From Catalyst Design to Molecular Devices: Theory and Experiments

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Abstract. Three different topics are presented herein. With the help of molecular-orbital analysis, the unique geometry and catalytic properties of d⁰ bent-metallocenes was analyzed in search for cyclopentadienyl substitutes.

To overcome the inherent racemization of coordinatively unsaturated piano-stool complexes, a ten-electron donor ligand was designed. This ligand incorporates an arene bearing two tethers: a phosphine and an imine (abbreviated PArN). It was shown that upon η²-η⁴-coordination of PArN to ruthenium, a configurationally stable piano-stool complex results [Ru(η²-η⁴-PArN)L]⁺⁺. A tripodal decadendate ligand, incorporating three soft bipyridine donors as well as three harder salicylamide chelates, was synthesized. This ligand allowed the investigation of the iron release from ferric enterobactin, suggesting a protonation/translocation into a salicylate-binding mode. In the presence of a single iron ion and depending on its oxidation mode, it was shown that this system displays switch-like properties.

1. Introduction

Catalysis is perhaps the word which best describes the spirit of chemistry: the miracle of consumption and regeneration [1]. Ever since my beginnings in science, I have been fascinated by all aspects of catalysis: bioinorganic, theoretical, organic, or as a tool to generate libraries [2].

After having identified a relevant problem from the current literature, I like to run qualitative molecular-orbital calculations to rationalize the published observations. Coincidentally, these form the basis for a synthetic project. Three distinct projects at different stages of achievement are presented herein: i) outlining a problem with the help of molecular orbital theory, ii) designing a ligand system, and, iii) applications.

2. The Geometry of d⁰ Pentacoordinate Complexes [3]

2.1. Background

In the field of homogeneous catalysis, the most versatile catalysts may well be the so-called bent-metallocene systems. These contain a d⁰-metal flanked by two cyclopentadienyls (abbreviated Cp). Most often, the catalyst precursors are [M Cp₂L₃]-like compounds. If one considers Cp as a six-electron donor occupying a single coordination site, such complexes are four-coordinate, distorted tetrahedrons (T-4) with a large CP₆ center-M-C₆ center angle [4]. To understand their unrivalled catalytic properties, however, we focus on five coordinate [M Cp₂L₃]-complexes. Pentacoordinate complexes play a pivotal role in transition-metal catalysis as five-coordinate transition states or intermediates have often been postulated either for associative reactions involving tetrahedral (T-4) or square planar (SP-4) complexes, or for dissociative reactions involving octahedral (OC-6) complexes [5].

The square pyramid (SPY-5) and the trigonal bipyramid (TB-5) represent prototypical geometries of five-coordinate complexes. The [M Cp₂L₃] compounds however cannot be categorized as either TB-5 or SPY-5. This is illustrated with three examples: [Ta Cp₂H₃] [1] is one of the first structurally characterized [M Cp₂L₃] complexes [6]; [Zr Cp₂(η²-C₅H₅CO)] 2 is an early example of an η²-bound acyl [7]; and 3 contains a planar four-coordinate carbon [8]. Interestingly, the proposed transition state 4 for the α-olefin polymerization catalyzed by bent metal-
locenes also displays this unusual geometry. Structural features common to these complexes are a bent \( \{\text{MCP}_2\} \)-fragment and a coplanar arrangement of the three ligands \( \text{L} \) with two acute \( \text{L}-\text{M}-\text{L} \) angles. We call this unusual \( \{\text{MCP}_2\text{L}_3\} \) geometry 'edge-bridged tetrahedral', abbreviated as EBT-5 (Fig. 1).

We reasoned that perhaps the unique catalytic properties of bent-metallocene complexes may be related to their unusual EBT-5 geometry of their pentacoordinate complexes. We thus set out to analyze the electronic origin of this geometry, with the aim of finding Cp-substitutes which would also favor EBT-5 geometries.

### 2.2. Theoretical Analysis

#### 2.2.1. \([\text{TiH}_5]^-\)

We begin our analysis with an extended \( \alpha \)-Hückel (\( \alpha \)H) description of the bonding of a trigonal bipyramidal five-coordinate \( \text{d}^0 \) complex containing pure \( \sigma \)-donors. These qualitative arguments were assessed by Density Functional Theory (DFT). A simplified molecular-orbital diagram for a \([\text{TiH}_5]^-\) model is sketched in the middle of Fig. 2. The HOMO is \( a^2_\alpha \) and is mostly ligand-centered. The \( d_{xy} \) and \( d_{yz} \) orbitals remain unperturbed and correspond to the LUMO (\( e^2_\alpha \)).

By varying the \( \alpha \)-Ti-H\(_{ax} \) angle from 130° to 55°, we find two minima at 120° (\( \text{E}_{\text{tot}} = 0.00 \) eV) and 70° (\( \text{E}_{\text{tot}} = +0.22 \) eV) which correspond to the SPY-5 and EBT-5 geometries, respectively. The TB-5 (\( \alpha = 90° \), \( \text{E}_{\text{tot}} = +1.00 \) eV) is a transition state in this diagram. The SPY-5 vs. EBT-5 preference can be traced back to a difference in ligand-ligand interactions associated with the \( 2a_\alpha \) orbital: artificially setting the \( \text{L}_{\text{eq}}-\text{Ti}-\text{H}_{\text{ax}} \) angle \( \alpha \) from 130° to 55°, we find two minima at 120° (\( \text{E}_{\text{tot}} = 0.00 \) eV) and 70° (\( \text{E}_{\text{tot}} = +0.22 \) eV) which correspond to the SPY-5 and EBT-5 geometries, respectively. The TB-5 (\( \alpha = 90° \), \( \text{E}_{\text{tot}} = +1.00 \) eV) is a transition state in this diagram. The SPY-5 vs. EBT-5 preference can be traced back to a difference in ligand-ligand interactions associated with the \( 2a_\alpha \) orbital: artificially setting the \( \text{L}_{\text{eq}}-\text{Ti}-\text{H}_{\text{ax}} \) angle \( \alpha \) from 130° to 55°, we find two minima at 120° (\( \text{E}_{\text{tot}} = 0.00 \) eV) and 70° (\( \text{E}_{\text{tot}} = +0.22 \) eV) which correspond to the SPY-5 and EBT-5 geometries, respectively. The TB-5 (\( \alpha = 90° \), \( \text{E}_{\text{tot}} = +1.00 \) eV) is a transition state in this diagram. The SPY-5 vs. EBT-5 preference can be traced back to a difference in ligand-ligand interactions associated with the \( 2a_\alpha \) orbital: artificially setting the \( \text{L}_{\text{eq}}-\text{Ti}-\text{H}_{\text{ax}} \) angle \( \alpha \) from 130° to 55°, we find two minima at 120° (\( \text{E}_{\text{tot}} = 0.00 \) eV) and 70° (\( \text{E}_{\text{tot}} = +0.22 \) eV) which correspond to the SPY-5 and EBT-5 geometries, respectively. The TB-5 (\( \alpha = 90° \), \( \text{E}_{\text{tot}} = +1.00 \) eV) is a transition state in this diagram. The SPY-5 vs. EBT-5 preference can be traced back to a difference in ligand-ligand interactions associated with the \( 2a_\alpha \) orbital: artificially setting the \( \text{L}_{\text{eq}}-\text{Ti}-\text{H}_{\text{ax}} \) angle \( \alpha \) from 130° to 55°, we find two minima at 120° (\( \text{E}_{\text{tot}} = 0.00 \) eV) and 70° (\( \text{E}_{\text{tot}} = +0.22 \) eV) which correspond to the SPY-5 and EBT-5 geometries, respectively.
360° and $55° \leq \alpha \leq 90°$. The resulting potential-energy surface (PES) is presented in Fig. 3, with ordinate $\cos \alpha \cdot \sin \beta$ and abscissa $\cos \alpha \cdot \cos \beta$. These coordinates represent the projection of $M-L_{ax}$ unit vectors onto the equatorial plane $ML_{eq}-L_{eq}'-L_{eq}$. This PES shows the expected Mexican-hat features with three minima and three saddle points corresponding to the SPY-5 ($\alpha = 60°, \beta = 60°, 180°$ and $300°$) and EBT-5 ($\alpha = 70°, \beta = 0°, 120°,$ and $240°$) geometries, respectively. The EBT-5 which appears as a minimum in the Walsh diagram $E = f(\alpha)$ (Fig. 3), is in fact a saddle point on the two-dimensional surface ($E = f(\alpha, \beta)$) and lies well below the maximum representing the TB-5.

We conclude that a $d^9$ complex containing five pure $\sigma$-donors should display SPY-5 geometry. A Cambridge Structural Database (CSD) search revealed a single homoleptic compound containing five $\sigma$-donors around a $d^9$ metal: $[\text{Ta(CH_2(4-MeC_6H_4)C_2H_4)]_{9}}$ [10]. This compound indeed displays an SPY-5 structure ($2\alpha = 138.1°, \beta = 177.2°$). Recently, the structure of $[\text{TaMe}_3]$ was determined by gas-phase electron diffraction. In contrast to its main group counterpart $[\text{SbMe}_3]$, the $d^9$ complex has an SPY-5 geometry [11] [12].

As can be appreciated from Fig. 2, the total energy of the $\bar{e}$-distortion follows mostly the fate of the $a_2^*$ orbital in $D_{3h}$ symmetry ($b_1$ irreducible representation in $C_{2v}$ point group). Introducing ligands capable of interacting with this orbital, which contains a large contribution of the $d_{xy}$ orbital (in both $C_{2v}$ geometries), may invert the SPY-5 preference, eventually leading to an EBT-5 ground state geometry.

2.2.2. $[\text{Ti(NH}_2)_2\text{H}_3]^+$

Adding two equatorial ligands capable of $\pi$-interaction, with their $\pi$-systems perpendicular to the equatorial plane fulfills this requirement: the in-phase combination of the two $p$ orbitals is of $b_1$ symmetry. Let us replace two equatorial hydrides by two amides, with their $p$-orbital perpendicular to the $xz$-equatorial plane $[\text{Ti(NH}_2)_2\text{H}_3]$. The Walsh diagram for the $\alpha$-distortion of $[\text{Ti(NH}_2)_2\text{H}_3]^+$ is presented in Fig. 4. As suspected, we compute the EBT-5 geometry ($\alpha = 70°, E_{EBT} = 0.00$ eV) to be preferred over the SPY-5 ($\alpha = 110°, E_{SPY} = 0.91$ eV), with a slightly distorted TB-5 ($\alpha = 95°, E_{TB} = 1.00$ eV) as transition state.

Computing the PES $E = f(\alpha, \beta)$, we find an EBT-5 minimum, with a soft potential along the $\beta$-precession coordinate. This feature will be important in discussing experimental structural data (Fig. 3b).

Introduction of double-faced $\pi$-donor ligands (rather than the single-faced $\pi$-donors presented above) does not alter the overall picture. This can be traced down to the fact that the second $\pi$-interaction (typically a $p$ orbital) does not have $b_1$ symmetry, and thus does not contribute significantly to the fate of the total energy in Fig. 2.

It thus appears that the geometry adopted by five-coordinate $d^9-[\text{MD}_{2}L_2]$ complexes with strong, single-or double-faced $\pi$-donors D as well as that adopted by $[\text{MCp}_{2}L_2]$ complexes is the result of the same 20JTDA along a reversed-Berry coordinate. From our model calculations, it
appears that all d0 systems containing only two strong single-faced π-donors in the equatorial plane with their filled p orbital perpendicular to this plane (pΔ) should display an EBT-5 geometry. In the following section, we test this model with structural data retrieved from the CSD.

2.3. Structure Correlation

2.3.1. Fragment Definition

In order to test the above hypothesis, we extracted all pentacoordinate d0 complexes from the CSD. After defining and retrieving the structures of interest, we mapped the available structures in the two-dimensional configuration space spanned by α and β.

To ensure that the geometry is not biased by ligand constraints, all polynuclear complexes were excluded, as well as those containing chelating- or η1-arene-ligands (n > 1). Only those compounds containing two strong π-donors were considered. To our surprise, this search yielded no more than seven pentacoordinated d0 complexes containing only two strong π-donors.

Eventually, we relaxed our stringent definition to incorporate complexes which contain two strong π-donors and up to three weaker π-donors. A total of 36 complexes matched these requirements. These results are not presented here.

For comparison, all [MCp2L3]-like complexes were retrieved from the CSD. Again here, only mononuclear complexes and those containing no chelates were considered, yielding a total of thirteen [MCp2L3]-complexes.

2.3.2. Ligand Labelling and Distortion Mapping

To unambiguously determine the relevant distortion angles, a consistent ligand-labelling scheme is required. Since the complexes can be viewed as distorted TB-5, one large (< 180°), three medium (ca. 120°) and six small (ca. 90°) interligand angles are expected. After computing all ten interligand angles for each complex, the largest angle was assigned as the L-M-Lax’ angle. The remaining three ligands were taken to define the equatorial plane.

In those cases where two large angles (ca. 150°) were computed, thus suggesting an SPY-5 coordination, the equatorial plane was defined in terms of the two strongest π-donor ligands D and D and the remaining equatorial ligand Leq.

The observed structural data for [MD2L3]-complexes (D = strong π-donor, L = pure π-donor) are displayed in Fig. 3, along with the eH-isoenergetic contour at 0.1 eV for the model [Ta(NH2)2H3]2−. In most compounds of this class, the axial substituents bend away from the π-donors and towards the pivot (2α < 180° and β < 90°). Five of the seven compounds are within the minimum-energy region calculated for the model complex [Ta(NH2)2H3]2−.

Inspection of [Ta(CHBu1hMes-PMe2)] (Entry 1), reveals an EBT-5 geometry. The presence of a very bulky mesitylene in the pivot position, prevents an efficient 2OJTD resulting in a large α-angle (2α = 166.3°).

Systems incorporating one strong and one weaker π-donor can be expected to adopt geometries intermediate between EBT-5, encountered with 2 strong π-donors, and SPY-5, a geometry prevalent with pentacoordinate compounds bearing a single π-donor [13][14]. Such an intermediate geometry is observed not only for [ReO2(NP3)] (Entry 4) but also for [WO(NEt2)2P3] (Entry 5) [15]. In both cases, the axial ligands precess towards the weaker π-donor, the longest, most distant o xo- and the amide-groups, respectively.

For [MCp2L3] complexes, the 2α angles fall in the range 148.0–102.1°. It is interesting to note that the complexes which are least bent are those with the most electronegative Lax. Electropositive axial donors favour the 2OJTD since in the TB-5 geometry, the HOMO is essentially located on the axial donor ligands (see Fig. 2). Good axial donors raise the energy of this orbital, and thus favor an efficient 2OJTD as this latter is inversely proportional to the HOMO-LUMO gap. This is nicely reflected with compounds containing axial silanes which all display very acute L-M-ax’ angles, despite significant steric interactions with Leq.

It should be noted that the minimum computed for our model [TaCp2H3] is very deep and small distortions both in the
α and β directions are costly in energy. The distortion along the β coordinate is disfavoured purely on steric grounds: at α = 65° and β = 30°, the shortest Hα-Hcp and Hα-Ccp contacts are 2.05 Å and 2.02 Å respectively. By artificially setting the Hα–Hcp and Hα–Ccp overlaps to zero, the shallow minimum observed for [Ti(NH2)2H3]− in EBT-5 is restored and the β-precession about the y-axis is soft.

### 3. Synthesis of Configurationally Stable Three-Legged Piano-Stool Complexes [20]

#### 3.1. Background

In the field of enantioselective transition-metal catalysis, ligand design plays a very prominent role. In the spirit of E. Fischer's 'lock and key' concept, the steric bulk on the chiral ligand is relayed by a metal template to a prochiral substrate, eventually giving rise to chiral induction. To simplify matters, C2-symmetric bidentate ligands were tailored, reducing the number of diastereomers from four to two upon complexation of a prochiral substrate.

In the early nineties, however, electronically asymmetric bidentate ligands were introduced and rapidly found many applications in enantioselective catalysis [21–23]. In such systems, in addition to steric arguments, electronic factors play a critical role in determining which diastereoisomer (or diastereoisomeric site) reacts faster to yield the enantiomerically enriched product. Such C2-symmetric bis-amide-systems should display bent-metallocene-like catalytic properties. We were pleased to see that such systems reported by McConville, Schrock and Gibson indeed display very promising olefin-polymerization properties [17–19].
dentate ligands offer the interesting prospective of studying the role of metal-based chirality. To our knowledge, this area has received only little attention, despite interesting preliminary reports.

As early as 1979, Faller et al. reported a chiral molybdenum-based promoter 5 for the functionalization of allylic substrates [24]. It was shown that, when coordinated to the [CpMo(CO)(NO)]2+-moiety, a symmetric allyl could be functionalized diastereoselectively at the carbon cis-positioned to the nitrosyl in the exo-conformation [25]. As a nitrosyl ligand is as bulky as a carbonyl ligand, there remains little doubt that the diastereoselectivity must be caused by electronic rather than steric arguments. Unfortunately, however, the system was stoichiometric and not catalytic. Similarly, Gladysz has extensively studied the Lewis-acidic [ReCp(NO)PPh3]2+-fragment 6 as a promoter for functionalizing prochiral substrates [26]. Again here, only stoichiometric applications have been reported.

One possible explanation for this fact could well be the configurational lability of the coordinatively unsaturated piano-stool complexes which are invariably involved in catalytic cycles. If a chiral-at-metal complex were to racemize during catalysis, this would have a dramatic effect on the enantiomeric excess of the reaction.

Before studying the role of chirality-at-the-metal in enantioselective catalysis, we analyzed theoretically the role of electronic asymmetry in the palladium-catalyzed allylic alkylation as well as the geometry of coordinatively unsaturated two-legged piano-stool complexes. Based on these results, we designed a chiral-at-metal piano stool complex which displays remarkable configurational stability.

### 3.2. Theoretical Considerations [27]

#### 3.2.1. On the Regioselectivity of a Nucleophilic Attack on [Pd(allyl)(phosphine)(imine)] Complexes

To understand the role of electronic asymmetry, we analyzed the frontier orbitals of a model [Pd(η2-C5H5)(PPh3)(NH3)]. We reasoned that since the coordinated allyl fragment undergoes a nucleophilic attack, the carbon atom which bears the greatest coefficient in the LUMO is most prone to be functionalized by the incoming soft nucleophile. The interaction diagram for [Pd(η2-C5H5)(PPh3)(NH3)] is built from the [Pd(PPh3)(NH3)]2+ and [η2-C5H5]+ (see Fig. 8).

The LUMO of such systems consists essentially of the out-of-phase combination of the dπ,π* orbital with the non-bonding orbital of the allyl π-system. Close inspection of the dπ,π* orbital of [Pd(PPh3)(NH3)]2+, however, reveals that this Fragment Molecular Orbital (FMO) is hybridized away from the nitrogen, a mere reflection of the electronic asymmetry caused by the P=N ligand. This hybridization allows mixing of both the π and π* orbitals of the allyl-fragment into the LUMO as their overlap with the hybridized dπ,π* orbital is no longer zero. Because of the good energy match between the π* and the LUMO, only this orbital contributes (and not the π orbital) significantly to the LUMO. Perturbation theory allows to predict that

\[ \text{LUMO} \approx d_{\pi,\pi^*} - (n) + (\pi^*) \]

As can be appreciated from Fig. 8, the Ctrans-P bears the greatest coefficient and thus is predicted to be most electrophilic. It should be pointed out that this picture is independent of the allyl conformation (exo or endo). As both these conformations interconvert rapidly under true catalysis conditions, we conclude that the nucleophilic attacks preferentially the Ctrans-P of the exo-conformation, yielding the observed enantiomer. This prediction was subsequently substantiated by DFT methods [28][29].

Qualitative MO arguments thus help rationalize the role of electronic asymmetry in enantioselective catalysis. Similar arguments were used with Faller’s piano-stool complex [CpMo(CO)(NO)(η2-allyl)] 5 to rationalize the site of nucleophilic attack on the coordinated allyl [25].

#### 3.2.2. Geometry of Coordinatively Unsaturated Two-Legged Piano-Stool Complexes [30]

Following the synthesis of chiral-at-metal piano-stool complexes, initiated by Brunner et al., the question of configurational stability of such systems was addressed by various groups [31]. Of particular interest in the context of catalysis are coordinatively unsaturated piano-stool complexes as these would be invariably involved in a catalytic cycle involving piano-stool complexes as catalysts.

It had been suggested by Hofmann that 16-electron complexes of the type [M(η2-C5H5)2(LL)] (n = 4–7) may have pyramidal and thus chiral-at-metal ground-state geometries [32]. Twenty years later, no firm experimental proof unambiguously validated this prediction. We thus re-analyzed these systems, in search of more quantitative predictions, i.e., inversion barriers. Our calculations suggest that, indeed, coordinatively unsaturated two-legged pi-
ano-stool complexes possess a pyramidal ground-state geometry. In all cases, however, the inversion barriers, via a planar, achiral geometry are low. The best candidate, \([FeCp(NO)SiR_3]^+\), incorporates an electropositive \(\sigma\)-donor (SiR_3) and an excellent \(\pi\)-acceptor (NO^+). Unfortunately, its inversion barrier is computed at 15 kcal/mol and thus is expected to readily racemize in solution at room temperature. Such systems have much in common with amines, which are pyramidal, but readily racemize in solution as their inversion barriers are low in most cases.

For both \(N\)-based and metal-based chirality, the pyramidalization is caused by a 2OJTDA away from the planar achiral geometry. For \(N\)-based chirality, electronic tuning of the substituents on nitrogen (i.e., electronegative substituents or incorporation into a small ring) suffices to prevent rapid racemization. Incorporation of the nitrogen in a bicyclic framework locks the configuration and allows the separation of enantiomers. This was elegantly achieved with the resolution of Tröger’s base by Prelog [33].

We reasoned that tethering of two donors on an arene would yield, after \(\eta^2: \eta^1: \eta^1\)-coordination to a metal center, a bicyclic-like framework, and thus prevent racemization (see Fig. 9).

### 3.3. Synthesis and Characterization of a Configurationally Stable Piano-Stool Complex [34]

Having analyzed in detail phosphine-imine systems (vide supra), we set out to synthesize a ten-electron donor ligand incorporating an electron deficient imine and a phosphine tethered to an arene (abbreviated PArN). The ligand synthesis as well as its coordination to ruthenium are summarized in Fig. 10. After \(\eta^2: \eta^1\)-coordination, a racemic, planar chiral complex \([Ru(\eta^2: \eta^1-ParN)Cl_2]\) (8) was obtained. After many unsuccessful derivatization- and crystallization experiments, we were pleased to find that the racemate could be resolved by preparative HPLC on Chiralpak AD using EtOH, to afford both enantiomers in nearly quantitative yield. Chloride abstraction in a coordinating solvent yields the chiral-at-metal complex \([\eta^2: \eta^1: \eta^1-(ParN)Ru(OH_2)](OTf)_2\) 9 which displays remarkable configurational stability. Its X-ray structure is depicted.

Fig. 8. Simplified interaction diagram between \([Pd(NH_2)PH_3]^+\) and \((C_3H_7J^\text{-}X\)

### 3.4. Outlook

Based on two theoretical analyses addressing the role of electronic asymmetry in enantioselective catalysis and the geometry of coordinatively unsaturated piano-stool complexes, we have synthesized a configurationally stable three-legged piano-stool complex which displays promising catalytic activities in various C–C-bond forming reactions (i.e., Mukaiyama aldol, Diels–Alder reaction and cyclopropanation). Although a considerable effort may be required to optimize the ligand design to obtain excellent levels of induction, we have shown that such systems are amenable to address the role of chirality at the metal in enantioselective catalysis.
4. An Iron-Based Molecular Switch [35]

4.1. Background

Once upon a time, ca. 2.5 billion years ago, the atmosphere surrounding the Earth contained very little dioxygen (<1%). As a consequence, the first multi-molecular units were anaerobic and used the surrounding organic compounds as the source of building materials and energy. Gradually, the primordial soup depleted.

Photosynthetic cells using light as an energy source may well have been the response to the dearth of energy [36]. The remarkable ability of these primitive organisms to switch to the use of H₂O as a reductant, with the concomitant production of dioxygen, probably produced the worst case of pollution in terrestrial history. Indeed, the photosynthesis reaction (Eqn. 1) produces carbohydrates, essential feedstocks for higher organisms, as well as equimolar amounts of dioxygen as a by-product:

\[ \text{CO}_2 + \text{H}_2\text{O} \xrightarrow{hv} \text{(CH}_2\text{O)}_n + \text{n O}_2 \]

Long before the appearance of dioxygen, organisms had developed an addiction to iron for various purposes. The choice of iron may well be due to its abundance (fourth most abundant element in earth’s crust) as well as its versatility as a catalyst thanks to its broad range of accessible oxidation states. Photosynthetic activity dramatically decreased the availability of iron in water, as dioxygen oxidizes iron to its ferric state with subsequent production of rust as illustrated in (Eqn. 2):

\[ 4 \text{Fe} + 3 \text{O}_2 + 6 \text{H}_2\text{O} \rightarrow 4 \text{Fe(OH)}_3 \rightarrow \text{RUST} \]

Thereafter, the dioxygen concentration in the atmosphere rose steadily and stabilized at about 20%, ca. 300 million years ago [37]. This elicited the appearance of aerobic cells that could not only withstand this pollution but could even turn it to their advantage by developing respiratory and oxidative processes capable of extracting energy more completely from nutrient molecules.

Paradoxically, the iron required as catalyst for photosynthesis became scarce because this reaction produces dioxygen and indirectly rust. Hard-pressed organisms eventually came up with an elegant solution to this threat. Iron-scavenging agents, referred to as siderophores, were released by organisms to collect the vital metal. Siderophores are chelating ligands which display very high affinity for iron. Typically, the binding constants of these ligands are higher than the solubility product of rust under physiological conditions, allowing siderophores to extract ferric ions from rust.

Almost all bacteria and fungi secrete low-molecular-weight siderophores to scavenge iron from their environment. Most natural and synthetic siderophores contain either three hydroxamate- or three catechol-binding sites. Enterobactin, a tris-catecholate ligand, is the most powerful siderophore with high affinity for a hard iron. Such high binding constants, the iron-release mechanism has attracted considerable attention [38].

To simulate the iron-uptake and -release mechanism, we designed a decaacetadentate ligand which mimics both a siderophore with high affinity for a hard ferric ion as well as an 'octahedral, por-
phyrin-like environment' to accommodate the softer ferrous ion [39][40]. We reasoned that in the presence of a single iron ion and depending on its oxidation state, the metal ion would bind selectively to one site or the other. Oxidation or reduction could be used to drive the metal reversibly and intramolecularly from one site to the other, as schematized in below:

4.2. Results and Discussion

In contrast to hydroxamate-based siderophores, and due to its stability, the reduction potential of \([\text{Fe(III)}(\text{enterobactin})]^{3-}\) lies outside the range accessible with natural reducing agents (i.e., NADH and FADH\(_2\)) [41]. Therefore, alternative release mechanisms have been investigated for \([\text{Fe(III)}(\text{enterobactin})]^{3-}\). The main pathway seems to occur via a hydrolysis of its tris-lactone backbone. An interesting alternative is a protonation of a catechol oxygen with a concomitant translocation in a 'salicylate-binding mode' [42].

To probe this, we synthesized a tripo-dial dodecadentate ligand consisting of three salicylamide-binding sites and three electron-deficient 2,2'-bipyridines (abbreviated \(\text{NNOO}_3\)). With this ligand at hand, we showed that these systems are coded for the oxidation-state-selective iron chelation and iron transport. The low-spin ferrous ion binds selectively to the soft tris-bipyridine pocket \([\text{Fe(II)}(\text{NNOO}_3)]^{2+}\), while the high-spin ferric ion binds to the harder tris-salicylamide pocket \([\text{Fe(III)}(\text{NNOO}_3)]^{-}\). Moreover, it was observed that oxidation or reduction induces intramolecular (depending on conditions), reversible iron translocation between these two sites, thus revealing switch-like properties. This is best illustrated with visible spectra resulting from the titration of the ferric complex \([\text{Fe(III)}(\text{NNOO}_3)]^{-}\) with aliquots of aqueous vitamin C resulting in the formation of the ferrous complex \([\text{Fe(II)}(\text{NNOO}_3)]^{2+}\) (see Fig. 11). Alternatively the ferrous complex may be oxidized with \(\text{H}_2\text{O}_2\) to yield the ferric complex. These two series of spectra are superimposable.

4.3. Outlook

The iron localization, oxidation state and translocation are conveniently addressed by visible spectroscopy. Furthermore, the Mössbauer spectrum for the ferric complex is fully consistent with that obtained by Raymond upon lowering the pH of \([\text{Fe(III)}(\text{enterobactin})]^{3-}\) solutions, thus supporting the iron-release mechanism from enterobactin via the salicylate-binding mode [42]. A summary of the spectroscopic data is presented in Fig. 12.

5. Conclusions

Three different projects were outlined in this paper:

- i) What makes \(d^0\) bent-metalloccenes so unusual?
  A MO analysis, coupled with a structure correlation revealed that \([\text{CP}_2\text{ML}_3]\) complexes can be viewed as trigonal bipyramidal structures which undergo distortion along a reversed-Berry pathway. Given the right electronic environment, this distortion is energetically favoured over the Berry distortion and is in fact quite common. Extensions of this work to metals with different electron counts as well as the synthesis of novel cyclopentadienyl substituents are planned [43].

- ii) What is the role of metal-based chirality in enantioselective catalysis?
  To probe this question, we developed a
Fig. 12. Summary of the spectroscopic data of the ferric complex \([\text{Fe(III)}(\text{NNOO})_3]^{2+}\) and the ferrous complex \([\text{Fe(II)}(\text{NNOO})_2]^+\)

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**General Approach for the Synthesis of Configurationaly Stable, Chiral-at-Metal Three-Legged Piano-Stool Complexes.** We are currently testing these as Lewis acids in various C–C-bond forming reactions.

**iii) How is iron released from ferric enterobactin?**

The synthesis of tripodal ligands incorporating salicylamide-binding sites has allowed us to give strong spectroscopic support for the iron release from enterobactin via a salicylate binding mode. In addition, we synthesized a fully functional redox-triggered molecular switch. Future directions include inclusion of this device in an artificial membrane as well as a detailed mechanistic investigation of the translaction mechanism.

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[1] R. Hoffmann, 'The Same and Not the Same', Columbia University Press, New York, 1995.
[2] C. Brändli, T. Ward, Helv. Chim. Acta 1998, 81, 1616.
[3] T.R. Ward, H.-B. Bürgi, F. Gilardoni, J. Weber, J. Am. Chem. Soc. 1997, 119, 1974.
[4] J.C. Green, Chem. Soc. Rev. 1998, 27, 263.
[5] T. Auf der Heyde, Angew. Chem., Int. Ed. Engl. 1994, 33, 823.
[6] R.D. Wilson, T.F. Koetzle, D.W. Hart, A. Krick, D.L. Tipton, R. Bau, J. Am. Chem. Soc. 1977, 99, 1775.
[7] G. Fachetti, C. Floriani, F. Marchetti, S. Merlino, J. Chem. Soc., Chem. Commun. 1976, 522.
[8] D. Rüttger, G. Erker, Angew. Chem., Int. Ed. Engl. 1997, 36, 812.
[9] T.A. Albright, J.K. Burden, M.-H. Whangbo, 'Orbital Interactions in Chemistry', John Wiley, New York, 1985.
[10] C.J. Piersol, R.D. Proillet, P.E. Fanwick, J.P. Rothwell, Polyhedron 1993, 12, 1779.
[11] C. Pulham, A. Haaland, A. Hammel, K. Rypdal, H.P. Verne, H.V. Volden, Angew. Chem., Int. Ed. Engl. 1992, 31, 1464.
[12] T.A. Albright, H. Tang, Angew. Chem., Int. Ed. Engl. 1992, 31, 1462.
[13] D.L. Dubois, R. Hoffmann, New J. Chem. 1977, 1, 479.
[14] W.A. Nugent, J. M. Mayer, 'Metal-Ligand Multiple Bonds', John Wiley & Sons, New York 1988.
[15] J.P.L. Ny, M.-T. Youinou, J.A. Osborn, Organometallics 1992, 11, 2413.
[16] E.L. Muetterties, L.J. Guggenberger, J. Am. Chem. Soc. 1974, 96, 1748.
[17] R. Bauman, W.M. Davis, R.R. Schrock, J. Am. Chem. Soc. 1997, 119, 3850.
[18] J.D. Scofield, D.H. McConville, J. Am. Chem. Soc. 1996, 118, 5008.
[19] U. Siegel, T. Bürkle, W.W. Schöller, C. Redshaw, V.G. Gibson, Inorg. Chem. 1998, 37, 4738.
[20] B. Herren, T.R. Ward, Angew. Chem. Int. Ed. Engl. 1998, in press.