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M_2L_4 Complexes for the Targeted Drug Delivery of Cisplatin and N-heterocyclic Silane and Silylene Pyridine Chelates – Findings on the Way to Novel Noble Metal Catalysts

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1 Zusammenfassung

Teil 1

Noch immer gehört Krebs zu den Haupttodesursachen in Deutschland, wenngleich sich Prognosen sowie Behandlungsmethoden im Verlauf der vergangenen Jahrzehnte gleichermaßen signifikant verbessert haben. Eines der bekanntesten und vielfältigsten eingesetzten Medikamente im Rahmen einer Chemotherapie ist hierbei Cisplatin, bei dessen Einsatz allerdings teils schwerwiegende Nebenwirkungen auftreten, wodurch das Interesse an einer zielgerichteten Applikation, sog. drug targeting, immer stärker in den Fokus der Forschung rückt. Eine Möglichkeit hierzu ist der Einschluss des Medikamentes in molekulare M_2L_4 Käfige, welche sich infolge ihrer Größe selektiv in malignem Gewebe anreichern; dieses Phänomen wird als EPR-Effekt bezeichnet (*engl.*: Enhanced Permeability and Retention).

Im Rahmen dieser Arbeit wurden aus methoxy-funktionalisierten, stark fluoreszenten Liganden und Pd- sowie Pt-Salzen neue, fluoreszente M_2L_4 Käfige hergestellt. Die neuen Pd-Verbindungen sind in der Lage Cisplatin einzuschließen; diese Einschlussverbindungen zeigen erhöhte Toxizität gegenüber A549 Zelllinien (humanes Lungenkarzinom) im Vergleich zu reinem Cisplatin, wohingegen Liganden und Käfige alleine nicht bis wenig toxisch sind.

Teil 2

Iridium- und Rhodiumkomplexe sind heute aufgrund ihrer Eignung als Katalysatoren für synthetisch wichtige Umsetzungen wie Hydrierungen elementarer Bestandteil der präparativen Chemie. Silane haben insbesondere als Reaktionsintermediate sowie als Quelle für weiche Silylradikale, welche vorteilhaft für Polymerisationen sein können, große Bedeutung erlangt.

In dieser Arbeit wurden neue Iridium- und Rhodiumkomplexe eines ambidenten, Pyridin-funktionalisierten N-heterocyclischen Silanliganden dargestellt. Iridium koordiniert an die Vorderseite des Liganden, wodurch ein Amin-Pyridin Chelat entsteht. Rhodium hingegen bindet das aromatische Rückgrat des Liganden *via* Aryl-π-Interaktion, was zu einem bisher beispiellosen Koordinationswechsel von 4 auf 5 am Siliciumzentrum führt, obwohl die direkte chemische Umgebung um Silicium nicht verändert wird. Dieser Wechsel in der Koordinationssphäre wird über eine räumliche Distanz von über 4,4 Å elektronisch induziert und könnte zukünftig für molekulare Schalter von Interesse sein.

2 Abstract

Part 1

Still today, cancer is one of the major causes of death in Germany, albeit prognoses and methods of treatment have signifigantly improved within the last decades. One of the most widely applied and famous drugs within chemotherapy is cisplatin, the application of which, however, is accompanied by partly severe side effects. This circumstance leads to a growing interest for drug targeting in today's research. One possibility for this is the encapsulation of cisplatin in molecular M_2L_4 cages, which selectively accumulate in malignant tissue as a consequence of their size; this phenomenon is known as the EPR effect (Enhanced Permeability and Retention).

Within this thesis new M_2L_4 cages have been synthesized from methoxy-functionalized, highly fluorescent ligands and Pd as well as Pt salts. The new Pd compounds are capable of encapsulating cisplatin; the clathrates exhibit an incresed toxicity towards A549 cancer cell lines (human lung carcinoma) in comparison to cisplatin alone, whereas ligands and cages themselves are non- or only mildly toxic.

Part 2

Iridium and rhodium complexes are an essential part within preparative chemistry due to their suitability as catalysts for synthetically important transformations such as hydrogenations. Silanes have gained a great repute as crucial reaction intermediates and as a source for soft silyl radicals, which can be beneficial for polymerizations.

Within this work new iridium and rhodium complexes of an ambident, pyridine-functionalized silane ligand have been synthesized. Iridium is coordinated by the ligand's front side, resulting in a pyridine-amine bidentate chelate. In contrast, rhodium binds to the ligand's aryl backbone through π-interaction, leading to an unprecedented change of the coordination mode at the silicon center from 4 to 5, although the direct chemical environment around the latter is not changed. This change is electronically induced over a spatial distance of more than 4.4 Å and might be of interest for future applications in molecular switches.

3 Introduction and motivation

3.1 Part 1: M_2L_4 complexes and their medical applications in targeted cancer treatment with cisplatin

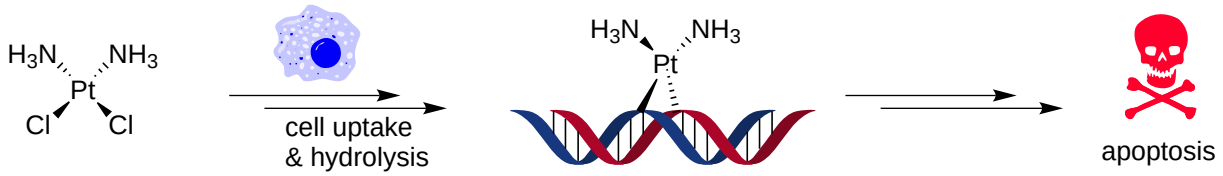
3.1.1 Cancer – spotlight on one of today's biggest medical challenges in consideration of historic developments

Cancer remains a pervasive and chameleonic disease that ranks among the major causes of death worldwide. In 2015, more than 28% of all deaths in Germany were the consequence of a malignant illness with only cardiovascular diseases causing more deaths (35%).[1] However, mortality from cancer in general has been decreasing throughout the years due to improved treatment with better remedies; *e.g.* the mortality rate for stomach-related cancer has decreased from about 50% in 1970 to under 15% in 2002.[2]

Within cancer treatment strategies, chemotherapy remains one of the most important components, since its introduction in the 1940s.[3] Physicians and other scientists had, during the treatment of mustard gas victims after World War I, discovered the myelodepressive (depression of the bone marrow) effects of these compounds.[4,5] They concluded that substances, which particularly attack fast-proliferating bone marrow cells, should have a similar effect on rapidly growing cancer cells, as well. The results from experimental treatment of mice with nitrogen mustard in the 1930's by researchers like Isaac Berenblum and of humans suffering from *e.g.* Hodgkin's lymphoma with analogous compounds like chlormethine in the 1940's *i.a.* by Louis Goodman and Alfred Gilman confirmed this assertion.[3,6] The compound chlormethine (*N*,*N*-bis(2-chloroethyl)-*N*-methylamine), which had only recently been developed as a chemical warfare agent, has been and is still used as a cytostatic in the USA.[7]

Since these first approaches, the variety of antiproliferative drugs has steadily increased. In 1978, the compound cisplatin [*cis*-diamminedichloridoplatinum(II)] was approved by the U.S. Food and Drug Administration (FDA) after it had successively been tested for its effectiveness against testicular cancer from 1974 onward. Once ingested, it is hydrolyzed in the cells and induces DNA crosslinking which leads to apoptosis, or programmed cell death (Scheme 1).[8,9]

The therapeutic scope of cisplatin has increased massively from 1978 and it has since become one of the most important cytostatic agents. However, like most contemporary



Scheme 1: Schematic representation of a DNA crosslinkage by cisplatin after uptake into a (cancer) cell and hydrolysis of the chloride ligands. Eventually, the crosslinkage leads to apoptosis, the programmed cell death.

drugs cisplatin is not selectively active in cancer tissue, but is more or less distributed over the majority of cells in the human body. Thus, the agent will also affect structures and actions that are not at all related to the cancerous processes it is indended to interfere with. Hence, along with a broad therapeutic scope come significant side-effects, ranging from nausea to severe issues such as myelosuppression, neuro- and nephrotoxicity. A targeted application of cytotoxic drugs is therefore highly desirable and would help to circumvent these downsides and wreaking havoc in noninvolved structures.[10,11]

3.1.2 Drug targeting – utilizing the so-called EPR effect

One possibility for drug targeting is to utilize the anomalous physiology of blood vessels in cancerous tissue. As a consequence of their huge demand for nutrients, due to the highly accelerated cell growth, most tumors express increased levels of nitrous oxide, peroxynitrite or bradykinin.[12–17] Consequently, blood vessels are dysplastic and the membranes are far more permeable and patchy than usual. Figure 1 illustrates a comparison between blood vessels in benign and malign tissue with the help of electron microscopic images.

The vessels' clear and regular structure in healthy tissue (**A** – **C**) is clearly recognizable, the tight and closed surface becomes apparent. In contrast, in metastatic, cancerous tissue the blood vessels look poriferous or even lacerated and frayed, especcially in contrast to adjacent healthy tissue (**D**; **E**).[18]

This special structure leads to the so-called EPR (Enhanced Permeability and Retention) effect, which has first been described by Yasuhiro Matsumura and Hiroshi Maeda in 1986.[19] Macromolecules of effectual size preferably exit the bloodstream in these structures and accumulate.[12] Thus, this can be utilized for passive drug targeting (*i.e.* without using a particular transporter) in oncology, to be specific through using a macromolecular drug or incorporation of the pharmaceutically active compound into a macromolecular vector (= carrier). Figure 1, picture **F** shows the result of treating a metastatic liver tumor

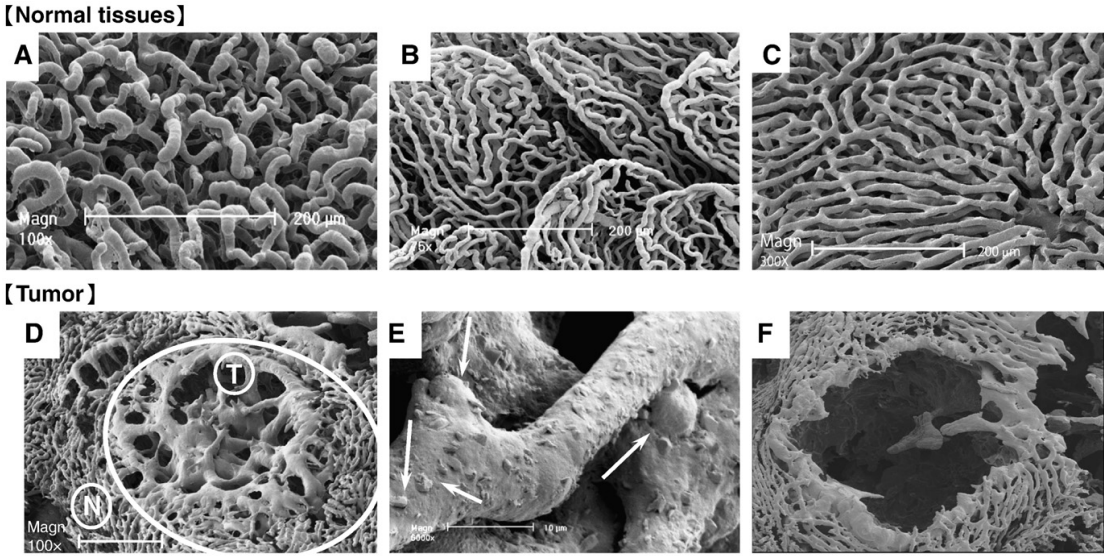


Figure 1: Top row, **A**–**C**: blood vessels in normal, benign tissue. Bottom row, **D**: blood vessels in a metastastatic tumor nodule (circled, marked with T) of the liver next to normal liver tissue (N), a magnification of the capillaries from the tumorous part (**E**) and the remains of the tumor (*cf.* **D**) after treatment with the macromolecular cytostatic SMA-pirarubicin (**F**).[18]

nodule with macromolecular SMA-pirarubicin. The tumor vascular bed has completely been disintegrated (*cf.* **D**).[18,20]

Investigation of selectivity for target tissue and verification of proposed pharmacokinetics can be achieved particularly well by fluorescence microscopy, in case the macromolecular vector is fluorescent. This technique is beneficial due to its high resolution and applicability in living cells.[21,22]

3.1.3 Molecular M_2L_4 cages – a promising drug delivery system?

One potential vector system to encapsulate oncological drugs, like cisplatin, are self-assembled molecular cages. Three-dimensional cages, in which stability is mainly based upon metal-ligand interactions, have received growing attention throughout the last decades.[23] With binding energies between $15 - 50\ \frac{\text{kJ}}{\text{mol}}$ coordination processes are supported insofar as they procure a balance between certain geometric rigidity but also a still sufficient kinetic reversibility. Thus, under suitable conditions, the thermodynamically most stable product will be formed, as "wrongly" formed bonds can dissociate and reassociate in a correct way after. The formation of cyclic or cage structures is therein usually favored over polymers because of entropic reasons.[24]

Many different kinds of these molecular cages have been synthesized so far and some show luminescence.[23,25–30] However, reports for the application of these complexes as drug delivery systems are still scarce.[23,31,32]

Due to their simple geometries as well as quick and straightforward synthesis through self-assembly, complexes consisting of two metal centers and four *bis*-monodentate ligands (M_2L_4) have been the focus of numerous studies, since first synthesized by Peter Steel *et al.* in 1998.[33] Not only can such capsules be utilized for molecular recognition,[34,35] they are also a promising drug delivery system.[23,31,32]

In most parts, palladium(II) is used as the metal center, but also some examples exist for other M^{2+} ions such as iron, cobalt, nickel, copper, manganese and zinc. Due to the fact that palladium often leads to fluorescence quenching, these alterntive metals might be a promising alternative for M_2L_4 capsules with auspicious optical properties.[23]

3.1.4 M_2L_4 molecular cages with metal ions different from palladium

Although most M_2L_4 cages in literature are based upon the interaction of ligands and the square planar coordinated d^8 ion palladium(II), some examples exist for other metals. Hani Amouri *et al.* isolated and characterized M_2L_4 molecular capsules, derived from a *bis*-benzimidazole-1,3-phenylene ligand with cobalt and copper as metal ions (Figure 2).[36,37]

Therein, the metal ions are coordinated in a distorted octahedral symmetry and the inner cavity is occupied by counterions BF_4^- or PF_6^-. These weakly coordinating anions interact with the two adjacent M^{2+} ions each at one of their axial positions. For the cobalt capsule the distances F–Co lie between 2.406(9) Å with BF_4^- and 2.361(5) – 2.426(4) Å with PF_6^- (in contrast, $d_{Co–N}$ averages to 2.09 Å). The outside axial positions are coordinated either by solvent molecules (MeCN) or counterions, interchangeably. In contrast, the encapsulated counterions cannot be replaced and are essential parts of the structure. Syntheses with more strongly coordinating anions such as chloride or nitrate led to metallacycles and polymers, respectively.[36–38]

Xian-He Bu *et al.* reported M_2L_4 capsules derived from highly flexible pyridyl dithioether ligands and $Co(ClO_4)_2$ as well as $Zn(ClO_4)_2$. In contrast, the respective manganese and cadmium salts gave polymeric structrures. The isostructural zinc and cobalt capsules could be crystallized and characterized by single crystal X-ray diffraction, the latter of which is shown on the left in Figure 3.[39]

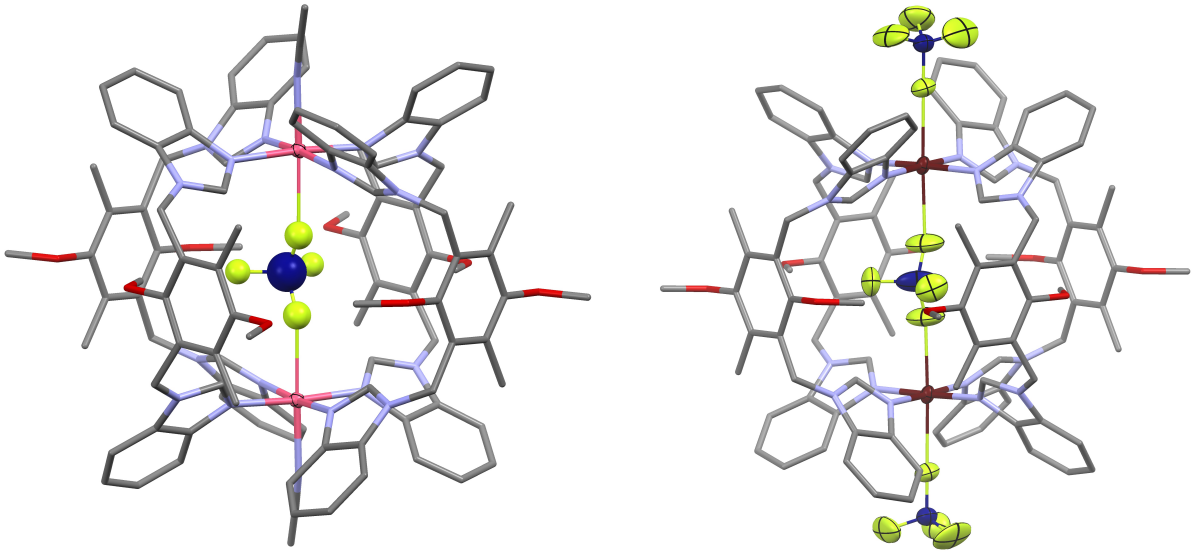


Figure 2: The cobalt (left) and copper (right) M_2L_4 cages with a *bis*-benzimidazole-1,3-phenylene ligand by Amouri *et al.* with encapsulated BF_4^- counterions. Ellipsoids for metal atoms and bound BF_4^- counterions shown at 50% probability level, all others as wireframe. Disorder, hydrogen atoms, non-bound counterions and solvent molecules omitted for clarity. Element colors: gray – carbon; light blue – nitrogen; red – oxygen; pink – cobalt; brown – copper; chartreuse – fluorine; dark blue – boron.[36,37]

The two cobalt atoms are coordinated in a Jahn-Teller-distorted octahedral geometry. Therein, four pyridine moieties are bound in one plane, the two axial positions are coordinated by water molecules. Interestingly, the Jahn-Teller-distortion leads to two different bond lengths $d_{Co–N}$ (2.119 vs. 2.170 Å); $d_{Co–O}$ are 2.162 – 2.168 Å.[41] For the zinc compound, as expected, all distances Zn–N are equal and amount 2.101 Å, $d_{Zn–O}$ are 2.148 Å (inside) and 2.394 Å (outside).[41] In contrast to the compounds by Amouri *et al.*, these cages do not encapsulate the counterions so they are located outside the structure.[36,37,39]

From another flexible pyridine thioether ligand and cobalt halides, Chunxi Zhang and Maochun Hong *et al.* reported a similar M_2L_4 cage, which can be obtained at temperatures around 10 °C (Figure 3, right). At higher reaction temperatures (25 and 30 °C), polymeric structures have been isolated.[40] The cages exhibit a distorted octahedral geometry around cobalt with four pyridine moieties in the equatorial positions ($d_{Co–N}$ = 2.137(2) – 2.160 Å).[41] The axial positions are occupied by halide counterions; each one Cl^- or Br^-, respectively, is encapsulated within the cage. The cobalt–halide distances vary: inside the cage they amount 2.818 Å for Cl^- and 2.904 Å for Br^-, outside they are significantly shorter with 2.424 Å (Cl^-) and 2.6045(5) Å (Br^-).[40,41] Apart from the abovementioned

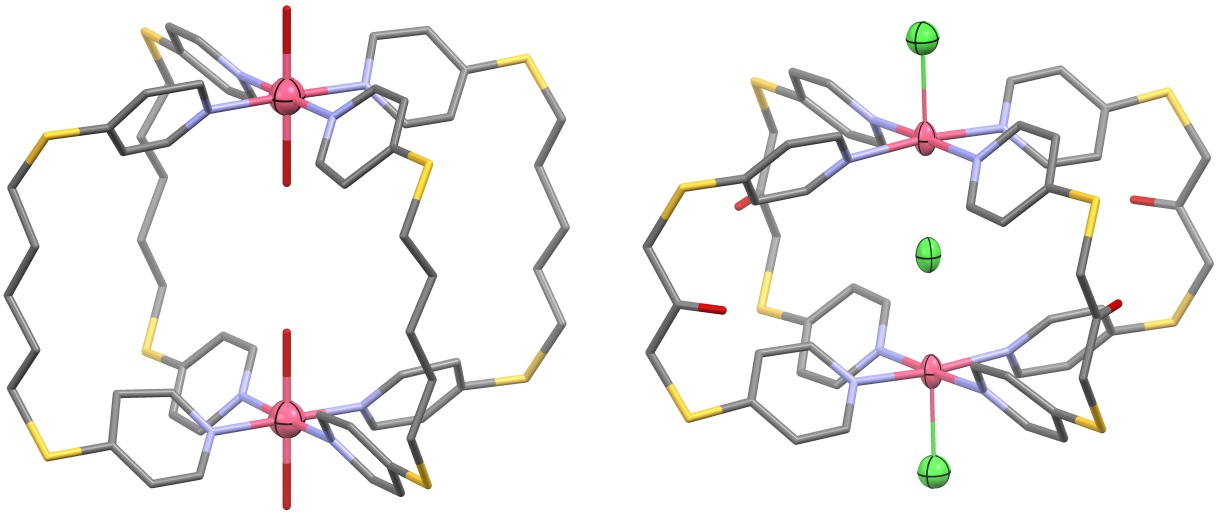


Figure 3: M_2L_4 capsules derived from highly flexible pyridyl dithioether ligands by Bu *et al.* (left) as well as Zhang and Hong *et al.* (right). Metal atoms, bound and encapsulated Cl^- counterions shown at 50% probability level, all other atoms as wireframe. Hydrogen atoms, non-bound counterions and solvent molecules omitted for clarity. Element colors: gray – carbon; light blue – nitrogen; red – oxygen; golden – sulfur; pink – cobalt; green – chlorine.[39,40]

examples, further examples for M_2L_4 cage compounds with M = Cu, Co, Ni, Zn and Fe exist.[42,43]

3.1.5 M_2L_4 molecular cages with highly fluorescent ligands

As mentioned before in Chapter 3.1.2, for the analysis of pharmacokinetics and cell uptake, fluorescent drug delivery vectors are highly beneficial, particularly with regard to fluorescence microscopy. In order to design fluorescent M_2L_4 capsules as vectors, it is neccessary to use highly emissive ligands. Only a few examples exist in literature so far, in which the fluorescence of ligands and M_2L_4 cage compounds has been investigated:

Richard Hooley *et al.* reported Pd_2L_4 capsules from several structurally similar phenylene-*bis*-ethynylpyridine ligands, some of which were luminescent with quantum yields of up to $\Phi = 87\%$ (exemplary structure in Figure 4 on the left).[44,45] Upon coordination to Pd^{2+}, in several cases the quantum yield is still considerably high (up to $\Phi = 83\%$), although it is significantly decreased in other cases.[45]

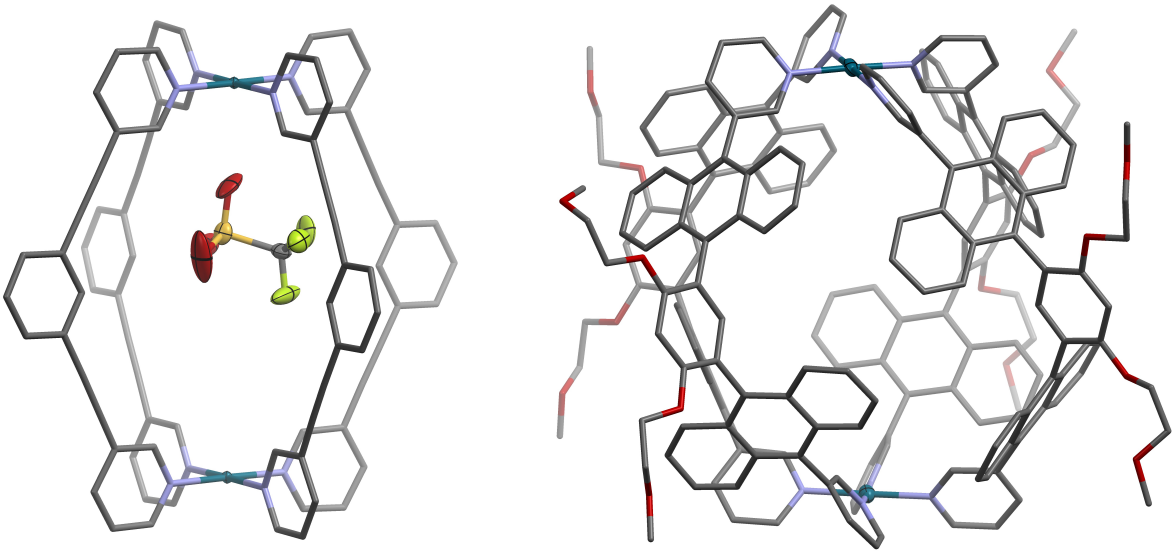


Figure 4: Exemplary structures for the M_2L_4 cage compounds by Hooley *et al.* (left) and Yoshizawa *et al.* (right). Ellipsoids for palladium atoms and encapsulated triflate-counterion shown at 50% probability level, all others as wireframe. Disorder, hydrogen atoms, non-encapsulated counterions and solvent molecules omitted for clarity. Element colors: gray – carbon; light blue – nitrogen; red – oxygen; turquoise – palladium; chartreuse – fluorine.[44–46]

Another fluorescent ligand motif, based upon an anthracene ligand, was introduced by Michito Yoshizawa *et al.* in 2011.[30] Isostructural complexes with similar ligands [methoxy groups partly or fully exchanged for MEM (methoxy-ethoxy-methyl)] and eight different metal cations (M = Zn, Cu, Pt, Pd, Ni, Co, Mn, Hg) could be isolated and characterized, four of them by single crystal X-ray diffraction (exemplary structure in Figure 4 on the right). The methoxy substituted ligand itself was highly emissive with a quantum yield of $\Phi = 79\%$. The capsules' fluorescence properties were highly dependent on the metal used. Pd, Pt, Co and Cu complexes were non-emissive, Ni and Mn complexes weakly emissive. With Hg, the absolute quantum yield was $\Phi = 16\%$, the Zn capsule however exhibited strong luminescence with $\Phi = 81\%$. Additionally, the copper capsule showed solvent-induced emission switching. While the fluorescence was not observed in MeCN, emission was detected in THF ($\Phi = 22\%$), DMF ($\Phi = 33\%$) and DMSO ($\Phi = 76\%$). The authors attribute this behavior to coordination of solvent to the apical positions of the Cu(II) centers.[46,47] Yet, not only are the cages by Yoshizawa *et al.* emissive, they are also capable of encapsulating various molecules – a behavior required for drug delivery vectors.

3.1.6 Molecular M_2L_4 cages with the ability to encapsulate molecules other than counterions and solvents

Although many M_2L_4 capsules have been described in literature, only a few have been investigated concerning their eligibility for host-guest interactions with smaller molecules. For example, the phenylene-*bis*-ethynylpyridine cage compound by Hooley *et al.* (and its platinum homologue) that is shown on the right in Figure 4 and has been described in Chapter 3.1.5 previously, shows affinity (up to $K_a = 12.1\ \text{M}^{-1}$) for several neutral organic guest molecules exhibiting both correct size as well as electrostatic complementarity, such as terephthalonitrile or 4-chlorobenzonitrile.[44]

Yoshizawa *et al.* reported the incorporation of Buckminsterfullerene C_{60} into a Pd_2L_4 cage that has been discussed in Chapter 3.1.5, as well.[48] Futhermore, they were able to include other molecules like methyl pyrene, coranullene, functionalized adamantane derivatives, and [2.2]-paracyclophane into this and structurally analogue capsules.[48–50] The structures of the host-guest assemblies with the bent coranullene (1:2) and the spherical [2.2]-paracyclophane (1:1) are shown in Figure 5.

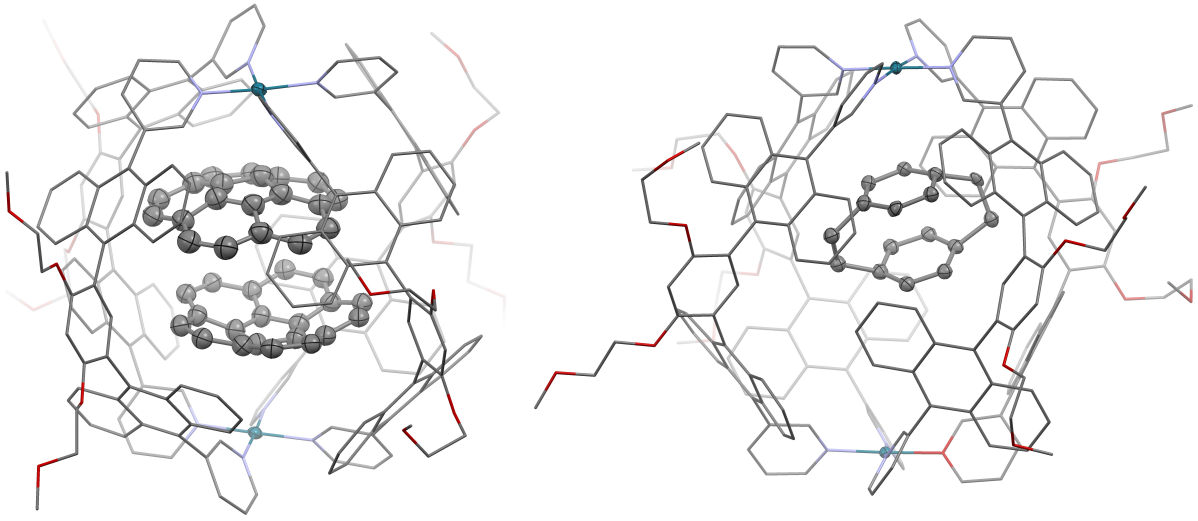


Figure 5: Host-guest assemblies of Pd_2L_4 cages with coranullene (1:2, left) and [2.2]-paracyclophane (1:1, right) by Yoshizawa *et al.* Ellipsoids for palladium atoms and encapsulated guest molecules shown at 30% probability level, all others as wireframe. Disorder, hydrogen atoms, counterions and solvent molecules omitted for clarity. Element colors: gray – carbon; light blue – nitrogen; red – oxygen; turquoise – palladium.[49,51]

Furthermore, the encapsulation of the fullerenes C_{60} and C_{70} into an analogous mercury capsule was reported in 2014. Additionally, this molecular cage transforms into a M_2L_2

molecular tube upon adjustment of the M:L-ratio through simple addition of more mercury salt which consequently releases the guest molecules.[47]

For the application as a drug delivery system, besides fluorescence and the ability to encapsulate small molecules, the cytotoxic properties of the vector, in this case the molecular cage, are of striking importance. However, the M_2L_4 cages (M = Pd and Pt) by Yoshizawa *et al.* and similar ones are more toxic than cisplatin itself in several cancer cell lines.[52,53] Thus, upon application, the major cytostatic effect arises from the vector, not the carried drug itself.

3.1.7 Encapsulation of cisplatin and other cytotoxic agents in nontoxic M_2L_4 molecular cages

Ideally, a drug delivery system does not itself exhibit cytotoxic effects, in order not to interfere with the carried cytostatic. However, reports about cytotoxicity of M_2L_4 compounds – especially combined with host-guest behavior with cytostatics – are still scarce. In this regard, James Crowley *et al.* reported the encapsulation of cisplatin into a M_2L_4 cage, that had previously been synthesized by Hooley *et al.* and been shown to exhibit slight luminescence (*cf.* chapter 3.1.5 and 3.1.6).[44,45,54] They have been able to trace the encapsulation process by ^{1}H NMR spectroscopy and HR ESMS. Single crystal X-ray diffraction unambiguously revealed the formation of a 1:2 adduct of M_2L_4 cage and cisplatin, which is shown in Figure 6 on the left. The comparatively low toxicity ($IC_{50} \geq 59$ μM in A549 and SKOV-3) of these kinds of ligands has been shown later.[55]

With similar ligands and M = Pd, Pt, Hani Amouri *et al.* were able to encapsulate one equivalent of the cytotoxic planar anion $[PtCl_4]^{2-}$. However, they did not investigate the cytotoxic properties of capsules and clathrates.[56]

Fritz Kühn *et al.* used modified, backbone-functionalized derivatives of Hooley's ligands to synthesize the respective M_2L_4 cages with improved photophysical properties.[44,45,55] They proved the encapsulation of cisplatin, amongst others, by single crystal X-ray diffraction. The structure of the clathrate is shown in Figure 6 on the right.

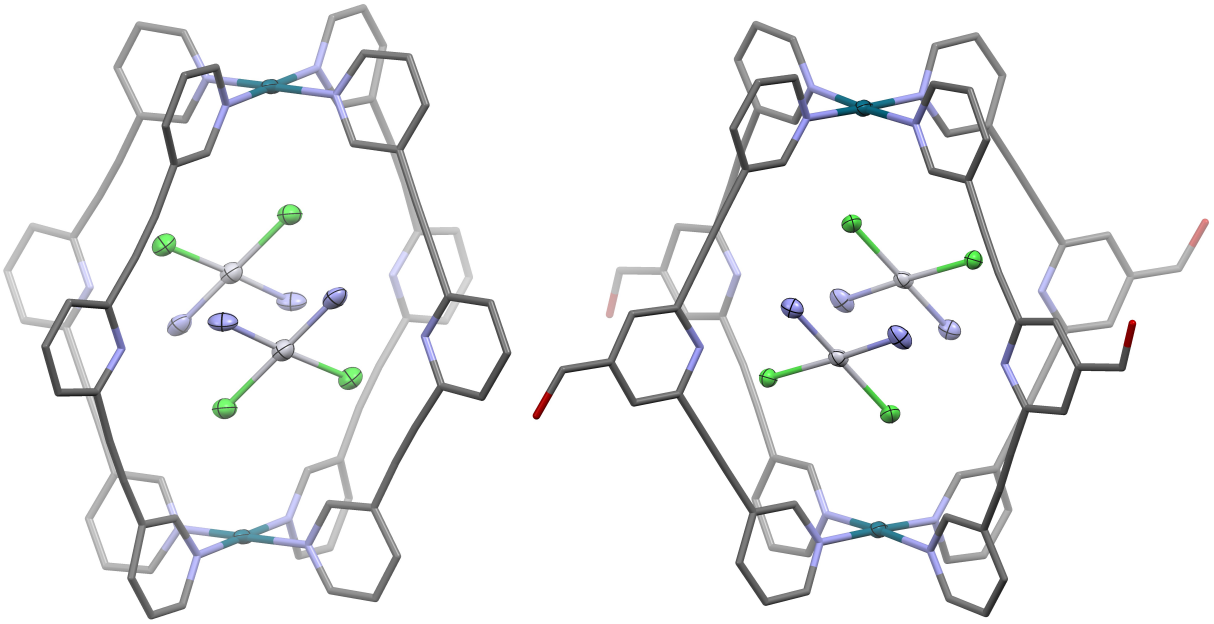


Figure 6: M_2L_4-cisplatin clathrates by Crowley *et al.* (left) and Kühn *et al.* (right). Ellipsoids for palladium atoms and encapsulated cisplatin molecules shown at 50% probability level, all others as wireframe. Hydrogen atoms, counterions and solvent molecules omitted for clarity. Element colors: gray – carbon; light blue – nitrogen; red – oxygen; turquoise – palladium; white – platinum.[54,55]

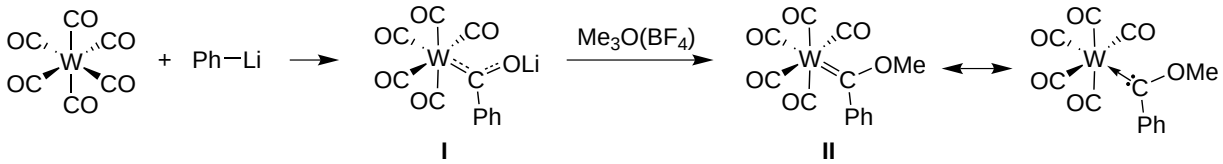
Furthermore, Kühn *et al.* investigated the cytotoxicity of ligands, cages and cage-cisplatin assemblies in comparison to cisplatin alone. The ligands used proved to be non- or only mildly toxic (*e.g.* $IC_{50} \geq 62.0 \pm 4.4$ μM in SKOV-3 – human ovarian cancer), while most of the palladium cages, except for the amine and hydroxymethyl functionalized ones, were only mildly toxic. Additionally, some of the cages exhibited weak fluorescence.[57]

By attachment of fluorophores or more/different functional groups to the ligands' backbone, emission could be increased further, an approach, that had successively been used before and shall be a topic of this thesis.[58,59]

3.2 Part 2: N-heterocyclic silane and silylene pyridine chelates – findings on the way to novel noble metal catalysts

3.2.1 Low valent group 14 compounds – from odd to essential

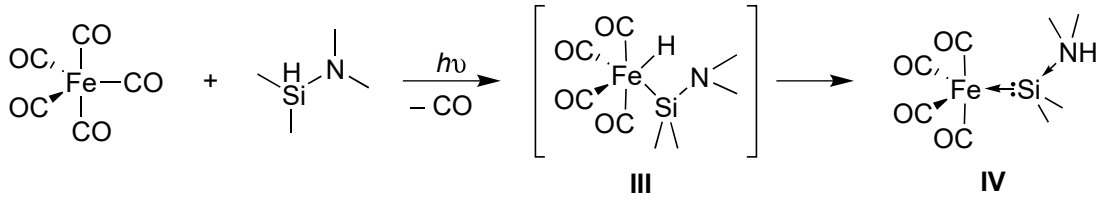
Among the first and most elementary rules not only in organic chemistry is the allegedly irrevocable principle of neutral carbon atoms always exhibiting four bonds in total. The scarce exceptions from this rule have been seen and treated as curiosities for decades, until Nobel Prize laureate Ernst O. Fischer *et al.* synthesized the first metal-stabilized carbene in 1964, *i.e.* formally a compound with a lone pair at the carbon atom (Scheme 2).[60,61]



Scheme 2: Synthesis of the first metal-carbene complex (**II**) by Ernst O. Fischer *et al.* through nucleophilic attack of phenyl lithium at a carbonyl C coordinated to W, followed by O-methylation with the Meerwein salt $Me_3O(BF_4)$. Improved synthetic route; initially, the anionic intermediate product **I** was precipitated as a tetrabutylammonium salt, protonated and then treated with diazomethane to yield **II**.[60–62]

However, it was not until more than 25 years later, that a free isolable carbene was reported by Guy Bertrand *et al.* (**V^a**, Figure 7).[63] Particularly the development of N-heterocyclic carbenes (NHCs) since the seminal work by Anthony J. Arduengo *et al.* in 1991 (**V^b**, Figure 7) triggered investigations in their applicability in catalysis, significantly favored by the perception of their isolobality to phosphines as ligands by Wolfgang A. Herrmann *et al.*[64–66] These early works cleared the way for extensive investigations in N-heterocyclic carbenes as ligands for transition metals, leading to several breakthroughs in the field of catalysis and the development of commercially available, industrially applied carbene catalysts, such as the second generation Grubbs catalyst, contributing to the Nobel Prize for its inventor Robert Grubbs in 2005.[67,68]

Consequently silylenes, the heavier group 14 homologues of carbenes have been investigated for their reactivity and catalytic properties as well, after they had mainly been recognized as important reaction intermediates before.[69] A stable silylene has first been isolated by Eckhard Welz *et al.* in 1977, when they irradiated a mixture of $Fe(CO)_5$ and HMe_2SiNMe_2 with a mercury vapor lamp (Scheme 3). Furthermore, they isolated a similar NHSi-iron complex from $Fe(CO)_5$ and 2-chloro-1,3-diphenyl-1,3-diaza-2-silacyclopentane.



Scheme 3: Synthesis of the first silylene by Eckhard Welz *et al.* from $Fe(CO)_5$ and HMe_2SiNMe_2 after irradiation with a mercury vapor lamp. The intermediate silyl iron hydride **III** is not stable under reaction conditions and rearranges to the amine-stabilized silylene complex **IV**.[70]

The first persistent free silylene however, was synthesized in 1994 (**VI**, Figure 7).[71] Since then, a growing variety of stable N-heterocyclic silylenes (NHSis) has been reported in literature and in 2001, the first example for a catalytically active metal-silylene complex was published by Alois Fürstner *et al.*[72]

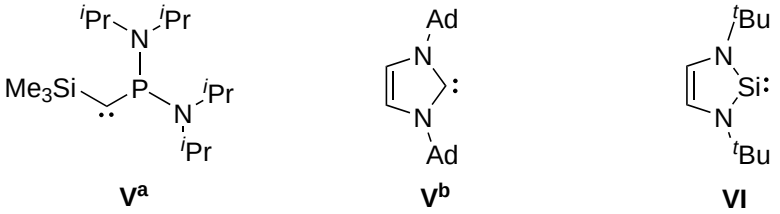


Figure 7: The first stable free carbene and N-heterocyclic carbene (left and middle, $\mathbf{V^a}$ and $\mathbf{V^b}$) and N-heterocyclic silylene (right, **VI**) by Bertrand, Arduengo and West *et al.*, respectively. Ad = adamantyl.[64,71]

3.2.2 Silylenes – properties and potential of these reactive species

Although they look very alike at first sight, NHSis and NHCs exhibit significant differences concerning electronic structure and reactivity. Due to a higher energy separation between s- and p-orbitals and a lower tendency to form hybrid orbitals, silylenes usually exhibit a singlet ground state, whereas carbenes also occur in a triplet state.[73] Compared to NHCs, NHSis have an empty p-orbital at silicon perpendicular to the N-heterocylic plane, that is less populated with electron density from the adjacent nitrogen π-donors. Secondary Lewis bases can be utilized to donate electron density into that orbital, thus additionally stabilize the electron deficient silylene and moreover increase the already high σ-donor strength even further.[74,75]

The majority of known, cyclic silylenes can be divided into four classes: (mostly five membered) N-heterocyclic silylenes (**A**), donor stabilized N-heterocyclic silylenes (**B**), donor

stabilized four membered ring silylenes (**C**) and donor stabilized six membered ring silylenes (**D**); their general structures are presented in Figure 8.[74]

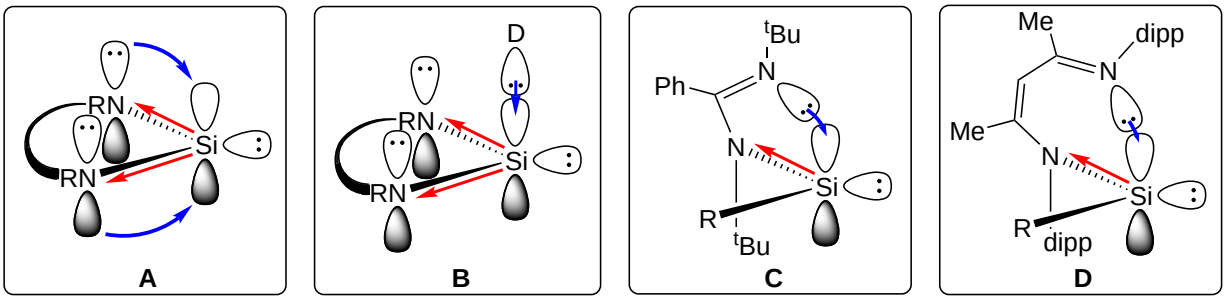


Figure 8: Structures of the four general classes of cyclic silylenes: (mostly five membered) N-heterocyclic silylenes (**A**), donor stabilized N-heterocyclic silylenes (**B**), donor stabilized four membered ring silylenes (**C**) and donor stabilized six membered ring silylenes (**D**). Blue arrows indicate π-electron donation to the "empty" p-orbital at the silicon center, red arrows the σ-electron withdrawal by the more electronegative nitrogen atoms. Abbreviations: D = Donor/ Lewis base; dipp = 2,6-diisopropylphenyl.[74]

The electron deficient silicon atom is sterically stabilized by the bulk of proximal R-groups and electronically by π-donation from adjacent N-atoms and/or additional electron donation by Lewis bases into the "empty" p-orbital. In general, the non-stabilized N-heterocyclic silylenes are weaker σ-donors than a comparable N-heterocyclic carbene (1,3-*bis*-(2,6-diisopropylphenyl)-imidazol-2-ylidene) and the phosphines PPh_3 and PCy_3 (Cy = cyclohexyl), according to calculated proton affinities as a measure of σ-donor strength. In contrast, the donor stabilized compounds (**B**–**D**) outperform the phosphines and some of them also the aforementioned NHC. The calculated π-acceptor-strengths of all silylene classes is in the vincinity of the comparative carbene, although some silylenes excel the latter by far. In contrast, the abovementioned phosphines exhibit no significant π-acceptor strengths at all.[74]

Due to these properties, silylenes are promising candidates for their utilization as ligands in transition metal catalysis. A high σ-donor strength promotes oxidative addition, a sufficient π-acceptor ability favors reductive elimination. Theses two are often key steps in many homogenous catalytic cycles.[76]

3.2.3 Noble metal silylene complexes in homogenous catalysis

Although examples for noble metal N-heterocyclic silylene-catalyzed reactions remain rather scarce in literature, considerable progress has been achieved in this field within the last five years. As shortly mentioned before in chapter 3.2.1, the first catalytically active silylene complex was reported in 2001 by Alois Fürstner *et al.* (Figure 9).[72]

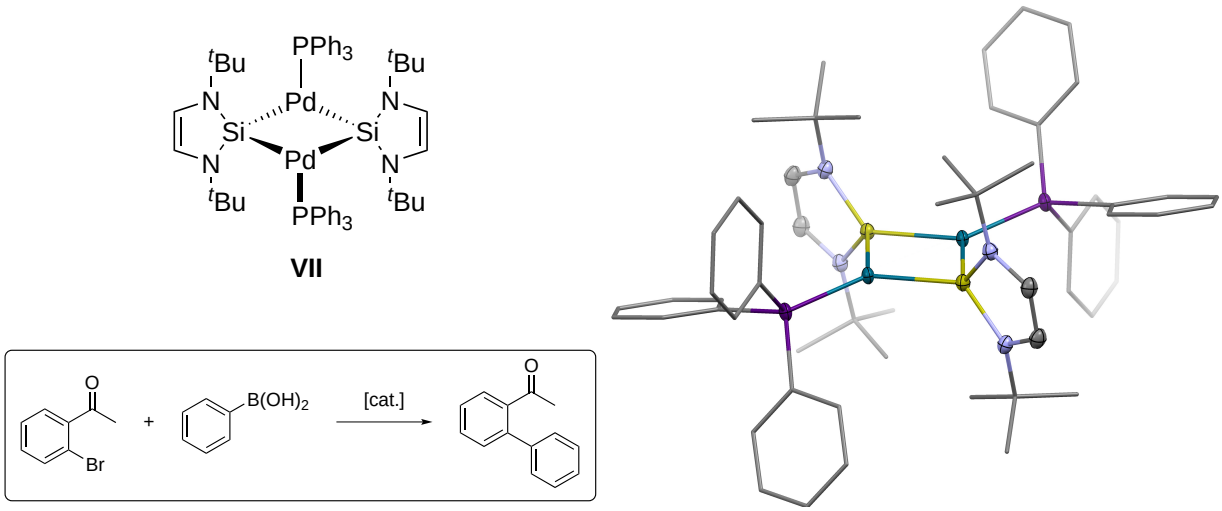
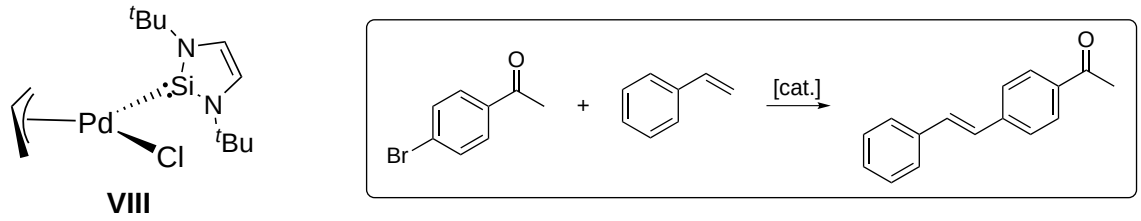


Figure 9: Lewis (top left) and X-ray (right) structure of the first catalytically active metal silylene complex **VII** by Fürstner *et al.* for Suzuki cross coupling reactions (bottom, exemplary). Catalytic conditions: 5 mol% **VII**, K_2CO_3, (glyme), 80 °C. Ellipsoids at 50% probability level, ^{t}Bu and Ph groups depicted as wireframe, hydrogen atoms omitted for clarity. Element colors: gray – carbon; light blue – nitrogen; golden – silicon; turquoise – palladium; purple – phosphorus. [72]

After treatment of $Pd(PPh_3)_4$ with free silylene **VI** they isolated the dimeric palladium complex **VII**. The compound was active as a catalyst in Suzuki type cross coupling reactions of activated aryl bromides with aryl boronic acids.[72]

A similar palladium compound, $[(\eta^3\text{-}C_3H_5)Pd(\mathbf{VI})Cl]$ (**VIII**), derived from free N-heterocyclic silylene **VI** and $[(\eta^3\text{-}C_3H_5)PdCl]_2$, has been reported by Herbert Roesky *et al.* in 2008. In contrast to **VII**, the authors claim that the complex is monomeric, although no direct evidence such as a single crystal X-ray structre or mass spectrometry has been provided. The complex has been successfully utilized as a catalyst in the Heck reaction between *p*-bromo acetophenone and styrene. The authors state that the catalyst is *in situ* activated by sodium actetate in dimethyl acetamide (DMA) as a solvent at high temperatures (140 °C), leading to almost quantitative yields within 4 h. In contrast, at 80 °C only 45% yield is achieved after 24 h.[77]



Scheme 4: The palladium silylene catalyst (left, **VIII**) for a Heck reaction of *p*-bromo acetophenone and styrene (right) by Roesky *et al.* Catalytic conditions: 1 mol% **VIII**, 1.5 eq NaOAc, 0.2 eq Bu_4NBr, (DMA), 140 °C, 24 h.[77]

From a donor stabilized six-membered N-heterocyclic silylene (*cf.* type **D**, chapter 3.2.2) and $[M(cod)Cl]_2$ (M = Rh, Ir, cod = 1,5-cyclooctadiene), Matthias Drieß *et al.* were able to isolate two catalytically active silylene complexes $\mathbf{IX^M}$ (Figure 10). Both complexes exhibit a similar structure, including pseudo square planar coordination around the transition metal and an almost rectangular N–Si–N angle of 96°, thus indicting a significant p-character within the N–Si bonds. The complexes are active catalysts for the reduction of a dibenzoazepin carboxamide with $PhSiH_3$ in toluene, as indicated in Figure 10.[78]

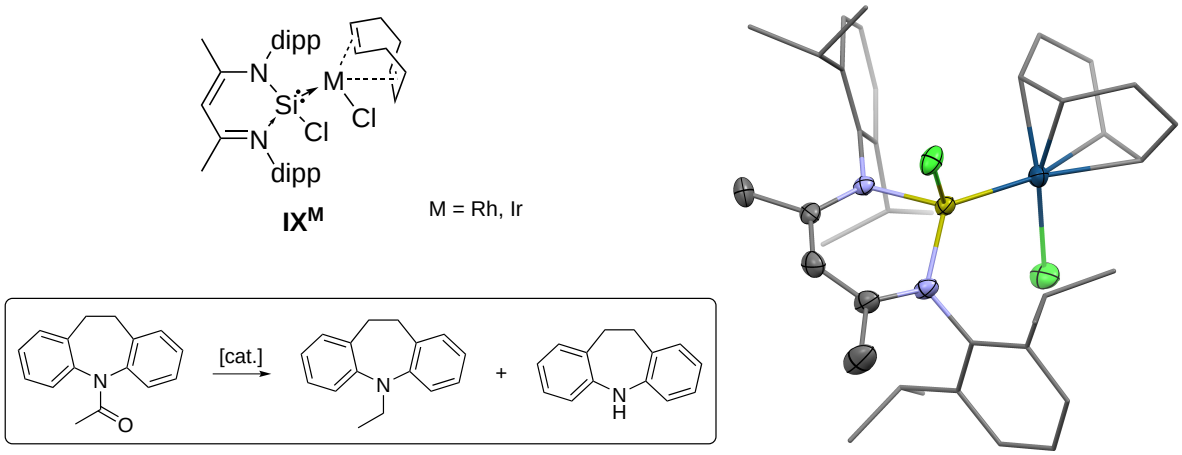
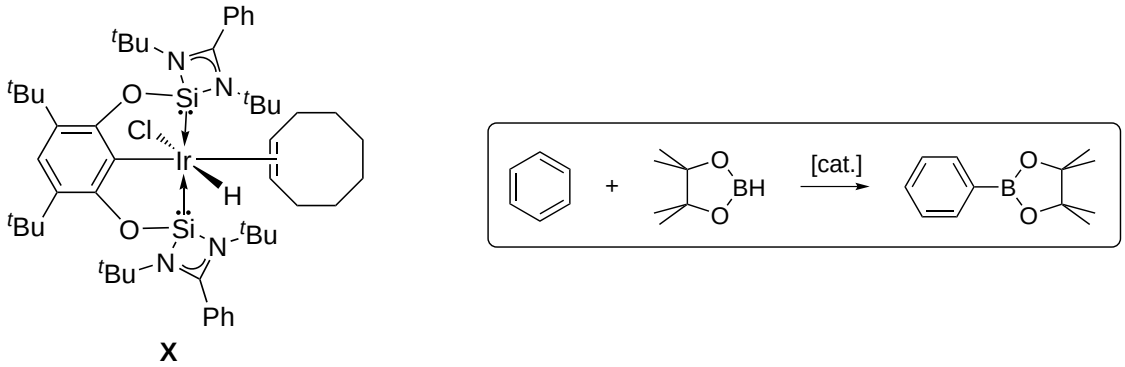


Figure 10: Catalyzed reduction of a dibenzoazepine derivative (bottom left) along with Lewis (top left) and X-ray structure (right, M = Ir) of the precatalysts $\mathbf{IX^M}$. Catalytic conditions: 2.5 mol% $\mathbf{IX^M}$, 2.5 eq $PhSiH_3$, (PhMe) r.t., 24 h. Ellipsoids at 50% probability level, cod and dipp groups depicted as wireframe, hydrogen atoms omitted for clarity; dipp = 2,6-diisopropyl phenyl. Element colors: gray – carbon; light blue – nitrogen; golden – silicon; ultramarine – iridium; green – chlorine.[78]

The rhodium compound $\mathbf{IX^{Rh}}$ induced selective C–O cleavage within the dibenzoazepine analogue depicted in Figure 10, whereas using the iridium $\mathbf{IX^{Ir}}$ compound led to a mixture of the C–O cleaved tertiary amine and the deacetylated product from N–C cleavage,

however featuring a higher total conversion. Under the applied catalytic conditions, the activity of $\mathbf{IX^{Rh}}$ is similar to the precursor $[Rh(cod)Cl]_2$, $\mathbf{IX^{Ir}}$ however outperforms the respective cod salt $[Ir(cod)Cl]_2$ by almost a factor of 3 (87% vs. 30% yield after 24 h).[78]

With a novel, strongly σ-donating *bis*-silylene Matthias Drieß and John F. Hartwig *et al.* reported the synthesis of new pincer-type noble metal silylene complexes. NMR spectroscopic investigations revealed a significantly higher σ-donor strength compared to isoelectronic phosphorus(III)-based systems. Iridium compound **X** is capable of catalyzing the CH-borylation of various arenes such as benzene, toluene and xylenes with pinacolborane (HBPin, Scheme 5) as a reagent.[79]



Scheme 5: Iridium catalyst **X** (left) for the CH-borylation of arenes with HBpin (right, for benzene) by Drieß and Hartwig *et al.* Catalytic conditions: 5 mol% **X**, 1 eq coe, (arene), 100 °C, 24 h.[79]

Addition of cyclooctene (coe) significantly boosts the reaction speed and yield (90% vs. 53% after 24 h). It reacts with the *in situ* generated hydrogen and can be detected as cyclooctane in the product mixture. In contrast, within comparative experiments with a phosphine-pincer iridium complex, addition of coe was disadvantagous and led to a reduction of the yield (21% vs. 55%) as well as an increasing amount of hydroborylated coe as a byproduct.[79] With another iridium silylene complex, Javier A. Cabeza and Pablo García-Álvarez *et al.* also reported a catalyst, capable of dehydrogenatively coupling benzene and toluene with HBPin.[80]

Antoine Baceiredo and Tsuyoshi Kato *et al.* reported a versatile and highly nucleophilic silacyclopropylidene ligand, which readily reacts with several noble metal fragments to form the respective silylene complexes.[81,82] The linear complex with copper(I) chloride catalyzed the hydrosilylation of ketones with H_2SiPh_2. Treatment with Karstedt's catalyst, widely used in industry and one of the benchmark systems for alkene hydrosilylations, yielded platinum(0) complex **XI** (Figure 11). According to the authors the new

compound exhibits increased persistence and selectivity within hydrosilylations, compared to Karstedt's catalyst and even outperforms carbene-enhanced Marko's catalyst in terms of "efficient catalytic activity." [82–84]

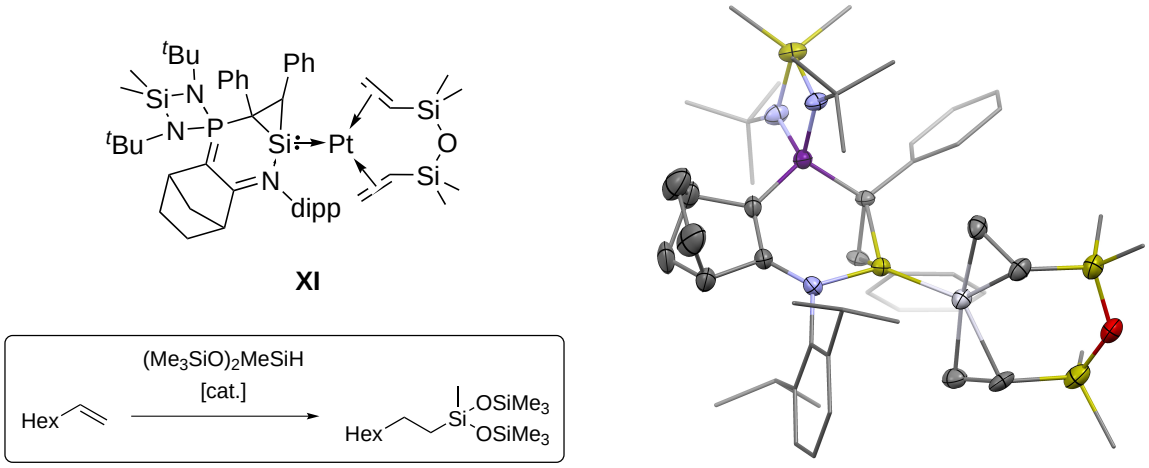


Figure 11: Catalyzed reduction of 1-octene (bottom left) along with Lewis (top left) and X-ray structure (right) of the catalyst **XI** by Baceiredo *et al.* Catalytic conditions: 10^{-5} – 10^{-3} mol% **XI**, 1 eq $HSiMe(OSiMe_3)_2$, (xylene), 72 °C. Ellipsoids at 50% probability level, dipp, Ph, ^{t}Bu and Me groups depicted as wireframe, hydrogen atoms and cocrystallized solvent omitted for clarity. Element colors: gray – carbon; light blue – nitrogen; golden – silicon; purple – phosphorus; white – platinum; red – oxygen. [82]

To determine its catalytic properties for hydrosilylations, new complex **XI** was mixed with equimolar amounts of 1-octene and $HSiMe(OSiMe_3)_2$ in xylene and heated to 72 °C. With catalyst loadings as dilute as 10^{-5} mol% they achieved 86% conversion, which relates to a turnover frequency (TOF) of $1.19 \cdot 10^5$ h^{-1}; almost twice as much as with Karstedt's catalyst (50% yield). The authors attribute the excelling catalytic performance of **XI** to the strong ligand-metal binding, providing better stabilization and protection for the reactive platinum(0) species. Furthermore, they regard it to the ligand's high steric bulk and π-accepting behavior, that equally promotes the dissociation of olefin ligands to create vacant sites and also reductive elimination as the rate determining step within the Chalk-Harrod hydrosilylation mechanism. [82,85–87]

Similar platinum(0) complexes, derived from Karstedt's catalyst and cyclic dialkyl- and alkylamino silylenes were reported by Takeaki Iwamoto *et al.* recently (Figure 12). The dialkylamino silylene complex **XII** was prepared by simply mixing Karstedt's catalyst and the respective free silylene in hexane and displayed outstanding catalytic activity in the hydrosilylation of terminal alkenes with $HSiMe(OSiMe_3)_2$ (for the catalytic reaction, *cf.* Figure 11). [88,89]

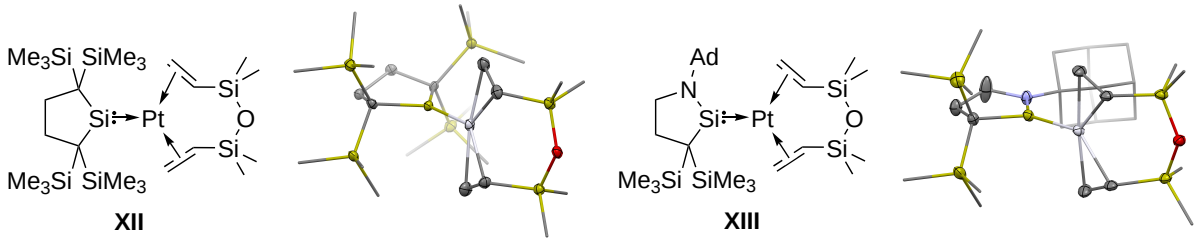
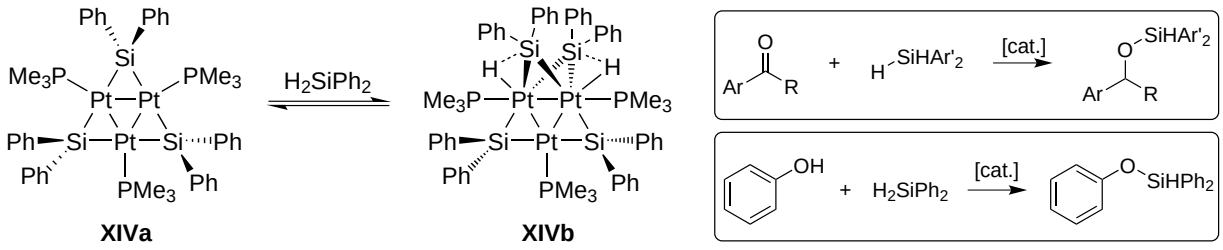


Figure 12: Silylene-platinum(0) complexes derived from Karstedt's catalyst and cyclic dialkyl- (left, **XII**) and alkylamino silylenes (right, **XIII**). Ellipsoids at 50% probability level, adamantyl (Ad) and Me groups depicted as wireframe, hydrogen atoms and disorder omitted for clarity. Element colors: gray – carbon; light blue – nitrogen; golden – silicon; white – platinum; red – oxygen.[88,89]

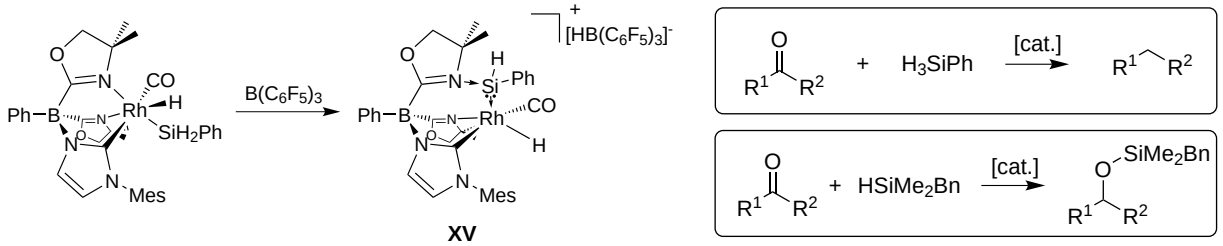
The catalytic activity was comparable to Karstedt's catalyst down to loadings of $3 \cdot 10^{-7}$ (w/w), yet the authors concede that it was not possible to irrevocably distinguish whether **XII** acted as a catalyst or merely as a source of active colloidal platinum. Interestingly, it tolerated the presence of functional groups such as ethers, epoxides and amines.[88] Platinum silylene **XIII** was prepared analogously to **XII** and exhibited similar activity and furthermore tolerated the presence of an ester moiety within the alkene substrate. According to calculations, the π-backbonding from platinum to the silylene is weaker than in the aforementioned dialkylsilylene complex. This is a result of the energetically higher empty 3p-orbital in **XII** due to the adjacent amino-moiety's π-donating properties.[89]

Another compound, that has been active as a catalyst in hydrosilylation, is a triangular triplatinum(0) silylene complex (**XIVa**, Scheme 6), which has been synthesized by Kohtaro Osakada *et al.* from equimolar amounts of $Pt(PPh_3)_4$ and H_2SiPh_2. However, due to the bridging coordination of silicon, the silyl ligands exhibit only limited siylene character. Upon treatment with an excess of diphenylsilane, the complex adds one equivalent of H_2SiPh_2 to form a 1:1 adduct with a bridging $SiPh_2$ moiety and two platinum-attached hydrides (**XIVb**, Scheme 6). The complexes are active in the hydrosilylation of benzaldehyde derivatives. The reaction is dependant on the aryl substitution, so that electron withdrawing *p*-fluoro or *p*-trifluoromethyl substituents significantly decrease the reaction rate (32% and 43% vs. 98% yield after 24 h). Acetophenone can be hydrosilylated as well, however significant amounts of side products such as dehydrosilylated silyl enole are formed (approximate ratio of desired hydrosilylated product $\approx$ 25%). Furthermore, **XIVa** slowly catalyzes the dehydrogenative coupling of phenol and H_2SiPh_2 with a yield of 79% in 4 d at ambient temperature (TOF = 2.7 $\frac{1}{h}$).[90]



Scheme 6: Triplatinum(0) silylene complex **XIVa** and its 1:1 adduct with H_2SiPh_2 **XIVb** (left). The complexes catalyze aldehyde and ketone hydrosilylations as well as the dehydrogenative coupling of phenol with H_2SiPh_2 (right). Catalytic conditions: 3–4 mol% **XIVa**, (C_6D_6), r.t., 24 h.[90]

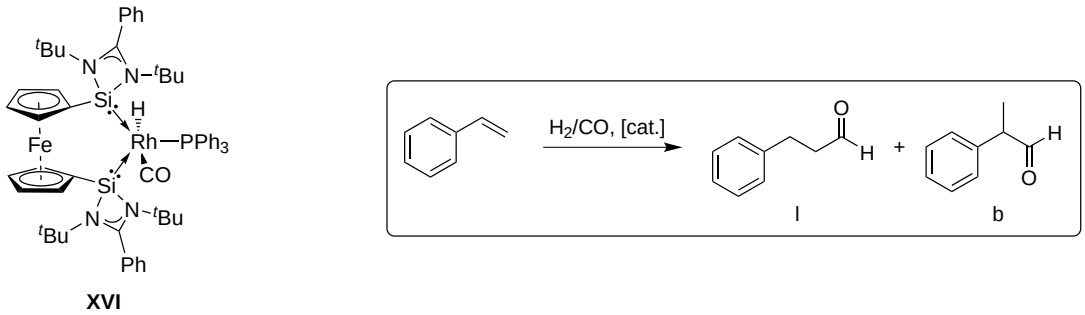
With a rhodium(I) silylene complex that is proposed to form upon hydride abstraction with $B(C_6F_5)_3$ and insertion into a N–Rh bond from the respective silane complex, Aaron D. Sadow *et al.* were able to catalyze carbonyl hydrosilylations with tertiary silanes and carbonyl deoxygenations with primary silanes. In the latter case, esters could be transformed into ethers, amides into amines, ketones and aldehydes into hydrocarbons using compound **XV** and H_3SiPh (Scheme 7).[91]



Scheme 7: Preparation of rhodium silylene catalyst **XV** (left) for carbonyl deoxygenations with H_3SiPh and carbonyl hydrosilylation with tertiary silane $HSiMe_2Bn$ (right). R_1, R_2 = -H, -alkyl, -alkenyl, -aryl, $-NMe_2$, -alkoxy, $-CF_3$. Catalytic conditions: 0.1–2 mol% **XV**, (various solvents), r.t.–80 °C, 0.5 – 72 h.[91]

Aside from hydrosilylations, hydroformylations ("Roelen reaction") are still of high importance for the chemical industry, since first discovered by Otto Roelen in the 1930s.[92] Matthias Drieß *et al.* reported and filed a patent for a new rhodium *bis*-(N-heterocyclic silylene) hydroformylation catalyst (Scheme 8).[75,93]

The catalyst **XVI** is prepared by simply mixing the free *bis*-silylene with $[HRh(CO)(PPh_3)_3]$. Its catalytic properties for the hydroformylation of styrene are highly temperature dependant. At 50 °C, only 10% conversion can be achieved, whereas at 100 °C the reaction gives complete conversion within 10 minutes, corresponding to a TOF of 9100 h^{-1}, hence outperforming similar, phosphine based catalysts, presumably due to its enhanced



Scheme 8: The new rhodium *bis*-silylene hydroformylation catalyst by Drieß *et al.* (left) and the tested catalytic hydroformylation of styrene to linear (l) and branched (b) aldehyde (right). Catalytic conditions: 30 bar H_2/CO, 0.03 mol% **XVI**, (PhMe), 50–100 °C, 10–60 min.[75]

σ-donor/π-acceptor properties. The linear-branched selectivity ratio however, is lower than with comparable phosphines (25:75 vs. 35:65 and 49:51, respectively)[75]

3.2.4 Designing novel noble metal N-heterocyclic silylene catalysts – potential and strategy

Today, several examples of noble metal N-heterocyclic silylene catalysts are known, as pointed out in the preceding chapter 3.2.3. However, particularly compared to N-heterocyclic carbene or phosphine based catalysts their role in catalysis is still rather negligible. For the design of new noble metal N-heterocyclic silylene catalysts for industrially relevant reactions like hydrogenation and hydrosilylation, it is important to combine beneficial properties of catalysts (*cf.* chapter 3.2.3) which are known today. Stability seems to be one of the most important properties of an outstanding catalyst, often achieved by the use of chelating ligands.[75,79,82,91] Ligands that are too sterically demanding however, might be disadvantageous, as they encumber the substrates' access to the active metal center. Furthermore, it has been observed that combination of strong σ-donors like N-heterocyclic carbenes and π-acceptors such as κ-*N*-heterocycles can promote catalytic activity.[94,95] Thus, bidentate chelates of iridium, rhodium and platinum, containing an N-heterocyclic silylene and a pyridine moiety have been initial target compounds within this doctoral project. However, on the way to these, complexes of rhodium and iridium containing silane rather than silylene moieties, which exhibited interesting and unprecedented properties, have been isolated instead.

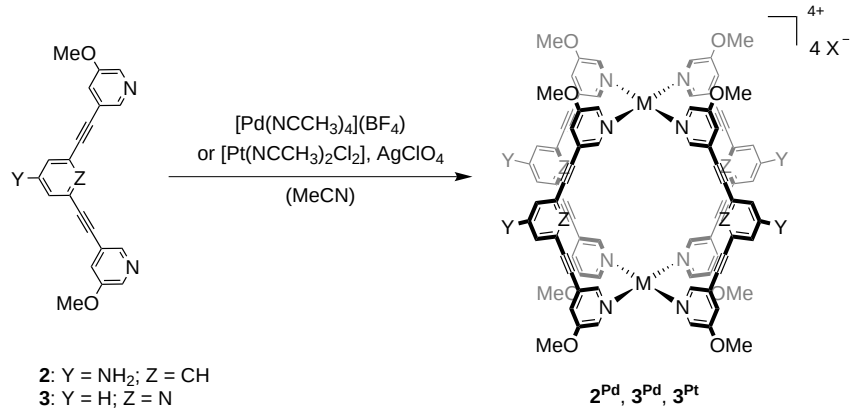
4 Results: Publication Summaries

Within the chapter at hand, the publications, prepared in the course of the doctoral project are briefly summarized. The respective reprint permissions aligned with detailed bibliographic data are located in chapters 5 and 6.

4.1 Self-Assembled Palladium and Platinum Coordination Cages: Photophysical Studies and Anticancer Activity

Cisplatin has been widely used as an anticancer drug against a plethora of diseases including ovarian, bladder and testicular cancer since its FDA approval in 1978. The wide area of application is opposed by its severe side-effects, thus limiting the applicable dose and creating a growing demand for drug targeting. One possibility therefore is the inclusion of cisplatin into molecular cages that selectively accumulate in malignant tissue due to the so-called EPR-effect (Enhanced Permeability and Retention). M_2L_4 molecular cages have the advantage of being easily accessible through self-assembly of bidentate ligands and M^{2+} ions. Thereby, the ligands and cages themselves are often nontoxic. The selection of metal ions is largely limited to palladium due to its unique coordination behavior. With the use of fluorescent cages, their pharmacokinetic properties could easily be monitored by fluorescence microscopy. Therefore, the utilization of fluorophores as ligands in M_2L_4 cages has been of high interest. In this article, new M_2L_4 (M= Pd, Pt) molecular cages, derived from highly fluorescent ligands with a quantum yield of up to $\Phi = 48\%$ have been synthesized; furthermore, the first Pt_2L_4 cage with a ligand, containing three pyridine subunits, is described (Scheme 9).

Formation of the cages is analytically evidenced by NMR (^{1}H, ^{13}C{^{1}H}, DOSY), high resolution ESI mass spectrometry and for the Pd cages single crystal X-ray crystallography. The photophysical properties of the ligands and cages were determined and the ligands were found to be highly emissive with an absolute quantum yield up to $\Phi = 48\%$. The cages, however, showed significantly reduced emission. The palladium cages were treated with cisplatin and evidence for inclusion was found. Eventually, ligands, cages and cisplatin inclusion compounds were tested for their antiproliferative effects against the two human cancer cell lines A549 (lung carcinoma) and HepG2 (hepatocellular carcinoma) *in vitro*. Whereas ligand and capsules show no significant toxicity themselves, the cisplatin inclusion compounds show increased toxicity towards A549 compared to free cisplatin (Figure 13), indicated by a lower IC_{50} (half maximal inhibitory concentration).



Scheme 9: Synthesis of M_2L_4 cages by self-assembly in acetonitrile using ligands **2** and **3** and $[Pd(NCCH_3)_4](BF_4)_2$ or $[Pt(NCCH_3)_2Cl_2]/AgClO_4$ as metal precursors ($X^- = BF_4^-/ClO_4^-$).

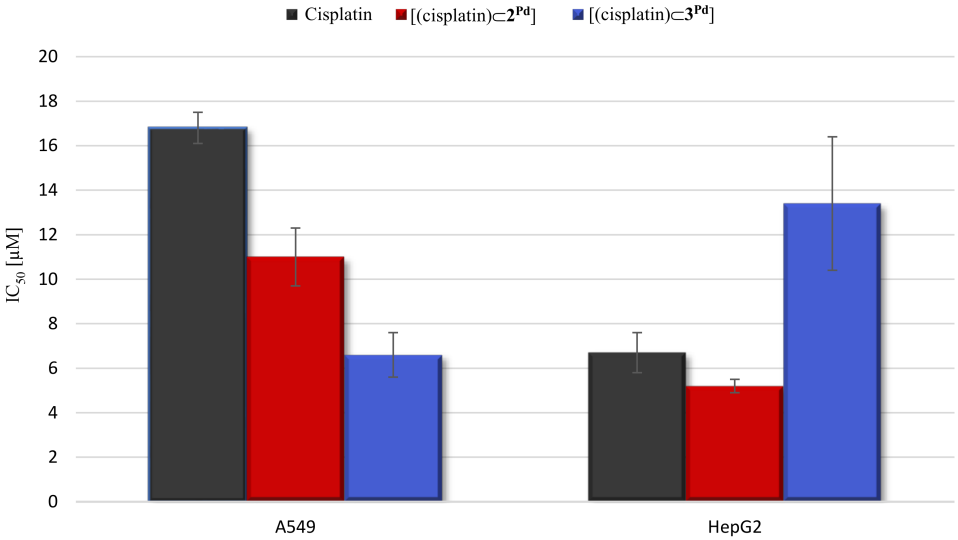
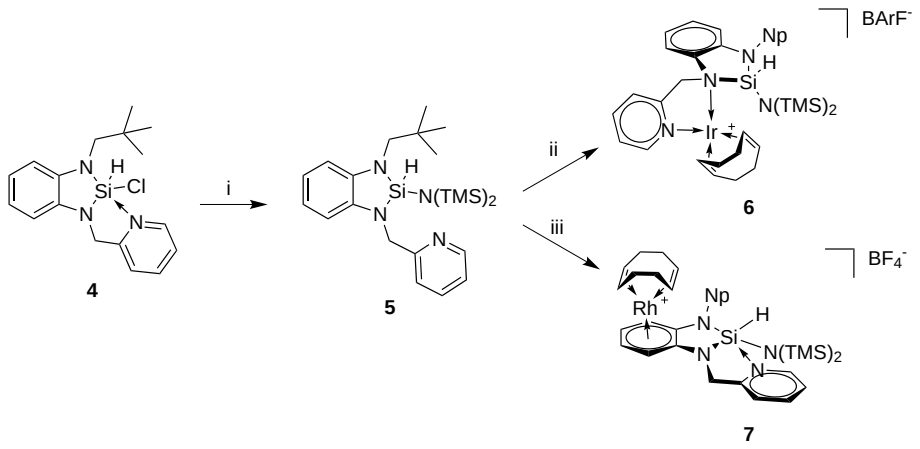


Figure 13: IC_{50} (half maximal inhibitory concentration) values of free cisplatin and the inclusion compounds [(cisplatin)⊂**2**$^{\mathbf{Pd}}$] and [(cisplatin)⊂**3**$^{\mathbf{Pd}}$], normalized to the respective concentration of cisplatin.

My individual contribution to this work comprised conception, experimental work including analyses and writing the manuscript.

4.2 Pyridine Functionalized N-Heterocyclic Silane Complexes of Iridium and Rhodium – An Unexpected Change in Coordination

Complexes of rhodium and iridium are of high interest for synthetic chemistry, as many of them readily activate small molecules like dihydrogen and silanes, and possess outstanding catalytic properties. Today, some of these complexes are even commercially available. Not only are N-heterocyclic silanes important intermediate products within the synthesis of N-heterocyclic silylenes (NHSis), they are also interesting potential sources for soft silyl radicals, which are beneficial for radical polymerization. Within this paper, novel pyridine functionalized N-heterocyclic silanes have been synthesized and their stability and reactivity investigated (Scheme 10).



Scheme 10: Synthesis of the four coordinate N-heterocyclic silane **5** from five coordinate precursor **4** and its reactivity towards particular Ir and Rh complexes. Reagents and solvents: (i): $LiN(SiMe_3)_2$, (hexanes); (ii): $[Ir(cod)_2](BAr^F)$, (CH_2Cl_2); (iii): $[Rh(cod)_2](BF_4)$, (CH_2Cl_2).

A nucleophilic substitution was observed upon treatment of **4** with $LiN(SiMe_3)_2$. Due to the increased steric bulk, coordination at silicon changes from 5 to 4 as a result of this transformation. Reaction of **5** with iridium and rhodium *bis*-cod salts did not result in an oxidative addition of the Si-H moiety but the formation of adduct complexes. Herein, ligand **5** shows ambident reactivity. With iridium, the ligand's front side reacts to form a pyridine-tertiary amine chelate whereas arene π-complexation of the backbone occurs for rhodium. Therein, by coordination of rhodium a coordination change at silicon from 4 back to 5 occurs, although the direct circumjacent chemical environment around silicon

remains unaltered. This unprecedented behavior is electronically induced through rhodium coordination over a spatial distance of more than 4.4 Å.

My individual contribution to this work included conception, experimental work including analytics and single crystal X-ray crystallography and writing of the manuscript.

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6 Bibliographical data for complete publications

6.1 Self-Assembled Palladium and Platinum Coordination Cages: Photophysical Studies and Anticancer Activity

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Eur. J. Inorg. Chem. **2016**, (33), 5189–5196.

DOI: 10.1002/ejic.201600811

6.2 Pyridine Functionalized N-Heterocyclic Silane Complexes of Iridium and Rhodium – An Unexpected Change in Coordination

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Organometallics, **2018**, *37* (1), 136–144.

DOI: 10.1021/acs.organomet.7b00769

7 List of Publications and Conference Contributions

7.1 Journal articles

[1] **Felix Kaiser**, Andrea Schmidt, Wolfgang Heydenreuter, Philipp J. Altmann, Angela Casini, Stephan A. Sieber and Fritz E. Kühn, „Self-Assembled Palladium and Platinum Coordination Cages: Photophysical Studies and Anticancer Activity“, *Eur. J. Inorg. Chem.* **2016**, (33), 5189–5196.

[2] **Felix Kaiser**, Robert M. Reich, Eric Rivard and Fritz E. Kühn, „Pyridine Functionalized N-Heterocyclic Silane Complexes of Iridium and Rhodium – An Unexpected Change in Coordination“, *Organometallics* **2018**, *37* (1), 136–144.

7.2 Talks and posters

11/2017 3rd annual ATUMS conference, Jasper, Alberta, Canada – Talk on „Noble metal complexes of silicon-containing ligands for homogenous catalysis“

06/2017 WACKER Symposium on silicon chemistry, Garching, Germany – Talk on „Noble metal silylene complexes for homogenous catalysis“

11/2016 2nd annual ATUMS conference, Raitenhaslach, Germany – Talk and poster on „Noble metal N-heterocyclic silylene chelates for homogenous catalysis“

11/2016 WACKER Symposium on silicon chemistry, Garching, Germany – Talk on „Noble metal silylene complexes for homogenous catalysis“

8 Notes and References

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