.

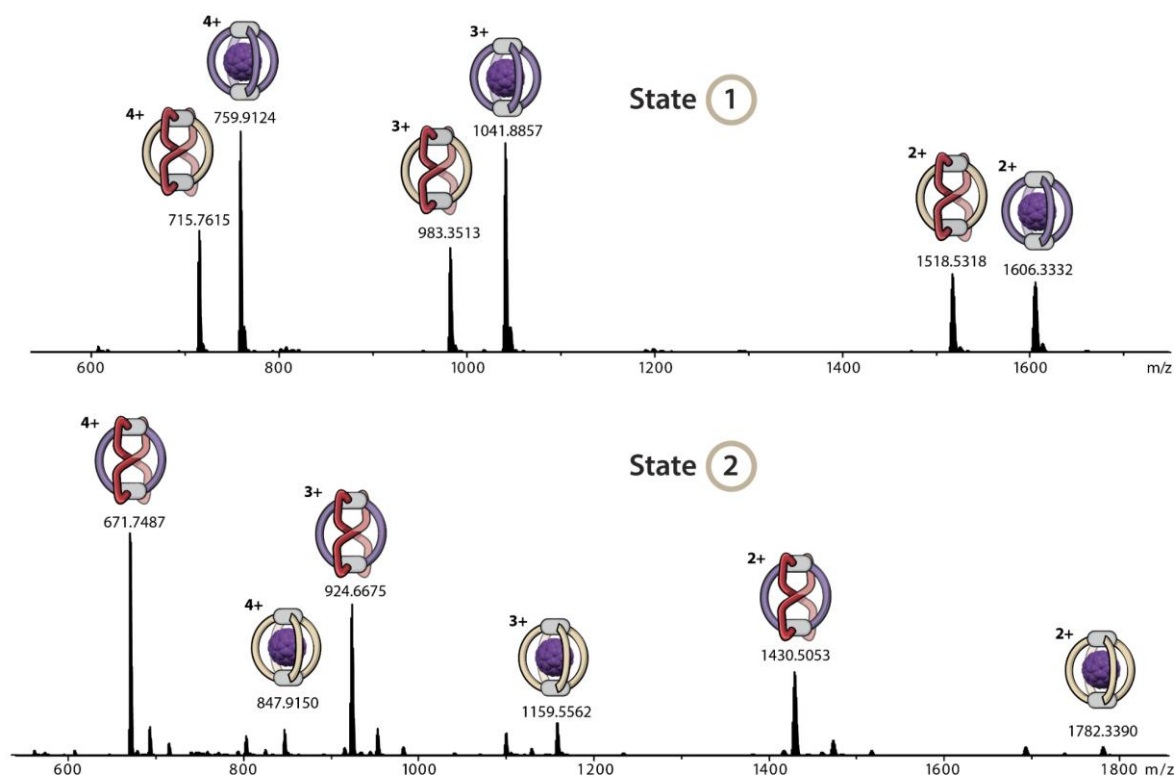


Figure S99: ESI-MS spectrum of a MeCN solution **State 1** and **State 2**. The observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ and $[\text{C}_{60}@\text{Pd}_2\text{B}_3\text{A}_4+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ for **State 1**. The observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{B}_3\text{A}_2+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ and $[\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4+n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ for **State 2**.

Subsection 3

Dissipative nature of the transformation

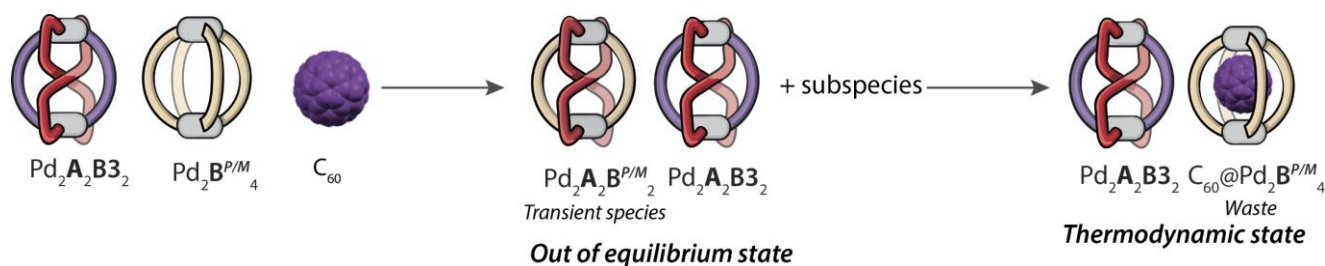


Figure S100: Schematic representation of the transient out-of-equilibrium state formation and decay during the transformation process.

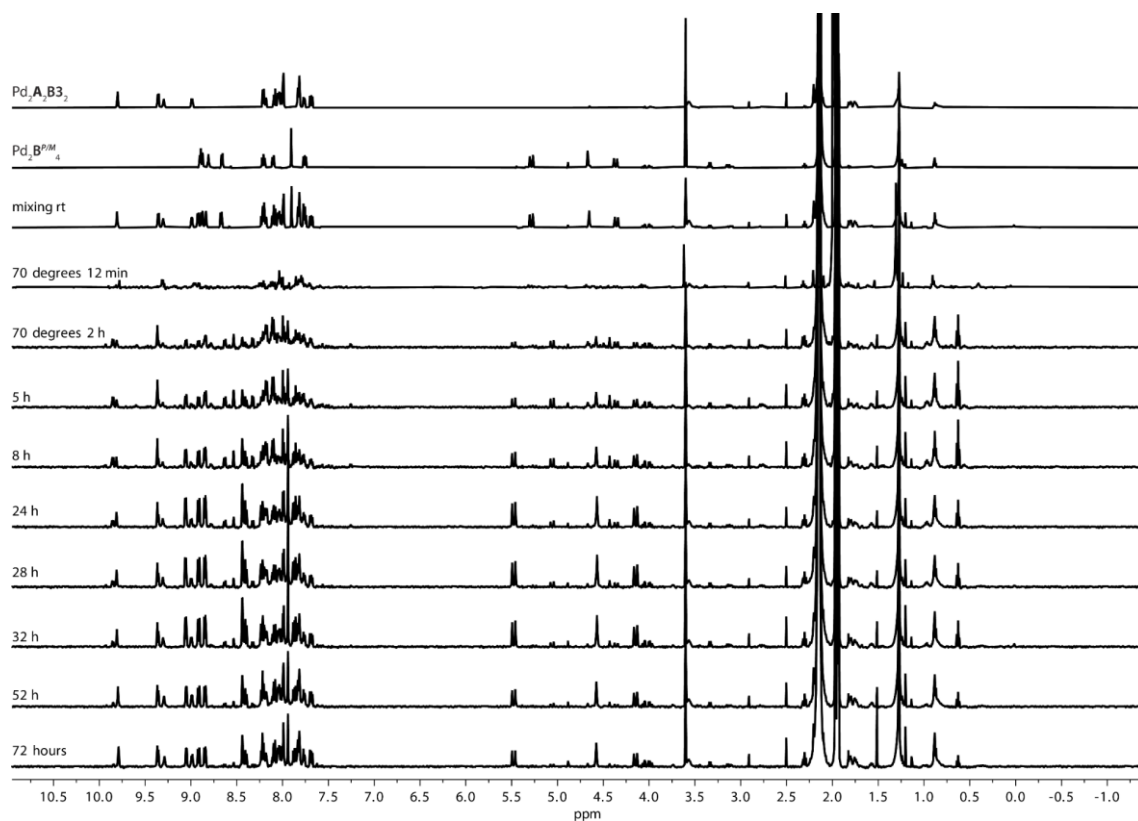


Figure S101: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation and showing the transient state. This is Cycle 1.

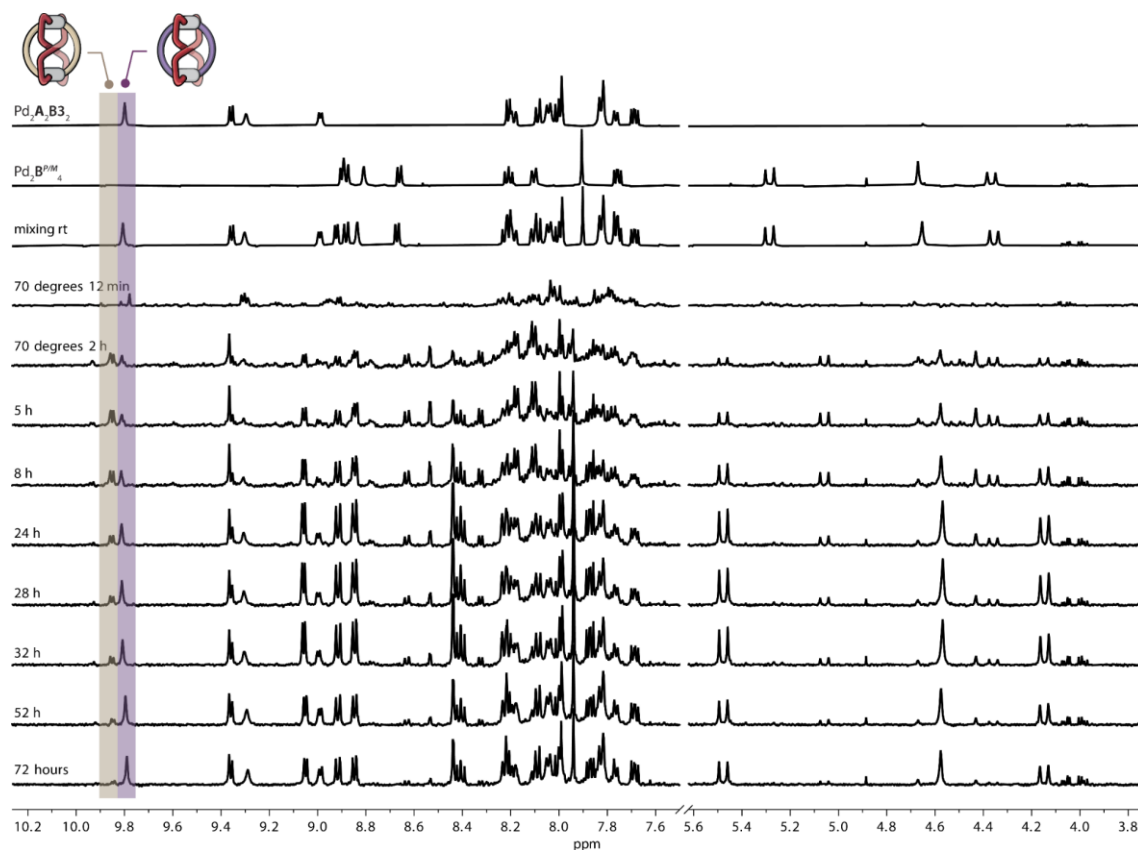


Figure S102: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) enlarged on the aromatic region following the transformation and showing the transient state.

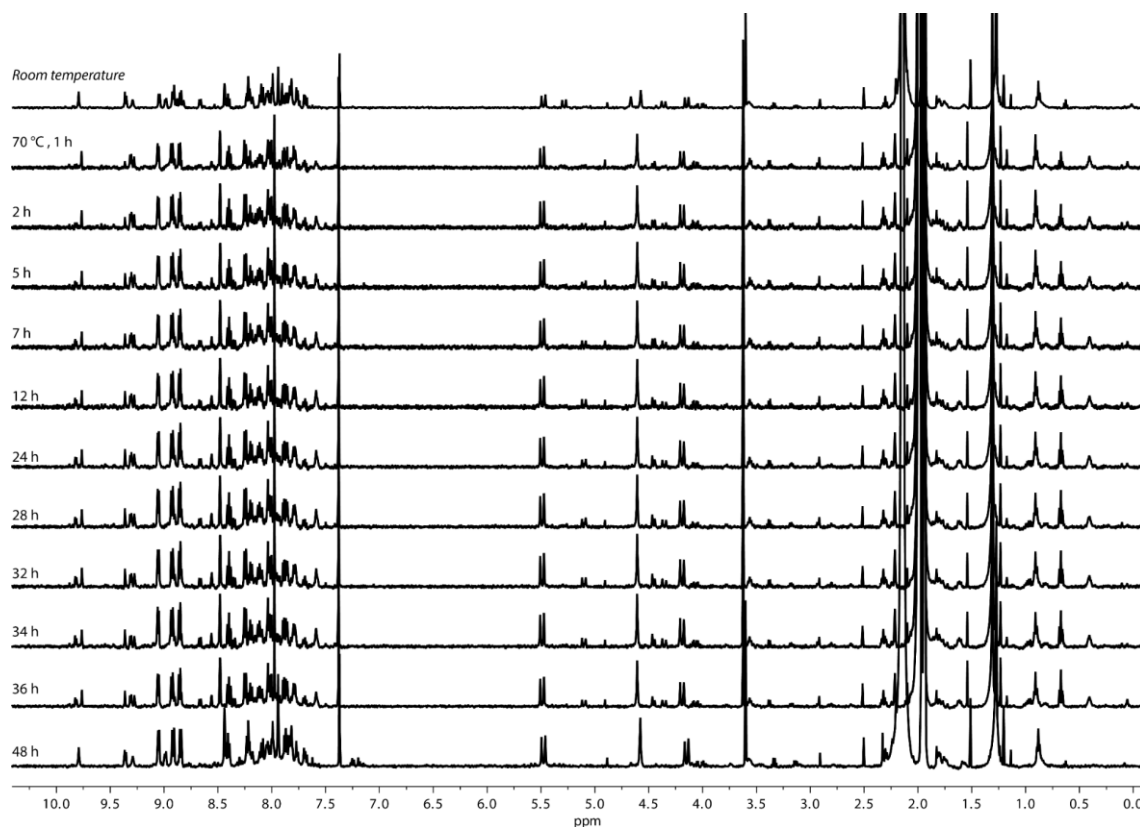


Figure S103: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) following the transformation and showing the transient state. This is Cycle 2.

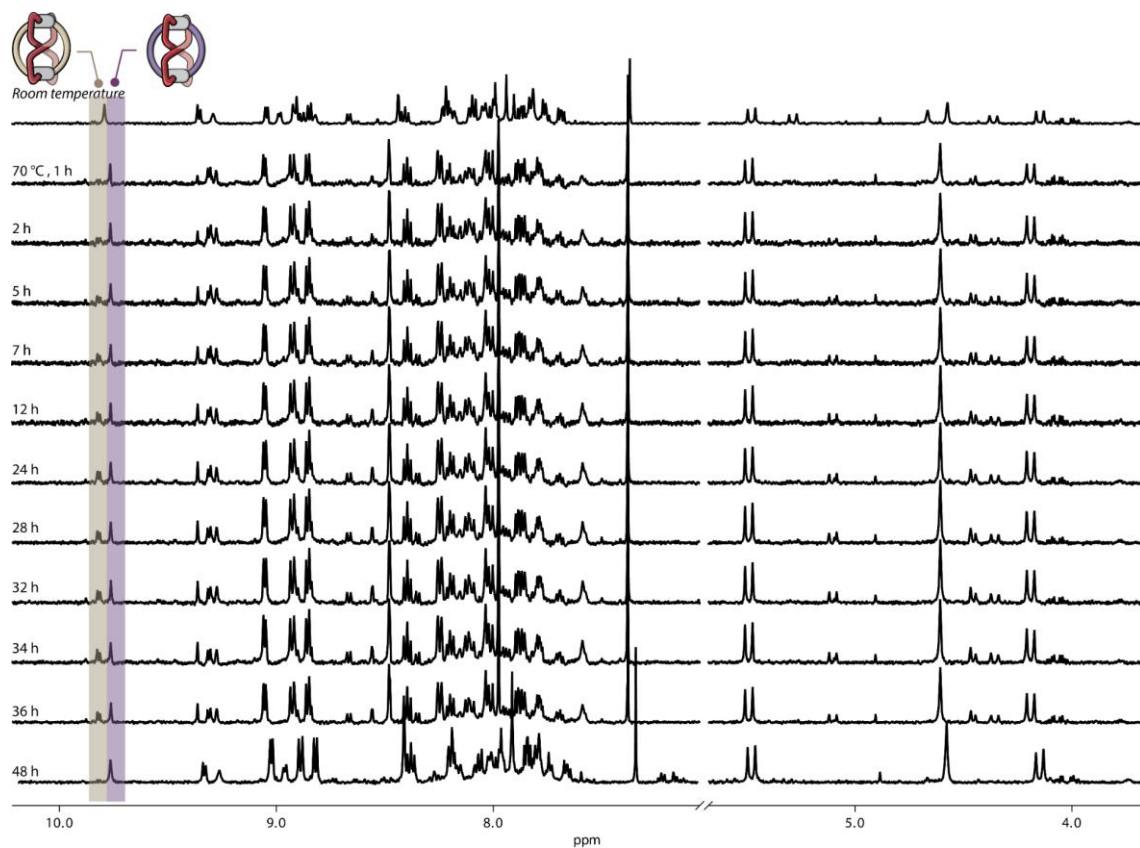


Figure S104: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) enlarged on the aromatic region following the transformation and showing the transient state. This is Cycle 2.

Signal transduction and complex population transformations

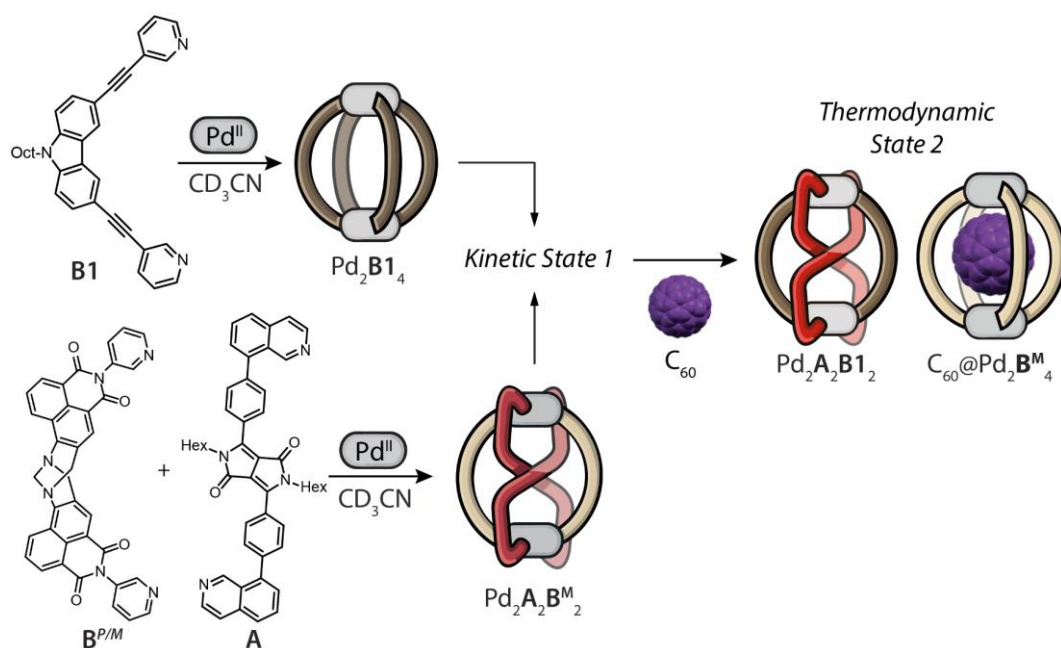


Figure S105: Schematic representation of the transformation process between $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_2\text{B1}_4$ in presence of fullerene C_{60} .

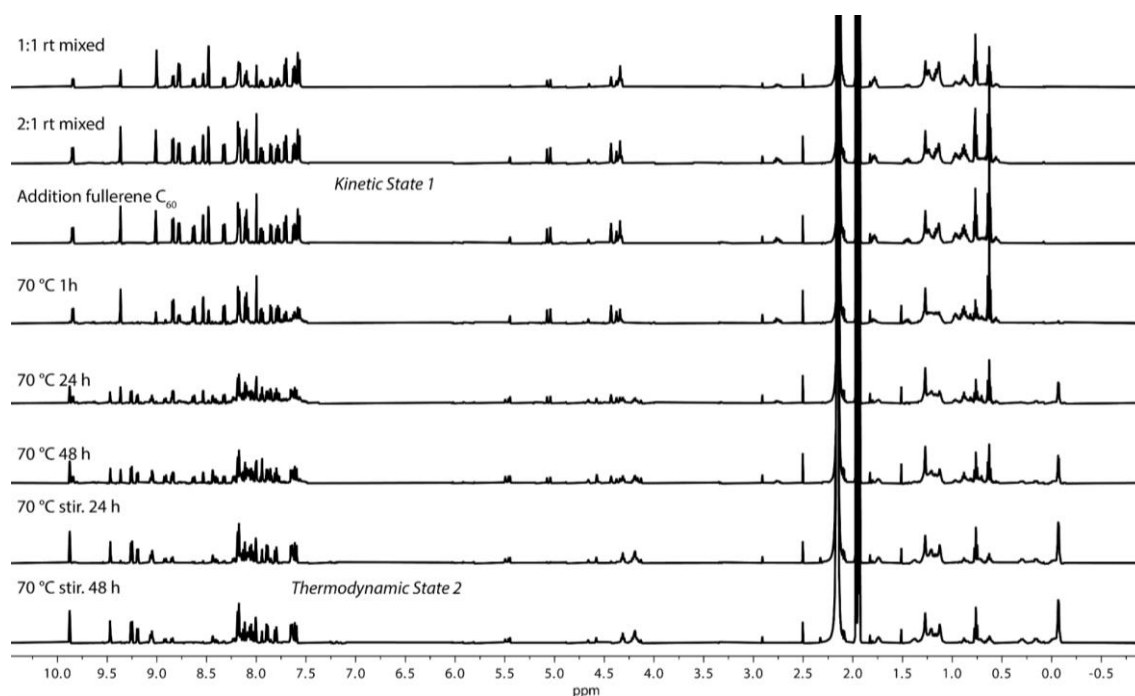


Figure S106: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) of the transformation process between $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_2\text{B1}_4$ in presence of fullerene C_{60} .

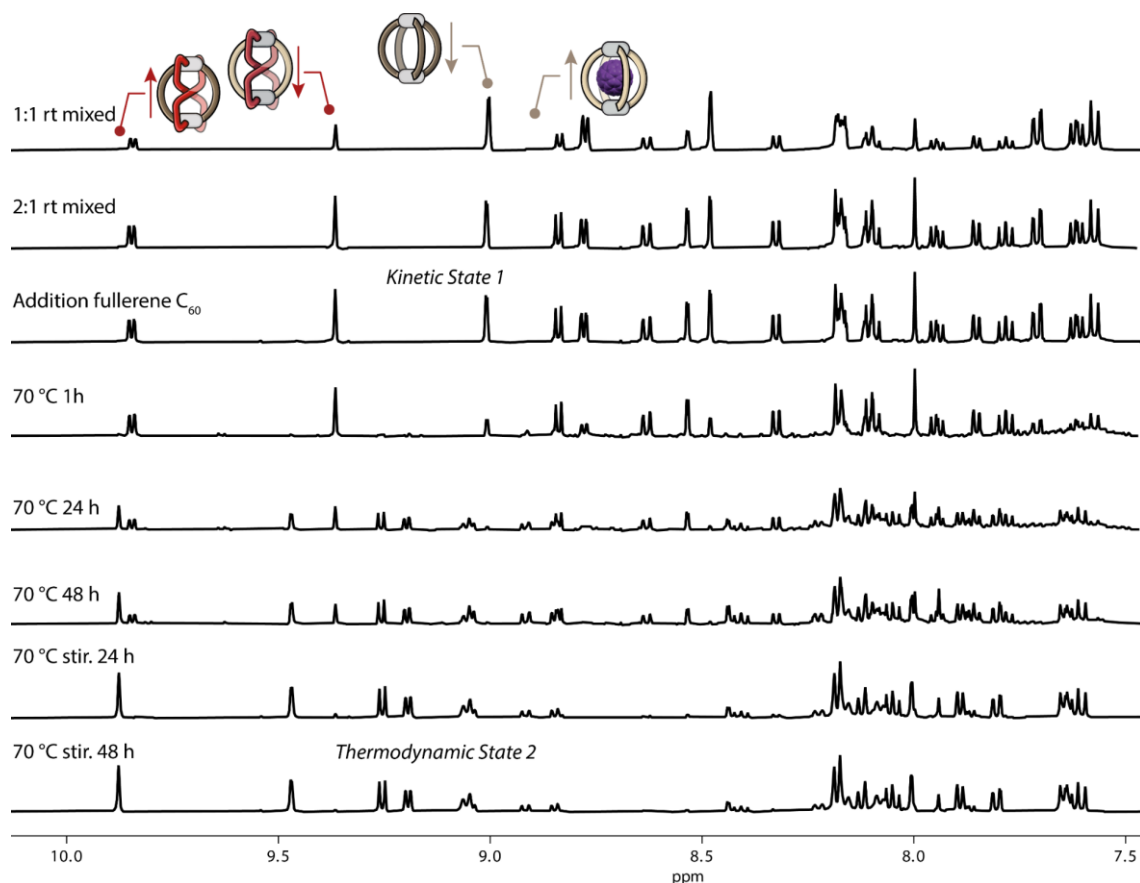


Figure S107: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the transformation process between $\text{Pd}_2\text{A}_2\text{Bp}_2$ and Pd_2B_{14} in presence of fullerene C_{60} .

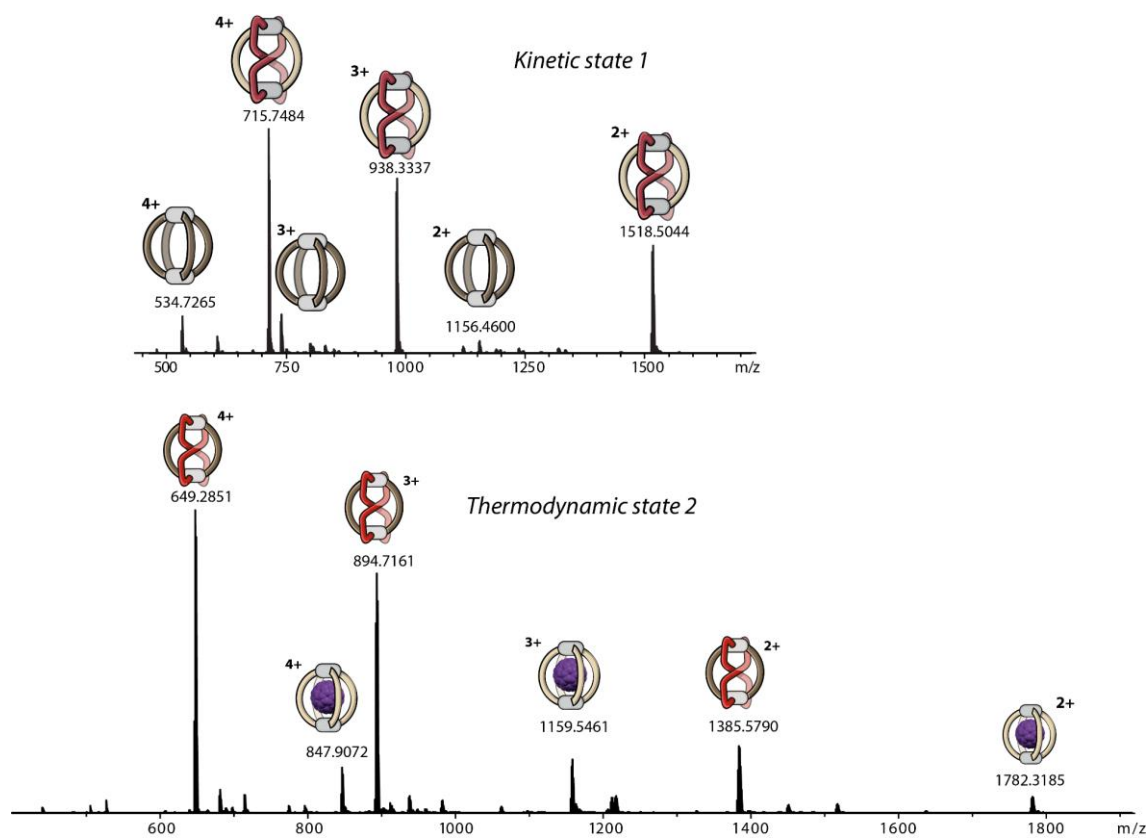


Figure S108: ESI-MS spectrum of a MeCN solution **State 1** and **State 2**. The observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ and $[\text{Pd}_2\text{B}^{\text{P}}_4 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ for **State 1**. The observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ and $[\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ for **State 2**.

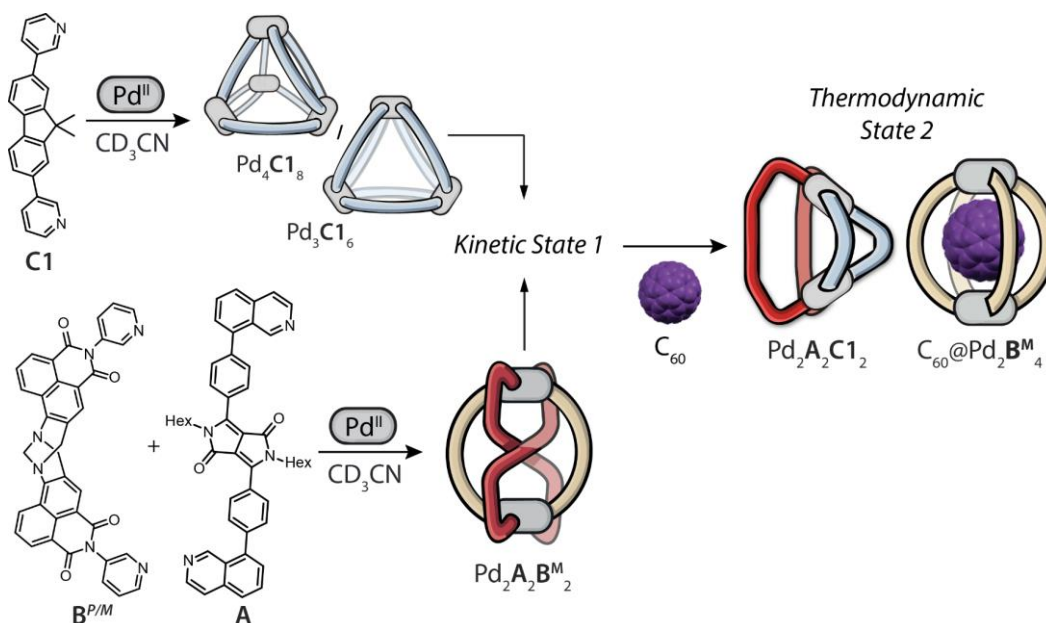


Figure S109: Schematic representation of the transformation process between $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_3\text{C1}_6/\text{Pd}_4\text{C1}_8$ in presence of fullerene C_{60} .

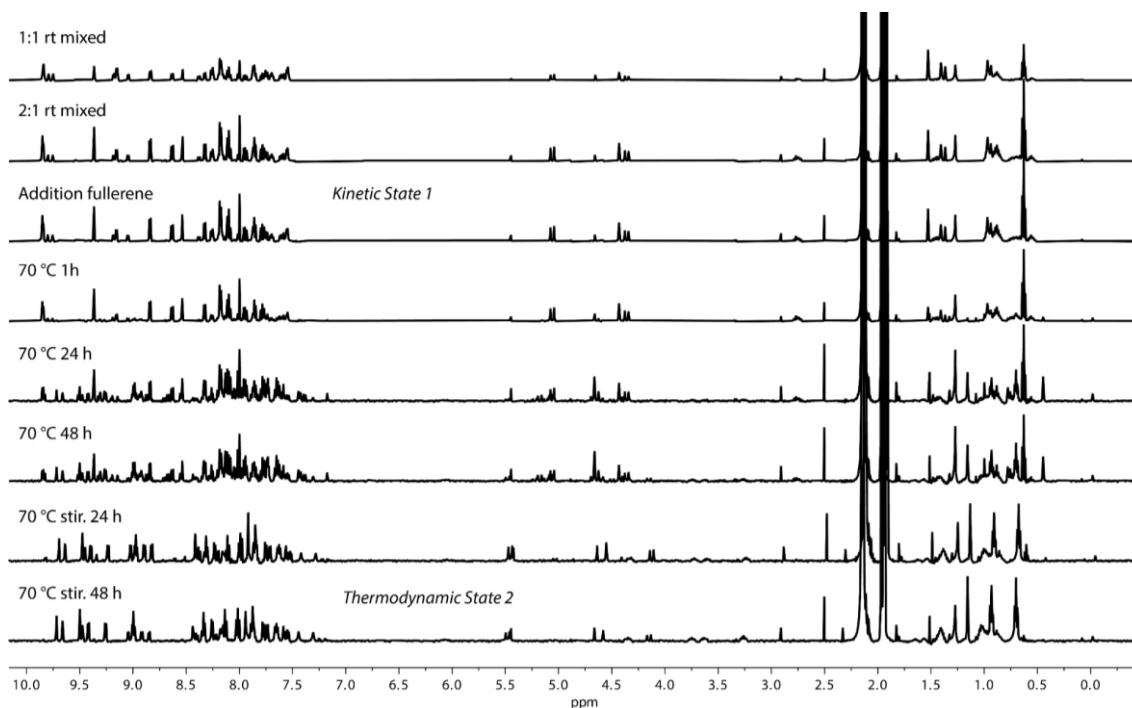


Figure S110: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) of the transformation process between $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_3\text{C1}_6/\text{Pd}_4\text{C1}_8$ in presence of fullerene C_{60} .

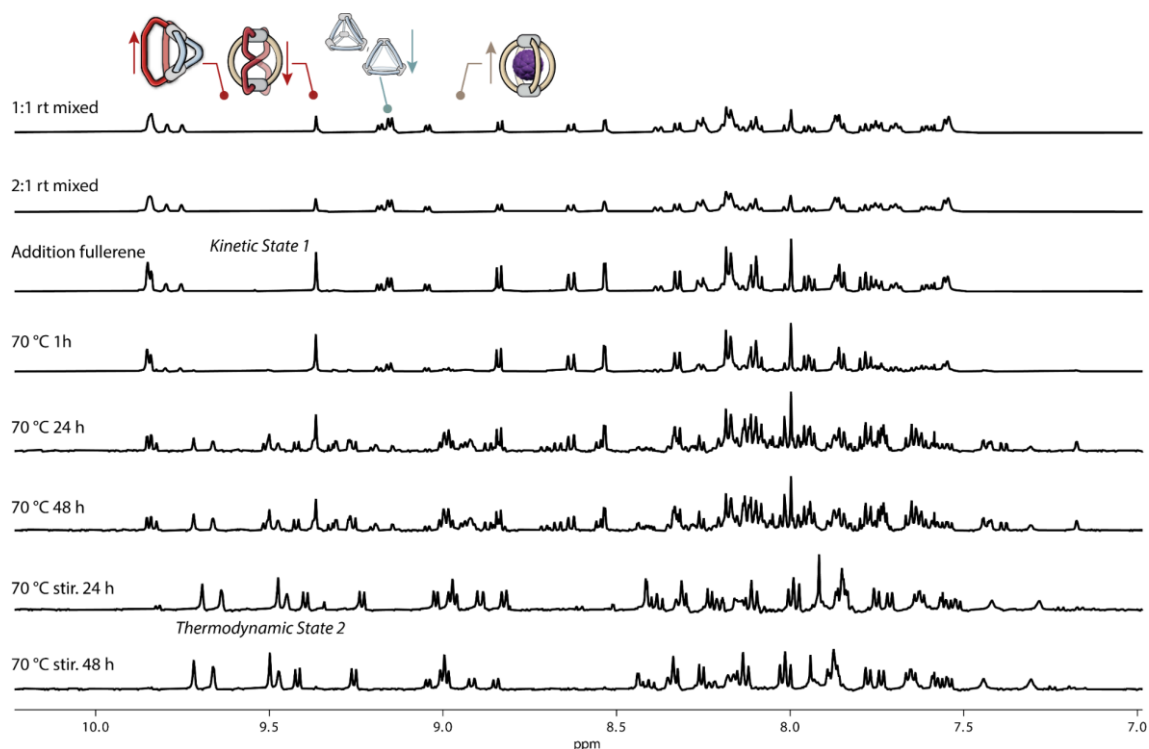


Figure S111: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the transformation process between $\text{Pd}_2\text{A}_2\text{B}_2$ and $\text{Pd}_3\text{C}_{16}/\text{Pd}_4\text{C}_{18}$ in presence of fullerene C_{60} .

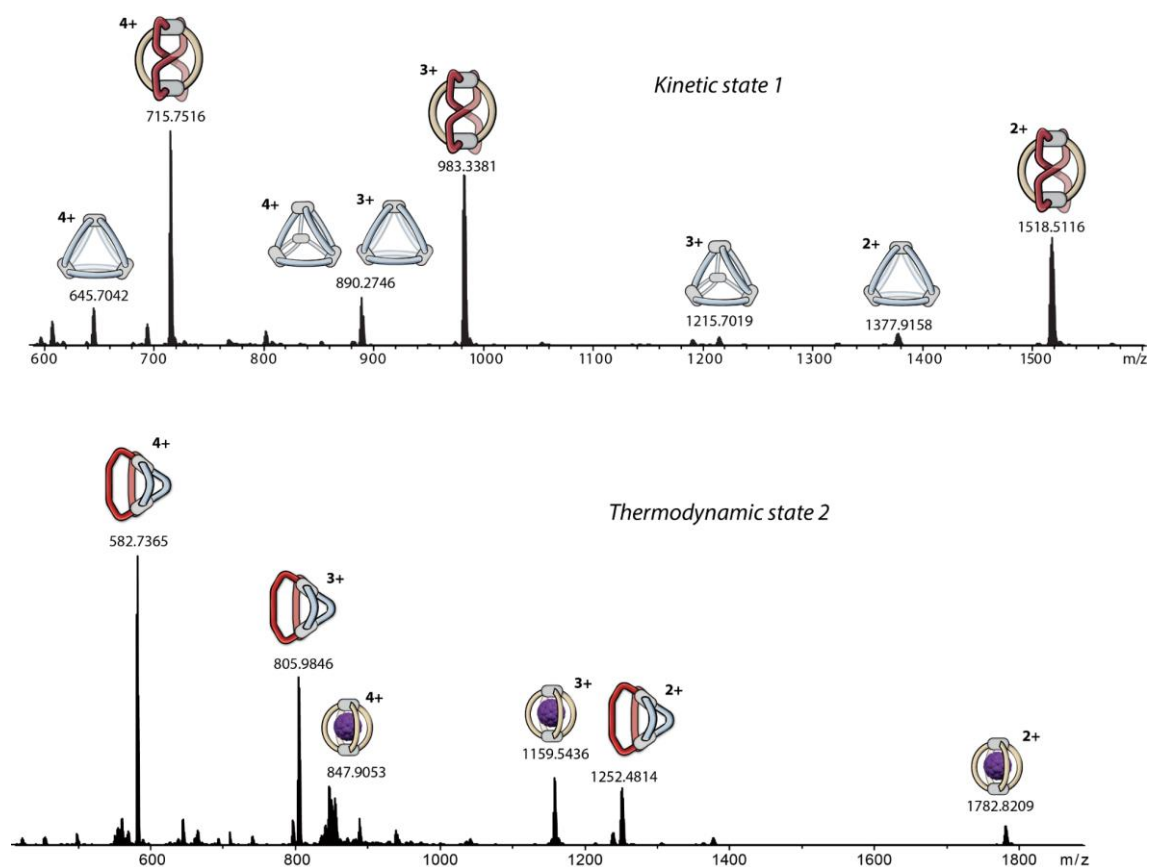


Figure S112: ESI-MS spectrum of a MeCN solution **State 1** and **State 2**. The observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{B}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ and $[\text{Pd}_3\text{C}_{16} + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ for **State 1**. The observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{C}_{12} + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ and $[\text{C}_{60}@\text{Pd}_2\text{B}_4 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ for **State 2**.

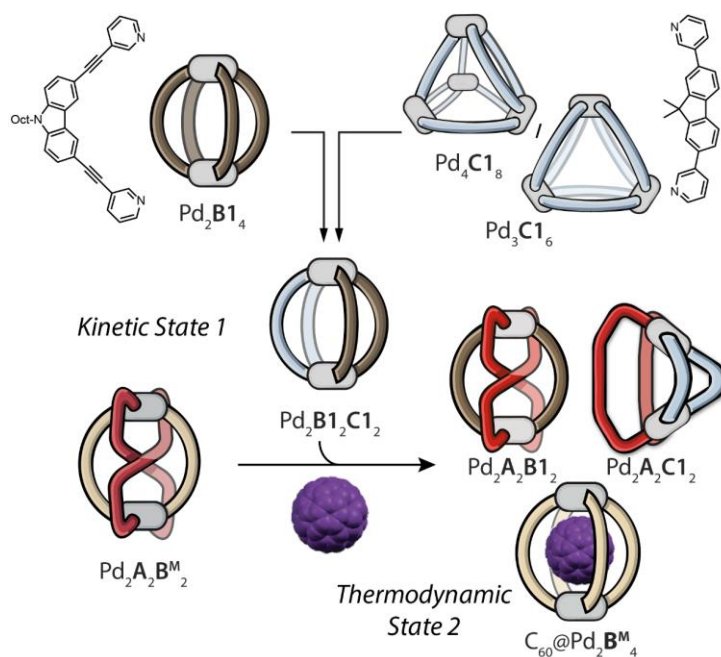


Figure S113: Schematic representation of the transformation process between $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_2\text{B}_{12}\text{C}_{12}$ in presence of fullerene C_{60} .

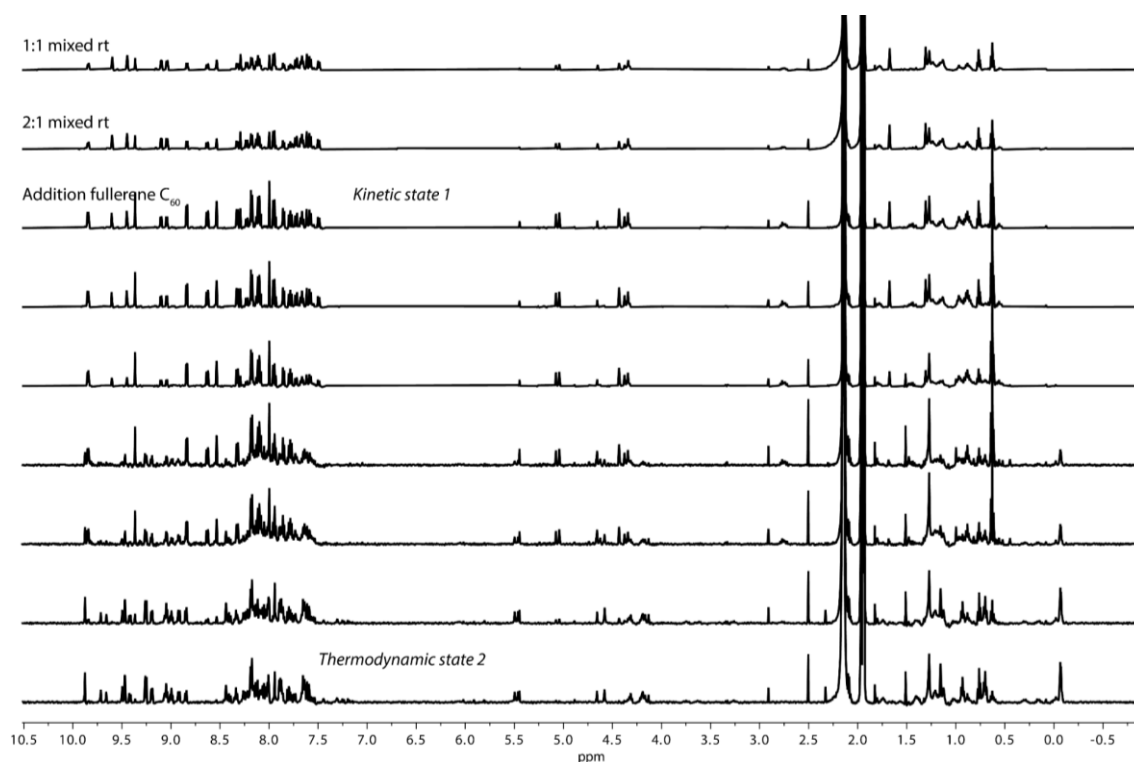


Figure 114: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) of the transformation process between $\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2$ and $\text{Pd}_2\text{B}_{12}\text{C}_{12}$ in presence of fullerene C_{60} .

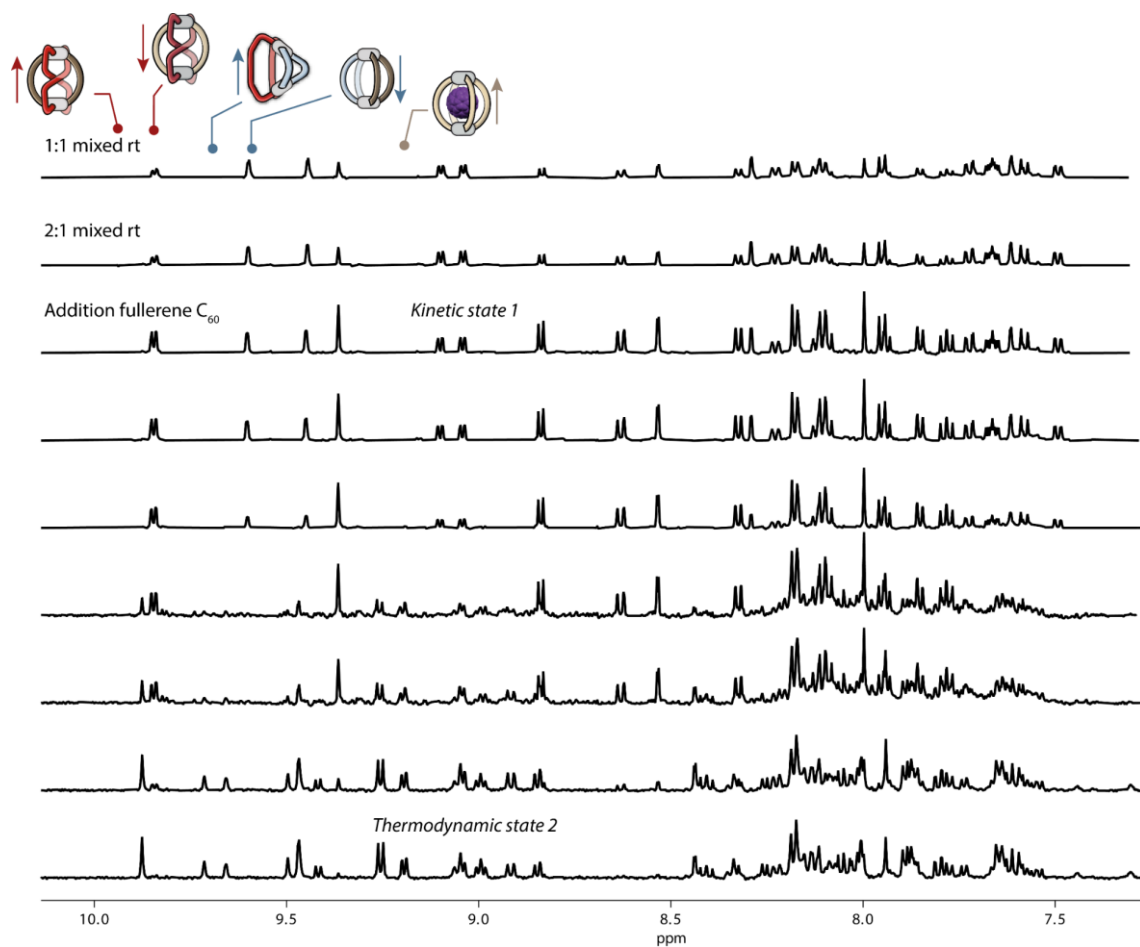


Figure S115: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the transformation process between $\text{Pd}_2\text{A}_2\text{BP}_2$ and $\text{Pd}_2\text{B}_{12}\text{C}_{12}$ in presence of fullerene C_{60} .

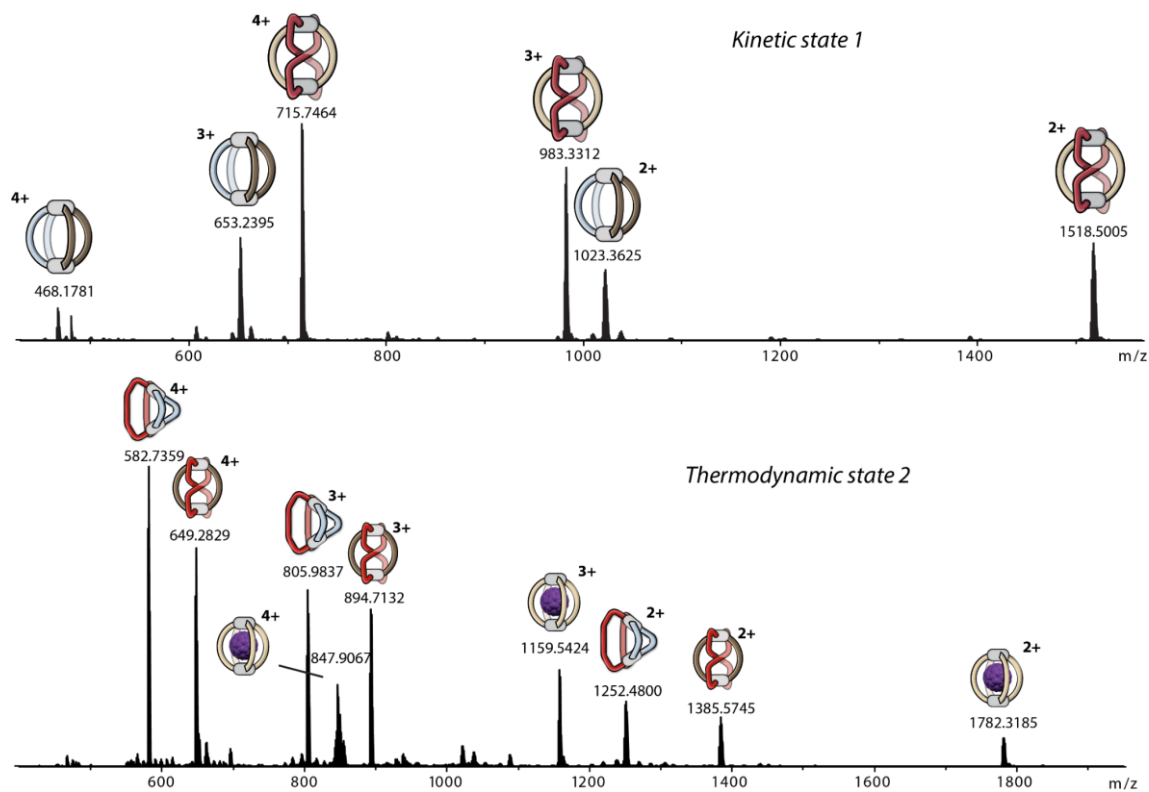


Figure S116: ESI-MS spectrum of a MeCN solution **State 1** and **State 2**. The observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{B}^{\text{P}}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ and $[\text{Pd}_2\text{B}_1\text{C}_1\text{C}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ for **State 1**. The observed peaks correspond to $[\text{Pd}_2\text{A}_2\text{B}_1\text{C}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$, $[\text{Pd}_2\text{A}_2\text{C}_1\text{C}_2 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ and $[\text{C}_{60}@\text{Pd}_2\text{B}^{\text{P}}_4 + n\text{BF}_4]^{(4-n)+}$ with $n=0-2$ for **State 2**.

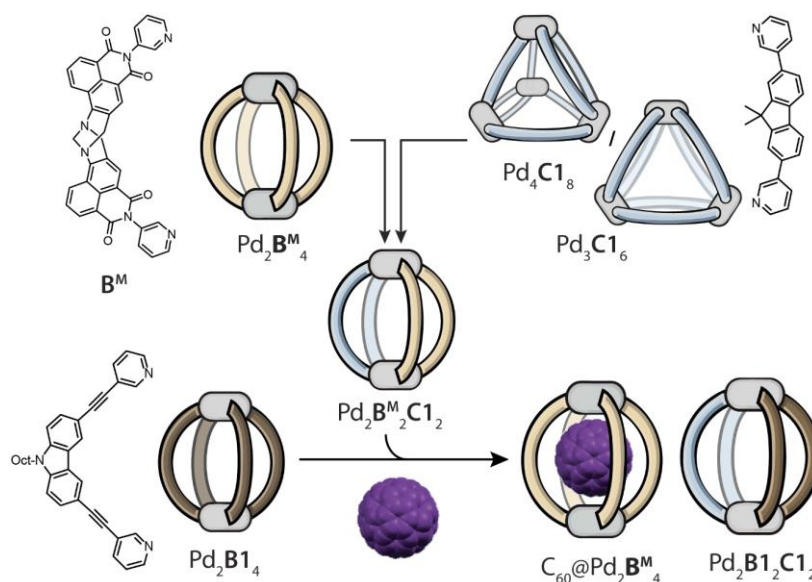


Figure S117: Schematic representation of the transformation process between $\text{Pd}_2\text{B}^{\text{P}}_2\text{C}_{12}$ and $\text{Pd}_2\text{B}_1\text{C}_4$ in presence of fullerene C_{60} .

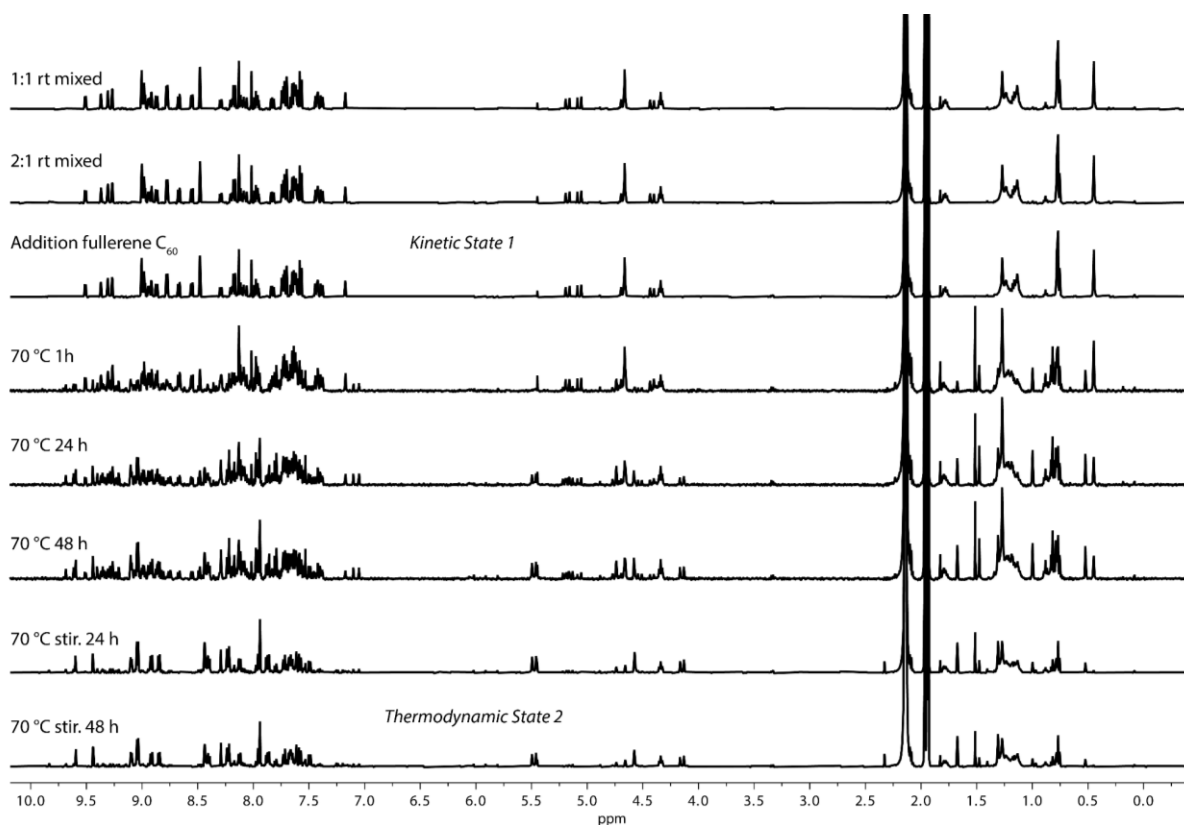


Figure 118: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) of the transformation process between $\text{Pd}_2\text{B}^{\text{P}}_2\text{C}_{12}$ and $\text{Pd}_2\text{B}_1\text{C}_4$ in presence of fullerene C_{60} .

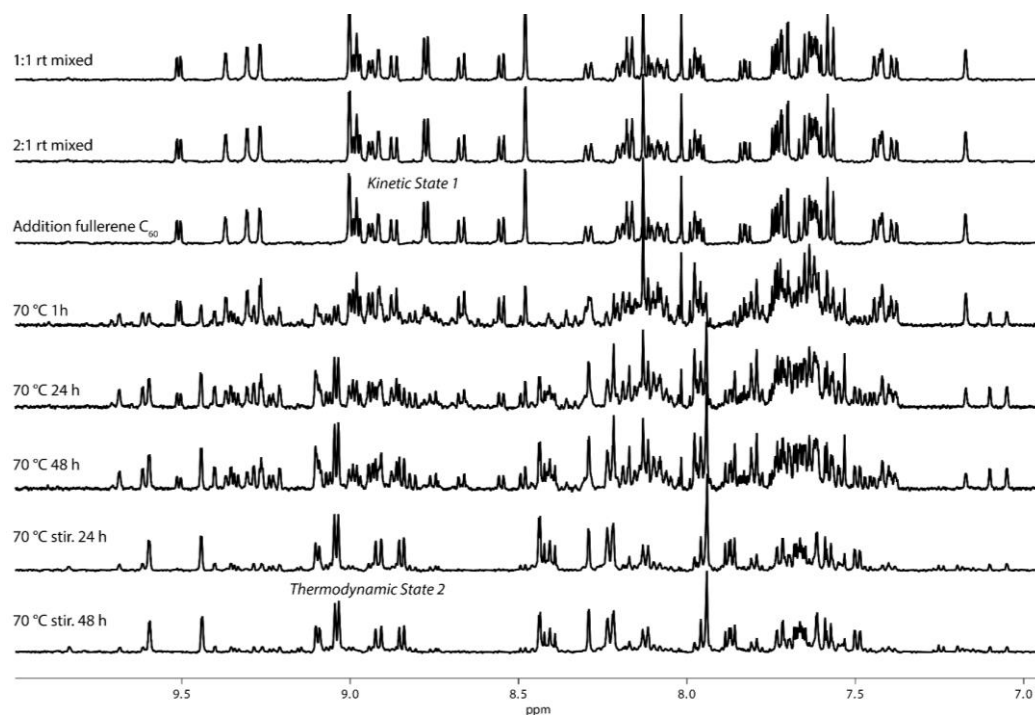


Figure S119: ^1H NMR spectra stack (500 MHz, 298K, CD_3CN) enlarged on the aromatic region of the transformation process between $\text{Pd}_2\text{B}^{\text{p}}_2\text{C}_{12}$ and Pd_2B_{14} in presence of fullerene C_{60} .

Photophysical Properties

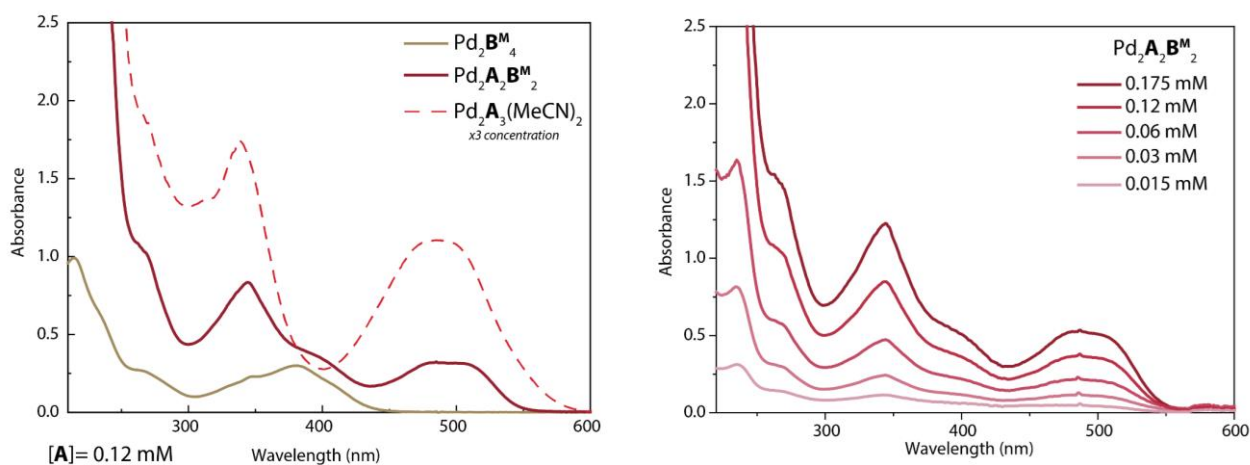


Figure S120: (left) UV-Vis spectra of $\text{Pd}_2\text{B}^{\text{M}}_4$, $\text{Pd}_2\text{A}_2\text{B}^{\text{M}}_2$ and $\text{Pd}_2\text{A}_3(\text{MeCN})_2$ in acetonitrile, 2 mm cuvette, 0.12 mM concentration in ligand. (right) concentration-dependent UV-Vis.

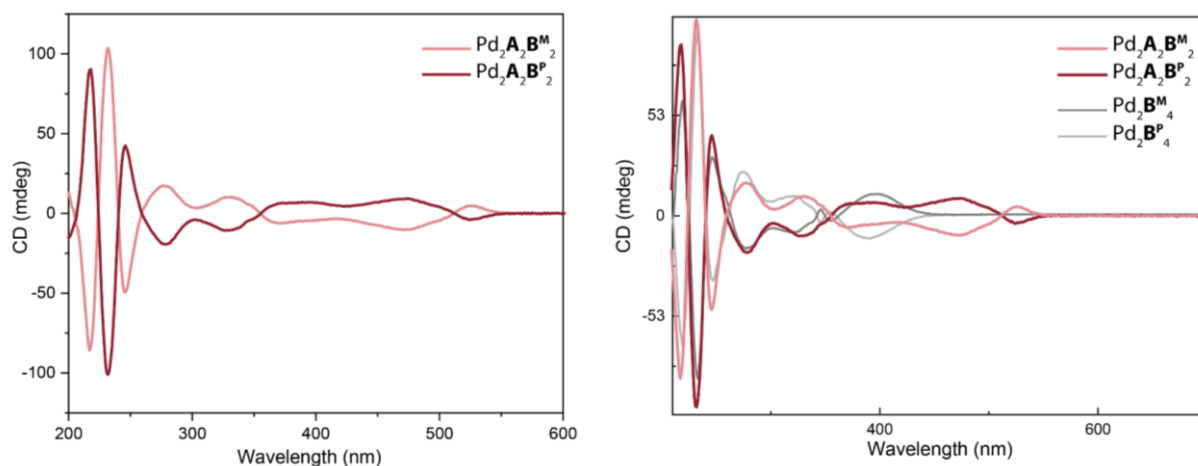


Figure S121: (left) CD spectra of the two diastereoisomers of the figure-eight $\text{Pd}_2\text{A}_2\text{B}_2^{\text{M}}$ and $\text{Pd}_2\text{A}_2\text{B}_2^{\text{P}}$ in acetonitrile, 2 mm cuvette, 0.12 mM concentration in ligand. (right) Stack of the two heteroleptic species with the corresponding homoleptic species $\text{Pd}_2\text{B}_4^{\text{M}}$ and $\text{Pd}_2\text{B}_4^{\text{P}}$.

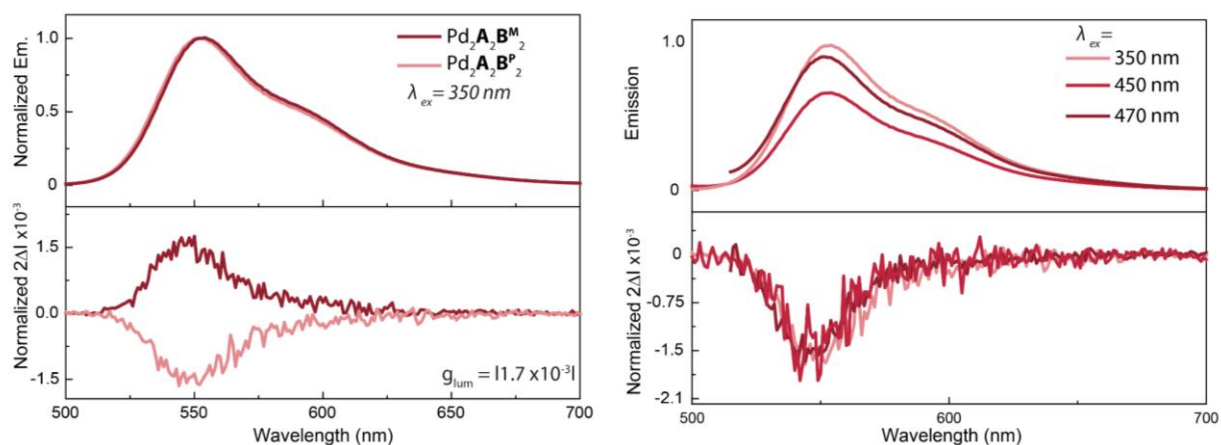


Figure 122: (left) Fluorescence and CPL spectra of the two diastereoisomers of the figure-eight $\text{Pd}_2\text{A}_2\text{B}_2^{\text{M}}$ and $\text{Pd}_2\text{A}_2\text{B}_2^{\text{P}}$ in acetonitrile, 2 mm cuvette, 0.12 mM concentration in ligand. (right) Stack of the Fluorescence and CPL spectra from $\text{Pd}_2\text{A}_2\text{B}_2^{\text{P}}$ excited at different wavelengths.

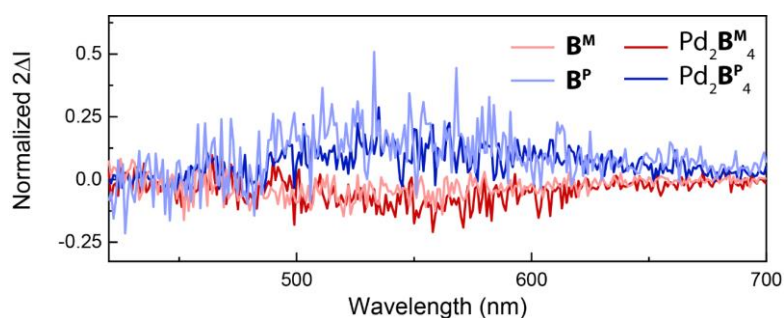


Figure S123: CPL spectra of the two enantiomers $\text{Pd}_2\text{B}_4^{\text{M}}$ and $\text{Pd}_2\text{B}_4^{\text{P}}$ and corresponding ligands in acetonitrile, 2 mm cuvette, 0.12 mM concentration in ligand.

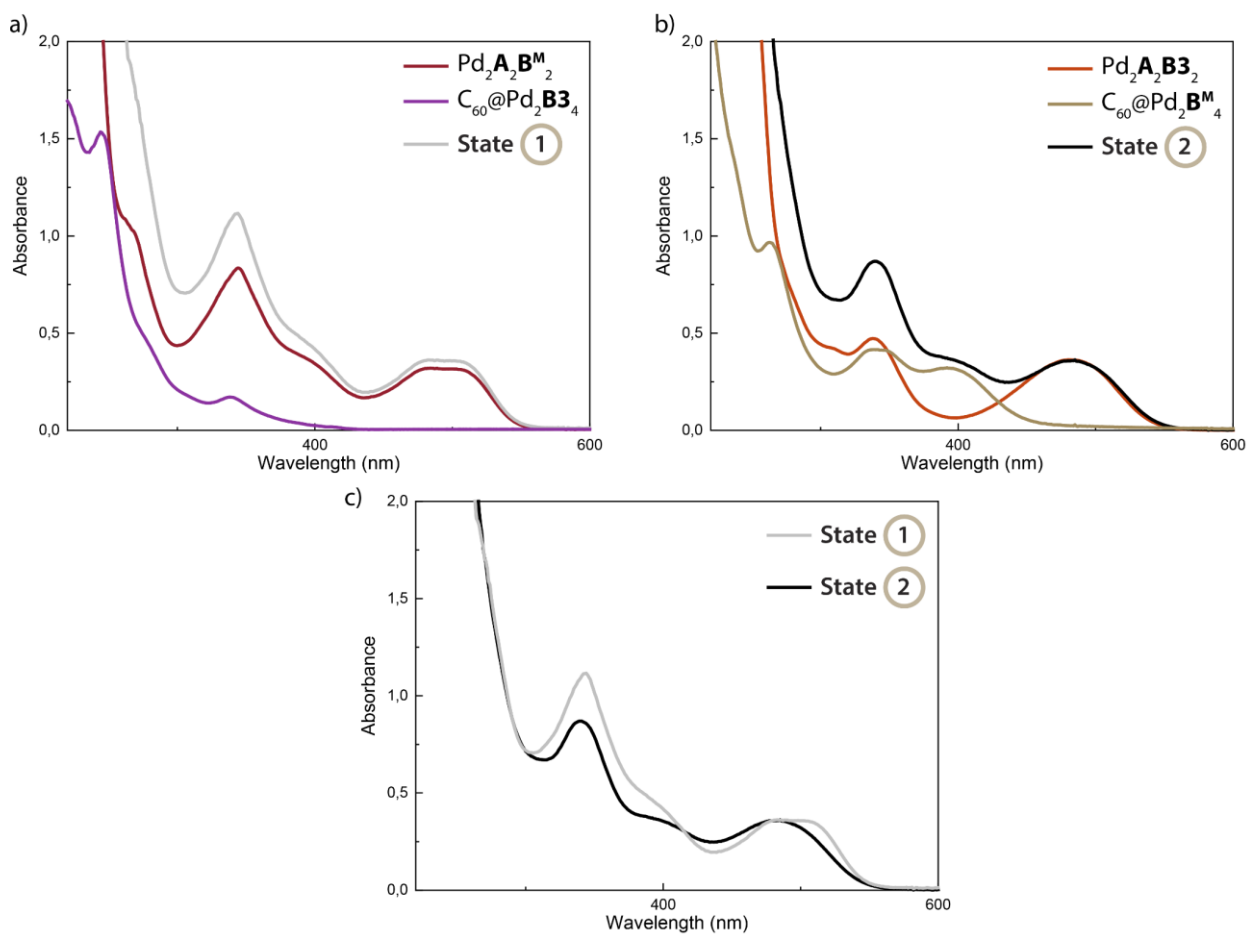


Figure S124: a) UV-Vis spectra overlap of **state 1** and its respective components. b) a) UV-Vis spectra overlap of **state 2** and its respective components. c) Overlap of **state 1** and **state 2** displaying their differences. Solvent= acetonitrile, 2 mm cuvette, 0.12 mM concentration in ligand.

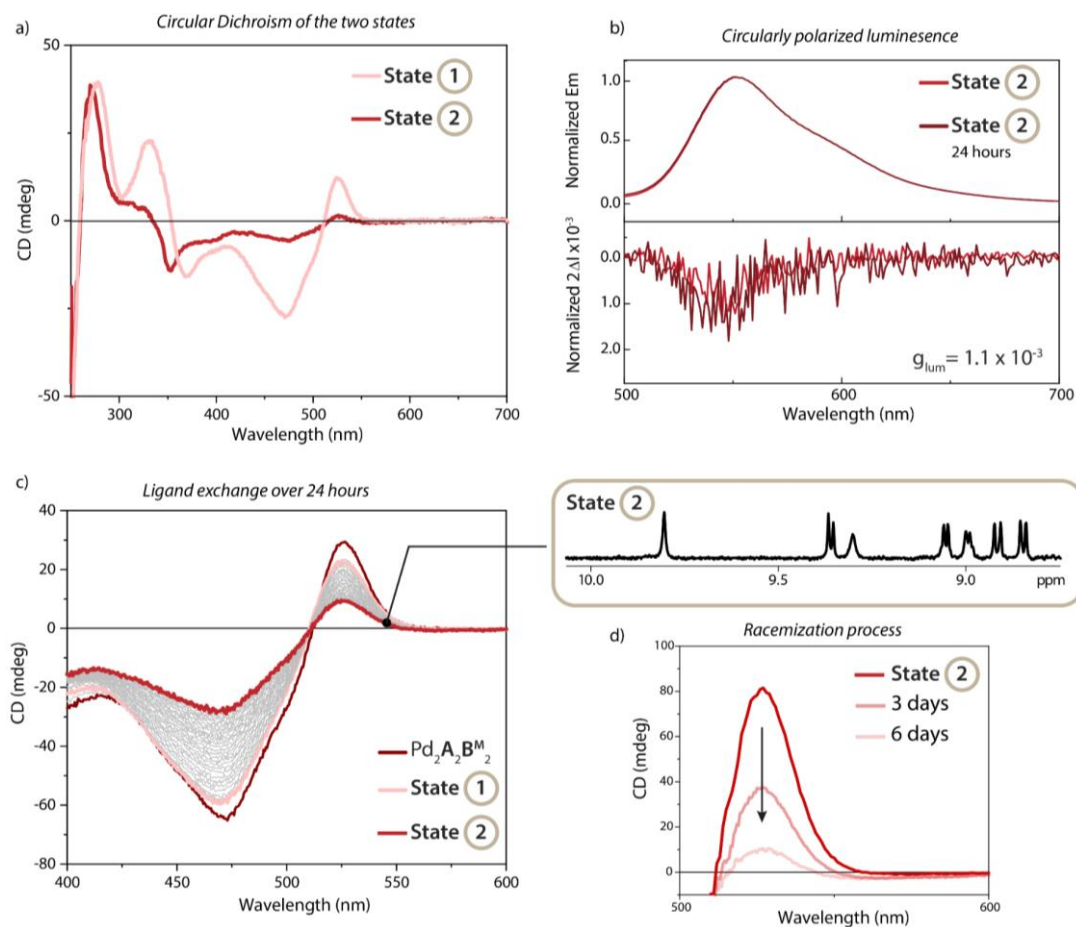


Figure S125: a) CD spectra of *state 1* and the resulting spectra after the conversion into *state 2*. 2 mm cuvette, 0.12 mM chromophore concentration. b) CPL spectra of *state 2* measured after CD and 24 hours resting at room temperature. Excitation at 350 nm. c) CD spectra following the transformation of *state 1* into *state 2*. The $\text{Pd}_2\text{A}_2\text{B}_2\text{M}_2$ spectrum is given as a reference. The inset highlights the ^1H NMR spectra of the system corresponding to the bright red curve where no trace of $\text{Pd}_2\text{A}_2\text{B}_2\text{M}_2$ can be detected. 2mm cuvette, 0.7 mM chromophore concentration. d) CD spectra of the racemization of the figure-eight over six days. 2 mM cuvette, 1.4 mM chromophore concentration.

Computational Studies Subsection 2

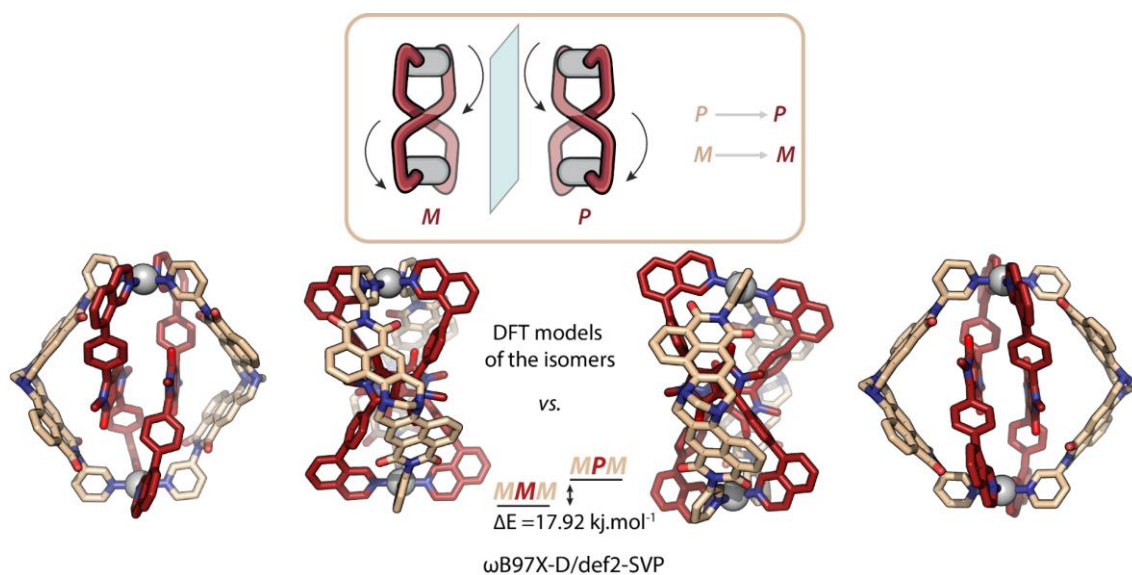


Figure S126: DFT ($\omega\text{B97X-D/def2-SVP}$) optimized structures and energies comparison between the two possible diastereoisomers of the chiral figure-eight. The outer ligand chirality dictates the δ chirality with B^{M} giving *M* and B^{P} giving *P*.

8. References

- [1] T. Weilandt, U. Kiehne, G. Schnakenburg, A. Lützen, *Chem. Commun.* **2009**, 0, 2320–2322.
- [2] U. Kiehne, T. Weilandt, A. Lützen, *Org. Lett.* **2007**, 9, 1283–1286.
- [3] A. Jarzebski, C. Tenten, C. Bannwarth, G. Schnakenburg, S. Grimme, A. Lützen, *Chem. Eur. J.* **2017**, 23, 12380–12386.
- [4] C. S. Arribas, O. F. Wendt, A. P. Sundin, C.-J. Carling, R. Wang, R. P. Lemieux, K. Wärnmark, *Chem. Commun.* **2010**, 46, 4381–4383.
- [5] U. Kiehne, T. Weilandt, A. Lützen, *Eur. J. Org. Chem.* **2008**, 2008, 2056–2064.
- [6] T. Weilandt, U. Kiehne, J. Bunzen, G. Schnakenburg, A. Lützen, *Chem. Eur. J.* **2010**, 16, 2418–2426.
- [7] J. I. Lovitt, D. Umadevi, P. R. Lakshmi, B. Twamley, T. Gunnlaugsson, S. Shanmugaraju, *Supramol. Chem.* **2021**, 1–14.
- [8] K. Matsumoto, S. Kusaba, Y. Tanaka, Y. Sei, M. Akita, K. Aritani, M. Haga, M. Yoshizawa, *Angew. Chem. Int. Ed.* **2019**, 58, 8463–8467.
- [9] T. Tsutsui, L. Catti, K. Yoza, M. Yoshizawa, *Chem. Sci.* **2020**, 11, 8145–8150.
- [10] K. Yazaki, S. Noda, Y. Tanaka, Y. Sei, M. Akita, M. Yoshizawa, *Angew. Chem. Int. Ed.* **2016**, 128, 15255–15258.
- [11] N. Kishi, Z. Li, K. Yoza, M. Akita, M. Yoshizawa, *J. Am. Chem. Soc.* **2011**, 133, 11438–11441.
- [12] M. Yamashina, T. Yuki, Y. Sei, M. Akita, M. Yoshizawa, *Chem. Eur. J.* **2015**, 21, 4200–4204.
- [13] Z. Li, N. Kishi, K. Hasegawa, M. Akita, M. Yoshizawa, *Chem. Commun.* **2011**, 47, 8605–8607.
- [14] Z. Li, N. Kishi, K. Yoza, M. Akita, M. Yoshizawa, *Chem. Eur. J.* **2012**, 18, 8358–8365.
- [15] S. Hasegawa, A. Baksi, B. Chen, G. H. Clever, *Org. Mater.* **2022**, 4, 222–227.
- [16] B. Chen, J. J. Holstein, S. Horiuchi, W. G. Hiller, G. H. Clever, *J. Am. Chem. Soc.* **2019**, 141, 8907–8913.
- [17] B. Chen, J. J. Holstein, A. Platzek, L. Schneider, K. Wu, G. H. Clever, *Chem. Sci.* **2022**, 13, 1829–1834.
- [18] X. Chang, Y. Xu, M. von Delius, *Chem. Soc. Rev.* **2023**, 53, 47–83.
- [19] G. D. Pantoş, J. Wietor, J. K. M. Sanders, *Angew. Chem. Int. Ed.* **2007**, 46, 2238–2240.
- [20] J. Kou, Q. Wu, D. Cui, Y. Geng, K. Zhang, M. Zhang, H. Zang, X. Wang, Z. Su, C. Sun, *Angew. Chem. Int. Ed.* **2023**, 62, e202312733.
- [21] S. Lo, T. Kitao, Y. Nada, K. Murata, K. Ishii, T. Uemura, *Angew. Chem. Int. Ed.* **2021**, 60, 17947–17951.
- [22] D. B. Straus, R. J. Cava, *Nano. Lett.* **2021**, 21, 4753–4756.
- [23] T. Kawauchi, J. Kumaki, A. Kitauro, K. Okoshi, H. Kusanagi, K. Kobayashi, T. Sugai, H. Shinohara, E. Yashima, *Angew. Chem. Int. Ed.* **2008**, 47, 515–519.
- [24] B. P. Bloom, Y. Paltiel, R. Naaman, D. H. Waldeck, *Chem. Rev.* **2024**, 124, 1950–1991.
- [25] I. S. Zlobin, Y. V. Nelyubina, V. V. Novikov, *Inorg. Chem.* **2022**, 61, 12919–12930.
- [26] A. V. Baskar, M. R. Benzigar, S. N. Talapaneni, G. Singh, A. S. Karakoti, J. Yi, A. H. Al-Muhtaseb, K. Ariga, P. M. Ajayan, A. Vinu, *Adv. Funct. Mater.* **2022**, 32, 202106924.
- [27] S. Hasegawa, S. L. Meichsner, J. J. Holstein, A. Baksi, M. Kasanmascheff, G. H. Clever, *J. Am. Chem. Soc.* **2021**, 143, 9718–9723.
- [28] W. M. Bloch, J. J. Holstein, W. Hiller, G. H. Clever, *Angew. Chem. Int. Ed.* **2017**, 56, 8285–8289.
- [29] I. Regeni, R. Chowdhury, K. Terlinden, S. Horiuchi, J. J. Holstein, S. Feldmann, G. H. Clever, *Angew. Chem. Int. Ed.* **2023**, 62, e202308288.
- [30] K. Wu, E. Benchimol, A. Baksi, G. H. Clever, *Nat. Chem.* **2024**, 16, 584–591.
- [31] N. Sieroka, T. Lossau, T. Neudecker, *Chem. Eur. J.* **2024**, 30, e202303868.
- [32] U. S. Bhalla, R. Iyengar, *Science* **1999**, 283, 381–387.
- [33] V. A. Seifert, *Commun. Chem.* **2022**, 5, 49.
- [34] J.-M. Lehn, *Chem. Soc. Rev.* **2007**, 36, 151.

Conclusion and personal perspectives

This dissertation has introduced a new concept to the field of coordination cages: the formation of cage populations. Although multiple cages could already coexist through *narcissistic* self-sorting, they were limited to homoleptic structures where no recognition/interplay between the different components (ligand) was taking place. Making heteroleptic species coexist necessitates both recognition between building blocks but also some sort of *narcissistic* exclusion between species, thus a higher degree of molecular information. Whether or not it will be possible to completely rationalize *heteromeric complete self-sorting* in the same way as *integrative self-sorting* for Pd(II) cages remains an open question. Further work on the combination of ligands as well as a deeper exploration of the influence of stoichiometry on sorting outcomes are needed. One could also envisage the coexistence of heteroleptic cages based on different metals and thus coordination modes or strategies. It might be that the recent advancements in heteroleptic Co(III) cages will find their way to this niche of the field and could potentially be orthogonally combined with Pd(II) cages. The logical next step will also be the study of more functional cage populations although this thesis has presented the premises of such systems. In a very fortunate way, most of the cages composing these populations contain one or more chromophores, some of them outstandingly retaining or combining their properties. It is therefore easy to foresee their use in orthogonal or cooperative *intra*-assembly processes within a population but obviously also in the exploration of *inter*-assemblies phenomena. Using these as exciton or electron transfer platforms for controlling reactions or other applications seems like the path to follow. This possible reaction control would also benefit from the ability to segregate substrates in specific cavities. The cage could be conceived as a sort of protecting group, a reservoir of reactant, or a stronger product binder in order to prevent side reactions, control the rate of reaction, catalyze a specific step or trigger a cascade. Many possibilities lie ahead.

Eventually, the last chapter of this dissertation might, at first, look heavy and could have been dissected in multiple ones with extended discussions. However, it contains the combinations of all the aspects I have developed and understood during my years as a PhD student. I started this journey with the wish of developing transformation networks similar to those described in the **General introduction** of this manuscript. I was also greatly interested in implementing photoswitchable ligands into such networks as light is a stimulus of choice for its controllability. Hard to admit that I did not manage the later part and somehow did not create either 'transformation networks' so to say. However, benefiting from numerous ligands both from the Clever lab members and collaborators, I slowly started exploring multiple combinations with a constant increase in the number of overall components. Among those ligands, the chiral ones definitely triggered my interest and the phenomenon of circularly polarized luminescence, brought to me by Dr. Jacopo Tessarolo, played an important role along the way. This last chapter is somehow composed of all of these little steps. Developing a chiral capsule with astonishing binding capabilities, mostly not presented in this thesis, and showing chiral induction on pristine fullerenes was the first one. Implementing this exact same ligand in my beloved DPP figure-of-eight and being able to create a chiral heteroleptic species displaying both CD and CPL was also an accomplishment. Eventually, the population transformation and chiral memory effect started mostly as what chemists would refer to as a "Friday afternoon experiment" and I would have not bet on such a neat process. The same remark applies to the final *transduction of signal* in the last subsection. The emergence of such properties coupled with the possibility of transient behaviors makes it an extremely complex system overall. While a considerable amount of work, mostly on studying the kinetics of the different phenomena, is still needed, this cage system has definitely stepped out of the traditional area explored to date and entered the field of system chemistry. It will stand as a proof of concept of the use of cages in such dynamic processes but will need to find further applications in the future. Again, if the fullerene guest of this system would be exchanged for a relevant reaction's substrate or if the process could be coupled to a more applied catalytic function, the system would attract greater interest.

Other scientific contributions

This dissertation has purposely focused only on my work on multi-cage systems. From this dissertation, one manuscript corresponding to the first part of **Chapter I** has been published but every subsection described corresponds to a manuscript in preparation (see (3) to (8) in the *in preparation* section of the publication list). However, as displayed in the list of publications I have contributed to or led several other works during the span of my Ph.D.

I have designed and written a published *Nature Chemistry* perspective summarizing the field of photoswitchable cages while foreseeing its future directions as one of the most exciting subfields for coordination cages. Similarly, helped by colleagues Laura Neukirch and Alexandre Walther, I have led and written a book-long review wrapping up the cages in which chromophores have been embedded and which can use light for different purposes such as electron or energy transfer, catalysis or (chiro)-optical recognition. This field has been vastly growing over the last years and the Clever Group has contributed to it through numerous works. This thesis has also presented a lot of this type of assembly.

In parallel to the works of this thesis, I published three other (co)-first-author papers which are not documented here. In the first one (***Chem. Commun.*** 2023, 59, 3467-3470), we reported ligand-to-ligand chiral induction in a $\text{Pd}_2\text{A}_2\text{B}_2$ cage and could observe both circular dichroism and circularly polarized emission on an otherwise non-chiral fluorenone chromophore. In a similar vein, we employed another fluorenone ligand and could demonstrate the formation of the first heteroleptic $\text{Pd}_3\text{A}_3\text{B}_3$ rings as well as $\text{Pd}_4\text{A}_4\text{B}_4$ saddle-like assemblies (***Angew. Chem. Int. Ed.***, 2024, DOI:10.1002/anie.202413323.). The $\text{Pd}_3\text{A}_3\text{B}_3$ rings were capable of encapsulating a chiral guest which led to guest-to-host chiral induction and allowed the observations of CD and CPL effects as mentioned above. Eventually, in the third paper (***Chem. Eur. J.*** 2024, DOI: 10.1002/chem.202401850), I employed a short acridone ligand showing a very high degree of conformational flexibility and allowing the formation of a wide range of architectures. Among those, an equilibrium between Pd_2L_4 helicate and mesocate was studied, a Pd_6L_{12} saw-toothed ring could be isolated in the solid state and finally heteroleptic cages featuring both diverging or converging binding vectors were obtained in association with the acridone ligand.

I also led and co-led two other studies for which the manuscripts are in preparation. In the first one, using a chiral ligand provided by Prof. Hosseini, I synthesized chiral heteroleptic trinuclear Pd(II) rings with an unprecedented $\text{Pd}_3\text{A}_2\text{B}_4$ topology and showed that the chirality of the ligands As can be transmitted to the ligands Bs within the assembly. Changing the ligands Bs for another set in which bulk has been installed enabled the formation of heteroleptic $\text{Pd}_4\text{A}_4\text{B}_4$ chiral tetrahedra which also show the chiral induction phenomenon. All those species demonstrated the possibility of binding chiral monosulfonate guests. In the second study, we created a chiral bis-monodentate ligand leading to an equilibrium between mono and double cage under a specific set of conditions. This is the first time such an equilibrium can be observed. It allowed us to study in depth the thermodynamics and kinetics of the equilibrium by using both temperature-dependent Van't Hoff analysis as well as pressure-dependent measurements. Multiple other stimuli could also be used to trigger the double to mono cage transformation and therefore this system stands as a complex transformation network.

I contributed to many works in collaboration with external groups which are not described in this manuscript. The first, with Prof. Nuernberger, was the study by time-resolved spectroscopy of the binding of guests within the cavity of a photoswitchable coordination cage (***Angew. Chem. Int. Ed.***, 2022, 61, e20221211) and how this event also affects the cage structure dynamics. I am part of a work in collaboration with the Nitschke Group on tetrahedral cages capable of changing their configuration upon guest binding. I measured solid-state CPL for the group of Prof. Lewandoski which has led to a first submitted manuscript and should also give a second one in the future. These measurements and the discussion around those systems allowed me to get a glimpse into material chemistry, which is drastically different from the science I conducted in Dortmund. I also contributed to CPL

measurements for the group of Prof. Stefankiewicz, and the study of host-to-guest chirality transfer in water-soluble coordination cages. To conclude on CPL collaborations, I have worked with Prof. Umakoshi both on chiral platinum and boron complexes.

In collaboration with Prof. Marc Sallé and Prof. Goebb from the University of Angers, I have helped Laura Neukirch and Jennifer Bou Zaid develop redox-responsive heteroleptic coordination cages and study the control of self-sorting upon stimulus application.

Eventually, I initiated two different collaborations to obtain photoswitchable stiff-stilbene, or so-called motor, ligands and study their implementation into heteroleptic cages. The first one was with Prof. Feringa, who provided us with a first-generation motor equipped with pyridine donors. I had started to explore the formation of cages with this ligand, but it was then mostly continued by Konstantin Jahn during his Bachelor Thesis under my supervision and we created the first heteroleptic cages bearing motor ligands. The second one was with Dr. Simon Krause who provided us a 2,7-fluorene-type motor. I synthesized the final ligand by installing pyridine moieties on it. Further work on heteroleptic assemblies was conducted mainly by Björn Schmidt with who I also strongly collaborated on other projects emerging from the use of Tröger base ligand(s).

List of abbreviations

AIBN	Azobisisobutyronitrile
AMBN	Azodi(2-methylbutyronitrile)
ATP	Adenine triphosphate
BODIPY	4,4-difluoro-4-bora-3a,4a-diaza-s-indacene
CD	Circular Dichroism
CPL	Circularly polarized light
CSE	Coordination sphere engineering
CV	Cyclic voltammetry
DA	Diels-Alder
DCM	Dichloromethane
DFT	Density functional theory
DMSO	Dimethylsulfoxide
DPP	Diketopyrrolopyrrole
DTE	Dithienylethene
ESI-MS	Electron spray ionization mass spectrometry
FRET	Forster resonance energy transfer
HOMO	Highest occupied molecular orbital
ICT	Intramolecular charge transfer
ISC	Intersystem-crossing
LUMO	Lowest occupied molecular orbital
MB	Methylene Blue
MeCN, CD ₃ CN	Acetonitrile and deuterated acetonitrile
NMR	Nuclear Magnetic resonance
PLQE	Photoluminescence quantum efficiency
SCA	Shape complementary assembly
TET	Triplet energy transfer
TREN	Tris(2-aminoethyl)amine
UV	Ultra-violet
VT	Variable temperature

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I want to thank Prof. Xavi Ribas for accepting to be part of the jury of my defense. I also need to thank him for the organization of the Girona Seminar 2024 in which I could, for the first time, stand on a big stage and give a talk in front of our community.

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I also have to give the right credit to all the external people I collaborated with. This manuscript might not show all the collaborations I created and made during my PhD but I benefited from amazing ligands, samples, measurements and discussions throughout my journey. I collaborated with scientists from all over the world, from Japan to Poland, from Ireland and Iceland to France and Spain, and from the US to India. That’s also one of the main reasons I am in love with Science.

And now come the more personal words. I am definitely smiling while writing those, as so many faces and memories come to my mind. But, as these are PhD thesis acknowledgments, I think that there are undeniably two people I have to start with, as all the work presented in this manuscript (but also myself) would have been different without them. I am so so so so so grateful for meeting my Italian “parents”, mentors, colleagues but most importantly friends: Jacopo and Irene, Irene and Jacopo; there is no order here. I am thankful for what you both brought to me, for taking me under your wings and for giving me all those projects! Ire, we clicked so much, both on the science and on the human level. From a discussion about a paragraph of your thesis that was supposed to “be a chem comm” to all that we have made together since. Thank you for your constant support and guidance, for your amazing friendship, for your unstoppable motivation and joy of life, for the random calls and the texts when we had hard times, for the trips in Leiden(bruuuuuuuudiiiiii) and everything else(there is too much). And Jaco, thanks for kicking my ass when I needed it, for pushing me and giving me trust in projects, but also for teaching me more and more stuff along the way. Thank you for all these discussions around beer, wine or food, for being a rugby fan with me and for all you have given me along this PhD. I looked and will continue to look up to both of you on my scientific journey.

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I am grateful for all the people I met during my time in Dortmund and around the world, and I will for sure have some in my head and my life for a long time. Some, more than others, have shaped my life and experiences on the way. Especially, grateful for meeting my dear Lea VdD, likely the kindest and most caring friend one can imagine but also an incredibly smart person and scientist. Lot of thoughts for Peter, Romana, Jasmin, Laurie, Andrea, Lukas my flatmates, and all the other people I won't cite here.

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To this little guy who wanted to understand the universe through theoretical physics, chemistry is not so bad.

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