Hypovalent substrates in transition metal catalysis: C-H bond functionalisation, ring-closing reactions & polymer synthesis

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Chapter 5

Towards Controlled Nitrene-Transfer Reactivity Using Co and Fe Porphyrin Catalysts.
Abstract

In this chapter we present our comparative mechanistic studies, based on experimental and computational studies, using Co II- and Fe II-porphyrins as catalysts for the activation of organic azides and subsequent nitrene-transfer to styrenes. We focused on the competition between 3-membered ring (aziridine) and 5-membered ring (tetrahydropyrrole) formation, the influence of the olefinic substrates, and the influence of the type of metallo-porphyrin and metallo-porpholactone used as catalyst for aziridination reactions. We found that the Co and Fe systems operate via very similar radicaloid mechanisms. Subtle differences in their electronic structures lead for Co to a discrete nitrene radical intermediate \([(\text{por})\text{Co}^{\text{III}}\{\text{N}•\text{R}–\}]\) upon activation of the azide, whereas Fe produces a nitrene intermediate with a more covalent Fe=NR $\pi$-bond, having each of its two $\pi^*$ Fe–N antibonding SOMOs half-filled. While this complicates the assignment of metal and ligand oxidation states (resonance structures: \([(\text{por})\text{Fe}^{\text{IV}}\{\text{NR}^{2–}\}] \leftrightarrow [(\text{por})\text{Fe}^{\text{III}}\{\text{N}•\text{R}–\}] \leftrightarrow [(\text{por})\text{Fe}^{\text{II}}\{\text{NR}^{0}\}])\), the species does contain a significant amount of spin density at the nitrene/imido nitrogen. This allows a description of its reactivity with styrene to proceed via its \([(\text{por})\text{Fe}^{\text{III}}\{\text{N}•\text{R}–\}]\) resonance form. Radical addition of \([(\text{por})\text{Fe}^{\text{III}}\{\text{N}•\text{R}–\}]\) to styrene produces a genuine Fe III $\gamma$-alkyl radical, comparable to the Co III $\gamma$-alkyl radical intermediate obtained by radical addition of \([(\text{por})\text{Co}^{\text{III}}\{\text{N}•\text{R}–\}]\) to styrene. These results highlight the importance of having discrete spin density located at the nitrene nitrogen in \((\text{por})\text{M}^{\text{III}}\{\text{N}•\text{R}–\}\) species prior to olefin attack (M = Co, Fe), which explains the reactivity displayed by these catalysts. Selectivity for formation of the aziridines (3-membered ring) vs. tetrahydropyrrole (5-membered ring) arises, from the competition between ring-closure and addition of the second styrene moiety. For all catalysts, we found almost barrierless ring-closure of the $\gamma$-alkyl radical species. Only for metallo-porpholactones, the barrier for the addition of the second unit becomes comparable to the ring formation barrier, and thus energetically competitive. Experimentally, tetrahydropyrrol formation is only observed when using metallo-porpholactones as catalysts and $p$-MeO-styrene as a substrate. In good agreement, also in the computational studies, the use of $p$-MeO-styrene further lowers the activation barrier for addition of the second styrene moiety, and in case of the Fe-porpholactone catalysts this path is nearly barrierless.
Towards controlled nitrene-transfer reactivity using Co and Fe porphyrin catalysts.

5.1 Introduction.

Nitrogen containing molecules are abundant in nature and their importance in biological systems has been widely documented. Therefore, metal catalysed nitrene/imido transfer reactions, such as aziridination of alkenes, sulfimidation of sulfides and amination/amidation of alkanes are important applications in organic synthesis. Nitrenes display important chemical reactivity and their capacity to insert into various bonds makes them attractive for the synthesis of nitrogen containing molecules. The ability of metal complexes to catalyse nitrene transfer reactions, demonstrated at the end of the 1960’s, brought attention to the field. Since then, research on synthesis of N–functionaized molecules has focused on methodologies for practical applications and it was the introduction of the hypervalent iodo precursors (i.e. PhI=NR) that led to a substantial expansion of the field. Following the pioneering work on nitrene-transfer reactions by MnIII-TPPCl and FeIII-TPPCl as heme model catalyst and PhI=NTs as the nitrene source described by Breslow in the early 80’s, other metal complexes based on Rh, Ru, Fe, Cu, and Co have been applied for nitrene transfer reactions, leading to development of important synthetic methodologies for the synthesis of N-containing products.

While most of the systems employ the high energy PhI=NR substrates, only a limited number of nitrogen-transfer catalysts are capable of employing more desirable organic azides as substrates. Among the examples with a broader scope in organic azides, CoII porphyrin have been shown to be efficient catalysts for olefin aziridination and amination of benzylic C–H bonds with organic azides (Scheme 1). The mechanism followed by the Co systems follows a multistep radical type mechanism (see Chapter 2 and 3). These reactions proved to be quite sensitive to the structure and nature of the employed organic azide, C–H or alkene substrate, and catalyst.

Early biomimetic applications of perhalogenated metallo-porphyrins were developed and these systems provided robust catalysts with enhanced activity in catalytic reactions such as hydroxylation by dioxygen. An advantage of these electron-deficient ligands is their ability...
to stabilise the more reduced species (i.e. ferrous state for iron) and a decreased reactivity towards \(O_2\), making the catalyst more stable towards highly oxidizing reagents. Applications of iron porphyrin systems in nitrogen transfer reactions are so far limited, with few literature examples and only recently the application of perhalogenated Fe metallo-porphyrins has been extended to C–N bond formation.\textsuperscript{11} Remarkably, the substitution of H– for F– at the phenyl rings on the \textit{meta}- positions increased the activity of Fe-porphyrin systems, leading to good yields in C–H bond activation and aziridination. Moreover, modification of the macrocycle (going from porphyrins to porpholactones or polycarbene cycles) has a positive effect on the activity of the Fe catalysts.\textsuperscript{11,12}

Mechanistic aspects concerning formation of the intermediate nitrene/imido species have been debated since the early developments of nitrene transfer reactions using metallo-porphyrins. Only recently, characterisation of the intermediate and mechanistic studies have shed some light on the nature of these intermediates and the mechanism by which they are formed.\textsuperscript{5e,9,13} However, nitrene-transfer reactions seem to be quite sensitive to the metal, the ligand, and the substrate. The presence of radical intermediates and redox cooperativity of the ligands appear to be important in the reactivity of many of the examples reported in literature (see Chapter 1). The lack of more general models in nitrogen-transfer reactions has motivated us to investigate the comparison of the mechanistic features of different metal centres in these porphyrin based catalysts. This information can provide a more accurate description of the factors influencing the catalytic process and should further aid the development of new catalytic systems. Additionally, a recent observation made by Zhang et. al. suggest that is possible to form 5-membered rings (tetrahydropyrroles) in reactions between electron-rich olefins and a nitrene source catalysed by iron-porpholactone complexes.\textsuperscript{11b} This reactivity was so far unknown and potentially provides a new and interesting way of synthesizing 5-membered ring compounds. In that perspective, we became interested in the mechanism behind these reactions, which is important for further developments. We were particularly interested in (1) the competition between 3-membered ring (aziridine) formation and 5-membered ring (tetrahydropyrrol) formation; (2) the influence of the olefinic substrates; and (3) the influence of the type of metallo-porphyrin and metallo-porpholactone used as catalyst (Co versus Fe, with or without electron-withdrawing groups) on the outcome of these reactions. Herein, we present our comparative mechanistic studies based on experimental results and computational studies.
5.2 Results.

Experimental catalytic studies on nitrogen-transfer reactions.

On the basis of the different yields and reaction conditions that have been reported for different metallo-porphyrin systems, we decided to evaluate the Fe and Co complexes depicted in Figure 1 under the same reaction conditions in order to have a precise picture of the factors that play a role in the activity of such systems.

We evaluated the activity of M(TPP), M(TF$_{20}$PP), and M(TF$_{20}$PPL) complexes (M = Co, Fe) in the formation of the 3-membered aziridines ring and the 5-membered tetrahydro-pyrrole (THP) ring from styrene and tosyl azide (TsN$_3$) (Scheme 2 and Table 1). The porphyrin complexes M(TPP) and M(TF$_{20}$PP) were compared with the porpholactone complexes M(TF$_{20}$PPL) because of the reported increased activity of the latter in these reactions. From data reported in literature, optimal catalytic results are expected for the Fe-catalyst using dichloroethane (DCE) as the solvent, while in general the activity of cobalt is enhanced using the less polar solvent chlorobenzene (PhCl). These results are confirmed by our observations; the use of DCE considerably reduces the already modest activity of CoTPP, and the iron systems show no activity when using PhCl instead of DCE.

Most notably, the 3-membered aziridine ring product was formed as the dominant product when using styrene as the substrate (Table 1, 4th column) and no THP was detected, irrespective of which Fe or Co catalyst was used. Formation of the 5-membered ring product (THP) was only detected when using the electron rich olefin $p$-MeO-styrene (5th column), and

![Figure 1](image-url)
only when using the porpholactone complexes $3_{Fe}$ and $3_{Co}$.

The catalytic observations in Table 1 correspond well with the reported data, and can be rationalised in the following manner:

1. For the Fe-systems, the improved activity when using the aprotic, high dielectric constant solvent DCE is used can probably be explained by an easier reduction of Fe$^{III}$ to Fe$^{II}$ in this solvent (See chapter 4). This is a likely requirement for catalytic activity.

2. Halogenated substituents on the porphyrin or porpholactone ring lead to enhanced catalytic activity only in the case of Fe, but not for Co (where it was reported to have a negative influence in the TS1 barrier; see chapter 3), again suggesting that the electron

![Scheme 2. Formation of 3-membered aziridine rings and 5-membered tetrahydropyrrole rings from styrenes and TsN$_3$ catalysed by metallo-porphyrin and metallo-porpholactone complexes.](image)

| Table 1. Aziridination of styrenes catalysed by metallo-porphyrins and metallo-porpholactones.$^a$ |
|---|---|---|
| **Entry** | **Catalyst** | **Solvent** | **Yield**$^b$ | **Yield**$^b$ |
| 1 | $1_{Fe}$ | DCE | 50 | -- |
| 2 | $2_{Fe}$ | DCE | 70 | -- |
| 3 | $3_{Fe}$ | DCE | 95 | 20 |
| 4$^e$ | $1_{Co}$ | PhCl | 18 | -- |
| 5$^e$ | $2_{Co}$ | PhCl | -- | -- |
| 6 | $3_{Co}$ | DCE | -- | <5$^f$ |

$^a$ Reaction conditions: alkene (0.6 mmol), azide (0.2 mmol), catalyst (0.001 mmol) in 2 ml 1,2-DCE at 80 °C for 18 hr under an inert (N$_2$) atmosphere using 4Å molecular sieves. $^b$ Determined by crude $^1$H NMR. $^c$ When the aziridine was detected, no tetrahydropyrrole was detected. $^d$ Tetrahydropyrrole was observed only when using p-MeO-styrene; all other olefins used produced only aziridines and no tetrahydropyrrole. $^e$ Data taken from ref 8d and 15, experiments carried in DCE gave no conversion. $^f$ 0.004 mmol catalyst.
withdrawing groups primarily facilitate reduction of Fe$^{III}$ to Fe$^{II}$. As a direct result of their less negative reduction potentials, the Fe(TF$_{20}$PP) and Fe(TF$_{20}$PPL) systems are expected to generate higher Fe$^{II}$ concentrations under the applied catalytic conditions.$^{17}$ There seems to be a clear relation between the redox potentials of the Fe$^{III}$/Fe$^{II}$ couple of compound 1$_{Fe}$, 2$_{Fe}$, and 3$_{Fe}$ (–0.89, –0.62, and –0.66 V vs Ag$^+$/Ag for 1$_{Fe}$, 2$_{Fe}$, and 3$_{Fe}$, respectively, moving in the expected direction with increasing electron-accepting properties of the porphyrin ligand) and their catalytic activity.

(3) For the cobalt systems, a non-coordinating mild polarity solvent seems to be required to enhance the lifetime of the radical intermediate. Since these systems do not require a pre-activation step, involving reduction of M$^{III}$ to M$^{II}$ prior to azide activation, electron-withdrawing groups have only a negative effect on the catalytic activity because the actual azide process involves electron transfer from the metal to the nitrene moiety (see Chapter 3). This leads to a higher energy barrier for TS$_{1-2Co}$ compared to TS$_{1-1Co}$.$^{17}$

We were intrigued by the fact that the use of the porpholactone complexes 3$_{Fe}$ and 3$_{Co}$ in reactions with the electron rich $p$-MeO-styrene substrate led to the formation of the 5-membered tetrahydropyrrole ring compound, while aziridines were not detected under these conditions. This point will be addressed in detail in the computational study described below.

**Computational studies.**

Our previous DFT studies on aziridination and C–H amination reactions with cobalt porphyrins and those of related cobalamin derivatives have shown that Co-ligand systems are best reproduced by the non-hybrid BP86 functional rather than hybrid functionals such as B3LYP.$^{18}$ We therefore consistently used the BP86 functional at the spin unrestricted DFT level as implemented in the Turbomole package. We first investigated the formation mechanism of the Fe=NR intermediates by DFT methods. The results are described in analogy with the previously reported data obtained for analogous Co-systems. In the experimental systems, the halogenated porphyrins in Fe-systems give higher yields than the non-halogenated ones, while the reverse is observed for the analogous Co$^{II}$-porphyrin systems (vide supra).$^{9b}$ Therefore, we included the effect of different porphyrin substituents in our studies. The non-substituted metalloporphyrins 1 act as a model for experimental metal-tetraphenylporphyrin [M(TPP)] complexes. Full atom models 2 were used to explore the effects of halogenated substituents (aryl groups) on the meta-position of the porphyrins (Figure ). Additionally, we explored the effect of changing porphyrin 2 to porpholactone 3. In
experimental studies, this has a remarkable influence on the activity of comparable Fe-systems. In 2012, Zhang\textsuperscript{11b} and coworkers reported the aziridination of olefins with 1 mol\% of [Fe\textsuperscript{III}(TFPPL)Cl] (TFPPL = tetrakis(pentafluoro-phenyl)porpholactone)\textsuperscript{14} as the best catalyst.

**Nitrene formation with substituted Co- and Fe-porphyrins.** We first investigated the influence of different porphyrin substituents on the activation of organic azides by Fe-porphyrins and Fe-porpholactones (Scheme 3). From the results presented in the previous chapter, it is clear that the reduced form of the iron-catalyst (ferrous porphyrin) has markedly lower transition barriers than the oxidised catalyst (ferric porphyrin), thus leading to increased activities (See chapter 4). Nonetheless, we included both Fe\textsuperscript{II} and Fe\textsuperscript{III} systems in our studies to investigate the influence of the aryl groups on the transition state barrier for formation of the nitrene/imido.

**Table 2.** Free energies for nitrene formation with Fe-porphyrins and Fe-porpholactones with different multiplicities and oxidation states.

<table>
<thead>
<tr>
<th>Species</th>
<th>Complex</th>
<th>∆G° (kcal mol(^{-1}))\textsuperscript{a}</th>
<th>Fe\textsuperscript{II}</th>
<th>Fe\textsuperscript{III}</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>S = 0</td>
<td>S = 1</td>
<td>S = 1/2</td>
</tr>
<tr>
<td>A</td>
<td>(^1)Fe</td>
<td>+12.3</td>
<td>0</td>
<td>+8.1</td>
</tr>
<tr>
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<tr>
<td></td>
<td>(^3)Fe</td>
<td>+11.3</td>
<td>0</td>
<td>+4.3</td>
</tr>
<tr>
<td></td>
<td>(^1)Fe</td>
<td>+20.9</td>
<td>+15.8</td>
<td>+31.4</td>
</tr>
<tr>
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<td>+17.2</td>
<td>+29.5</td>
</tr>
<tr>
<td></td>
<td>(^3)Fe</td>
<td>+21.2</td>
<td>+17.1</td>
<td>+30.4</td>
</tr>
<tr>
<td></td>
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<td>-24.2</td>
<td>-26.4</td>
<td>-4.7</td>
</tr>
<tr>
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<td>(^2)Fe</td>
<td>-22.1</td>
<td>-24.1</td>
<td>-5.5</td>
</tr>
<tr>
<td></td>
<td>(^3)Fe</td>
<td>-20.9</td>
<td>-22.7</td>
<td>-6.0</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Free energies corrected for the condensed phase reference volume in a Trouton-like approach.
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complex \( (\text{TS}1_{\text{Fe}}; \text{Table 2}) \). For \( \text{Fe}^{II} \) slightly higher barriers are observed for halogenated porphyrins \( 2_{\text{Fe}} \) and \( 3_{\text{Fe}} \) \( (\Delta G^f \sim 2 \text{ kcal mol}^{-1}; \text{Figure 2}) \), and this behaviour has also been observed for Co-porphyrin systems (see Chapter 3). The electron-withdrawing groups seem to hamper electron-transfer from \( \text{M}^{II} \) to \( \text{M}^{III} \) to the nitrene/imido nitrogen atom formed in the process.\(^9b\) Coordination of the azide prior to its activation, involving a discrete intermediate B (Figure 10 in chapter 2) may not be a strict requirement. Although optimisation at the SV(P) level led to convergence to minimum B, optimisations using the larger functional (def2-TZVP) did not support coordination of the azide. While this may be counter-balanced by attractive Van der Waals interactions, not included in DFT, a more detailed study is required to explore this phenomenon. This is beyond the scope of the present study, and hence we will not discuss complex B. In any case, formation of the Fe-nitrene/imido species is a combination of approach of the \( \alpha \)-nitrogen atom of the azide to the metal centre followed by \( \text{N}_2 \) loss (Scheme 3).

The calculated thermodynamic parameters associated with formation of iron nitrene/imido complexes at different spin state surfaces and using complexes in different oxidation states are summarised in Table 2. For \( \text{Fe}^{II} \), the most populated spin state in all three models is the intermediate spin \( (S = 1) \) system.\(^{19}\) Species derived from \( \text{S}^{=0} \text{A} \) have a considerably higher energy compared to species on the pathway from \( \text{S}^{=1} \text{A} \) in case of \( \text{Fe}^{II} \) \( (10 \text{ kcal mol}^{-1} \) difference). For \( \text{Fe}^{III} \), although to a lesser extent, the doublet pathway is also higher in energy than the quartet pathway \( (5–8 \text{ kcal mol}^{-1} \) consistent with previous studies.\(^{19,20}\) The \( \text{Fe}^{II} \) pathway on the intermediate spin (IS) triplet surface \( (S = 1) \) has lower energy barriers than the

![Figure 2](image_url). Energy profile for the formation of nitrene species C with \( \text{Fe}^{II} \) and \( \text{Fe}^{III} \) in the low spin (LS; \( S = 0 \) or \( S = 1/2 \)) and intermediate spin (IS; \( S = 1 \) or \( S = 3/2 \)) states, respectively. Energies corrected for the entropy using a Trouton-like approach \( (6.2 \text{ kcal mol}^{-1}) \).
pathway on the low spin (LS) singlet surface (S = 0). This is not the case with Fe\textsuperscript{III}, for which formation of species C can proceed via the close lying doublet (S = 1/2) and quartet (S = 3/2) spin state surfaces. For Fe\textsuperscript{III} an inversion of spin state stability occurs upon nitrogen release, leading to lower free energies of \(\frac{1}{2}\text{TS}_1\) and \(\frac{1}{2}\text{C}\) compared to \(\frac{3}{2}\text{TS}_1\) and \(\frac{3}{2}\text{C}\) (See Table 2 and Figure 2). However, this does not affect the fact that the energy barriers \(\text{TS}_1\) are remarkably higher for Fe\textsuperscript{III} (both spin states) than for Fe\textsuperscript{II} (\(\frac{1}{2}\text{TS}_1 > \frac{1}{2}\text{TS}_1\), ~10 kcal) for all porphyrin and porpholactone models studied here, in agreement with the findings described in Chapter 4. These results, combined with the experimental catalytic studies presented in the previous section and the results described in Chapter 4 all point to the importance of reduction of Fe\textsuperscript{III} to Fe\textsuperscript{II} as a prerequisite for catalytic activity. Hence, we concluded that the mechanism by which the Fe-complexes operate proceeds via Fe\textsuperscript{II} complexes.

For the computed reaction sequences for aziridination and THP ring formation, we calculated the pathways on both the triplet and the open-shell singlet spin surface. In most of the cases, the triplet energies of the intermediates are lower in energy (exceptions are mentioned in the discussion) and in all cases the barriers on the triplet surface proved to be significantly lower than on the open shell singlet surface (see experimental section for complete data). Therefore, we restrict further discussions to the lowest-energy triplet surface, which should represent the preferred reactivity surface of the Fe-porphyrins and Fe-porpholactones (see Chapter 4, Figure 2 and Table 2).

In chapters 2 and 3, we investigated the radical-type mechanism of Co\textsuperscript{II}-porphyrin mediated activation of azides\textsuperscript{9}. The formation of the nitrene radical intermediate was described by DFT calculations as an exergonic process (\(\Delta G^0 \sim 17\) kcal mol\(^{-1}\)) and we were able to characterise the Co\textsuperscript{III}-nitrene radical (TPP)Co((N\•SO\(_2\)C\(_6\)H\(_4\)p-NO\(_2\)) and (3,5-Di'Bu-ChenPhyrin) Co(N\•Troc) species with EPR techniques (Chapter 2 and 3). In line with these findings, we were also able to characterise with spectroelectrochemical techniques the exergonic (\(\Delta G^0 \sim 26\) kcal mol\(^{-1}\)) formation of Fe-nitrene/imido.

\[\text{Figure 3. Free Energy (}\Delta G^1\text{) profile for the formation of nitrene species C for Co}^{\text{II}}.\text{ Energies corrected for the entropy using a Trouton-like approach (6.2 kcal mol}^{-1}\text{).}\]
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complex [TPPFe=NTs] starting from Fe$^{II}$ (see Chapter 4). In analogy with these data and based on our theoretical models, we propose that in all cases reduction of the ferric precatalysts to the active ferrous species ($^{S=1/2}A_{Fe(III)} + e \rightarrow ^{S=1}A_{Fe(II)}$) is crucial for activation of the azide. This leads to a similar mechanism for the formation of the complexes $^{S=1}C-1_{Fe}$, $^{S=1}C-2_{Fe}$, and $^{S=1}C-3_{Fe}$, with comparable energy barriers $^{S=1}TS1$ for all three iron porphyrinoid models studied herein, which partially parallels the cobalt-mediated pathway.

We further investigated the influence of the porphyrin/porpholactone structure on the activation barriers for nitrene formation at the cobalt systems. While the electron withdrawing –C$_6$F$_5$ groups of 2$_{Co}$ have a rather small influence on the TS1 activation barrier compared to the barrier from non-functionalised 1$_{Co}$ ($\Delta G^\ddagger$ +20.3 vs. +21.0 kcal mol$^{-1}$ for $^{S=1/2}TS1-1_{Co}$ compared to $^{S=1/2}TS1-2_{Co}$), moving from a porphyrin to a porpholactone has a much larger influence for cobalt. For porpholactone complex 3$_{Co}$ the $^{S=1/2}TS1-3_{Co}$ barrier is considerably higher in energy (+30.3 kcal mol$^{-1}$) than the comparative barriers $^{S=1/2}TS1-1_{Co}$ and $^{S=1/2}TS1-2_{Co}$. This is a result of the lower energy of the HOMO orbital of the starting species A, which hampers electron transfer to the organic azide during nitrene formation required to form C.$^{14,21}$

The above results can be summarised in the following manner: efficient formation of the nitrene intermediate requires catalysts which bear mild electron-withdrawing groups to favour coordination of the azide substrate, but it is of crucial importance that these groups are not too strongly electron-withdrawing because this hampers charge transfer from the metal to the substrate during formation of the nitrene intermediate (See chapter 3). An important difference between the Co- and Fe- systems is the electronic structure of species C. While the (por)Co$^{III}$-nitrene complexes C$_{Co}$ bear a nitrene centred radical, (por)Fe-imido complexes C$_{Fe}$ have nearly covalent Fe-N $\pi$-bonds with two half-filled (near covalent) $\pi^*$-based SOMO orbitals (See chapter 4). This leads to a resonance description best described being in between an Fe$^{IV}$-imido and an Fe$^{II}$-nitrene species ([$(RN=Fe^{III}(por^2-)) \leftrightarrow [R\cdot N=Fe^{III}(por^2-)] \leftrightarrow [RN^2-]=Fe^{IV}(por^2-)$]), but the nitrene/imido ligand does bear substantial radical spin density (see Chapter 4). Hence, also the intermediate Fe$^{III}$-nitrene radical resonance form (Fe$^{III}$-{$N\cdot R$}) contributes significantly to the electronic structure of this species. See Figure 4. In fact, this leads to interesting radical-type reactivity

![Figure 4. Resonance structures of species C$_{Fe}$.](image)

of nitrene/imido intermediates generated from Fe\textsuperscript{II}-porphyrinoids, somewhat comparable to the behaviour of their Co\textsuperscript{II}-analognes.

**Single and double styrene addition to species C: 3-membered versus 5-membered ring formation.** The electronic structure of species C is such that these species are best described as “nitrene radical” complexes for all Co complexes studied (\(S=1/2\text{C-1}_\text{Co},\ S=1/2\text{C-2}_\text{Co},\) and \(S=1/2\text{C-3}_\text{Co}\)). For the iron complexes \(S=1\text{C-1}_\text{Fe},\ S=1\text{C-2}_\text{Fe},\) and \(S=1\text{C-3}_\text{Fe}\), the metal and ligand oxidation states are not as straightforward to interpret due to the presence of two rather covalent Fe–N \(\pi\) bonds (see Chapter 4, Figure 4, and the discussion above). In terms of reactivity, however, these species basically react via their Fe\textsuperscript{III}-nitrene radical resonance form Fe\textsuperscript{III}–\{N•R\} (Figure 4, middle), and accordingly the calculated (unrestricted) DFT pathway reveals a step-wise radical mechanism for nitrene transfer from \(\text{C}_\text{Fe}\) to styrene, somewhat similar to the cobalt-mediated pathway. Approach of the double bond of styrene to the nitrene nitrogen atom of \(\text{C}_\text{Fe}\) leads to a migration of spin density from the nitrene moiety to an olefinic carbon (benzylic \(\gamma\)-carbon in intermediate D) to form biradical species D (Scheme 4). Species D are best described as genuine Fe\textsuperscript{III}-species containing a \(\gamma\)-radical amido ligand (\{NR-CH\textsubscript{2}-CH•Ph\}), the spin of which is either ferro- (\(S=1\text{D}\)) or antiferromagnetically (\(S=0\text{D}\)) coupled to the unpaired electron of the low spin Fe\textsuperscript{III} centre (Scheme 4, Table 3, and Figure 5).

Overall the mechanistic features of the Fe\textsuperscript{II} and Co\textsuperscript{II} pathways bear many similarities, but the electronic structure differences between these systems lead to interesting effects. For the

![Scheme 4](image-url)

Scheme 4. Species found along pathway for addition of alkenes to Fe- and Co-nitrene radical complexes.
Towards controlled nitrene-transfer reactivity using Co and Fe porphyrin catalysts. We previously reported (see Chapter 2) that the energy barrier $S=1/2TS1_{Co}$ for styrene ($\Delta G^\ddagger \approx 20$ kcal mol$^{-1}$) leading to a mechanism with two rate determining steps during the reaction of aziridination. Remarkably, the structure of $S=1/2D-1_{Co}$ species has a doublet ground state ($S = 1/2$) with a broken symmetry, in which two $\alpha$–spin electrons at cobalt ($S_{Co} = 1$; $d_z^2$ and $\pi^*_{Co-N}$ ($d_z-C_p$) orbitals) are antiferromagnetically coupled to a $\beta$–spin electron mainly located at the $\gamma$–carbon of the olefin ($S_{ligand} = 1/2$). This situation arises after radical addition of doublet Co$^{III}$-nitrene radical species $S=1/2C-1_{Co}$ (with its spin density mostly located at the ‘nitrene’ nitrogen atom) to styrene, followed by a low spin (LS) to intermediate spin (IS) transition of the cobalt(III) centre.

Olefin addition to $S=1C-1_{Fe}$ follows a similar path, but with important subtle electronic differences. First of all, the reaction starts with an intermediate spin state ($S = 1$) iron, and the metal spin state does not change over the course of this process. Species $S=1C_{Fe}$ has two unpaired electrons, each located in one of the two Fe=NR $\pi^*$orbitals (~65% Fe character and ~35% nitrogen character each, based on spin density calculations; Table 3). Despite the rather covalent character Fe–N bond, radical-type addition of the metal-imido moiety of $C_{Fe}$ to styrene occurs relatively easily. As an example, the process is illustrated for $S=1TS2-1_{Fe}$ in Figure 5, showing the changes in spin densities upon approach of the $\pi$-orbital of styrene to the singly occupied $\pi^*_{Fe-N}(d_z-C_p)$ orbital on the side of the nitrogen (see also Table 3). As a result, the C=C double bond of styrene breaks and the $\pi^*_{Fe-N}(d_z-C_p)$ orbital gets fully occupied (formally breaking one of the half bond-order Fe–N bonds) in species $S=1D-1_{Fe}$, which allows the radical-type addition to the olefin. This highlights the importance of having discrete spin density located at the nitrene nitrogen in $C_{Fe}$ prior to olefin attack.

The resulting electronic structure of $D_{Fe}$ is best described as a biradical with its $\alpha$ spin in

<p>| Table 3. Mulliken spin density populations for species $S=1C_{Fe}$, $S=1TS2_{Fe}$, and $S=1D_{Fe}$. |
|------------------|------------------|------------------|------------------|
| $S=1C_{Fe}$      | $S=1TS2_{Fe}$    | $S=1D_{Fe}$      |</p>
<table>
<thead>
<tr>
<th>Fe</th>
<th>NR</th>
<th>Fe</th>
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<th>NR</th>
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<td>0.89</td>
<td>0.18</td>
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<td>0.89</td>
<td>0.20</td>
<td>0.96</td>
<td></td>
</tr>
<tr>
<td>3</td>
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<td>0.74</td>
<td>1.24</td>
<td>0.51</td>
<td>0.26</td>
<td>1.01</td>
<td>0.25</td>
<td>0.83</td>
<td></td>
</tr>
</tbody>
</table>
the mostly Fe $\pi$ *Fe–N ($d_{xz}$–$p_x$) orbital and another unpaired electron located at the $\gamma$–carbon of the olefin (Table 3). In contrast with the cobalt system, for species $\text{DFe}$ the energy of the singlet ($S=1$D-1Fe with a $\beta$–spin in the $\gamma$–carbon) and the triplet ($S=1$D-1Fe with an $\alpha$–spin in the $\gamma$–carbon) are almost degenerate (See Figure 5). The associated energy barrier ($\text{TS2}$, $\Delta G^\ddagger = \sim 21$ kcal mol $^{-1}$) for radical addition of $\text{CFe}$ to styrene is comparable to the corresponding barrier for the (por)Co catalyst (See Figure 6 and Figure 8). However, different from cobalt, for iron $\text{TS1}$ is $\sim 5$ kcal mol $^{-1}$ lower in energy than $\text{TS2}$ (roughly two orders of magnitude faster), hence $\text{TS2}$ becomes the rate determining step.

The formation of aziridine adduct ($E$) through ring-closure from species $S=1/2\text{DCo}$ was found to be almost barrierless ($S=1/2\text{TS3Co}$) in the cobalt catalysed process (see ref. 9a and Figure 7). When iron-porphyrins are used as catalyst the mechanism is quite similar, but ring closure to form the aziridine has a higher (but still small) barrier $S=1\text{TS3Fe}$ ($\Delta G^\ddagger \sim +4$ kcal mol $^{-1}$) compared to cobalt. The difference in energy for cobalt and iron for $\text{TS3}$ seems to be an electronic effect, and can in part be explained by the differences in nitrogen radical character as determined by the relative atomic orbital coefficients in the SOMO orbitals. The multi-radical character of species $D$ arises from (anti)ferromagnetic coupling between the unpaired electrons located on the SOMOs determined by the $\gamma$–carbon p-orbital and the $\pi$ *M–N ($d_{xz}$–$p_x$) orbital. During the ring closure, the $\gamma$–carbon radical orbital must mix-in with the $\pi$ *M–N ($d_{xz}$–$p_x$) orbital, in which the attack occurs from the side of the ‘amido’ nitrogen moiety. For Fe, the nitrogen radical character is considerably smaller than for cobalt (18% spin density for $S=1\text{D-1Fe}$, and 31% spin density for $S=1/2\text{D-1Co}$; see Table 3 and Chapter 2), which likely contributes to a higher barrier. Additionally, the ring-closing process for iron on the lowest energy triplet surface requires an energy costly spin flip process (while on the higher energy open-shell singlet surface ring closure simply produces a high energy species having

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**Figure 5.** a) Simplified reactivity scheme for $\text{TS2Fe}$ representing the addition of the olefin to species $\text{CFe}$. b) Isosurface plot (0.08) of the $\text{TS2Fe}$ orbital involved in olefin addition to $\text{C-1Fe}$. 

![Figure 5](image-url)
Towards controlled nitrene-transfer reactivity using Co and Fe porphyrin catalysts.

Effect of different styrenes on 3-membered versus 5-membered ring formation. As is clear from the catalytic studies described in the previous section and data taken from literature, the use of $p$-MeO-styrene as a substrate does not lead to aziridines. Instead, a five membered ring (tetrahydropyrrole, THP) was isolated, albeit in rather low yields (<20%). Zhang et al.\textsuperscript{11b} in their studies with A-3Fe investigated nitrene transfer reactions to several aryl substituted styrene substrates and found that the only substrates that can afford the THP product are those with methoxy substituent in the para- and meta-position. In our own experiments, we extended the catalytic screening to all our catalysts with Fe and Co and found that also A-3Co can form the THP ring (Table ; entry 3 and 6), although it should be noted that a higher catalyst loading was necessary than with A-3Fe. It proved impossible to increase the THP yields by changing the reaction conditions, and remarkably the expected aziridines were not detected when THP was formed. In control experiments, we tested if THP could be formed from the aziridine as an intermediate, but the addition of 2-($p$-MeOC$_6$H$_4$)-N-tosyl aziridine to para-methoxystyrene under the same catalytic conditions did not produce the THP product.\textsuperscript{23}

To shine some light on this unusual behaviour we decided to investigate the formation of THP heterocycles computationally.\textsuperscript{24} Addition of a second styrene unit to the γ–carbon radical

**Figure 6.** a) Normalised (on the resting state species $S=1\text{C}_\text{Fe}$) free energy pathway for alkene addition to nitrene species $C_\text{Fe}$. Solid lines: sequential addition of two alkene units (5-membered ring formation via TS4). Dashed lines: ring-closure pathway after the first alkene addition to species $C_\text{Fe}$ (3-membered aziridine ring formation via TS3). b) Scheme of TS3 and TS4. c) Spin density plot of $S=1\text{TS4-1}_\text{Fe}$. an unfavourable electronic configuration for Fe$^{11}$, thus contributing to an even higher energy transition state barrier).
of species $D$ (Scheme 4) leading to species $E$ is associated with a relatively low transition state barrier ($TS_4$), in fact lower than the first addition ($TS_2 > TS_4 \approx 5$ kcal mol$^{-1}$). However, the $TS_4$ barrier is considerably higher than $TS_3$. As we can see from Figure 6, the energy barrier $TS_4$ is remarkably different for the Fe complexes. $TS_{4-2Fe}$ has the highest barrier in the series 1–3 (+19.3 kcal mol$^{-1}$), and compared to $TS_{4-2Fe}$ it is clear that aziridine formation is preferred over the addition of $D$ to a second olefin. However, porpholactone 3 has a marked influence over $TS_{4-3Fe}$ and clearly diminishes the energy barrier, leading to the smallest difference in energy of $TS_{3-3Fe}$ and $TS_{4-3Fe}$ in this series.

Another factor that needs to be included in the discussion is a comparison between the standard gas phase conditions in our model and the actual experimental conditions in solution. The theoretical model represents standard gas phase (1 bar; 22.4 L mol$^{-1}$ each species) free energies ($\Delta G^\circ$). Experimentally, however, there is a 600 fold excess alkene:catalyst, which is far from standard conditions. With such a concentration ratio we need to consider the chemical potential ($Q$), which cannot be neglected in a comparison of the pathways for 3-membered and 5-membered ring formation. Corrections for the thermodynamic activity will strongly affect the $TS_4$ barrier (equation 1) because this pathway is associated with a change in the number of species.

\[ D + styrene \rightarrow [TS_4]^+ \rightarrow E \quad (1) \]

\[ \Delta G^\circ' = \Delta G^\circ + RT \ln Q \quad (2) \]

\[ Q = \frac{[E]}{[D][styrene]} \quad (3) \]
Towards controlled nitrene-transfer reactivity using Co and Fe porphyrin catalysts.

The 3-membered ring closure pathway from D via TS3, on the other hand, is an intramolecular process, and hence is not affected in the same manner as TS4 by the chemical potential. As an estimation (the active catalysts concentration is unknown, and the substrate:catalyst ratio changes during the course of the reaction), the corrected intermolecular free energies under the applied catalytic conditions corresponds roughly to equation 4:

\[ \Delta G^\circ' = \Delta G^\circ + RT \ln \frac{1}{n} \]  

(4)

The thus corrected free energies (\(\Delta G^\circ' = \Delta G^\circ - 3.8 \text{ kcal mol}^{-1}\)) are compared in Figure 8. Note that the \(S_{\text{Fe}} = \text{TS4-3Fe}\) barrier for formation of the 5-membered ring under these conditions is low enough and close to compete with the transition state TS3 for formation of the aziridines (3-membered ring formation).

For cobalt the scenario looks slightly different, and larger differences between TS3\(_{\text{Co}}\) and TS4\(_{\text{Co}}\) are observed. As in case for TS4\(_{\text{Fe}}\)-3Fe, the addition of the second olefin has the lowest barrier for catalyst 3Co. However, TS4-3Co is still \(~10\) kcal mol\(^{-1}\) higher than TS3-3Co after correction for the chemical potential. This is in line with results found experimentally.

**Comparison of styrene and para-methoxy styrene as a substrate.** The above results clearly show that upon switching from the porphyrin complexes 1 and 2 to the porpholactone complexes 3 (both Fe and Co), the probability of 5-membered THP ring formation increases. For the porphyrin complexes 1 and 2, formation of a 3-membered aziridine ring via TS3 is clearly favoured, while THP formation via TS4 becomes competitive with TS3 for the porpholactones 3. A further effect of the substrate must play a role, since THP formation has experimentally only been detected for \(\text{para}\)-methoxy-styrene, not for styrene. The electronic effects that govern the selectivity are likely dependent both on the reactivity of the radical species D and the electronic properties of the olefin. Hence, we investigated also the latter, and we sought to find the influence of a \(\text{para}\)-methoxy group in the styrene substrate on TS4. Figure 9 shows the free energies corresponding to the addition of the second olefin, TS4\(_{\text{pMeO}}\).
Notably, for all catalysts TS$_{4pMeO}$ (for para-methoxy-styrene) is lower than its counterpart TS$_{4}$ (for styrene). Hence, switching from styrene to para-methoxy-styrene further increases the selectivity for the formation of the probability to form the 5-membered THP ring product (Figure 9). After correction for the chemical potential, the barrier TS$_{4pMeO}$-$3Fe$ is very low ($\Delta G^\ddagger = +2.6$ kcal mol$^{-1}$). Also in the case of cobalt, the free energy barriers TS$_{4}$ are lowered significantly, which corresponds well with THP formation from para-methoxy-styrene using porpholactone catalysts 3 detected experimentally.$^{25}$

### 5.3 Summary & Conclusions

Catalytic activation of organic azides and subsequent nitrene-transfer to styrenes using Co$^{II}$- and Fe$^{II}$- porphyrins proceed via related radicaloid pathways. Both for Co and for Fe, the

![Diagram](image)

**Figure 9.** Effect of the alkene in reactivity towards five member ring THP. Addition of the second p-methoxy styrene to species D$_{pMeO}$. a) Free energies with no corrections included; b) corrected free energies according to eq. 4; c) Enthalpic energies; d) corrected free energies for TS$_4$-$3$ (styrene) and TS$_{4pMeO}$-$3$ (p-methoxy styrene) for Fe and Co.
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reaction involves formation of a discrete nitrene/imido moiety, which undergoes ‘radical addition’ to the styrene substrates. The Co systems prefer reactivity on the doublet surface in which intramolecular electron transfer from $d^7$ cobalt(II) to the nitrene nitrogen atom during activation of the azide surface generates a (por)Co$^{III}$-N•R ‘nitrene radical’ intermediate C$_{Co}$. The Fe system reacts in a similar way, but with interesting subtle differences. The Fe$^{III}$ precursors must first get reduced to the active Fe$^{II}$ species to activate the organic azide, leading to the nitrene/imido intermediate C$_{Fe}$, which has near covalent Fe=NR $\pi$-bonds with an unpaired electron in each of the two antibonding $\pi^*$ SOMOs. Nonetheless, this species has a substantial amount of spin density at the nitrene/imido nitrogen atom ($\sim$0.35 e$^–$ per SOMO orbital). Species C$_{Fe}$ is, therefore, best described by the resonance structures (por)Fe$^{IV}${NR$_2$–} $\leftrightarrow$ (por)Fe$^{III}${N•R–} $\leftrightarrow$ (por)Fe$^{II}${NR$^0$}. Subsequent reaction of C$_{Fe}$ with styrenes is best described as a reaction of C$_{Fe}$ in its (por)Fe$^{III}${N•R–} resonance form to produce (por)Fe$^{III}${NR-CH$_2$-CH•Ar} species D$_{Fe}$, which contains a $\gamma$-radical amido ligand, similar to the pathway for cobalt. The Fe systems prefer reactivity on the triplet surface. Formation of the nitrene species C from the organic azides is highly exergonic in all cases Co$^{II}$ ($\Delta G^\circ \sim$ $-15$ kcal mol$^{-1}$) and Fe$^{II}$ ($\Delta G^\circ \sim$ $-23$ kcal mol$^{-1}$). Addition of styrenes to species C$_{Co}$ (TS$_{2Co}$) is associated with a comparable energy barrier as the barrier for nitrene formation (TS$_{1Co}$). Interestingly, for Fe the energy barrier for nitrene formation (TS$_{1Fe}$) is calculated to considerably lower than the olefin addition step (TS$_{2Fe}$), hence suggesting that the latter should be rate determining.

The $\gamma$-radical (por)M$^{III}${NR-CH$_2$-CH•Ar} species D have a strong tendency to ring-close, thus forming the 3-membered aziridine ring compounds. For the porpholactone iron and cobalt systems, however, addition of a second styrene moiety becomes energetically competing according to DFT, allowing the formation of 5-membered tetrahydropyrrole (THP) ring compounds. Experimentally, this reaction is only observed for more electron-rich styrene substrates, such as para-methoxystyrene. Also computationally, 5-membered THP ring formation from this substrate is more favourable.

Electron-withdrawing groups at the porphyrin meta-positions influence the computed energies barriers. In general, the nitrene formation has a high barrier TS$_1$ is higher ($\sim$2 kcal mol$^{-1}$) for porphyrins with polyfluorinated groups at the meta-position. However, does not modify the overall mechanistic pathway. The same occurs with porpholactone ligand in compounds 3. Overall, the electron-withdrawing groups increase the barriers slightly. For Fe
this effect is (largely) compensated by the fact that these same electron-withdrawing groups facilitate reduction of Fe\textsuperscript{III} to Fe\textsuperscript{II}, thus giving rise to a higher amount of active species.

5.4 Experimental details

All manipulations were performed under a nitrogen atmosphere using standard Schlenk techniques. All solvents were dried, either distilled or from an M-Braun SPS (Solvent Purification System) and deoxygenated with freeze-thaw techniques, and stored over 4Å molecular sieves. All other chemicals were used as received without further purification, unless described otherwise. Styrene and \textit{p}-methoxystyrene were distilled under vacuum before use. NMR spectroscopy experiments were carried out on a Bruker AV-400 spectrometer (400 and 100 MHz for \textsuperscript{1}H and \textsuperscript{13}C, respectively) or a Bruker DRX-500 spectrometer (500 and 125 MHz for \textsuperscript{1}H and \textsuperscript{13}C, respectively). High resolution mass spectra (HR-MS) were recorded on a JEOL JMS SX/SX102A four sector mass spectrometer; for FAB-MS, 3-nitrobenzyl alcohol was used as a matrix. The UV-Vis spectra were obtained by scanning between 180-900 nm in a 2 mm glass cuvette on a Hewlett-Packard 8453 UV-Visible Spectrophotometer and a Varian Cary 3 UV-Visible spectrometer.

\textit{5,10,15,20-tetrakis-(pentafluorophenyl)-porphyrin (H\textsubscript{2}TFPP)} was synthesised according the procedure of Volz and Schneckenburger.\textsuperscript{26} \textit{5,10,15,20-tetrakis-(pentafluorophenyl)-porpholactone} as synthesised via osmylation of H\textsubscript{2}TFPP to form the 5,10,15,20-tetrakis-(pentafluorophenyl)-2,3-dihydroxychlorin osmate ester bipyridine according the procedure of Bruckner.\textsuperscript{27} \textit{5,10,15,20-tetrakis-phenyl-porphyrin (H\textsubscript{2}TPP)} was purchase from Aldrich and Fe(TPP)Cl was purchased from strem chemicals and was used with any further purification.

\textbf{Fe\textsuperscript{III}TFPPCl.} 0.049 g (0.05 mmol) H\textsubscript{2}TFPP and 0.0814 g (0.5 mmol) of FeCl\textsubscript{3} were added to a Schlenk flask and dissolved in 10 ml of 4:1 DCM:THF. 0.4 ml of N\textsubscript{2}N-diisopropylethylamine (freshly distilled) was added, and the reaction mixture was heated under reflux for 19 hours. The reaction was monitored by TLC (CH\textsubscript{2}Cl\textsubscript{2}:hexane = 10:1) until the starting material had disappeared. The solvent was evaporated under reduced pressure and the metallated porphyrin was washed with 10 ml of water and dried overnight at 80 °C under vacuum. UV-Vis: 351, 412, 506, 569, 643 nm. HRMS (FAB\textsuperscript{+}) (C\textsubscript{44}H\textsubscript{8}F\textsubscript{20}N\textsubscript{4}Fe): \textit{m/z} calc. 1028.9858, found 1028.9847.

\textbf{Fe\textsuperscript{III}TFPLCl.} 0.03 g (0.03 mmol) H\textsubscript{2}TFPL and 0.045 g (0.28 mmol) FeCl\textsubscript{3} were added to a Schlenk flask and dissolved in 5 ml of DMF. The reaction mixture was refluxed for 10 hours and monitored by TLC (CH\textsubscript{2}Cl\textsubscript{2}:MeOH = 100:1) until the starting material had disappeared.
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The solvent was evaporated under reduced pressure and the metallated porpholactone was washed with 10 ml of water and dried overnight at 80 °C under vacuum. UV-Vis: 387, 413, 512, 576, 628 nm. HRMS (FAB+) (C43H6F20N4O2Fe): m/z calc. 1046.9600; found 1046.9573.

CoTPP. 0.50 g (0.8 mmol) H2TPP and 1.64 g (6.60 mmol) Co(OAc)2.4H2O were added to a Schlenk flask and dissolved in 10 ml of DMF. The reaction mixture was heated under reflux for 5 hours, followed by addition of 20 ml of water. The reaction mixture was cooled to room temperature with an ice bath, filtered and washed with 50 ml of water. The product was dried in a vacuum oven overnight. UV-Vis: 414, 527, 584, 645 nm. HRMS (FAB+) (C44H28N4Co): m/z calc. 672.1724, found 672.1732.

CoTFPP. 0.05 g (0.05 mmol) H2TFPP and 0.11 g (0.43 mmol) Co(OAc)2.4H2O were added to a Schlenk flask and dissolved in 2 ml of DMF. The reaction mixture was heated under reflux for 4 hours, followed by addition of 15 ml of water. Dichloromethane was added, and the layers were separated. The reaction mixture was subsequently washed with water, dried with MgSO4 and filtered. The solvent from the filtrate was evaporated under reduced pressure to obtain the product. UV-Vis: 408, 526, 549 nm. HRMS (FAB+) (C44H8F20N4Co): m/z calcd 1031.9840, found 1031.9835.

CoTFPL. 0.05 g (0.05 mmol) H2TFPL and 0.10 g (0.39 mmol) Co(OAc)2.4H2O were added to a Schlenk flask and dissolved in 2 ml of DMF. The reaction mixture was heated under reflux for 5 hours, followed by addition of 4 ml of water. The mixture was cooled to room temperature with an ice bath, filtered and washed with 10 ml of water. DCM was added to the mixture and the layers were separated. The reaction mixture was subsequently washed with water, dried with NaSO4 and filtered. The solvent from the filtrate was evaporated under reduced pressure to obtain the product. HRMS (FAB) (C43H6F20N4OCo): m/z calc. 1049.9582, found 1049.9592.

General procedure for styrene aziridination / THP formation. 1,2-dichloroethane (2 mL) was added to a mixture of alkene (0.60 mmol), azide (0.20 mmol), catalyst (0.001 mmol) and 4 Å pre-activated molecular sieves (120 mg). The reaction mixture was heated at 80 °C under nitrogen atmosphere for 16 hours, after which the reaction mixture was concentrated under reduced pressure. The crude reaction mixture was analysed with 1H NMR.

Computational methods.

Geometry optimisations were carried out with the Turbomole program package28 coupled to the PQS Baker optimizer29 via the BOpt package,30 at the spin unrestricted ri-DFT level using
the BP86\textsuperscript{31} functional and the resolution-of-identity (ri) method.\textsuperscript{32} We used the SV(P) basis set\textsuperscript{33} for the geometry optimisations of all stationary points. Stationary points on the potential energy surface were characterised as either minima or transition states by the presence of zero or exactly one significant imaginary frequency, respectively, in the BP86/SV(P) vibrational spectrum, obtained by numerically calculating the Hessian matrix. ZPE and gas-phase thermal corrections (entropy and enthalpy, 298 K, 1 bar) from these analyses were calculated. Improved energies were obtained with single point calculations at the spin unrestricted DFT/BP86 level using the Turbomole def-TZVP basis set.\textsuperscript{34} All free energy values refer to 298.15 K and 0.1 MPa (1 bar) pressure. As the reaction does not take place in an ideally diluted gas phase, the standard statistical thermodynamic free energy values were corrected for all species, except dinitrogen in a Trouton-like approach by adding 6.25 kcal mol\textsuperscript{−1} assuming $\Delta S_{\text{vap}}$ of all liquids to be +21 kcal mol\textsuperscript{−1}.\textsuperscript{35} For the cobalt complexes, the energies of each species in their doublet ($S = \frac{1}{2}$) and quartet ($S = 3/2$) states were compared. For all species, the doublet state represents the ground state, with the quartet states being $>$10 kcal mol\textsuperscript{−1} higher in energy (except $D$, for which $4D$ is only +2 kcal mol\textsuperscript{−1} higher in energy than $2D$). The discussion in the main text focuses on the lowest energy doublet energy surface, unless stated otherwise. For the iron complexes, the energies of each species were calculated in their low spin ($S = 0$), intermediate spin ($S = 1$) and high spin ($S = 2$) states for the Fe\textsuperscript{II} species, and in their low spin ($S = 1/2$), intermediate spin ($S = 3/2$) and high spin ($S = 5/2$) states for the Fe\textsuperscript{III} species. In both cases the high spin state showed to be remarkably higher than the lower multiplicities. Thus, only the low spin and intermediate spin states are discussed in the text. The corrected broken symmetry energies $\varepsilon_{\text{BS}}$ of the doublets ($S = 1/2$) or the open-shell singlets ($S = 0$) was estimated from the energy from the energy $\varepsilon_S$ of the optimised single-determinant broken symmetry solution and the energy $\varepsilon_{S+1}$ from a separate unrestricted quartet or triplet calculation at the same level, using the approximate correction formula:\textsuperscript{36}

$$\varepsilon_S \approx \frac{S_{S+1}^2 \varepsilon_{S} - S_S^2 \varepsilon_{S+1}}{S_{S+1}^2 - S_S^2}$$
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Figure 10. Complete free energy profiles for $^{1}\text{Fe}$, $^{2}\text{Fe}$, and $^{3}\text{Fe}$ in their low ($S=0$) and intermediate ($S=1$) spin state for Fe$^{III}$ (left) and Fe$^{II}$ (right).

5.6 Acknowledgments.

We thank Esther Vleugel and dr. V. Lyaskovskyy for their contribution to this chapter.

5.7 References


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14 Porpholactones are porphyrin analogues that have one of their pyrrole groups replaced by an oxazolone ring. The saturation of one of the rings reduces the normal conjugation of 22 aromatic electrons in porphyrins. The resulting (anti-aromatic) 20e conjugation resembles that of the chlorins, however in porpholactones the lone pair of the carbonyl group can participate in the aromaticity and thus porpholactones are regarded as systems in between porphyrins and chlorins. M. Gouterman, R.J. Hall, G.E. Khalil, P.C. Martin, E.G. Shankland, R.L. Cerny, *J. Am. Chem. Soc.* **1989**, *110*, 3702–3707.

15 Experiments of C–H amination were carried with neat olefin and PhCl in presence of catalyst [Co(TF$_2$0PP)] and no conversion was observed: See ref. 7d.

16 The experimental reason of starting with a Fe$^{III}$(por) pre-catalyst, instead of Fe$^{II}$(por), is because Fe$^{II}$(por) catalysts suffer very high reactivity towards oxidation. While Fe$^{III}$(por) can be normally handle in air, most of the Fe$^{II}$(por) complexes show immediate oxidation to [Fe(por)]$_2$O dimers.

17 The positive effect that electron-withdrawing groups have on the reduction probability of the Fe-porphyrin systems easily compensates for the negative effect, observed for Co- and Fe-porphyrins, of having somewhat higher TS$_1$ barriers (~2 kcal mol$^{-1}$; *vide infra*) with halogenated catalysts.


19 We also calculated the (high spin) S = 5/2 and S = 2 spin states of the corresponding Fe$^{II}$ and Fe$^{III}$ complexes. However, the metallo-porphyrin alone is the only one that lies very close in energy to the corresponding intermediate spin state ($^{HS}A$ vs $^{IS}A$). Thus, we focused on the comparison of the IS and LS. The energy values for the high spin states are reported in chapter 4. M. Zerner, M. Gouterman, H. Kobayashi, *Theoret. Chim. Acta*, **1966**, 363–400.


23 In fact, a similar control experiment was mentioned in reference 11b. However, we found insufficient information and therefore we decided to perform the control reaction also
with our catalysts. There is an alternative experiment that involves addition of the \( m \)-MeO-styrene and 2-(\( p \)-MeOC\(_6\)H\(_4\))-N-tosyl aziridines in order to observe a possible mixing (scrambling) of the substitution pattern on the phenyl ring of the THP. However, due to the low yields we were not able to distinguish such products.

24 Different alternative pathways were explored, but only a stepwise radical mechanism in which methoxy-styrene adds to D leading to intermediate E followed by ring closure made any sense. Attempts to find a reasonable pathways proceeding via (1) ring opening at adduct F followed by addition of the olefin, or (2) concerted insertion of the olefin into the N–C bond of adduct F all failed to give any satisfactory results. Using different constraints in these systems always led to dissociation of the substrates from the metal centre instead of the desired olefin insertion.

25 Comparison of the \( \text{TS3}_{\text{pMeO}} \) and \( \text{TS4}_{\text{pMeO}} \) should give a more accurate comparison. However, our geometry optimisations of the \( \text{TS3}_{\text{pMeO}} \) transition states suffered from severe convergence problems.


