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Exploring the Reactivity of Supramolecular Organometallic Complexes Based on Macrocyclic NHC Ligands

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If I had listened to the naysayers,
I would still be in the Austrian Alps yodeling.

— Arnold Schwarzenegger

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Abstract

Supramolecular coordination complexes (SCCs) are well-defined discrete structures that result from the directed self-assembly of metal ions and organic ligands. Their synthetic accessibility and modularity make them attractive platforms for functional applications, ranging from molecular sensing to catalysis. However, the broader utility of SCCs is often limited by the lability of conventional metal–ligand bonds used for their construction, especially under harsh reaction conditions or in the presence of competing ligands. The incorporation of *N*-heterocyclic carbene (NHC) ligands into supramolecular frameworks overcomes these limitations, as these ligands often form exceptionally stable metal–carbon bonds. This dissertation systematically explores design principles for introducing and controlling reactivity in supramolecular organometallic complexes (SOCs), with a particular focus on tubular pillarplexes, investigating two main sites of reactivity: the metal centers embedded within the cavitand walls and the electron-deficient macrocyclic rim.

The first major contribution demonstrates metal-centered reactivity through the synthesis of a Cu^{I}-based pillarplex, **[Cu$_8$L$_2$](OTf)$_4$**, based on a macrocyclic calix[4]imidazolylidene[2]pyrazolate ligand scaffold. This SOC exhibited endohedral guest binding driven primarily by metal–ligand coordination, as evidenced by the accommodation of tetrahydrofuran (THF). As a hydrophilic model substrate, THF was held within the pore through Cu–O interactions despite a significant steric mismatch between the pore and the guest. Electrochemical analysis of a mechanically interlocked rotaxane, **Rot[Cu$_8$L$_2$](OTf)$_4$**, revealed $Cu^{II/I}$ redox activity of the pillarplex, establishing this system as a synthetic mimic of multinuclear copper enzymes with potential for confined-space catalysis.

The second major contribution explores rim-centered reactivity arising from the electron-deficient pillarplex periphery. For this purpose, a [2]rotaxane, **[Fmoc*-Rot][Ag$_8$L$_2$](PF$_6$)$_4$**, was synthesized by threading an Ag^{I} pillarplex **[Ag$_8$L$_2$](PF$_6$)$_4$** onto a 1,12-diaminododecyl axle capped with bulky 2,7-^{t}Bu$_2$-9-fluorenylmethoxycarbonyl (Fmoc*) stoppers. Kinetic analysis revealed that the electron-deficient pillarplex rim significantly enhances the reactivity of the Fmoc* stoppers within the mechanically interlocked molecule (MIM), accelerating base-induced Fmoc* deprotection by 36-fold compared to a non-interlocked control. This rate enhancement is rationalized by preorganization of the ring and stopper components *via* directional CH–π interactions and hydrogen bonding, which expose the reactive site of the Fmoc* group for efficient deprotonation by piperidine. To generalize this behavior beyond the specific Fmoc*–pillarplex pairing, a structural rationale was established, introducing the concept of the *mechanosteric effect* to describe how

macrocycles can tune the reactivity of functional groups in MIMs. A *positive mechanosteric effect* denotes reactivity enhancement through spatial preorganization or electronic activation, while the inhibition of reactivity (*e.g.* by steric shielding) constitutes a *negative mechanosteric effect*.

In addition to the main projects of this dissertation, complementary studies highlight how the structure and functionality of the pillarplex platform can be controlled through targeted modifications. For example, replacing pyrazolate groups with triazolate units in the macrocyclic ligand led to the formation of a shape-adaptive pillarplex, $\mathbf{[Au_8L^t_2](PF_6)_4}$, with compressed portal openings in the solid state. In principle, this illustrates that the geometry of pillarplexes can be tuned through ligand design. Likewise, metal variation in SOCs enabled the introduction of photophysical functionality, as exemplified by the synthesis of a photoluminescent bimetallic Pt^{II} complex, $\mathbf{[Pt_2L](PF_6)_2}$, based on the established calix[4]imidazolylidene[2]pyrazolate ligand scaffold.

Zusammenfassung

Supramolekulare Koordinationskomplexe (SCCs) sind wohldefinierte, diskrete Strukturen, die sich durch die gezielte Selbstassemblierung von Metallionen und organischen Liganden bilden. Ihre synthetische Zugänglichkeit und Modularität machen sie zu attraktiven Plattformen für funktionelle Anwendungen – von der selektiven Erkennung von Molekülen bis zur Katalyse. Ihre breitere Nutzung wird jedoch oft dadurch eingeschränkt, dass die zugrunde liegenden Metall–Ligand-Bindungen unter harschen Reaktionsbedingungen oder in Gegenwart konkurrierender Liganden nicht stabil genug sind. Die Integration von *N*-heterocyclischen Carbenliganden (NHCs) in supramolekulare Strukturen überwindet diese Limitationen, da diese Ligandenklasse oft außergewöhnlich stabile Metall–Kohlenstoff-Bindungen ausbildet. Im Mittelpunkt dieser Arbeit steht daher die systematische Untersuchung der gezielten Einführung und Steuerung von Reaktivität in supramolekularen organometallischen Komplexen (SOCs), mit besonderem Fokus auf tubuläre Pillarplexe. Zwei Hauptreaktionszentren stehen dabei im Fokus: die in den Wänden des Kavitätsmoleküls eingebetteten Metallzentren sowie der elektronenarme Rand des Makrozyklus.

Der erste wesentliche Beitrag dazu demonstriert metallzentrierte Reaktivität durch die Synthese eines auf Cu^{I}-Ionen und einem makrozyklischen Calix[4]imidazolyliden[2]pyrazolat-Liganden basierenden Pillarplexes, **[Cu_8L_2](OTf)**. Dieser SOC kann Gastmoleküle endohedral, primär beruhend auf koordinativen Wechselwirkungen zwischen Metall und Liganden, binden – wie die Einlagerung von Tetrahydrofuran (THF) in die Pillarplex-Pore zeigt. Obwohl eine erhebliche sterische Inkompatibilität zwischen Pore und Gast besteht, wird das hydrophile Modellsubstrat THF durch Cu–O Wechselwirkungen in der Pore gehalten. Elektrochemische Untersuchungen an einem mechanisch verzahnten Rotaxan, **Rot[Cu_8L_2](OTf)$_4$**, belegen $Cu^{II/I}$-Redoxaktivität des Pillarplexes. Damit stellt dieses System ein synthetisches Analogon mehrkerniger Kupferenzyme dar und zeigt Potenzial für Katalyse in räumlich eingeschränkter Umgebung.

Ein weiterer zentraler Teil dieser Arbeit widmet sich der Reaktivität am elektronenarmen Randbereich von Pillarplexen. Zu diesem Zweck wurde ein [2]Rotaxan, **[Fmoc*-Rot][Ag_8L_2](PF_6)$_4$**, synthetisiert, indem ein Ag^{I}-basierter Pillarplex **[Ag_8L_2](PF_6)$_4$** auf eine 1,12-Diaminododecyl-Achse mit sterisch anspruchsvollen Fmoc*-Stoppern aufgefädelt wurde (Fmoc* = 2,7-$^{t}Bu_2$-9-fluorenylmethoxycarbonyl). Kinetische Analysen zeigten, dass der elektronenarme Rand des Pillarplexes die Reaktivität der Fmoc*-Stoppers im mechanisch verzahnten Molekül (MIM) deutlich erhöht: Die basenkatalysierte Fmoc*-Abspaltung verlief 36-mal schneller als in einer nicht-verzahnten Referenzverbindung. Diese Geschwindigkeitssteigerung beruht auf der präzisen räumli-

chen Anordnung von Ring und Stopper im Rotaxan, die durch gerichtete CH–π-Wechselwirkungen und Wasserstoffbrücken stabilisiert wird. Dadurch wird das reaktive Zentrum der Fmoc*-Gruppe für eine effiziente Deprotonierung durch Piperidin exponiert. Um dieses Phänomen über das spezifische Fmoc*–Pillarplex-System hinaus zu verallgemeinern, wurde ein strukturelles Konzept eingeführt, das den Begriff des *mechanosterischen Effekts* innerhalb mechanisch verzahnter Moleküle definiert. Ein *positiver mechanosterischer Effekt* beschreibt eine Reaktivitätssteigerung einer chemischen Funktionalität durch räumliche Präorganisation oder elektronische Aktivierung der beteiligten Komponenten, während ein *negativer mechanosterischer Effekt* durch Reaktivitätshemmung hervorgerufen wird (z. B. durch sterische Abschirmung).

Ergänzende Studien zu den beiden Hauptprojekten dieser Arbeit zeigen, wie sich Struktur und Funktionalität der Pillarplex-Plattform durch gezielte Modifikationen steuern lassen. So führte etwa der Austausch von Pyrazolat- durch Triazolat-Gruppen im makrocyclischen Liganden zur Bildung eines strukturell adaptiven Pillarplex, $\mathbf{[Au_8L^t_2](PF_6)_4}$, dessen röhrenförmige Struktur im Festkörper an den Rändern komprimiert ist. Das zeigt, dass die Geometrie von Pillarplexen durch Ligandendesign prinzipiell steuerbar ist. Ebenso ermöglichte die Variation der Metallzentren in SOCs die Einführung photophysikalischer Funktionalität, wie die Synthese eines photolumineszenten bimetallischen Pt^{II}-Komplexes, $\mathbf{[Pt_2L](PF_6)_2}$, auf Basis des etablierten Calix[4]imidazolyliden[2]pyrazolat-Liganden demonstriert.

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But I am very poorly today and very stupid and hate everybody and everything.

— Charles Darwin

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1 Introduction

1.1 Supramolecular Chemistry

1.1.1 Principles

The synthesis of molecules has been a cornerstone of chemistry for two centuries, with some of its key principles established already well before the advent of quantum mechanics and the modern understanding of chemical bonding. Molecular chemistry is fundamentally based on covalent bonds and provides a conceptual framework for linking the microscopic structure of a compound to its macroscopic properties.[1] In contrast, supramolecular chemistry extends beyond individual molecules to study the interactions that occur between them. Jean-Marie Lehn, a pioneer of the field, famously defined it as the "*chemistry beyond the molecule*",[2] concerned with the organization of two or more components into complex assemblies through non-covalent interactions. These include hydrogen bonding, π–π interactions, *van der Waals* forces, electrostatic interactions, metal–ligand coordination, and hydrophobic effects, all of which are individually weaker than covalent bonds.[3] It is through their cumulative effect that a combination of these forces give rise to structurally defined, stable and (often) functional supramolecular architectures.[3]

A key requirement for the formation of complex supramolecular assemblies is the presence of highly complementary structural features in the individual molecular components, enabling them to selectively associate through specific non-covalent interactions. The conceptual roots of this principle date back to 1894, when Emil Fischer proposed the "lock-and-key" model to describe enzyme–substrate interactions based on the geometric and chemical complementarity of the binding partners.[4] A seminal synthetic example of this *molecular recognition* is the discovery of crown ethers – cyclic molecules capable of selectively binding alkali metal ions of particular sizes (**Figure 1A**).[5] Since this landmark discovery, increasingly sophisticated host architectures based on macrocyclic platforms (so-called *cavitands*) have been developed to host small molecules and ions in high selectivity and efficiency (**Figure 1B**).[6-11] The majority of reported cavitands are cyclic oligomers based on organic building blocks with nanoscale shapes ranging from cage-like (*e.g.*

ExCage), to conical (*e.g.* calix[*n*]arenes) and tubular (*e.g.* pillar[*n*]arenes). Depending on the nature and number of included monomers, they vary in pore size and properties. These macrocyclic compounds can act as *receptors* (or *hosts*), designed to recognize and bind specific *substrates* (or *guests*). The reversible association between host and guest under equilibrium conditions to form a defined supramolecular *host–guest complex* is known as *self-assembly*. Such behavior is not limited to synthetic systems; it is a fundamental aspect of biological processes,[12] including protein–protein interactions and enzyme–substrate recognition.[2]

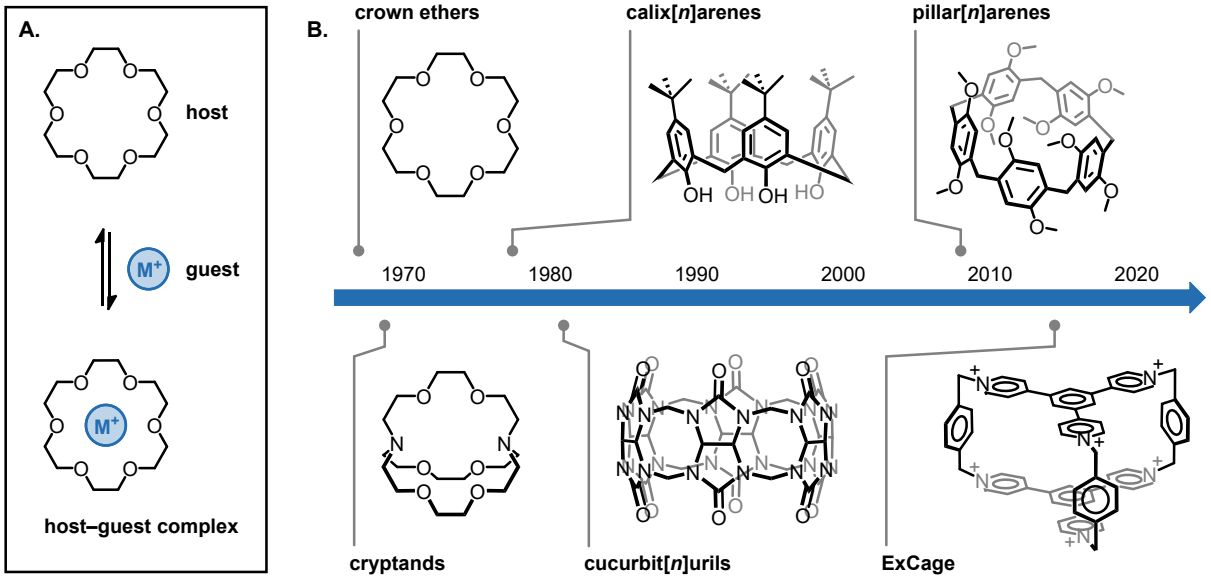

Figure 1 | **A**. Host–guest complex formation as exemplified by the self-assembly of a crown ether (*host*) and a metal ion (*guest*). **B**. Progression toward more complex macrocyclic host architectures within the last 50 years, illustrating the evolution of molecular recognition in supramolecular chemistry by harnessing non-covalent interactions.[7-11]

For a receptor and its substrate to bind effectively, they must exhibit complementarity on both steric and electronic levels.[2,6] This complementarity is encoded in the molecular features of the binding sites of the interacting molecules, which are defined by geometric properties (*e.g.* shape, size, and spatial arrangement) and electronic characteristics (*e.g.* charge, polarity, and polarizability).[6] Although individual non-covalent interactions are weak compared to covalent bonds, the presence of multiple, strategically positioned interaction sites can result in strong and selective binding.[6] This interplay enables the formation of complex supramolecular structures by assembly of multiple discrete components.[6]

One of the defining characteristics of supramolecular systems is their dynamic and reversible nature. Efficient and selective binding between components often relies on the preorganization of their structure by optimizing enthalpic stabilization, while minimizing entropic penalties associated with self-assembly.[1] The balance between enthalpic stabilization and entropic cost is central to highly selective guest binding, enabling systems to discriminate between closely related guests.[13] Targeted molecular recognition, in turn, enables applications in separation techniques,[14-16] molecular reaction vessels,[17-18] and specialized drug carriers.[19]

Moreover, the dynamic behavior of supramolecular systems allows them to adapt to external stimuli (*e.g.* pH, light, temperature), making them inherently *responsive* and *tunable*. These properties form the basis for numerous applications across chemical sensing,[20-21] catalysis,[22-23] drug delivery,[24-26] and materials science,[27-29] where reversible molecular recognition governs both structure and function.[3,30]

1.2 Metallosupramolecular Chemistry

1.2.1 Principles

In the broad context of supramolecular chemistry, metal ions play a key role as adaptable building blocks for creating self-assembled structures. Metallosupramolecular systems are formed through the specific interactions of metal ions and organic ligands with complementary metal binding sites.[31] While weaker forces such as hydrogen bonding and π–π interactions typically still contribute to the overall structure, metal–ligand coordination is the dominant organizing force for assembly. The strength of coordinative bonds (typically < 200 kJ/mol) strikes a balance between the robustness of covalent bonds and the reversibility of weaker non-covalent interactions.[32] Metal–ligand bonds are thus strong enough to provide structural stability but are cleaved readily enough to enable the dynamic behavior necessary for thermodynamically controlled self-assembly and error correction. This directional and tunable nature of coordination enables precise geometric control over the resulting supramolecular structures.

The modularity of this *coordination-driven self-assembly* has led to the systematic exploration of increasingly complex metallosupramolecular architectures, ranging from discrete supramolecular coordination complexes (SCCs) to extended coordination networks (**Figure 2**).[33] The key consideration is whether the combination of building blocks leads to convergent or divergent assembly pathways. Metal ions hereby act as structure-directing elements with well-defined coordination geometries, ranging from square planar (*e.g.* Pd^{II}, Pt^{II}), octahedral (*e.g.* Fe^{II}, Co^{II}, Ru^{II}), and tetrahedral (*e.g.* Zn^{II}) to linear (*e.g.* Ag^{I}, Au^{I}). The geometric constraints imposed by a specific metal ion dictate the overall shape, size, and properties of the resulting supramolecular assembly (**Figure 2**). Likewise, the organic ligands function as linkers with specific encoded angular information to direct the self-assembly process toward a desired geometric outcome.[31,34] Through careful selection of complementary building blocks with appropriate geometries, precise control over the thermodynamic stability of the resulting assemblies may be achieved – in many cases yielding a single product, provided that it is considerably lower in energy than others.[31]

When metals and ligands are combined in a geometrically divergent manner, they can give rise to extended coordination polymers (CPs). These extended structures are defined by bridging ligands that connect metal nodes into one-dimensional chains or further into two- or three-dimensional networks.[35] Among the broad variety of coordination polymers, metal-organic frameworks (MOFs), in particular, have attracted significant attention due to their promising applications in areas such as gas storage,[36-37] molecular separation,[38] and catalysis.[39-40]

Discrete metallosupramolecular platforms are formed by convergent metal–ligand combinations, giving rise to well-defined two-dimensional structures such as polygons (*e.g.* triangles, squares,

rectangles, and hexagons), and three-dimensional polyhedra (*e.g.* tetrahedra, cubes, octahedra, prisms) (**Figure 2**).[41-42] The outcome is influenced not only by the intrinsic coordination preferences of the metal centers and the spatial constraints of the ligands but also by external factors such as concentration, temperature, and solvent (polarity). Through precise control over these parameters, vastly different shapes, including helicates,[43] coordination cages,[44] and capsules,[45] can form.

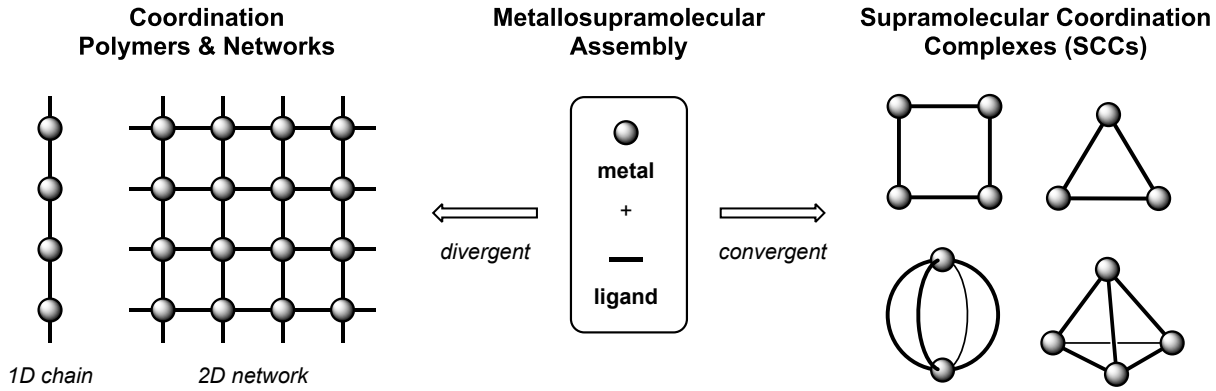

Figure 2 | Schematic illustration of metallosupramolecular assemblies: Coordination polymers and extended networks formed *via* divergent combinations of metal centers and organic ligands (left), and discrete supramolecular complexes (SSCs) from convergent metal–ligand bonding (right). Both building blocks encode specific angular constraints that govern the overall geometry.[31] (Adapted from A. Pöthig and A. Casini, *Theranostics* **2019**, *9*, 3150. © 2019 Pöthig and Casini. Licensed under CC BY-NC 4.0. Changes were made to the original.)

1.2.2 Structural Overview of SCCs

Owing to the structural diversity of organic ligands and the well-defined coordination preferences of many transition metal ions, a wide range of SCCs with diverse geometries have been developed (**Figure 3B**). Among the earliest examples are binuclear Cu^{II} macrocycles based on a bis(*β*-diketone) ligand, reported by Maverick and Klavetter in the 1980s.[46-47] Already at the time of their discovery, these SCCs were recognized for the ability to engage in host–guest chemistry, reminiscent of organic cavitands. Since then, a variety of SCCs with tailored geometries have been reported, guided by the synthetic strategies outlined below.

Conceptually, the synthesis of SCCs follows either a *face*-directed or *edge*-directed approach.[48] Illustrative examples of *face*-directed assemblies include metallorectangles introduced by the Fujita group, which consist of planar bipyridyl ligands that coordinate to convergently oriented metal centers, forming the faces of supramolecular polygons.[49] Conversely, in the *edge*-directed strategy developed by Stang and co-workers,[50-51] bent bidentate pyridyl ligands are employed as the building blocks that define the edges of the assembly,[33] typically bound to Pd^{II} or Pt^{II} ions as structure-directing counterparts.[52] Raymond and co-workers advanced both approaches by investigating the dynamic behavior,[53] chirality,[54-55] and catalytic properties[56-57] of SCCs.[33] Additionally, with the concept of "*subcomponent self-assembly*",[58] the Nitschke group introduced an efficient method in which ligand formation occurs *in situ*. For example, imine condensation of aldehydes and amines enabled the straightforward assembly as well as covalent post-synthetic

functionalization of SCCs.[59] A remarkable demonstration of the scalability of *coordination-driven assembly* is the synthesis of a '$Pd_{48}L_{96}$' cage by Fujita and co-workers,[60] which to date is the largest known discrete polyhedral SCC obtained *via* the *edge*-directed approach.

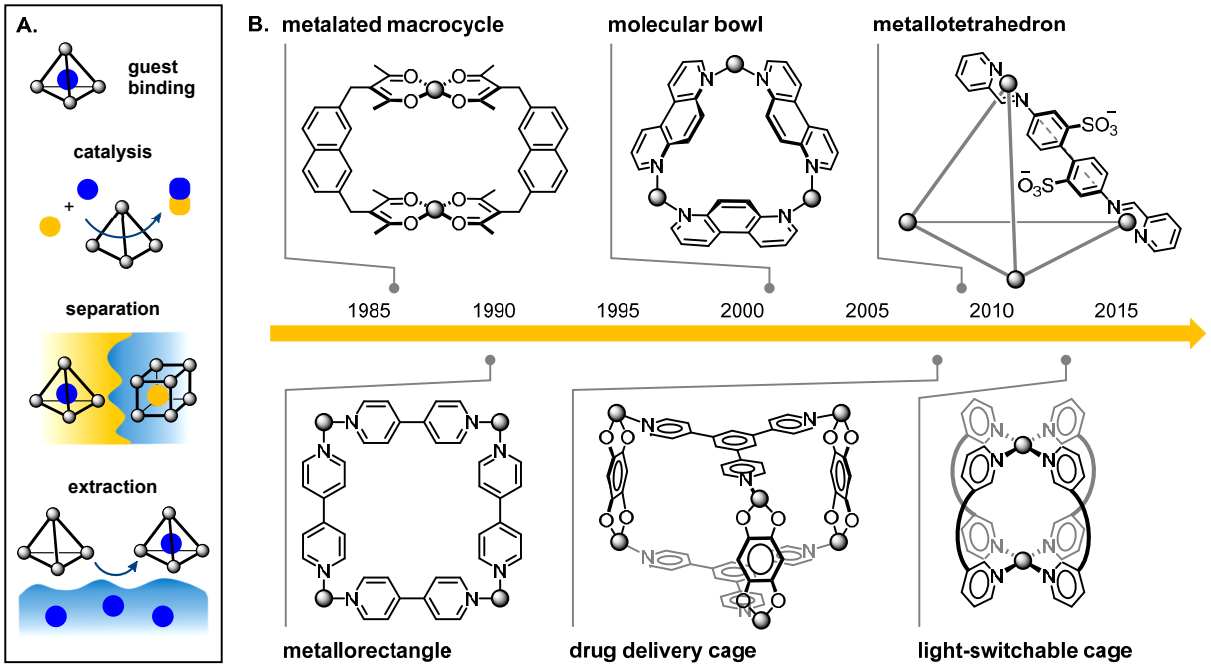

Figure 3 | **A**. Overview of selected applications of supramolecular coordination complexes (SCCs). **B**. Schematic illustration of representative SCCs,[47,61-65] highlighting structural and functional complexity. Capping ligands coordinated to the structure-directing metal ions, as well as capping ligands and certain parts of the organic linkers (black or grey lines) are omitted for clarity.

1.2.3 Reactivity in SCCs

A defining structural feature of many SCCs is an internal cavity capable of encapsulating guest molecules. Paired with the ability to selectively bind the guests through a combination of non-covalent interactions, SCCs are inherently well-suited to function as reactive synthetic receptors.[44] Thus, they are typically applied in molecular recognition and sensing, stabilization of reactive species, and catalysis (**Figure 3A**).[58] In this context, a key advantage of SCCs lies in the tunability and modularity of their structure, allowing selective substrate uptake and efficient product release within the confined space of the cavity.[44] In some cases, SCCs have even been shown to accommodate geometrically mismatched guests by undergoing reversible structural deformations to adapt the pore dimensions accordingly without cleaving metal–ligand bonds.[66] Moreover, certain SCCs are inherently chiral, offering a platform for enantioselective catalysis.[67-68] Complementing this, the embedded metal ions may even add functionality beyond structurally defining the metallosupramolecular assembly: Due to their positive charge, they can stabilize reactive intermediates through electrostatic interactions, introduce photochemical activity,[69-70] or function as Lewis acids if the metal is accessible for further coordination.[71] Taken together, these

characteristics position SCCs as synthetic analogs to enzymatic catalysts, as both systems facilitate chemical transformations through proximity effects, discrimination between substrates (including different isomers), and highly specific modulation of reactivity.[72]

To design reactive SCCs with such desirable catalytic properties, two principal strategies have been developed. In the first approach, a component with *intrinsic* catalytic activity is incorporated into the scaffold of the SCC.[44] Metal–porphyrins are often employed in this context as they are versatile synthetic building blocks. In such systems, catalysis is an *enhanced* property within the cavity of the SCC.[44] This can be achieved by steric shielding, regulation of substrate access, tuning of reactivity through spatial confinement, or cooperative and synergistic effects based on multiple active sites brought into proximity within the cavity.[44,72] Catalysis may occur either inside the cage or at its portals, depending on how the active sites are positioned.[44]

An alternative strategy relies solely on the geometric and chemical properties of the assembled SCCs, even though neither the isolated constituent metal centers nor the ligands show any intrinsic catalytic activity.[44] Rather, catalysis can be considered an *emergent* property resulting from substrate preorganization, stabilization of intermediates, or transition states within a highly defined cavity.[44,72] This behavior parallels enzyme catalysis, wherein most individual amino acids show no catalytic potential on their own, yet highly effective catalysis emerges from creating a functional confined space through protein folding.[44]

Both design approaches have been employed successfully over the past decades, enabling reactive SCCs to mediate a variety of chemical transformations. A schematic overview of some representative reaction types catalyzed by SCCs is shown in **Figure 4**, including the transformation of a single substrate, coupling of two substrates, as well as cleavage of one substrate to two products, and functional group transfer *via* a shared intermediate or transition state.

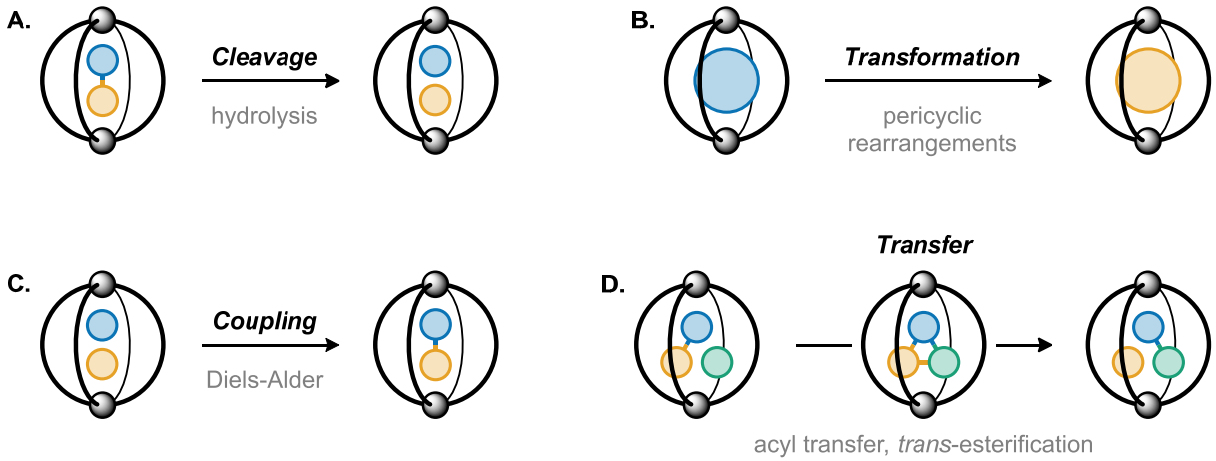

Figure 4 | Schematic overview of selected reaction types mediated by supramolecular coordination complexes (SCCs): **A**. substrate cleavage, **B**. transformation of a single substrate, **C**. coupling of two substrates, **D**. transfer of functional groups between substrates *via* a shared intermediate or transition state.[44,73] (Adapted from T. K. Piskorz, V. Martí-Centelles, R. L. Spicer, F. Duarte, and P. J. Lusby, *Chem. Sci.* **2023**, *14*, 11300. © 2023 The Royal Society of Chemistry. Licensed under CC BY-NC 3.0. Changes were made to the original.)

Interestingly, despite the vast number of SCCs reported over the past decades, only a few platforms have been explored extensively for catalysis. Apart from functionalized SCCs with large pores constructed from components with inherent catalytic activity, many studies have focused experimentally on unfunctionalized SCCs with small pores.[44,50,56,72,74] Although these systems are structurally diverse and often unrelated, they share a defining characteristic: the presence of relatively small, well-defined cavities capable of precisely orienting substrates, intermediates, or even transition states. The following section presents a few selected examples of such SCCs that highlight their architectural and catalytic features.

The development of SCC-based catalysis was significantly shaped by the pioneering efforts of the Fujita group. One of the key contributions was demonstrating how encapsulation in $[Pd_6L_4]$ cages can accelerate chemical transformations by co-encapsulation of reactants in confined, hydrophobic cavities.[75-80] This approach proved especially effective for apolar substrates such as dienes and dienophiles, which exhibit increased binding affinity in water, leading to substantial rate enhancements in cycloaddition reactions.[75-80] A distinctive feature of Fujita's $[Pd_6L_4]$ cages is their ability to control regioselectivity through spatial confinement. For instance, encapsulated anthracenyl dienes undergo Diels–Alder reactions that selectively yield the unusual 1,4-regioisomer, contrasting with the typical 9,10-product seen in bulk solution (**Figure 5**, top).[76] Though these Pd^{II}-based SCCs are generally achiral, they can still influence stereochemical outcomes. A notable example is the photochemical [2+2] dimerization of 1-methylacenaphthylene, which occurs exclusively in the head-to-tail *syn*-configuration within the $[Pd_6L_4]$ cavity, in contrast to the isomeric mixture obtained without the SCC (**Figure 5**, bottom).[81]

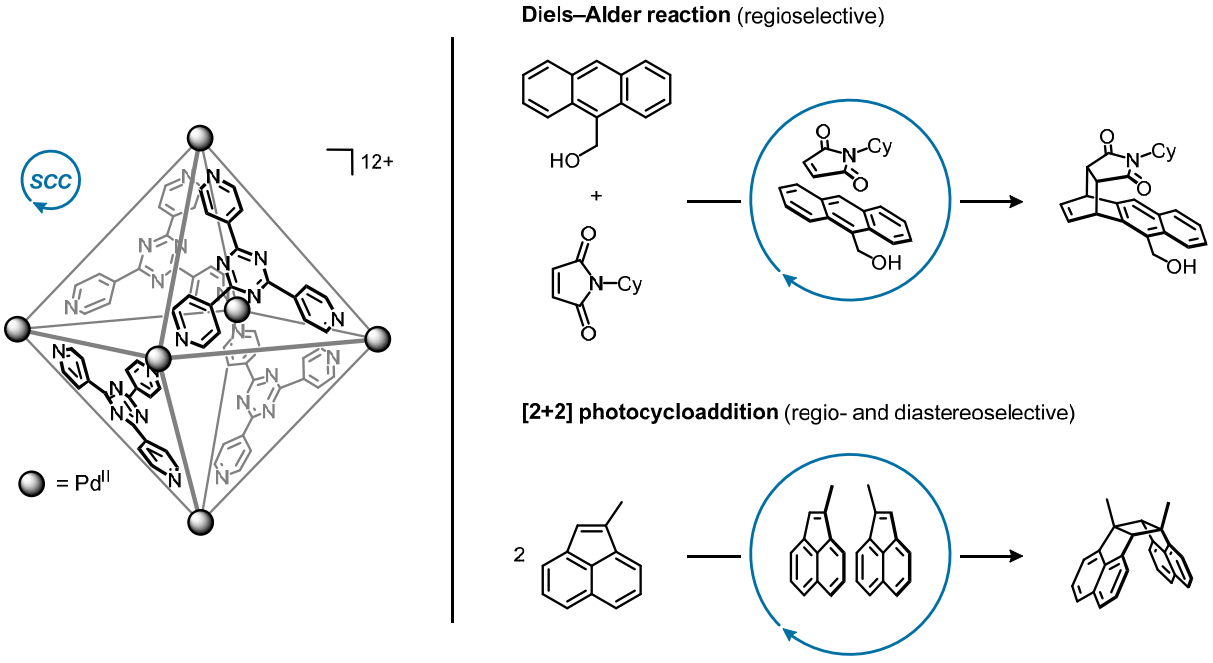

Figure 5 | Reactivity control enabled by substrate encapsulation within a $[Pd_6L_4]$ metallooctahedron. Top: Regioselective Diels–Alder reaction of 9-anthracenemethanol with *N*-cyclohexylmaleimide, yielding the atypical 1,4-adduct.[76] Bottom: *Syn*-selective photodimerization of 1-methylacenaphthylene, driven by spatial confinement inside the cage.[81]

Another early example of a SCC-based catalyst is a [Ga_4L_6] tetrahedron developed by Raymond and Bergman, which has since become one of the most extensively studied SCC catalysts.[82-83] This anionic, water-soluble Ga_4L_6 cage provided a fundamentally different catalytic environment than Fujita's [Pd_6L_4] cage, defined by a compact, highly charged cavity resembling organic capsules. The cage has served as a prototypical platform for exploring *constrictive binding catalysis*, where flexible substrates are forced into reactive conformations within the cavity of the SCC.[44] Its well-defined structure, strong binding affinity for cationic guests, and ability to stabilize reactive intermediates have made it a foundational system for elucidating both entropic and enthalpic contributions to supramolecular reactivity.[44,84]

The concept of *constrictive binding catalysis* as an entropic effect in the context of SCCs was first demonstrated in the *aza*-Cope rearrangement of diene-enammonium cations (**Figure 6**, top).[82] Catalytic turnover was enabled by endohedral hydrolysis of the iminium intermediate to a neutral aldehyde, which readily dissociates. Owing to the rigid cavity of the [Ga_4L_6] cage, catalysis depends critically on the size and shape of the substrate. Smaller or overly flexible molecules benefit less from the enforced preorganization, resulting in minimal rate enhancement.[82] Constrictive binding has since been extended to other reactions, including the Nazarov reaction (**Figure 6**, middle),[85] and (*aza*-)Prins cyclization (**Figure 6**, bottom).[86-87] In these cases, rate enhancement also arises from enthalpic contributions, specifically electrostatic stabilization of charged intermediates within the negatively charged SCC.[44]

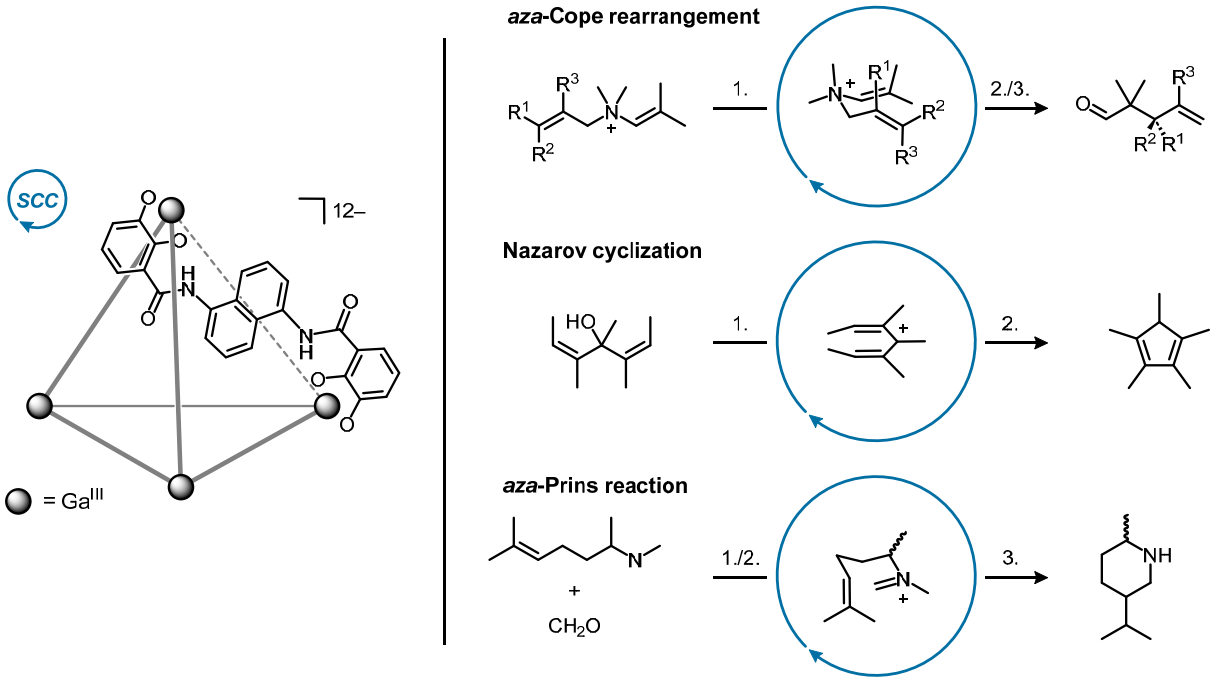

Figure 6 | Selected reactions catalyzed by a [Ga_4L_6] metallotetrahedron *via* constrictive binding. Top: *Aza*-Cope rearrangement of diene-enammonium cations (1. Substrate folding, 2. [3,3]-Sigmatropic shift, 3. Hydrolysis).[82] Middle: Nazarov cyclization facilitated by entropic and electrostatic stabilization (1. Substrate Folding and Cationic stabilization, 2. 4π-Electrocyclization).[85] Bottom: *Aza*-Prins reaction within the cavity of the anionic SCC.[87]

Beyond entropic preorganization, SCCs can also catalyze reactions by stabilizing high-energy intermediates *via* enthalpic interactions.[44] This is particularly valuable for transformations that proceed through charged species. For instance, Raymond's [Ga_4L_6] metallotetrahedron catalyzes the reductive elimination of organometallic complexes like [$(R_3P)Au^{III}(CH_3)_2$] by stabilizing a cationic Au^{III} intermediate within the anionic cage (**Figure 7**).[88] The reaction proceeds through halide dissociation, followed by encapsulation of the reactive intermediate, which then undergoes rapid reductive elimination. Steric tuning of the phosphine ligands proved critical, with intermediate-sized substituents favoring optimal encapsulation and reactivity.[88]

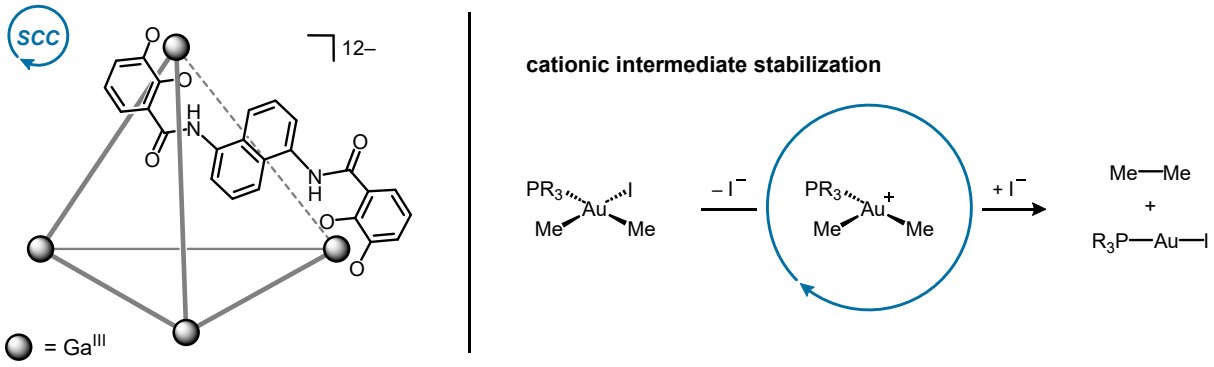

Figure 7 | Reductive elimination of an Au^{III} complex catalyzed by a [Ga_4L_6] metallotetrahedron through electrostatic stabilization of a cationic intermediate. The anionic cavity stabilizes a reactive Au^{III} intermediate formed after halide dissociation from [$(R_3P)Au^{III}(CH_3)_2$], promoting rapid reductive elimination.[88]

While anionic cages have proven highly effective for stabilizing cationic intermediates, analogous reactivity in cationic cages is less developed. Several limitations contribute to this asymmetry: 1) anions are generally hard to desolvate, 2) cation–π interactions between guests and the flat aromatic ligands constituting many SCCs are more stabilizing than anion–π interactions, and 3) strongly coordinating anions may disrupt the SCC's constituent metal–ligand bonds.[44] Despite this, cationic SCC catalysts stabilizing anionic species have been reported (**Figure 8**).

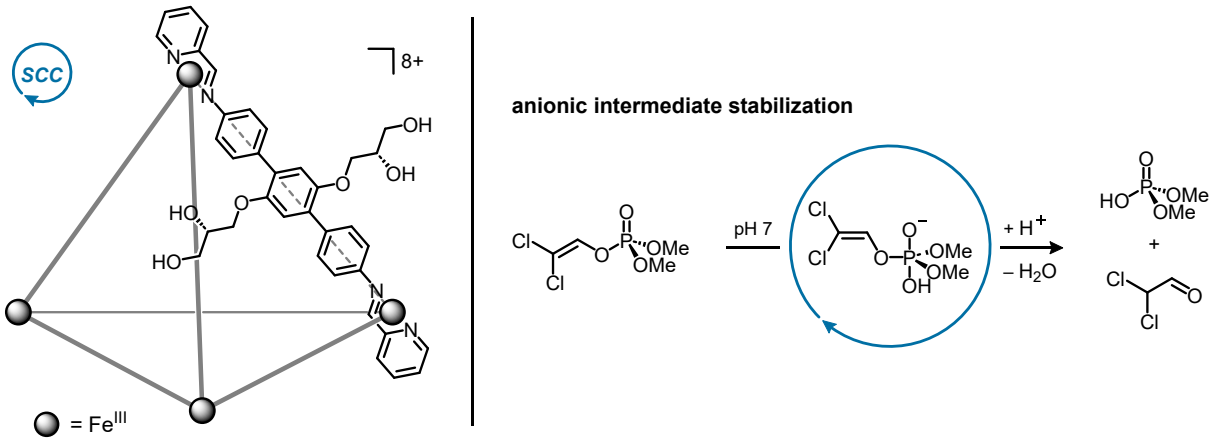

Figure 8 | Hydrolysis of dichlorvos catalyzed by a [Fe_4L_6] cage. The positively charged cavity is proposed to stabilize an anionic phosphate intermediate, facilitating bond cleavage and promoting reactivity in aqueous solution.[89]

A $[Fe_4L_6]$ metallotetrahedron by the Nitschke group catalyzes the hydrolysis of dichlorvos (2,2-dichlorovinyl dimethyl phosphate), likely by stabilizing an anionic phosphate intermediate within its cavity (**Figure 8**).[89]

While most SCC catalysis mentioned so far has been performed in aqueous media relying on the hydrophobic effect to drive substrate binding, an alternative strategy involves more "polar" SCCs operating in less polar, organic solvents. These systems exploit direct polar interactions between the cage and substrate to facilitate guest insertion.[44] Prominent examples include the large family of $[Pd_2L_4]$ cages,[90-96] whose ligands are oriented perpendicular to the cavity, creating large portals that do not favor hydrophobic encapsulation.[97] **Figure 9** shows a $[Pd_2L_4]$ cage, which effectively catalyzes Michael additions in dichloromethane, with reactivity observed even under "base-free" conditions, only requiring trace water for deprotonation. This implies that the cage environment significantly perturbs the substrate's pK_a, demonstrating the power of electrostatic modulation within a confined environment.

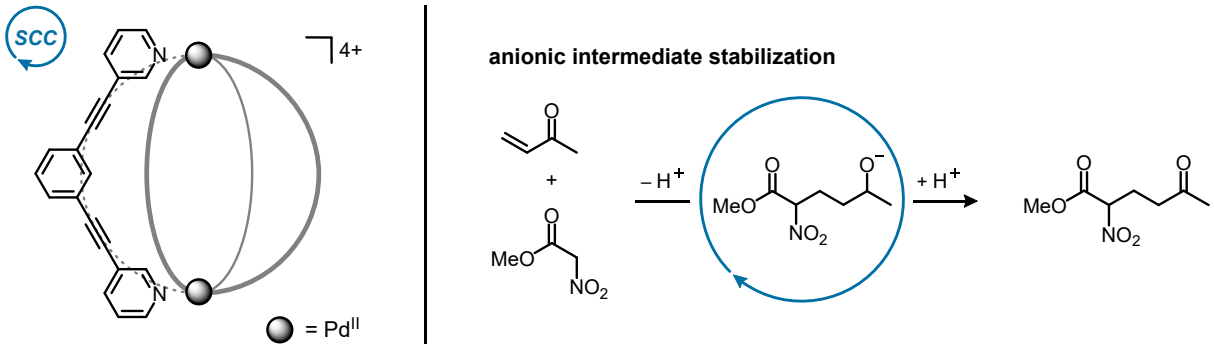

Figure 9 | Michael addition catalyzed by a $[Pd_2L_4]$ cage in dichloromethane. Unlike hydrophobic SCCs operating in water, this "polar" cage functions in organic solvent by exploiting direct electrostatic interactions with the substrate. The reaction proceeds efficiently with only trace water required for deprotonation.[97]

The development of SCC catalysts capable of allosteric regulation represents an advanced approach that mimics the sophisticated control mechanisms found in biological systems. Unlike the majority of synthetic catalysts, which lack regulatory mechanisms, allosteric supramolecular systems can modulate their catalytic activity in response to external stimuli.[50] Mirkin and co-workers have pioneered the design of SCCs with distinct structural and catalytic domains that respond to external stimuli. Among them, the group reported Rh^I- and Cu^I-based SCCs that reversibly bind allosteric effectors CO and Cl^- *via* coordination to the metals (**Figure 10**).[98-99] Upon effector binding, the assembly undergoes a conformational change, exposing previously buried catalytic sites based on chiral Zn^{II}–salen motifs. In this activated state, the SCC allows substrate access to both active sites within the cavity and accelerates acyl-transfer reactions in a bimetallic fashion. Similarly, instead of Zn^{II}, a Cr^{III}–salen variant catalyzes the ring opening of epoxides approximately twice as fast in its activated form compared to its form before binding of CO and Cl^-.[100] This design allows for "on-demand" catalysis, mimicking the functional complexity of enzymes.

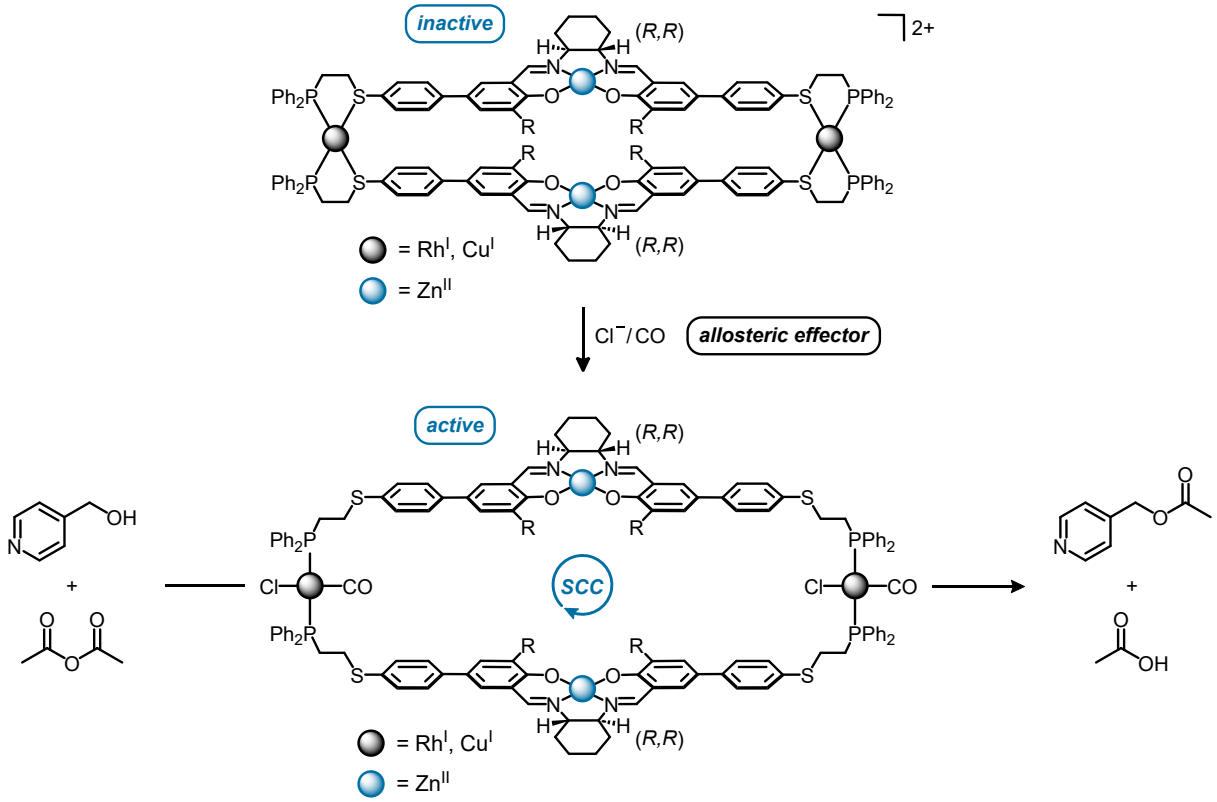

Figure 10 | Allosteric activation of SCC catalysts by effector binding: Rh^{I}- and Cu^{I}-based SCCs reversibly coordinate CO and Cl^{-} to induce a conformational switch that exposes buried Zn^{II}–salen catalytic sites, enabling bimetallic acyl-transfer within the cavity.[98-99]

1.3 Supramolecular Organometallic Complexes

1.3.1 Principles and Structural Overview of SOCs

Coordination-driven self-assembly has enabled the efficient synthesis of supramolecular coordination complexes (SCCs), in which metal nodes and organic linkers are traditionally connected through Werner-type coordination involving *O*-, *N*-, or *P*-donor atoms. However, a key limitation of SCCs lies in their reduced stability compared to fully covalent systems.[44] This reduced robustness can limit the practical utility of SCCs in catalysis, especially under harsh reaction conditions or in the presence of excess substrate capable of displacing the coordinating ligands that hold the structure together.[44]

In the past decades, supramolecular organometallic complexes (SOCs) have emerged as a more robust subclass of supramolecular assemblies. In contrast to traditional SCCs based on Werner-type coordination, SOCs feature strong metal–carbon bonds as structure-directing elements.[33] By definition, the carbon donors must be directly involved in the bonding at the interface between the metal centers and the connecting linkers, such that the M–C bond is critical to the overall architecture of the assembly.[33] In contrast, assemblies that incorporate organometallic fragments only in the linker backbone (*e.g.* ferrocenyl-dicarboxylic acids) or in the metal nodes (*e.g.* metal carbonyl complexes, η^5-cyclopentadienyl or η^6-arene half-sandwich metal complexes), but where

the assembly itself still relies on Werner-type coordination chemistry, are more appropriately classified as SCCs.[33]

In SOCs, exceptionally stable metal–carbon bonds must play a decisive structural role. Common carbon donor motifs include alkynyl groups (forming strong σ-bonds with electron-rich metals),[50] arenes (providing π-coordination particularly to late transition metals),[50] and *N*-heterocyclic carbenes (offering exceptional σ-donor strength and synthetic versatility).[101-104] The extensive development of multidentate NHC ligands by the groups of Baker, Hahn, and Peris has demonstrated the successful implementation of these principles in the design of SOCs, capitalizing on both the stability and tunability inherent to NHCs (**Figure 11**).

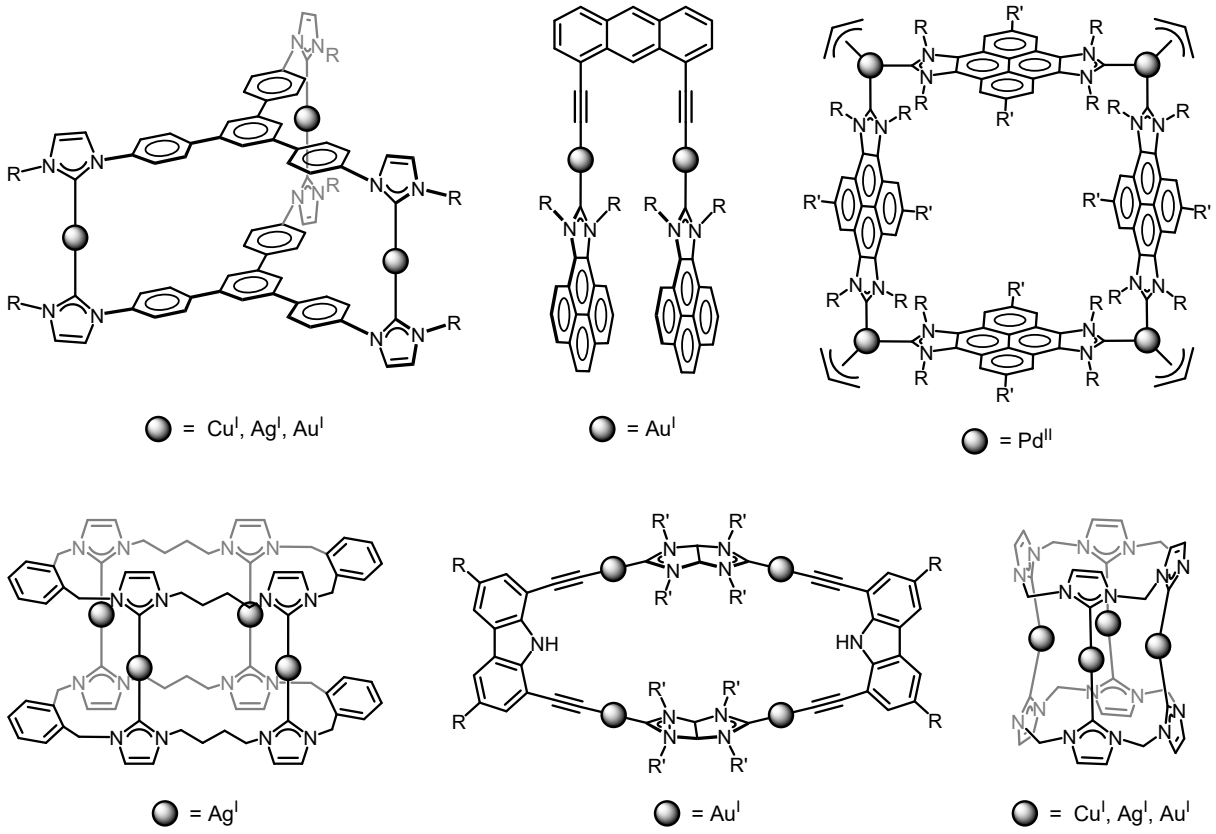

Figure 11 | Representative SOCs based on multidentate NHC ligands. These systems highlight the structural diversity achieved through strong metal–carbon bonding, including cyclophanes, cages, tweezers, and tubes.[105-111] Group 10 and 11 metals are especially well-suited for NHC-based SOCs due to their electron-rich nature and predictable coordination geometries. Overall charges and counterions are omitted for clarity.

1.3.2 Excursus: *N*-Heterocyclic Carbenes (NHCs)

Among different carbon donors employed for SOC construction, *N*-heterocyclic carbenes (NHCs) have emerged as particularly promising building blocks. NHCs are a class of stable carbenes characterized by a divalent carbon center incorporated into a heterocyclic ring that contains at least one nitrogen atom adjacent to the carbene carbon. The archetypal and most extensively studied NHCs are imidazolylidenes, first introduced as ligands in metal complexes by Wanzlick[112] and

Öfele[113] as early as 1968, and eventually isolated as stable free carbenes by Arduengo and co-workers in 1991.[114] These five-membered heterocycles have since become the predominant NHC variants due to their optimal balance of stability, accessibility, and tunability (**Figure 12**).[115]

The exceptional stability of imidazolylidene NHCs stems from a combination of electronic effects that stabilize the singlet ground state of the carbene.[115] The adjacent nitrogen atoms provide π-donation to the vacant p-orbital of the carbene carbon, while simultaneously withdrawing electron density through their electronegativity (σ-withdrawal).[115] The aromaticity of the imidazole ring facilitates charge delocalization, further enhancing electronic stabilization.[115] Additionally, the nitrogen substituents provide kinetic stabilization through steric shielding of the reactive carbene site (**Figure 12**).[115]

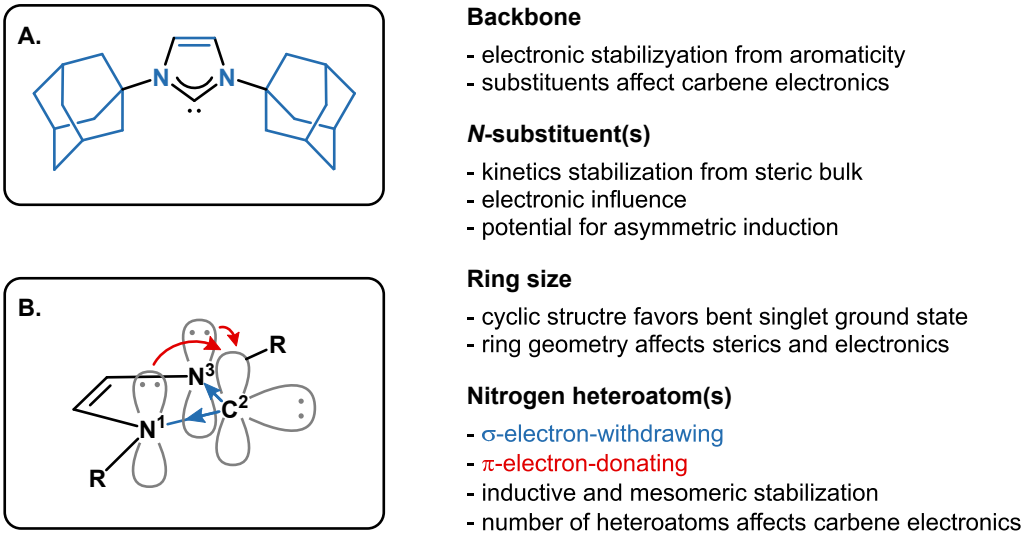

Figure 12 | Structural and electronic features of NHCs: **A**. General structure of an imidazolylidene, showing how ring size, backbone, and nitrogen substituents (in this case, adamantyl residues) influence the stability and reactivity of the carbene. **B**. Ground-state electronic configuration of the carbene, stabilized by the σ-withdrawing and π-donating effects of adjacent nitrogen atoms.[115] (Adapted from M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485. © 2014 Springer Nature Limited. Changes were made to the original.)

The structural rigidity of NHCs, combined with the strong σ-donor character of the carbene lone pair, leads to metal–carbon bonds that are generally stronger than those formed with phosphine ligands, while exhibiting minimal π-backbonding.[115] Moreover, the electronic properties of NHCs can be systematically tuned through structural modifications: Backbone substitution (*e.g.* heteroatoms or alkyl groups at the 4,5-positions) influences both the σ-donor strength and steric bulk of the carbene. Variation of the *N*-substituents ("*wingtips*") allows for fine-tuning of electronic properties and introduction of functional groups.

Synthetically, NHCs are commonly accessed *via* imidazolium salts, prepared through cyclization reactions.[116] This process often involves condensation of tethered diamines (derived by reductive amination of glyoxal derivatives) with a C_1 synthon such as trialkyl orthoformate, followed by

ring closure to form imidazolium salts.[116] Alternatively, acid-mediated cyclization of paraformaldehyde with the 1,2-diimines,[116] or alkylation of existing imidazole derivatives also affords imidazolium salts. These stable, isolable precursors can be subsequently deprotonated at the C^2 position with strong bases (*e.g.* KO^{t}Bu, NaH) to generate the free carbene (**Figure 13**).[117] Metal–NHC complexes can also be prepared by *in situ* deprotonation of imidazolium salts in the presence of metal precursors, avoiding isolation of free carbenes.[117] This strategy is particularly useful for moisture- and air-sensitive carbenes. Another common approach involves transmetalation from readily accessible Ag^I–NHC complexes, which serve as carbene transfer reagents.[117]

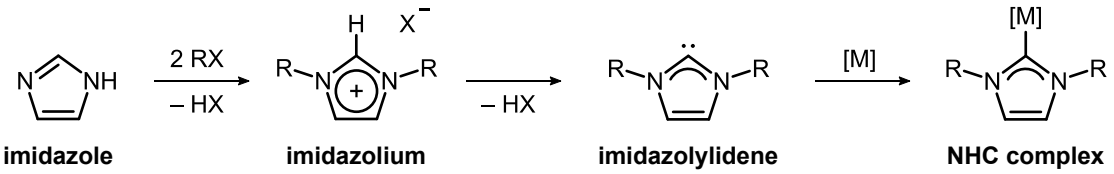

Figure 13 | Transformation from imidazole to metal–NHC complex: The imidazole is first alkylated to form an imidazolium salt, which is then deprotonated at the C^2 position using a strong base to generate the free carbene. Subsequent metalation with a suitable precursor yields stable metal–carbene complexes.

The combination of exceptional stability, structural versatility, strong σ-donor ability, and synthetic accessibility has established NHCs as ideal spectator ligands in homogeneous catalysis.[115] Their ability to remain coordinated under harsh conditions that typically lead to ligand dissociation makes them particularly attractive for SOC assembly, where the robustness of metal–NHC bonds directly translates to assemblies with enhanced stability.

1.3.3 Reactivity in SOCs

Despite their promising structural properties, studies on the reactivity and functionality of SOCs remain relatively scarce compared to traditional SCCs. Existing studies have primarily focused on two main areas: molecular recognition and (enantioselective) catalysis. The following selected examples illustrate the current scope and potential of SOCs.

The rigid, preorganized cavities of many SOCs enable the selective binding of guest species, including transition metal ions and polycyclic aromatic hydrocarbons (PAHs). For instance, the Mukherjee group reported a metallorectangle based on anthracene-based fluorophores and an imine-derived metal-binding site (**Figure 14**, top). This system exhibits selective fluorescence quenching upon binding moderately hard first-row transition metal ions (Mn^{II}, Fe^{III}, Ni^{II}, and Cu^{II}), while soft d^{10} metal ions (Zn^{II}, Cd^{II}) do not show such a response.[118] Similarly, the Stang group designed a metallorectangle, incorporating a phenanthroline-derived binding pocket, that functions as an efficient sensor for Ni^{II}, Cd^{II}, and Cr^{III} (**Figure 14**, bottom).[119]

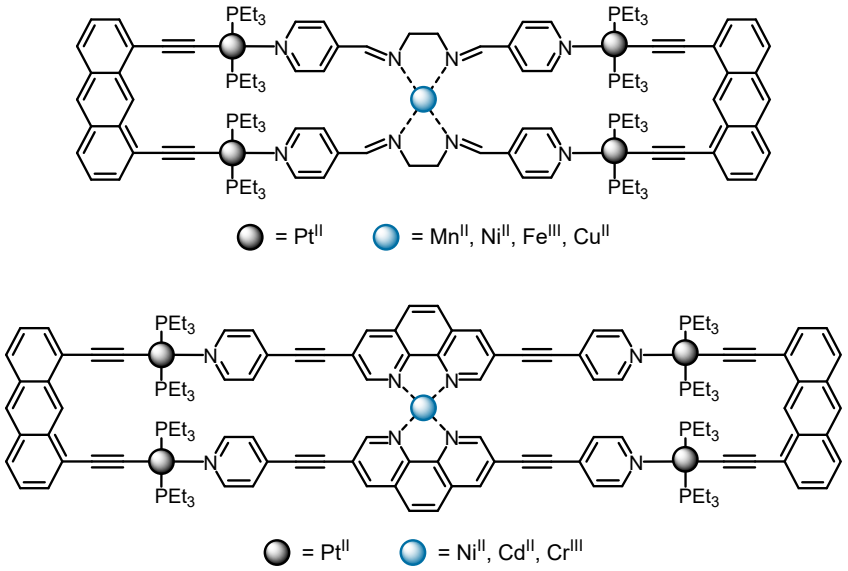

Figure 14 | Metallorectangles with an embedded metal binding site for transition metal sensing.[118-119]

A more advanced example of hierarchical guest recognition was achieved by a family of Pt^{II}-based metallorectangles assembled from 4-ethynylpyridine ligands (**Figure 15**). These structures first bind Ag^{I} ions *via* a "*π-tweezer effect*" between acetylene units.[120] The resulting Ag^{I}-coordinated metallorectangles act as Lewis acidic hosts capable of further encapsulating neutral Lewis basic guests such as pyrazine, phenazine, and 4,4'-dipyridyl ketone. This cooperative, stepwise binding demonstrates a modular recognition strategy enabled by metal-mediated π-interactions to activate the host toward secondary guest binding.[120]

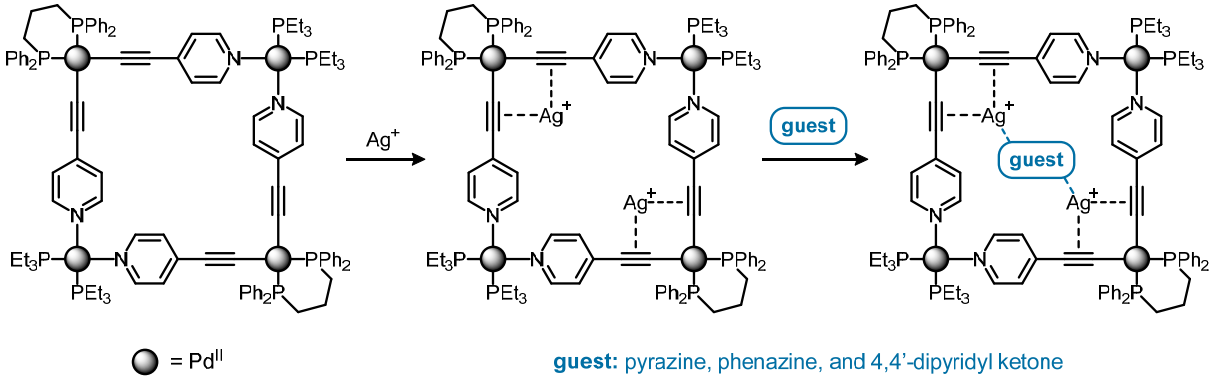

Figure 15 | Stepwise guest recognition *via* metal-mediated cooperativity: A metallorectangle binds Ag^{I} ions through a "*π-tweezer effect*" between acetylene ligands, followed by encapsulation of neutral Lewis basic guests.[120]

On another note, SOCs based on extended π-conjugated multidentate NHC ligands are particularly well suited for binding PAHs and fullerenes.[103] For example, a trigonal-prismatic hexanuclear Au^{I}-NHC complex bearing triphenylene-tris(NHC) ligands strongly binds coronene in solution, enabled by π–π interactions between host and guest within the shape-complementary pore of the SOC.[121] Similarly, a tetranuclear Au^{I}-based SOC constructed from extended π-conjugated

bidentate NHC ligands exhibits high affinity for binding electron-rich PAHs such as anthracene, pyrene, triphenylene, perylene, coronene (**Figure 16**, right).[122]

Binuclear Au^{I}-based metallotweezers constructed from a 1,8-diethynylanthracene linker with pyrene–NHC arms have also been employed for the recognition of "naked" metal cations (Cu^{I}, Ag^{I}, Tl^{I}) and PAHs.[123] However, these systems tend to self-aggregate in solution through a combination of π–π stacking and Au–Au metallophilic interactions. To prevent this, bite angles can be tuned by replacing the central linker with a bis(alkynyl)carbazole core, forcing the pyrene–NHC arms apart and suppressing self-aggregation while maintaining guest binding ability (**Figure 16**, left).[124]

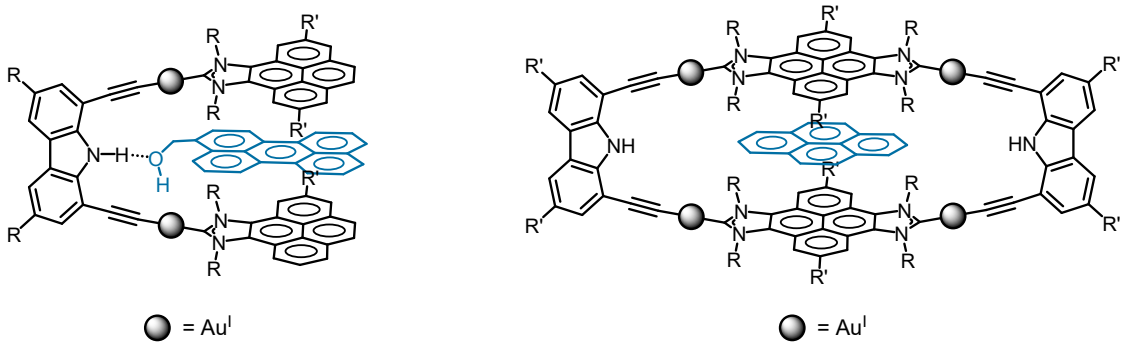

Figure 16 | Au^{I}-based SOCs for PAH binding. Left: Metallotweezer with pyrene–NHC arms binding 3-perylenylmethanol *via* π–π interactions.[124] Right: Metallorectangle based on extended bis-NHC ligands encapsulating PAHs.[122]

Metallorectangles based on Ni^{II} or Pd^{II} ions with extended π-conjugated bidentate NHC ligands have also demonstrated host–guest interactions with PAHs, dominated by the π-systems of the incorporated pyrenes.[125-127] In the Pd^{II} congener, combinations of electron-rich and electron-deficient PAHs assemble inside the cavity in donor–acceptor–donor–acceptor–donor (D–A–D–A–D) arrays, stabilized by π-stacking and electronic complementarity.[127] The same SOC also binds fullerenes such as C_{60} and C_{70} (**Figure 17**).[110]

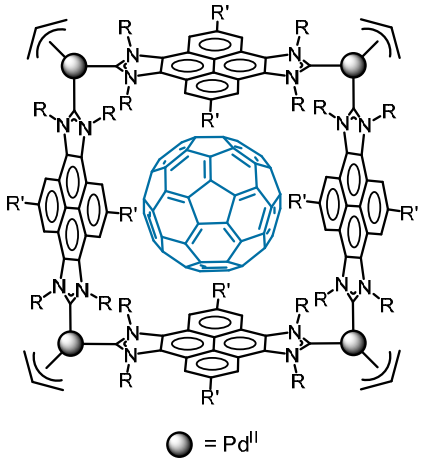

Figure 17 | Pd^{II}-based metallorectangle for fullerene binding, based on extended π-conjugated bidentate NHC ligands.

In terms of reactivity, SOCs have been employed as catalysts, where their rigid, multimetallic architectures enable both *enhanced* and *emergent* catalysis. An example of *enhanced* catalysis is a trinuclear Cu^{I}–NHC complex featuring a chelating tridentate NHC ligand, which catalyzes Ullmann-type *N*-arylation reactions of azoles (and phenols) under relatively mild conditions (**Figure 18**).[128] The catalyst displays broad substrate scope, efficiently converting various azoles with aryl iodides, bromides, and even activated chlorides.[128]

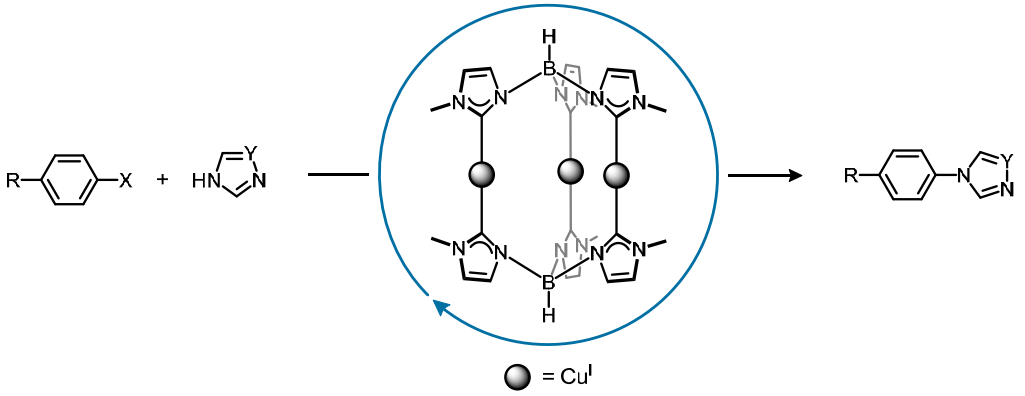

Figure 18 | *N*-Arylation of azoles with substituted aryl halides catalyzed by a Cu^{I}-based trinuclear NHC complex in the presence of Cs_2CO_3 in DMSO at 100 °C (Substituents: R = Me, OMe, C(O)Me; X = Cl, Br, I; Y = CH, N).[128]

In the context of enantioselective catalysis, chiral SOCs have been explored as catalysts with *emergent* catalytic properties by the Lin group. For example, Pt^{II}-based metallocyclophanes assembled from three bis(alkynyl) ligands incorporating a chiral 1,1'-bi-2-naphthol (BINOL) moiety have been shown to stereoselectively catalyze the addition of diethylzinc to aromatic aldehydes to afford the corresponding chiral secondary alcohols (**Figure 19**, right).[129-130]

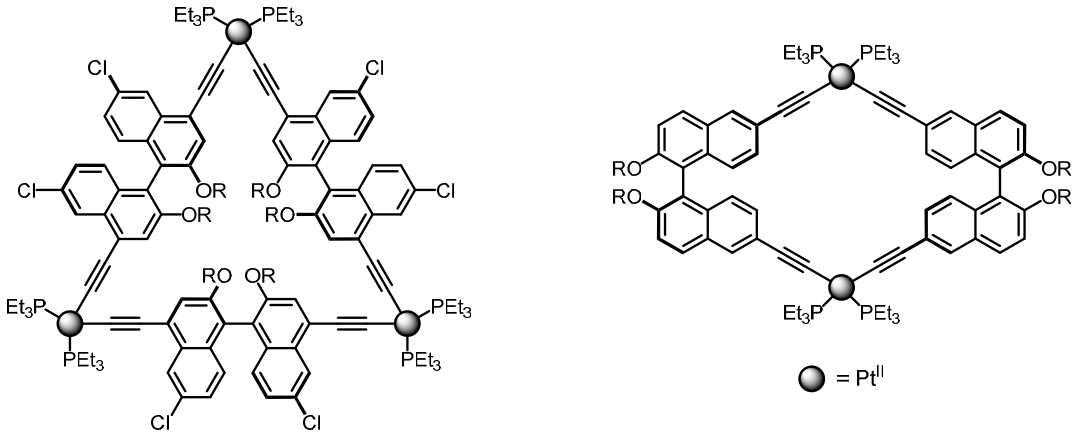

Figure 19 | Chiral supramolecular organometallic complexes (SOCs) as enantioselective catalysts: Pt^{II}-based metallotriangles and metallocyclophanes incorporating chiral BINOL–bis(alkynyl) ligands catalyze the addition of diethylzinc to aromatic aldehydes in the presence of $Ti(OiPr)_4$.[130-131]

With 1-naphthaldehyde as the substrate and in the presence of $Ti(O^iPr)_4$, a 95% conversion with 94% enantiomeric excess was observed. Interestingly, enantioselectivity decreases for smaller aromatic aldehydes as substrates, which the authors attribute to insufficient substrate confinement within the rigid cavity of the SOC.[130] A metallotriangle composed of the same BINOL–bis(alkynyl) building blocks but with altered connectivity showed even higher enantioselectivity across all tested substrates (**Figure 19**, left).[131]

Duan and co-workers reported the cyanosilylation of imines by a chiral cylinder-shaped trinuclear Ag^I–NHC complex assembled from a macrocyclic tris(imidazolium) salt and Ag_2O.[132] The SOC achieved nearly quantitative conversion, but the enantioselectivity remained modest (≤28% enantiomeric excess), despite the homochiral architecture of the catalyst. The authors attributed this to the overall architecture of the SOC, which lacked a sufficiently rigid or spatially confined chiral environment around the reactive center, preventing effective asymmetric induction during substrate conversion (**Figure 20**).[132]

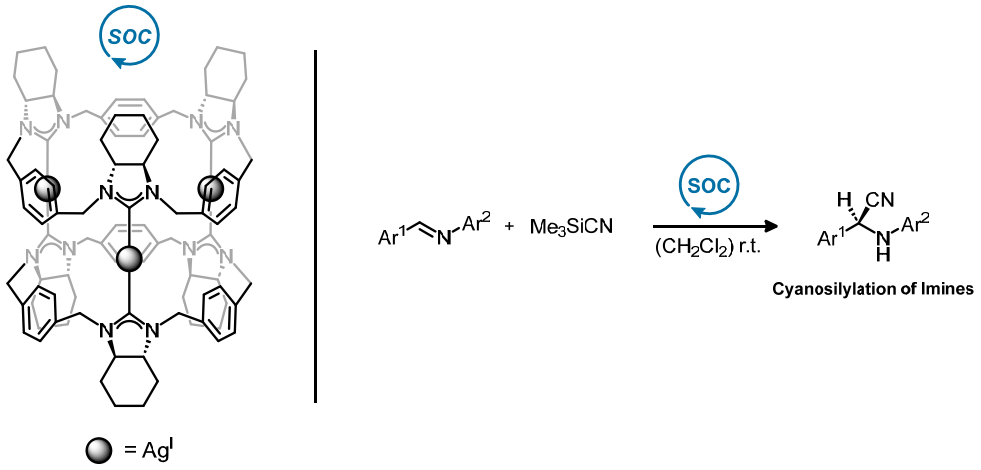

Figure 20 | Asymmetric cyanosilylation of imines with Me_3SiCN catalyzed by a trinuclear Ag^I–NHC complex (Ar^1 = Ph, *p*-(Me_2N)-Ph, *n*-pentyl; Ar^2 = Ph, *p*-tolyl, *n*-pentyl). Overall charges and counterions are omitted for clarity.[132]

Beyond guest recognition and catalysis, SOCs can also exhibit intrinsic reactivity, functioning as structurally preorganized platforms for the formation of otherwise challenging molecular architectures. A prominent example is the use of metallocyclophanes for the synthesis of highly strained cyclopara[*n*]phenylenes ([*n*]CPPs).[133-138] The Yamago group demonstrated that a tetranuclear Pt^{II} metallorectangle, constructed from four biphenylene-4,4'-diyl ligands, undergoes oxidative bromination with bromine, thereby reductively eliminating [8]CPP in the process (**Figure 21**, left).[133] Similarly, Tsuchido, Osakada and co-workers reported a hexanuclear Au^I metallotriangle, assembled from the same ligands, which also can undergo oxidative chlorination with $PhICl_2$ under the formation of [6]CPP (**Figure 21**, right).[138] These transformations illustrate how SOCs can act as reactive macrocyclic scaffolds, in which the metal centers actively mediate the formation of new covalent (C–C) bonds within the cavity.

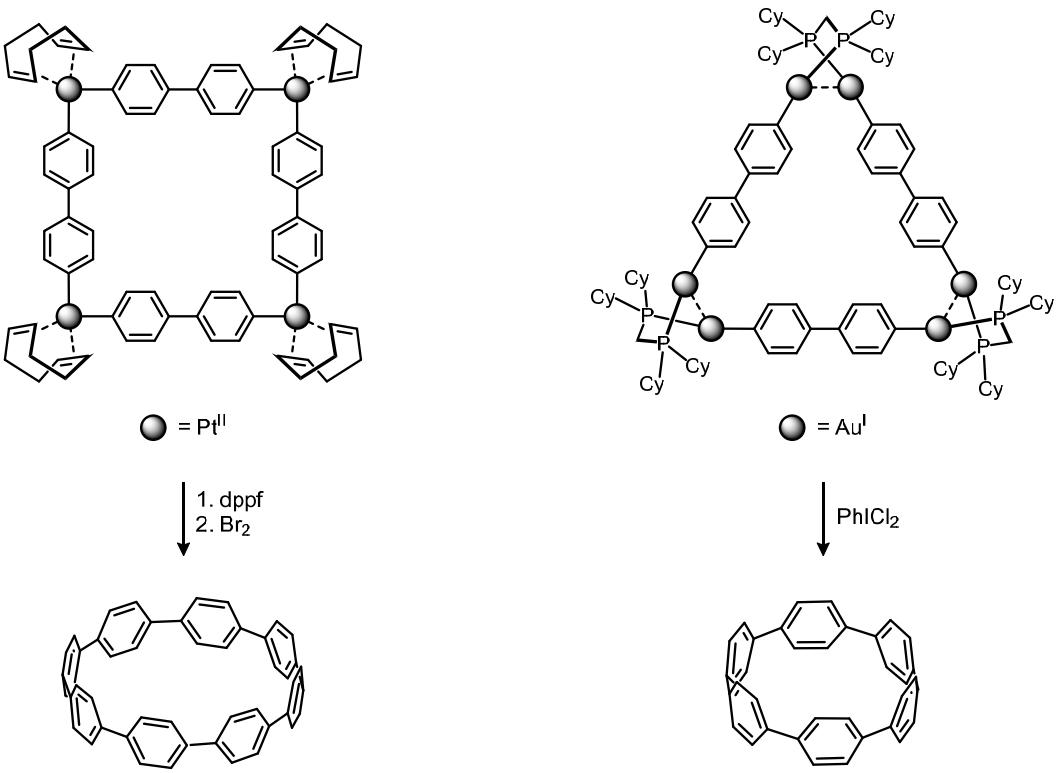

Figure 21 | Formation of cyclo[*n*]paraphenylenes from a tetranuclear Pt^{II}-based metallorectangle (*n* = 8) and a hexanuclear Au^{I}-based metallotriangle (*n* = 6) *via* reductive elimination of the organic macrocycles under oxidative conditions (dppf = 1,1-bis(diphenylphosphino)ferrocene).[133,138]

1.4 Pillarplexes

Pillarplexes represent a distinct class of functional tubular-shaped SOCs, first introduced by Altmann and Pöthig in 2016.[139] These barrel-like assemblies uniquely combine features of classical supramolecular chemistry (*e.g.* host–guest recognition) with defining traits of organometallic complexes. They incorporate strong, directional metal–carbon bonds, which confer high thermal and chemical stability, imparting a 4+ overall charge to the SOCs. Structurally, pillarplexes are octanuclear *N*-heterocyclic carbene (NHC) complexes of group 11 metal ions (M = Ag^{I}, Au^{I}), formed by two macrocyclic calix[4]imidazolylidene[2]pyrazolate ligands. The metal ions serve primarily as structure-directing elements: Each metal is linearly coordinated by one NHC and one pyrazolate donor from two opposing macrocycles, resulting in a ring of eight coinage metal centers sandwiched between the two poly(NHC) ligands (**Figure 22**). This arrangement yields a rigid, tubular architecture with a narrow, well-defined pore.

Pillarplexes readily self-assemble in high yields *via* deprotonation of macrocyclic ligand precursor $\mathbf{H_6L(PF_6)_4}$ in the presence of a basic metal source, such as Ag_2O, affording $\mathbf{[Ag_8L_2](PF_6)_4}$ (**Figure 22**). Transmetalation with $(Me_2S)AuCl$ provides the corresponding Au^{I} congener $\mathbf{[Au_8L_2](PF_6)_4}$. Notably, the same ligand scaffold also gives access to structurally well-defined group 10 metal–NHC complexes *via* a similar synthetic approach. Deprotonation of $\mathbf{H_6L(PF_6)_4}$ with Cs_2CO_3 in the presence of $NiCl_2(PPh_3)_2$ leads to the formation of binuclear saddle-shaped complex $\mathbf{Ni_2L(PF_6)_4}$.[140]

The overall geometry of the SOCs based on this macrocyclic ligand is governed by the preferred coordination mode of the metal centers: d^8 metals favor square-planar coordination, while d^{10} metals adopt linear geometries.

Beyond the metal centers, the counter anions also play an active role in modulating key material properties. By strategic choice of anion, the solubility of pillarplexes can be finely tuned. For example, acetate (OAc^-) salts are water-soluble, hexafluorophosphate (PF_6^-) salts dissolve exclusively in polar organic solvents, and triflate (OTf^-) salts are soluble in both aqueous and polar organic media.

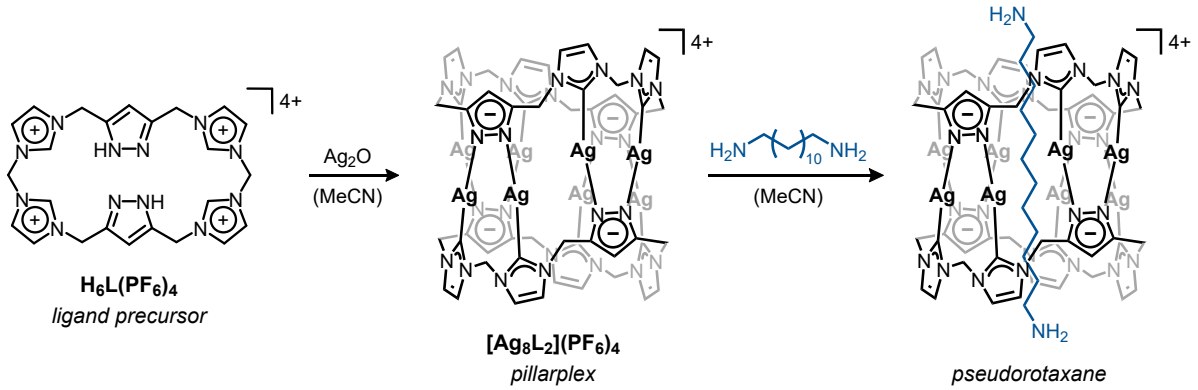

Figure 22 | Synthesis of Ag^I pillarplex **$[Ag_8L_2](PF_6)_4$** *via* deprotonation of macrocyclic ligand precursor **$H_6L(PF_6)_4$**, followed by guest insertion of 1,12-diaminododecane into the shape-compatible pillarplex pore.[139]

The unique properties of pillarplexes arise from 1) their intrinsic polarity and accumulated positive charge, 2) a shape-persistent cavity, and 3) structural rigidity conferred by strong metal–carbon coordination to planar NHC and pyrazolate ligands. The narrow tubular pore functions as a molecular recognition site, capable of selectively binding linear guest molecules, such as diaminoalkanes, based on size complementarity and favorable intermolecular interactions (**Figure 22**).[139] In contrast, bulkier species like six-membered aromatic guests are excluded due to steric constraints. Guest uptake can be monitored using various analytical methods, including NMR spectroscopy and isothermal titration calorimetry (ITC). Additionally, Au^I pillarplexes exhibit photoluminescence, and guest-induced quenching provides a sensitive probe of host–guest interactions. From a stability perspective, it is also the Au^I pillarplexes that are generally more robust than their Ag^I counterparts, likely due to the high bond dissociation energy of Au^I–NHC bonds,[141] as demonstrated under acidic conditions.[142] Accordingly, Au^I pillarplexes show reduced cytotoxicity compared to their Ag^I analogs.[142]

The differing stabilities observed for pillarplexes depending on the metal ion also raise the question about how strictly they conform to the defining SOC criterion of persistent structural integrity. In particular, Ag^I pillarplexes exhibit pronounced dynamic behavior, including reversible coordination and ligand exchange, as evidenced by competitive self-sorting experiments.[143] In contrast, Au^I pillarplexes clearly satisfy the stability requirements associated with SOCs.

Building on this chemical stability, cationic nature, and tubular shape, Au^{I} pillarplexes have recently been shown to selectively bind to DNA Holliday junctions – four-way branched structures central to DNA recombination and repair.[144] In particular, **$[Au_8L_2](OAc)_4$** interacts with the open conformation of these junctions *via* shape-complementary insertion into their central cavity.[144]

1.4.1 Excursus: Mechanically Interlocked Molecules (MIMs)

Mechanically interlocked molecules (MIMs) are supramolecular assemblies composed of discrete molecular components topologically entangled in such a way that they cannot be separated without breaking covalent bonds.[145] This form of connectivity, termed *mechanical bonding*, was introduced by J. F. Stoddart in the 1990s and led to the emergence of the field of *mechanostereochemistry*.[145-146] Since then, a wide variety of structurally different MIMs have been reported. Among the most prominent are rotaxanes, in which a ring component is threaded onto an axle terminated with bulky stoppers that prevent the ring from dissociating.[145]

Several synthetic strategies have been developed for rotaxane construction.[147] One of the most widely used is the *capping approach*, wherein a pseudorotaxane is first formed through reversible molecular recognition, commonly *via* metal–ligand coordination or hydrophobic interactions (**Figure 23A**).[148] The mechanically interlocked structure is then formed by covalently or coordinatively attaching bulky stopper groups to the axle termini.

Rotaxanes have become key building blocks in the design of *molecular machines*, defined as assemblies of molecules capable of performing controlled, mechanical-like movements in response to external stimuli.[149] Such systems are fundamental to biology (*e.g.* in DNA replication and ATP synthesis) and have inspired artificial counterparts including molecular shuttles, switches, motors, and sensors (**Figure 23B**).[149] Foundational contributions in this area by J. P. Sauvage, J. F. Stoddart, and B. L. Feringa were recognized with the Nobel Prize in Chemistry in 2016. Beyond their role in molecular machines, rotaxanes are an active area of research.[150] They have been constructed from diverse components such as fullerenes (**Figure 23B**),[151] and also integrated into higher-order architectures. Notably, rotaxane-based linkers have been employed to assemble one-, two-, and three-dimensional arrays by coordination with metal ions, giving rise to *metal–organic rotaxane frameworks* (MORFs) and interlocked coordination polymers (**Figure 23B**).[152-153] In addition, rotaxanes have attracted considerable attention as catalysts. The mechanical bond in catalytically active rotaxanes enables the spatial arrangement of catalytic sites in ways not accessible to conventional, covalently linked systems.[154] This interlocked topology allows for dynamic control over the proximity and orientation of functional groups, often resulting in enhanced activity, selectivity, and even switchable catalytic behavior in response to external stimuli such as pH, light, or redox changes.[154] The catalytic site can be part of the axle or the macrocycle; in the former case, its accessibility and thus activity can be tuned by the macrocycle's position, which can conceal or expose the active site.[155-156] The use of inherently chiral rotaxanes has also enabled the development of enantioselective catalysts, where the mechanical chirality of the MIM imparts stereocontrol in asymmetric transformations.[157-158]

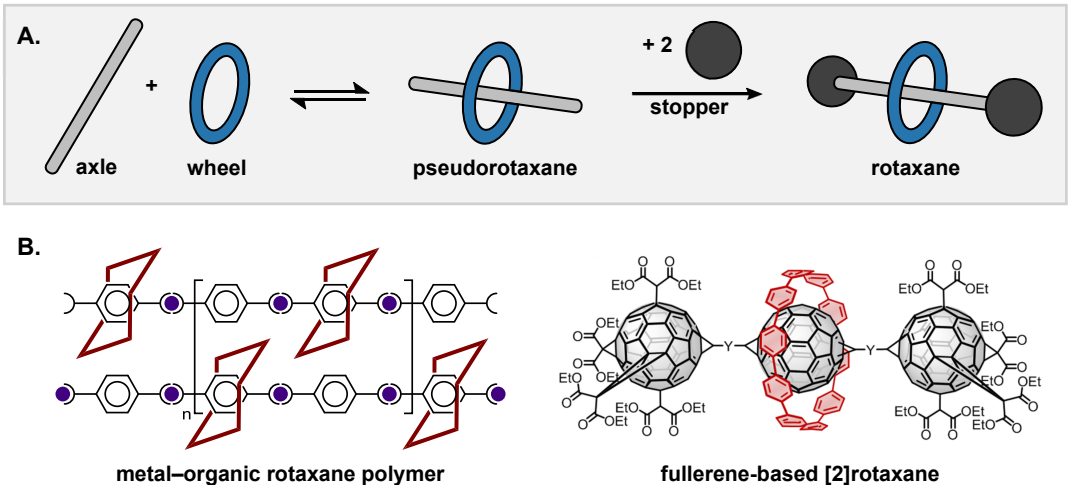

Figure 23 | Rotaxanes and their applications: **A**. Schematic representation of [2]rotaxane formation *via* the capping approach, where a ring is threaded onto an axle, followed by attachment of bulky stopper groups. **B**. Examples of rotaxanes in modern supramolecular chemistry, including interlocked coordination polymers and fullerene-based MIMs (Y = macrocyclic spacer).[151-152] (Reprinted with permission from Y. Xu, R. Kaur, B. Wang, M. B. Minameyer, S. Gsänger, B. Meyer, T. Drewello, D. M. Guldi, M. von Delius, *J. Am. Chem. Soc.* **2018**, *140*, 13413. © 2018 American Chemical Society. Changes were made to the original.)

1.4.2 Pillarplex-Based Rotaxanes

The rigid, tubular architecture and high guest selectivity of pillarplexes provide an ideal scaffold for mechanically interlocked architectures. Building on these features, Pöthig and Altmann pioneered a new type of MIM in which linear diaminoalkanes are threaded through the pillarplex pore and capped to yield rotaxane **Rot[Ag_8L_2]$(PF_6)_4$** in near-quantitative yield (**Figure 24**).[159]

Despite the chemically distinct environment introduced by the interlocked architecture, the key properties of the pillarplex are preserved. Even in the rotaxane, the Ag^I pillarplex can still undergo transmetalation to the corresponding Au^I congener. Moreover, at low pH or in presence of chloride ions, the Ag^I pillarplex disassociates, releasing the metal ions and yielding a purely organic *mechanically interlocked ligand* (MIL). This process is three orders of magnitude faster than the dissociation of the corresponding non-interlocked pillarplex. In analogy to the *catenand effect* described by Sauvage,[160] this difference in stability between rotaxane and pillarplex disassembly been termed *rotaxand effect*. The resulting MIL is a [3]rotaxane composed of two interlocked poly(imidazolium) macrocycles threaded onto the capped axle. Remarkably, this process is fully reversible. Under basic conditions, the metal ions can be reintroduced to regenerate the organometallic [2]rotaxane (**Figure 24**).[159] Thus, pillarplex–rotaxanes function as pH-responsive molecular switches, controllably switching between organometallic and organic states.

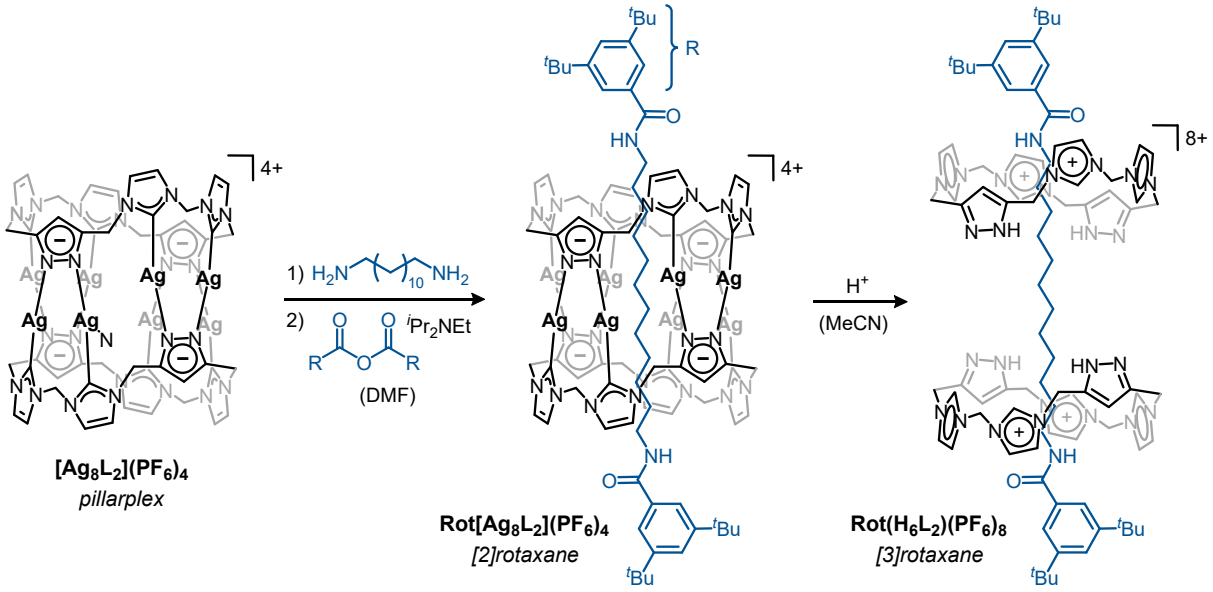

Figure 24 | Formation and reversible demetalation of a pillarplex–rotaxane **Rot[Ag_8L_2](PF_6)$_4$**. Capping a diaminoalkane guest threaded through the pillarplex yields the organometallic [2]rotaxane **Rot[Ag_8L_2](PF_6)$_4$**, which reversibly converts to a purely organic [3]rotaxane, **Rot(H_6L_2)(PF_6)$_8$**, upon acidic demetalation.[159]

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If you don't know where you are going, any road will get you there.

— Lewis Carroll

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2 Objective

Reactivity as a leitmotif

Supramolecular organometallic complexes (SOCs) based on *N*-heterocyclic carbene (NHC) ligands offer remarkable robustness, setting them apart from traditional supramolecular coordination complexes (SCCs), which are typically held together by labile, *Werner*-type coordination. This enhanced stability under harsh conditions or in the presence of competing ligands overcomes a key limitation that often limits the practical utility of SCCs in applications such as catalysis. At the same time, SOCs retain the primary advantages of their classical counterparts, including a modular design and facile synthetic pathways based on coordination-driven self-assembly.

While the intrinsic reactivity of SCCs is well-studied and remains central to their applicability, the field of SOCs is relatively young in comparison. This dissertation aims to systematically investigate the reactivity of SOCs, with a focus on tubular *pillarplexes* based on NHC ligands and coinage metals. A central question is how to leverage the architecture of pillarplexes to create reactive or even catalytic systems. Foundational studies on pillarplexes have demonstrated that their structure offers at least two distinct regions where chemical reactivity can occur. The specific objectives of this work are organized around these reactive sites:

1. At the metal centers embedded in the cavitand walls

The first part of this thesis explores metal-centered reactivity within the pillarplex platform. To date, these SOCs have been constructed exclusively from linearly coordinating Ag^{I} and Au^{I} ions, which contribute to the high stability of the structures through strong metal–carbon bonds. However, both Ag^{I} and Au^{I} possess limited intrinsic chemical reactivity. As a logical progression, this work introduces Cu^{I} as a structure-directing building block. Copper not only favors the required linear coordination geometry for pillarplex formation but also offers significantly enhanced reactivity compared to its heavier homologues. The design of a Cu^{I}-based pillarplex lies at the core of the first part of this thesis. It is investigated whether such a SOC can accommodate guests (and potentially substrates for subsequent catalysis), which is a prerequisite for any reactivity to occur within the pore of the SOC. Moreover, the redox activity of the embedded Cu^{I} ions is examined

as a critical prerequisite for building reactive pillarplexes. Together, these aspects lay the foundation for developing reactive SOCs and ultimately achieving *enhanced* catalysis in the confined space of pillarplexes.

2. At the pillarplex rim

The second focus of this thesis investigates reactivity at the pillarplex rim. Prior studies on the properties of the macrocyclic ligand framework used for pillarplex assembly indicate that the rim of these SOCs is quite electron-deficient, likely arising from polarization of the NHC and pyrazolate backbone protons, induced by metal coordination. This is evidenced by SC-XRD structures of related metal complexes, in which hydrogen bond acceptors are often located in close proximity to the NHC/pyrazolate backbone protons defining the rim of the SOC.

Owing to the rigidity and spatial orientation of the ligands, the rim presents a well-defined environment capable of engaging in selective, directional interactions with structurally and electronically complementary systems, *e.g.* electron-rich aromatic compounds or hydrogen-bonding acceptors. The quasi-parallel alignment of the backbone protons enables precise positioning of such molecules, potentially modulating their reactivity through non-covalent interactions at the rim, in a manner reminiscent of organocatalytic activation. This effect may be further enhanced through the formation of a mechanically interlocked molecule (MIM), in which part of the complementary system is threaded through the pillarplex pore, thereby enabling preorganization of the reactive site directly at the activating rim. The design of such a MIM, with the aim of inducing *emergent* catalytic properties, constitutes the second main objective of this thesis.

The systematic investigation of these two distinct modes of reactivity in pillarplexes aims to provide fundamental insights into the design principles for reactive SOCs and their potential applications in catalysis.

Complementary studies on functional SOCs

In addition to the two main areas of investigation, this work includes studies on structurally related systems that provide broader insight into reactivity in SOCs. These systems were examined to probe key physicochemical properties relevant to the design of functional SOCs, including coordination behavior, ligand rigidity, host–guest interactions, photophysical features, and electronic structure. Collectively, these studies contribute to a foundational understanding of how reactivity can be introduced into SOCs and thereby support the overarching objective of this thesis.

The great tragedy of science – the slaying of a beautiful hypothesis by an ugly fact.

— Thomas Huxley

3 Results – Summary and Context

3.1 Endohedral Coordination of Bulky Substrates in Metalloenzyme-Like Organometallic Nanotubes

Chem. Eur. J. **2025**, *31*, e202500775

Summary

This study introduces a Cu^{I}-based pillarplex **[Cu$_8$L$_2$](OTf)$_4$** as a synthetic receptor, mimicking key structural and functional properties of metalloenzymes, specifically multinuclear copper enzymes. By integrating eight Cu^{I} centers directly into the cavitand walls of the SOC, we built a system with (1) a structurally adaptable cavity, (2) the ability to bind substrates *via* metal–ligand coordination, and (3) metal-based redox activity.

The organometallic nanotube **[Cu$_8$L$_2$](OTf)$_4$** was synthesized through deprotonation of its calix[4]imidazolium[2]pyrazole ligand precursor **H$_6$L(OTf)$_4$** using Cu_2O as an intrinsically basic Cu^{I} source. The structure was confirmed through comprehensive characterization including ^{1}H and ^{13}C NMR spectroscopy, elemental analysis, high-resolution mass spectrometry, and SC-XRD.

A key finding is the receptor's ability to accommodate tetrahydrofuran (THF), despite a significant steric mismatch between the host's narrow pore (d_{pore} ≈ 5.2 Å, d_{inner} ≈ 3.7 Å) and the cyclic guest (d_{THF} ≈ 5.2 Å). SC-XRD analysis revealed that the insertion is driven by endohedral metal–ligand coordination. Specifically, the THF oxygen atom coordinates to two adjacent Cu^{I} centers in a μ_2-bridging mode, with Cu–O_{THF} distances of 2.591(9) Å and 2.75(1) Å, significantly shorter than the sum of the van der Waals radii. This coordination induces structural flexibility, with Cu–Cu distances shortening from 2.9664(8) Å to 2.8715(9) Å upon THF binding.

Density Functional Theory (DFT) calculations at the ωB97X-V/def2-TZVP level of theory corroborated these findings, quantifying the THF insertion as exergonic (ΔG = −41 kJ mol^{-1}) and strongly driven by enthalpy (ΔH = −101 kJ mol^{-1}) despite a high entropic penalty (TΔS = −60 kJ mol^{-1}). In

addition, Quantum Theory of Atoms in Molecules (QTAIM) analysis confirmed Cu–O coordination through the identification of bond critical points between the Cu^{I} ions and the THF oxygen atom. A control calculation using cyclopentane as a non-coordinating analogue of THF showed a significantly lower binding affinity *in silico* ($\Delta G = -4$ kJ mol^{-1}), owing to a reduced enthalpic stabilization. This demonstrated the crucial role of metal–ligand coordination in driving substrate insertion.

Solution-phase binding studies of THF and **[Cu_8L_2](OTf)$_4$** using ^1H NMR titration in D_2O revealed strong host–guest association ($K_a = 2730\ M^{-1}$), despite the rather hydrophilic nature of THF typically limiting guest recognition in aqueous media. The titration data confirmed the high affinity of **[Cu_8L_2](OTf)$_4$** for THF coordination and suggested that the solid-state binding behavior translates well to solution.

Beyond substrate binding, we investigated the system's redox properties, a critical feature of metalloenzymes. To isolate and study the metal centers without interference from guest dynamics, we synthesized a pillarplex-based [2]rotaxane, **Rot[Cu_8L_2](OTf)$_4$**, where the cavity of the SOC is mechanically blocked. Cyclic voltammetry (CV) studies suggested that the Cu^{I} centers are redox-active, exhibiting a quasi-reversible oxidation at a half-wave potential of +1.05 V, which is activated by trace components present in aged acetonitrile. Spectroelectrochemical EPR analysis unambiguously confirmed Cu^{II} formation upon electro-oxidation, with characteristic *g*-values ($g_1 = 2.279$, $g_2 = 2.058$, $g_3 = 2.027$) and hyperfine coupling ($A_1 = 44$ mT) consistent with copper-centered redox activity. A control experiment with an analogous, redox-inert Ag^{I} rotaxane showed no such activity, ruling out a ligand-based redox event.

Taken together, this work establishes the Cu^{I} pillarplex as a new class of metalloenzyme mimic, integrating reactive metal sites directly into the receptor's walls. Exhibiting key features of metalloenzymes, such as structural flexibility, coordination-driven substrate uptake, and metal-based redox activity, the platform demonstrates a novel receptor topology and sets the stage for developing advanced functional systems for catalysis and sensing.

Author Contributions

T.P. carried out most of the experimental work and data analysis, including NMR spectroscopy, NMR titrations, and SC-XRD. T.P. also performed DFT calculations, supported the conceptual development of the study, and wrote the initial draft of the manuscript. P.M. and D.P.H. performed electrochemical measurements and analyzed the data. D.P.H. and O.S. conducted EPR spectroelectrochemical experiments. M.R.A., F.S., and K.G. assisted with experimental work. D.P.H. supported data analysis, project coordination, and manuscript preparation. A.P. led the project and the conceptual development of the study, framed the narrative, secured funding, and provided overall guidance. A.P., D.P.H., and T.P. reviewed, edited, and revised the manuscript.

3.2 Spotlight on Mechanosterics: A Bulky Macrocycle Promotes Functional Group Reactivity in a [2]Rotaxane

J. Am. Chem. Soc. **2025**, *147*, 27192

Summary

This study explores pillarplexes as *promoters* of the reactivity of functional groups within a mechanically interlocked molecule, harnessing the reactivity of the rim of these SOCs. Our work demonstrates how these bulky macrocycles *enhance* the reactivity of 2,7-^{t}Bu$_2$-9-fluorenylmethoxycarbonyl (Fmoc*) stoppers in the pillarplex-based [2]rotaxane **[Fmoc*-Rot][Ag$_8$L$_2$](PF$_6$)$_4$**. Specifically, the pillarplex accelerates the base-induced deprotection of the Fmoc* stoppers by more than 35-fold compared to a non-interlocked control compound **[Fmoc*-NH-(CH$_2$)$_6$]$_2$**. This dramatic rate enhancement is counterintuitive and contrasts with the prevailing mechanistic paradigm that steric encumbrance of macrocycles often suppresses functional group reactivity. To contextualize this, we introduced the term "*mechanosteric effect*" to describe *positive* and *negative* influences of a macrocycle on the reactivity of such a functional group within a mechanically interlocked architecture.

The target [2]rotaxane **[Fmoc*-Rot][Ag$_8$L$_2$](PF$_6$)$_4$** was synthesized through a two-step protocol involving guest insertion of 1,12-diaminododecane into the pillarplex **[Ag$_8$L$_2$](PF$_6$)$_4$** in acetonitrile, followed by stoppering with Fmoc* *N*-hydroxysuccinimide, affording the MIM in 68% isolated yield. The corresponding non-interlocked analogue **[Fmoc*-NH-(CH$_2$)$_6$]$_2$** was prepared as a kinetic reference, enabling direct comparison of deprotection rates.

Base-induced Fmoc* deprotection was monitored by ^{1}H NMR spectroscopy in acetone-d_6, tracking the decay of the C^9–H methine proton signal in the presence of piperidine. Kinetic analysis revealed pseudo-first order kinetics for both systems, consistent with a base-promoted E1cB mechanism where initial C9–H deprotonation is rate-determining. The rotaxane showed a second-order rate constant of 20.5 $M^{-1}h^{-1}$ compared to 0.56 $M^{-1}h^{-1}$ for the control, representing a 36-fold acceleration.

Single-crystal X-ray diffraction elucidated the molecular origin of this enhancement, revealing a distinctive "*wrapped*" conformation in which one Fmoc* stopper folds around the electron-deficient aromatic rim of the pillarplex. This geometry exposes the reactive C^9–H proton, facilitating base-promoted deprotonation. The preorganized arrangement is stabilized through highly directional CH–π interactions between the fluorenyl π-system and pillarplex C–H protons, complemented by hydrogen bonding between the carbamate oxygen and ligand backbone protons.

^{1}H NMR spectroscopy in solution confirmed the persistence of this conformation. Significant upfield shifts (Δδ = 0.16–0.25 ppm) were observed for pillarplex protons located "*beneath*" the fluorenyl ring, consistent with aromatic shielding effects. Short interproton distances (4.7 Å and 4.3 Å) between the Fmoc* group and the pillarplex rim were estimated from 2D ^{1}H,^{1}H ROESY exper-

iments, supporting the presence of a "*wrapped*" conformation matching the crystal structure geometry. Control experiments with an amide-stoppered rotaxane showed no comparable shielding effects, confirming that CH–π interactions are specific to the Fmoc*-pillarplex pairing.

DFT calculations corroborated the thermodynamic preference for the "*wrapped*" conformation. Conformational sampling (GFN2-xTB) and reevaluation of selected conformers on the r^{2}SCAN-3c level of theory revealed that structures lacking CH–π interactions and hydrogen bonding were significantly destabilized compared to the "*wrapped*" orientations.

This work establishes the *positive* mechanosteric effect as a general design principle for functional mechanically interlocked molecules, demonstrating that mechanical entanglement combined with targeted non-covalent interactions can preorganize functional groups to actively enhance reactivity. We show that mechanical bonding does not necessarily inhibit nearby reactivity through steric effects, instead revealing how precise spatial control through interlocking can modulate local chemical environments. Thereby, we provide fundamental insights into practical design principles for functional molecular machine design.

Author Contributions

T.P. carried out the experimental work and data analysis, including NMR spectroscopy, kinetic analyses, and SC-XRD, and performed DFT calculations. T.P. also led the conceptual development of the study and wrote the initial draft of the manuscript. C.S. and D.B. assisted with experimental work. M.C. contributed to interpreting the kinetic data. A.P. led the project, supported the conceptual development of the study, framed the narrative, secured funding, and provided overall guidance. A.P. and T.P. reviewed, edited, and revised the manuscript.

3.3 Crystal Structure Elucidation of a Geminal and Vicinal Bis(trifluoromethanesulfonate) Ester

Acta Cryst. C **2024**, *80*, 278

Summary

This study presents the first structural analysis of geminal and vicinal bis(trifluoromethanesulfonate) esters. These compounds are highly reactive synthons used to construct macrocyclic precursors for supramolecular hosts like pillarplexes. Their structural characterization by SC-XRD was previously unachieved due to their nature as air- and moisture-sensitive oils.

By employing a low-temperature crystallization protocol at 277 K, we successfully obtained single crystals of methylene bis(trifluoromethanesulfonate) and ethylene bis(trifluoromethanesulfonate) for SC-XRD analysis. Both compounds were found to crystallize as two-component non-merohedral twins. The geminal methylene bis(triflate) crystallizes in the chiral, monoclinic space group $P2_1$. In contrast, the vicinal ethylene bis(triflate) crystallizes in the centrosymmetric, triclinic space group $P\overline{1}$, with two independent conformers co-existing in the asymmetric unit that differ primarily by their C–C–O–S torsion angles.

The crystal packing of both bis(triflates) reveals a self-sorting behavior, governed by a combination of non-classical C–H···O hydrogen bonds and intermolecular C–F···F–C interactions. This results in the formation of distinct, alternating two-dimensional layers of polar (non-fluorous) and non-polar (fluorous) domains within the crystal lattice.

To rationalize this observation, we performed DFT calculations to visualize the Molecular Electrostatic Potential (MEP) of both molecules. The MEP surfaces confirmed the high positive charge on the alkylene protons, consistent with their known electrophilicity. It also correctly predicted the high negative charge on the sulfonate oxygen atoms, explaining their participation in C–H···O hydrogen bonding within the polar domains. Conversely, the less polarized trifluoromethyl groups aggregate to form the non-polar, fluorous domains.

In conclusion, this study offers fundamental structural insights into a class of highly electrophilic synthons, paving the way for a deeper understanding of their structure-property relationships.

Author Contributions

T.P. performed the SC-XRD measurements, analyzed the crystallographic data, and carried out DFT calculations. T.P. also led the conceptual development of the study and wrote the initial draft of the manuscript. J.Z. and J.S. assisted with experimental work, including crystal growth attempts and crystal picking under cryogenic conditions. A.P. secured funding and provided overall guidance. A.P. and T.P. reviewed, edited, and revised the manuscript.

3.4 Triazolate-Based Pillarplexes: Shape-Adaptive Metallocavitands via Rim Modification of Macrocyclic Ligands

Org. Chem. Front. **2021**, *8*, 4061

Summary

This study introduces a new subclass of pillarplexes through strategic modification of their macrocyclic ligand rim. We show that strategically replacing a pyrazolate unit with a 1,2,4-triazolate group within the ligand framework yields a pillarplex with shape-adaptive properties. This modification was achieved *via* a macrocycle-templated synthesis using calix[4]imidazolium[2]triazole ligand precursor $\mathbf{H_6L^t(OTf)_4}$ as a supramolecular building block for the self-assembly of Ag^I and Au^I pillarplexes, $\mathbf{[Ag_8L^t_2](OTf)_4}$ and $\mathbf{[Au_8L^t_2](PF_6)_4}$.

The central finding of this work is the remarkable structural flexibility of the gold(I) complex, $\mathbf{[Au_8L^t_2](PF_6)_4}$, observed in the solid state. While the Ag^I analogue adopts a tubular geometry with a large pore size (d_{pore} ≈ 4.8 Å), SC-XRD of the Au^I complex revealed a significant distortion where the portals of the cavitand are compressed, drastically reducing the portal diameter (d_{pore} ≈ 2.9 Å). This "*squeezed*" conformation is driven by strong, charge-assisted intermolecular hydrogen bonds between PF_6^- counter-anions and C–H groups at the pillarplex rim. We propose that the lower steric demand of the triazolate nitrogen atom, compared to the C–H group in the parent pyrazolate pillarplexes, enables this pronounced deformation.

DFT calculations support this hypothesis, revealing a significantly lower energetic penalty for portal compression in the triazolate-based system compared to its pyrazolate analogue. This indicates that the rim modification intrinsically enhances the structural adaptability of the portal of the SOC.

To assess whether the solid-state compression observed in triazolate-modified pillarplexes impacts their host–guest behavior in solution, we performed ^{1}H NMR titration experiments. The Au^I congener $\mathbf{[Au_8L^t_2](PF_6)_4}$ exhibited a strong binding affinity for 1,8-diaminooctane as a model guest, with an association constant (K_a) of (4.6 ± 3.5) × 10^4 M^{-1}, closely matching that of the pyrazolate-based parent pillarplex $\mathbf{[Au_8L_2](PF_6)_4}$. These results indicate that the shape-adaptive compression is primarily a solid-state packing effect, and that the cavitand remains fully accessible for guest binding in solution.

In conclusion, this work establishes that targeted rim modification of the ligand is a powerful strategy to tune the structural properties of pillarplexes. By incorporating a triazolate moiety, we have created a shape-adaptive organometallic tube with enhanced structural flexibility and the capacity for inter-cationic self-recognition. Moreover, this study validates the macrocyclic templation approach as a tool for introducing new functionality at the rim of the SOCs (in the solid state) without compromising their core host–guest chemistry (in solution).

Author Contributions

S.G., L.S., X.Z., and P.J.A. carried out the experimental work of this study. C.J. performed SC-XRD measurements. T.P. performed DFT calculations. S.G. and T.P. led data analysis and interpreted the results. S.G. and T.P. wrote the initial draft of the manuscript. A.P., T.P., and S.G. reviewed, edited, and revised the manuscript.

3.5 Bimetallic Platinum Group Complexes of a Macrocyclic Pyrazolate/NHC Hybrid Ligand

Organometallics **2021**, *40*, 3056

Summary

In this study, we report the synthesis, characterization, and photophysical properties of dinuclear Pd^{II} and Pt^{II} complexes, **$[Pd_2L](PF_6)_2$** and **$[Pt_2L](PF_6)_2$**, derived from the same macrocyclic ligand platform used in pillarplexes. Designed as heavier homologues of a previously reported Ni^{II} complex, these compounds were investigated to assess the influence of the metal ions on the structure and, in particular, on the emission properties of the Pt^{II} congener.

The metal complexes were prepared by two different routes: (1) direct deprotonation of the macrocyclic calix[4]imidazolium[2]pyrazole ligand precursor **$H_6L(PF_6)_4$** in the presence of $Pd(OAc)_2$ or $PtCl_2$(cod) (cod = cyclooxtadiene) and base; and (2) for **$[Pt_2L](PF_6)_2$**, additionally by transmetalation from the Ag^I pillarplex **$[Ag_8L_2](PF_6)_4$**. Structural analysis by SC-XRD and NMR spectroscopy confirmed that both NHC complexes are essentially isostructural to the Ni^{II} analogue, adopting a rigid, saddle-shaped conformation. Within this framework, the d^8 metal ions are bound in a slightly distorted square-planar coordination geometry.

Photophysical analysis revealed that, while the Ni^{II} and Pd^{II} complexes are non-emissive, the Pt^{II} congener **$[Pt_2L](PF_6)_2$** exhibits blue photoluminescence both in acetonitrile solution and in the solid state ($\lambda_{em} \approx 420$ nm) dispersed in PMMA. Notably, the emission lifetime is in the nanosecond range ($\tau_{av} = 5.4$ ns), which is unusually short for Pt^{II} complexes and more characteristic of fluorescence than the typical microsecond-scale phosphorescence of mononuclear Pt^{II} systems. This behavior is attributed to the nature of the ligand, as **$H_6L(PF_6)$** itself emits weakly with a similarly short lifetime. DFT and TDDFT calculations supported this conclusion, showing that the lowest-energy transitions are mainly localized on the π-system of the ligand, with little contribution from the metal centers.

In conclusion, this work demonstrates that, in analogy to the reported Ni^{II} congener, the heavier group 10 metals can be successfully incorporated in our macrocyclic NHC/pyrazolate ligand platform. Importantly, it also shows that photophysical functionality can be introduced through metal selection, as exemplified by the emissive Pt^{II} complex.

Author Contributions

T.P. carried out most of the experimental work and data analysis, including NMR spectroscopy, NMR titrations, and SC-XRD. T.P also performed DFT calculations, supported the conceptual development of the study, and wrote the initial draft of the manuscript. A.P. led the project and the conceptual development of the study, framed the narrative, secured funding, and provided overall guidance. A.P. and T.P. reviewed, edited, and revised the manuscript.

The task proved hard indeed, yet in the end it was done.

— J. R. R. Tolkien

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4 Conclusion and Outlook

This dissertation presents a systematic investigation of the reactivity of supramolecular organometallic complexes (SOCs), with a particular emphasis on tubular pillarplexes, derived from *N*-heterocyclic carbene (NHC) ligands and coinage metals. While prior studies have established a profound structural understanding of pillarplexes, this thesis shifts the focus toward their reactivity. It establishes fundamental design principles, synthetic strategies, and mechanistic insights for the development of reactive pillarplexes and derived SOCs.

The key findings demonstrate that reactivity can be induced and modulated through strategic selection of the metal centers and the ligand framework, as well as through mechanical interlocking of the pillarplex macrocycle within larger supramolecular assemblies. Reactivity was studied at two principal sites: (1) the *metal centers* embedded within the cavitand walls and (2) the pillarplex *rim*.

In the context of metal-centered reactivity, the first main objective of this dissertation is the introduction of Cu^{I} as a reactive, structure-directing building block in pillarplexes. The successful synthesis and characterization of Cu^{I} pillarplex **[Cu$_8$L$_2$](OTf)$_4$** have demonstrated that intrinsically reactive metals can be incorporated into the cavitand platform without compromising its structural integrity. Specifically, the structural adaptability of the Cu^{I} pillarplex enables accommodation of a model substrate despite a significant steric mismatch, as exemplified by the endohedral coordination of tetrahydrofuran (THF). The μ_2-bridging coordination mode observed in the solid state, with Cu–O_{THF} distances significantly shorter than van der Waals radii, demonstrates that metal–ligand coordination can drive substrate insertion even in sterically demanding environments. The calculated thermodynamic favorability of this process underscores the potential for substrate preorganization within the cavity. Guest binding studies in D_2O indicate that the solid-state binding behavior translates well to solution, as confirmed by a strong affinity towards THF insertion (K_a = 2730 M^{-1}).

Extending this approach, a pillarplex-based [2]rotaxane, **Rot[Cu$_8$L$_2$](OTf)$_4$**, was synthesized to demonstrate metal-centered redox activity as an example of reactivity introduced into the SOC. Cyclic voltammetry established a quasi-reversible oxidation in acetonitrile, corresponding to the

formation of Cu^{II} ions, as confirmed by EPR spectroelectrochemistry. This accessible Cu^{I} oxidation, combined with the ability to coordinate substrates within the pore, positions the Cu^{I} pillarplex as a mimic for multinuclear copper enzymes.

The second type of reactivity explored in this work revolves around the rim of the pillarplex scaffold, shifting the focus from metal-centered chemistry to supramolecular interactions involving the backbone protons and aromatic ligands of pillarplexes. Prior studies have established this aromatic rim as a structurally well-defined, electron-deficient region capable of engaging in precise non-covalent interactions, such as hydrogen bonding.

To quantify this rim-centered reactivity, a [2]rotaxane, **[Fmoc*-Rot][Ag_8L_2](PF_6)$_4$**, was synthesized by threading Ag^{I} pillarplex **[Ag_8L_2](PF_6)$_4$** onto a 1,12-diaminododecyl axle capped with 2,7-$^{t}Bu_2$-9-fluorenylmethoxycarbonyl (Fmoc*) stoppers. Kinetic studies monitored by ^{1}H NMR spectroscopy revealed that the base-induced Fmoc* deprotection within the mechanically interlocked molecule (MIM) proceeds over 35 times faster than in the non-interlocked control, **[Fmoc*-NH-(CH_2)$_6$]$_2$**. This dramatic rate enhancement reflects a phenomenon we termed the "*mechanosteric effect*", which we define as the influence of a macrocycle on the reactivity of a functional group within a MIM. Conventionally, steric crowding between these two components is assumed to *inhibit* reactivity, resulting in a *negative* mechanosteric effect. In contrast, our system displays a *positive* mechanosteric effect, where the macrocycle actively *enhances* the reactivity of an Fmoc* stopper by preorganizing it near the pillarplex rim.

Structural analysis in the solid state (SC-XRD) suggested that this preorganization results from folding of the fluorenyl system around the pillarplex rim, which exposes the reactive site and facilitates deprotonation. This arrangement is stabilized by directional CH–π interactions and hydrogen bonding between the Fmoc* group and the pillarplex backbone. ^{1}H NMR spectroscopy in acetone-d_6 solution supports this activation mode under reaction conditions, as evidenced by significant upfield shifts of selected pillarplex proton signals associated with Fmoc* interactions. In addition, quantitative 2D ^{1}H,^{1}H NOESY experiments estimated interproton distances between key Fmoc* and pillarplex protons that match well with the folded, preorganized conformation observed in the crystal structure. Eventually, a structurally similar control [2]rotaxane with 3,5-$^{t}Bu_2$-benzamide instead of Fmoc* stoppers did not show any rate enhancement of Fmoc* deprotection of **[Fmoc*-NH-(CH_2)$_6$]$_2$**, confirming that specific stopper–macrocycle pairing is required for this effect. Together, these findings demonstrate that the rigid orientation and electron-poor nature of the pillarplex ligands can create well-defined formally organocatalytic microenvironments. By exploiting mechanical interlocking and supramolecular preorganization, the system achieves selective substrate activation, thereby offering a novel strategy for the design of functional MIMs.

In addition to the two main contributions focusing on reactive pillarplexes, complementary studies explored the design and functionality of pillarplexes and derived SOCs. The investigation into triazolate-based pillarplexes demonstrated the *programmability* of the pillarplex rim. By subtly modifying the ligand backbone (*i.e.* replacing the pyrazolate motifs with triazolate ligands), we created a shape-adaptive pillarplex, **[$Au_8L^{t}_2$](PF_6)$_4$**, that exhibited a compressed, "*squeezed*" pore opening in the solid state, driven by anion interactions at the rim. While it is not entirely clear to

which degree this structural change is also present in solution, the study underscored that the rim's chemical and physical properties can be precisely tuned through ligand design without compromising the core host–guest chemistry in solution.

Similarly, structural and photophysical studies of bimetallic platinum group complexes of the same macrocyclic ligand platform used for pillarplex assembly established that functional properties can be systematically introduced into SOCs through strategic metal selection. Analogous to the previously reported Ni^{II} complex **[Ni_2L](PF_6)$_2$**, the heavier Pd^{II} and Pt^{II} congeners form saddle-shaped SOCs **[Pd_2L](PF_6)$_2$** and **[Pt_2L](PF_6)$_2$**, driven by their preference for a square-planar coordination geometry. Notably, **[Pt_2L](PF_6)$_2$** exhibits blue photoluminescence ($\lambda_{em} \approx 420$ nm, $\tau_{av} = 5.4$ ns) as an emerging property directly attributed to the choice of metal. Although the quantum yield remains modest, the Pt^{II} complex serves as a reference for evaluating the photophysical and coordination behavior of pillarplex-derived SOCs, paving the way for further exploration in light-harvesting and sensing applications.

In conclusion, this dissertation has demonstrated that reactivity can be systematically introduced into SOCs without compromising their inherent stability and modularity. The exploration of both metal-centered and rim-based reactivity has established complementary strategies for designing functional SOCs. The foundational work presented herein opens several promising research directions.

Outlook

Among the conceptual advances,[†] a central contribution of this dissertation is the definition of the *positive* mechanosteric effect, as exemplified by the accelerated Fmoc* deprotection observed within pillarplex-based rotaxane **[Fmoc*-Rot][Ag_8L_2](PF_6)$_4$**. While macrocycle-induced effects on the reactivity of functional groups in MIMs are known, this work is the first to clearly formalize the concept and demonstrate its utility in a molecular machine model. Systematic exploration of macrocycle–stopper and macrocycle–bump pairings may reveal broader applicability of this effect, potentially enabling reactivity modulation across a wide range of functional groups. For example, rim-functionalized pillarplexes incorporating functionalized (*e.g.* halogenated) pyrazolate or triazolate ligands (synthetically accessible through the modular approach outlined above) could create steric environments that exhibit either *positive* or *negative* mechanosteric effects, depending on the specific pairing.

Finally, preliminary studies have already shown that pH-induced interconversion of [2]rotaxane **[Fmoc*-Rot][Ag_8L_2](PF_6)$_4$** to a fully organic [3]rotaxane **[Fmoc*-Rot](H_6L)$_2$(PF_6)$_8$** is possible in the presence of strong acid (HPF_6), as evidenced by ^{1}H NMR and SC-XRD (**Figure 25**). Such an orthogonal stimulus-responsive transformation adds another layer of switchability, expanding the functional repertoire of pillarplex-based MIMs. This may prove valuable for the development of sophisticated molecular machines constructed from pillarplex-based components.

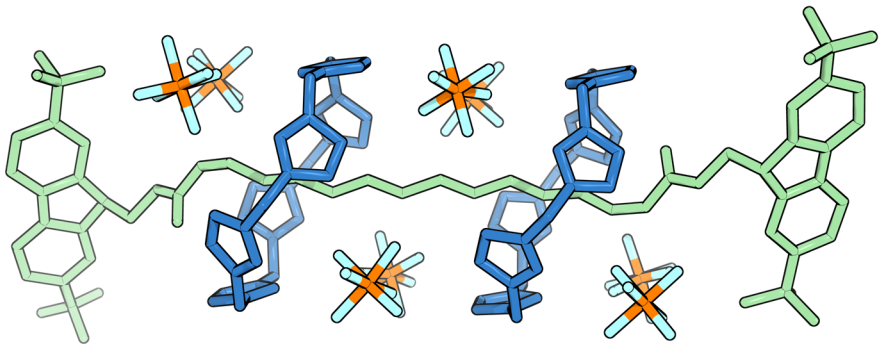

Figure 25 | Electron diffractometry (ED) structure of [3]rotaxane **[Fmoc*-Rot](H_6L)$_2$(PF_6)$_8$** in capped-sticks representation (color code: green = Fmoc*-stoppered 1,12-diaminododecyl axle, blue = calix[4]imidazolium[2]pyrazole macrocycle, orange = phosphorus, turquoise = fluorine), as determined by electron diffraction. Special thanks to *Rigaku Europe SE* for the opportunity to conduct ED measurements at their facility.

[†] *It is a minor but genuine regret that, despite dedicated efforts, pillarplexes exhibited no affinity for capsaicin as a "spicy" guest. Thus, for now, the question whether these cavitands could be used as molecular agents against chili heat remains unanswered.*

Everything works out in the end.
If it didn't, it's because it hasn't yet come to an end.

— Fernando Sabino

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5 Appendix

5.1 Complete List of Publications

5.1.1 First Author Publications

[1] *Endohedral Coordination of Bulky Substrates in Metalloenzyme-Like Organometallic Nanotubes*

T. Pickl, P. Mollik, M. Anneser, F. Sixt, K. Geißer, O. Storcheva, D. Halter, A. Pöthig
Chem. Eur. J. **2025**, *31*, e202500775

Contribution: *support with conceptual approach, experimental and data analysis (NMR, titrations, SC-XRD) except for (spectro-)electrochemical measurements, computational modelling (DFT), co-conception and writing of manuscript*

[2] *Spotlight on Mechanosterics: A Bulky Macrocycle Promotes Functional Group Reactivity in a [2]Rotaxane*

T. Pickl, C. Stark, D. Briganti, M. Curcio, A. Pöthig
J. Am. Chem. Soc. **2025**, *147*, 27192

Contribution: *conceptual approach, experimental and data analysis (NMR, kinetics, SC-XRD), computational modelling (DFT), co-conception and writing of manuscript*

[3] *Crystal Structure Elucidation of a Geminal and Vicinal Bis(trifluoromethanesulfonate) Ester*

T. Pickl, J. Zuber, J. Stephan, A. Pöthig
Acta Cryst. C **2024**, *80*, 278

Contribution: *conceptual approach, experimental and data analysis (SC-XRD), computational modelling (DFT), conception and writing of manuscript*

[4] *Triazolate-Based Pillarplexes: Shape-Adaptive Metallocavitands via Rim Modification of Macrocyclic Ligands*

S. Guan,‡ **T. Pickl**,‡ C. Jandl, L. Schuchmann, X. Zhou, P. J. Altmann, A. Pöthig
Org. Chem. Front. **2021**, *8*, 4061

Contribution: *computational modelling (DFT), data analysis, co-writing of manuscript*

[5] *Bimetallic Platinum Group Complexes of a Macrocyclic Pyrazolate/NHC Hybrid Ligand*

T. Pickl, A. Pöthig
Organometallics **2021**, *40*, 3056

Contribution: *support with conceptual approach, experimental and data analysis (NMR, SC-XRD) except for photoluminescence measurements, computational modelling (DFT), writing of manuscript*

‡ = These authors contributed equally.

5.1.2 Co-Author Publications

[1] *Enantioselective Photochemical Generation of a Short-Lived, Twisted Cycloheptenone Isomer: Catalytic Formation, Detection, and Consecutive Chemistry*

M. Stierle, C. Jaschke, D. J. Grenda, M. Peschel, **T. Pickl**, N. Gessner, P. Nuernberger, B. Fingerhut, C. Ochsenfeld, R. de Vivie-Riedle, T. Bach
Angew. Chem. Int. Ed. **2025**, *64*, e202501433

[2] *Monomeric M(II) (M = Fe, Co, Ni) Complexes Supported by Bulky Aryloxide Ligands Tethered to an Arene Functionality; Synthesis, Electrochemistry and Study of the M(II)–Arene Interaction*

I. Vagiakos, N. Tsoureas, T. Huang, S. Christodoulou, L. Maron, **T. Pickl**, J. Mink, D. P. Halter
Dalton Trans. **2025**, *54*, 8683

[3] *Photochemical Deracemization of 4,7-Diaza-1-isoindolinones by Unidirectional Hydrogen Atom Shuttling*

P. Freund, M. Pauls, D. Babushkina, **T. Pickl**, C. Bannwarth, T. Bach
J. Am. Chem. Soc. **2025**, *147*, 1434

[4] *A Chiral Nanohoop as Highly Efficient Asymmetric Organocatalyst*

A. Sacristán-Martín, F. Schwer, **T. Pickl**, A. Lebzelter, A. Pöthig, M. von Delius
Preprint (*ChemRxiv*) **2024**, DOI: 10.26434/chemrxiv-2024-srqv5-v2

[5] *Rim-Brominated Pillarplexes and Their Assembly via Self-Sorting*

J. Zuber, **T. Pickl**, A. Heidecker, M. Baron, C. Jandl, A. Pöthig
Dalton Trans. **2024**, *53*, 19116

[6] *Screening Privileged Alkyl Guanidinium Motifs under Host-Mimicking Conditions Reveals a Novel Antibiotic with an Unconventional Mode of Action*

D. Schum, F. Elsen, S. Ruddell, K. Schorpp, H. Junca, M. Müsken, S.-Y. Chen, M. Fiedler, **T. Pickl**, D. Pieper, K. Hadian, M. Zacharias, S. A. Sieber
JACS Au **2024**, *4*, 3125

[7] *Benzene-1,4-di(dithiocarboxylate) Linker-Based Coordination Polymers of Mn^{2+}, Zn^{2+}, and Mixed-Valence $Fe^{2+/3+}$*

M. Aust, M. Schönherr, D. Halter, L. Schröck, **T. Pickl**, S. Deger, M. Hussain, A. Jentys, R. Bühler, Z. Zhang, K. Meyer, M. Kuhl, J. Eichhorn, D. Medina, A. Pöthig, R. Fischer
Inorg. Chem. **2023**, *63*, 129

[8] *Photochemical Isomerization of Cyclohept-1-ene-1-carbaldehyde: Strain-Release Cycloadditions and Ene Reactions*

D. Schwinger, **T. Pickl**, T. Bach
J. Org. Chem. **2023**, *88*, 12844

[9] *Dual-Phosphorescent Heteroleptic Silver(I) Complex in Long-Lasting Red Light-Emitting Electrochemical Cells*

S. Lipinski, L. Cavinato, **T. Pickl**, G. Biffi, A. Pöthig, P. Coto, J. Fernández-Cestau, R. D. Costa
Adv. Opt. Mater. **2023**, *11*, 2203145

[10] *Synthesis of Boronates with a Protoilludane Skeleton*

J. Proessdorf, C. Jandl, **T. Pickl**, T. Bach
Synthesis **2023**, *55*, 2311

[11] *Arene Activation through Iminium Ions: Product Diversity from Intramolecular Photocycloaddition Reactions*

J. Proessdorf, C. Jandl, **T. Pickl**, T. Bach
Angew. Chem. Int. Ed. **2022**, *61*, e202208329

[12] *Rhodium(CAAC)-Catalyzed Arene Hydrogenation of Benzo-Fused N-Heterocycles to Saturated Building Blocks with an all-cis Configuration*

C. Schiwek, S. Stegbauer, **T. Pickl**, T. Bach
Adv. Synth. Catal. **2022**, *364*, 3360

5.1.3 Conference Contributions

[1] **Poster**: *Solution and Solid-State Interactions of a Copper(I)-Based Metallocavitand with a Cyclic Guest*

33rd Annual Meeting of the German Crystallographic Society
Hannover (DE), **2025**

T. Pickl, M. Anneser, A. Pöthig

[2] **Poster**: *Coordination-Driven Insertion of a Guest Molecule into the Pore of a Copper(I)-Based Metallocavitand*

18th International Symposium on Macrocyclic and Supramolecular Chemistry
Hangzhou (CN), **2024**

T. Pickl, F. Sixt, A. Pöthig

[3] **Poster**: *First Molecular Structure Elucidation of a Geminal and Vicinal Bis(triflate) Ester*

32nd Annual Meeting of the German Crystallographic Society
Bayreuth (DE), **2024**

T. Pickl, J. Zuber, J. Stephan, A. Pöthig

[4] **Poster**: *Pillarplexes as Versatile Supramolecular Building Blocks*

SupraChem 2024
Ulm (DE), **2024**

T. Pickl, J. Zuber, J. Preinl, A. Pöthig

[5] **Poster**: *Copper(I) Pillarplexes as Redox-Active Building Blocks for Rotaxane Electrocatalysts*

17th International Symposium on Macrocyclic and Supramolecular Chemistry
Reykjavík (IS), **2023**

T. Pickl, M. Anneser, O. Storcheva, D. Halter, A. Pöthig

[6] **Poster** & **Flash Talk**: *Coordination-Driven Insertion of a Guest Molecule into the Pore of a Copper(I)-Based Metallocavitand*

31st Annual Meeting of the German Crystallographic Society
Frankfurt am Main (DE), **2023**

T. Pickl, F. Sixt, A. Pöthig

[7] **Poster**: *Copper(I)-Based Pillarplexes: Platforms for Supramolecular Assemblies with Intrinsic Reactivity*

16th International Symposium on Macrocyclic and Supramolecular Chemistry
Eugene (US), **2022**

T. Pickl, D. Halter, M. Anneser, A. Pöthig

[8] **Poster**: *Expanding the Scope of Macrocyclic Poly-NHC Ligands: Bimetallic Palladium(II) and Platinum(II) Complexes*

1st Women in Supramolecular Chemistry Workshop
Cagliari (IT), **2021**

T. Pickl, A. Pöthig

5.2 Reprint Permissions

5.2.1 Endohedral Coordination of Bulky Substrates in Metalloenzyme-Like Organometallic Nanotubes

T. Pickl, P. Mollik, M. Anneser, F. Sixt, K. Geißer, O. Storcheva, D. Halter, A. Pöthig
Chem. Eur. J. **2025**, *31*, e202500775

5.2.2 Spotlight on Mechanosterics: A Bulky Macrocycle Promotes Functional Group Reactivity in a [2]Rotaxane

T. Pickl, C. Stark, D. Briganti, M. Curcio, A. Pöthig

J. Am. Chem. Soc. **2025,** *147*, 27192

5.2.3 Crystal Structure Elucidation of a Geminal and Vicinal Bis(trifluoromethanesulfonate) Ester

T. Pickl, J. Zuber, J. Stephan, A. Pöthig

Acta Cryst. C **2024**, *80*, 278

5.2.4 Triazolate-Based Pillarplexes: Shape-Adaptive Metallocavitands via Rim Modification of Macrocyclic Ligands

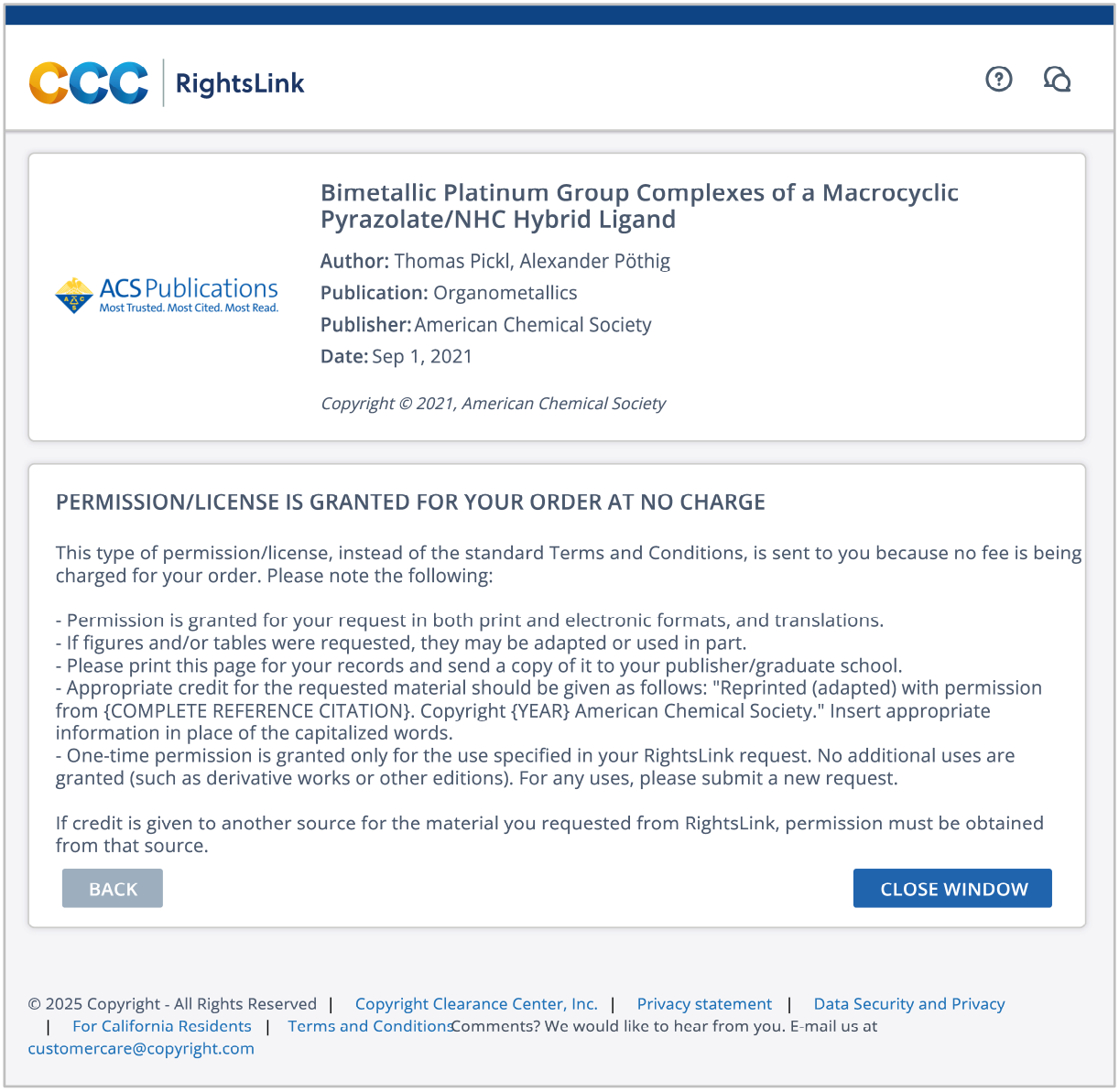
S. Guan,‡ **T. Pickl**,‡ C. Jandl, L. Schuchmann, X. Zhou, P. J. Altmann, A. Pöthig

Org. Chem. Front. **2021**, *8*, 4061

5.2.5 Bimetallic Platinum Group Complexes of a Macrocyclic Pyrazolate/NHC Hybrid Ligand

T. Pickl, A. Pöthig

Organometallics **2021**, *40*, 3056



With this, we close the situation.

— Roland A. Fischer