

10 Summary

This thesis consists of theoretical studies on various aspects of the oxidative addition reaction, as well as the mechanism of halogen bonding interactions. As stated in the introduction, the purpose of these studies was to not only be descriptive, but to provide insights and reveal causal relationships. Therefore, the following summary will discuss only the most important findings from the preceding chapters, in order to focus on their explanatory character.

All results are obtained using density functional theory (DFT) computations performed with the ADF software package. A red thread throughout this thesis is the interpretation of the numerical results using a combined approach of the activation strain model and molecular orbital (MO) theory. Within the activation strain model (discussed in section 2.5), the energy change that accompanies a chemical process is analyzed in terms of the original reactants. The relative energy is split into two terms: (i) the strain energy that accounts for the geometrical changes that occur during the chemical process, and (ii) the interaction energy between the deformed fragments. Both the strain energy and the interaction energy can be further analyzed using MO theory.

In chapter 3 this approach is used to understand why some d^{10} - ML_2 transition metal complexes have nonlinear equilibrium geometries, that is, bent $L-M-L$ angles, instead of the generally expected linear $L-M-L$ angles. We have investigated the ML_2 complexes where M is varied along Co^- , Rh^- , Ir^- , Ni , Pd , Pt , Cu^+ , Ag^+ and Au^+ , and the ligands L are varied along NH_3 , PH_3 and CO . Based on detailed analyses of the bonding between an ML fragment and a second ligand L , we have traced back the origin of this nonlinearity to π backdonation: when the second ligand L binds to ML perpendicular to the first ligand, its π^* acceptor orbitals interact with d orbitals on the metal that are not yet stabilized by interactions with the first ligand. These d orbitals are therefore higher in energy, resulting in more strongly stabilizing $d-\pi^*$ donor-acceptor interactions than in the linear $L-M-L$

geometry. When this additional stabilization is stronger than the induced steric repulsion upon bending, the ML_2 complex obtains a nonlinear L–M–L angle.

In practice, however, catalyst complexes often feature bulkier ligands. Therefore, we have addressed in chapter 4 the effect of steric bulk on the geometry and activity of a series of $Pd(PR_3)_2$ catalyst complexes, where the substituents R are varied along H, Me, *i*Pr (isopropyl), *t*Bu (*tert*-butyl), Cy (cyclohexyl) and Ph (phenyl). From $Pd(PH_3)_2$ to $Pd(P*t*Bu_3)_2$, we find that all complexes have linear L–M–L angles, except $Pd(P*i*Pr_3)_2$ for which it is bent slightly. More interestingly, we find significantly nonlinear L–M–L angles in both $Pd(PCy_3)_2$ and $Pd(PPh_3)_2$. These small angles can not be explained satisfactorily with the electronic mechanism described in chapter 3, although this mechanism does contribute to the flexibility of these complexes. Our analyses show that ligands that are large but to some extent flat (instead of isotropically bulky) build up relatively strong dispersion interactions between their large surfaces (“sticky pancakes”) when they bend toward each other. The resulting stabilization, a form of steric attraction, favors bending and thus enhances the flexibility of the bite angle, eventually leading to nonlinear ligand-metal-ligand angles. When methane C–H oxidative addition to these catalyst complexes is investigated, the more flexible, or even nonlinear geometry of these complexes appears to translate into lower reaction barriers.

Chapter 5 discusses yet another series of palladium bisphosphine catalysts, but now the substituents are varied from hydrogen in PH_3 , to halogens in the series of PX_3 ligands, where X = F, Cl, Br or I. This series allows to study simultaneously the electronic effects, as described in chapter 3, and the steric effects as described in chapter 4, since both the size and the electronegativity of the substituents is changing significantly. Although $Pd(PH_3)_2$ is linear, all halogenated $Pd(PX_3)_2$ catalyst complexes have nonlinear ligand-metal-ligand angles. Counterintuitively, we also find that, as the size of the halogens increases, the complexes become more bent. This trend originates partly from the attractive dispersion interactions between the ligands, revealing again a contribution from steric attraction. But, besides this steric effect, also the electronic factors have to be taken into account. All halogenated PX_3 ligands are better π acceptors than PH_3 , which results in improved π back-bonding and nonlinear ligand-metal-ligand angles in the $Pd(PX_3)_2$ complexes. However, our analyses reveal another electronic factor, namely the repulsive overlap between the highest occupied MOs (HOMOs) on the PX_3 and $PdPX_3$ fragments. When the substituents X are varied from F to I, the repulsive HOMO-HOMO overlap decreases, resulting

in less destabilizing Pauli repulsion upon bending the $\text{Pd}(\text{PX}_3)_2$ complexes, and therefore more strongly bent equilibrium geometries.

Applying the $\text{Pd}(\text{PX}_3)_2$ complexes for the oxidative addition of the methane C–H bond, we find very similar reaction barriers as for the archetypal $\text{Pd}(\text{PH}_3)_2$. Activation strain analyses reveal a similar bite-angle effect as described in chapter 4, but also show that this is counteracted by a simultaneous weakening of the catalyst-substrate interaction as one goes from $\text{Pd}(\text{PH}_3)_2$ to $\text{Pd}(\text{PX}_3)_2$, and along the $\text{Pd}(\text{PX}_3)_2$ series as X is varied from F to I. The weaker interaction is a direct result of (i) a decreased electron-donating capability of the catalyst, and (ii) an increase in repulsive catalyst-substrate interactions.

For chapters 6 and 7, we return to the same series of $d^{10}\text{-ML}_n$ catalyst complexes that were the subject of chapter 3. In chapter 6, the reactivity of these complexes towards methane oxidative addition is investigated. It is shown that, when going from the anionic group 9 metal complexes to the cationic group 11 metal complexes, reaction barriers go up significantly, due to the decreased electron-donating capability of the catalysts, and therefore weaker catalyst-substrate donor-acceptor interaction. When going from first row to third row transition metal centers, the highest reaction barrier is typically found for the catalyst with a metal center from the second transition metal row. For catalyst complexes with a metal center from the first row the reaction barrier is generally lower, because the d-derived orbital energies of these complexes are higher, leading to stronger donation from catalyst to substrate. When, instead, a catalyst complex with a metal center from the third row is compared to a second transition metal row complex, it is the larger orbital overlap of the former with the substrate σ^* orbital that results in stronger interactions, and consequently a lower reaction barrier. Also relativistic effects become important for third row transition metals. These tend to stabilize the electron-accepting metal s orbital, thereby further enhancing catalyst-substrate interaction.

Ligand effects can be explained by considering their influence on the electron-donating and electron-accepting capabilities of the metal center. Adding a good π -accepting ligand reduces the electron-donating capability of the metal center, whereas a strong σ -donating ligand will enhance the electron-donating capability. To correctly predict how this will affect reaction barriers, we have introduced in chapter 6 the concept of electronic regimes. In what we designate the ‘d regime’, ligand effects are dictated by their influence on the metal d orbitals. In this regime, reaction barriers become higher when π -accepting ligands are attached to the metal, as these reduce the electron-donating capability of the catalyst. In the ‘s regime’ the reactivity of the catalyst depends to a large extent

on the electron-accepting capability of the s orbital. Adding a strong π -accepting ligand to an s -regime catalyst enhances its electron-accepting capability, and lowers the reaction barrier. It follows that ligands can have completely opposite effects on the reaction barrier, when added to metal centers from different electronic regimes.

Furthermore, in chapter 6 we elaborated on the concept of bite-angle flexibility. We have shown that, for the complexes for which we encountered nonlinear ligand-metal-ligand angles in chapter 3, the reaction barrier for oxidative addition of methane is lowered, due to the smaller amount of catalyst deformation that is required to bend away its ligands. More interestingly, however, we find a similar effect along series of catalysts that all have linear ligand-metal-ligand angles in their equilibrium geometry, but become more flexible towards bending.

In chapter 7, the reaction barriers have been analyzed for oxidative addition of ethane, via activation of either the C–H or the C–C bond. For both bonds, the trends in reaction barriers are very similar to those described for activation of the methane C–H bond in chapter 6. However, there are subtle differences between these bonds, which influence the interaction of the substrates with the catalysts. A detailed understanding of these differences, and the nature of the catalyst–substrate interactions, allowed us to devise catalyst complexes that selectively activate either bond. Thus, starting with the ethane C–H and C–C bonds, activation of the latter usually occurs with a higher reaction barrier, despite the fact that it is weaker. This is due to a delay in the build-up of stabilizing interactions, caused by the additional nodal plane present in the $\sigma_{\text{C-C}}^*$ orbital, compared to the $\sigma_{\text{C-H}}^*$ orbital, which diminishes favorable overlap with the donating metal d orbitals. To shift the selectivity towards activation of the weaker C–C bond, this effect has to be mitigated, which can be achieved by applying a catalyst complex from the s regime, for which donation into the σ^* orbitals plays only a moderate role.

To distinguish between the methane and ethane C–H bonds, a similar approach is taken. The ethane C–H bonds are slightly weaker than the methane C–H bonds, but, upon stretching, the methane $\sigma_{\text{C-H}}^*$ LUMO drops faster in energy than the ethane $\sigma_{\text{C-H}}^*$ LUMO. Thus, we found that strongly donating d -regime catalysts prefer activation of the methane C–H bond, because the lower $\sigma_{\text{C-H}}^*$ orbital energy leads to a strengthening of the catalyst–substrate interaction that is significant enough to overcome the higher bond dissociation energy. For s -regime catalysts, the difference between the interaction energy curves for activation of the methane and ethane C–H bonds is smaller, and these catalysts therefore prefer ethane C–H activation, as dictated by the lower strain energy.

The final two chapters of this thesis deal with the bonding mechanism of halogen bonds. Chapter 8 contains detailed analyses of the hydrogen bonds in $\text{DH}\cdots\text{A}^-$ and halogen bonds in $\text{DX}\cdots\text{A}^-$ where D, X and A are varied along the halogens F, Cl, Br and I. Consistent comparisons of variations along series of both types of complexes revealed that hydrogen bonds and halogen bonds arise due to a very similar bonding mechanism, which is easily explained in the framework of MO theory. Both halogen bonds and hydrogen bonds have, besides an electrostatic component, a sizable covalent component that originates from charge transfer from the halide lone pair to the DX or DH σ^* orbital. The electrostatic component is usually stronger for hydrogen bonds, due to the more favorable polarization along the DH hydrogen halide, compared to the dihalogen DX. Nevertheless, halogen bonds can be stronger than hydrogen bonds, because of a stronger contribution from the covalent component to the bonding energy. The reason for this is that the empty σ^* orbital on DX is lower in energy than the σ^* orbital on the hydrogen halides DH.

By consistent variation of either D, X or A, and considering how this affects the electronic structure of the fragment, the change in bonding characteristics of $\text{DH}\cdots\text{A}^-$ and $\text{DX}\cdots\text{A}^-$ can be readily explained. For example, replacing A^- with a heavier halide, reduces the strength of both the hydrogen bonds and halogen bonds, in part because the electron-donating capability of the halide decreases when going down the periodic table. This is true also for the fluorine-bonded complexes, although the final trend in bond strength is reversed due to a subtle interplay of factors, which are related to the significant stretch of the relatively weak D–F bonds and the low energy of the $\sigma_{\text{D-F}}^*$ acceptor orbitals.

Variation of the hydrogen- or halogen-donating atom D has opposite effects on the bond strength of the hydrogen bonds and halogen bonds. However, activation strain analyses along the bond formation process reveal that the strain and interaction energies follow the same trends as D becomes heavier. The interaction energy weakens, because the increased electropositivity of D results in a less favorable polarization of the electron density across DH or DX, thereby reducing the electrostatic attraction with A^- , and, mainly for the halogen bonds, also strengthening the Pauli repulsion. Simultaneously, the strain energy curves soften, because the D–H and D–X bonds get weaker when D becomes heavier. For the DX fragments, these differences are moderate, and the total bond strength therefore follows the same trend as the interaction energy. The differences in D–H bond strength are, however, much larger. From FH to IH, the D–H stretch upon hydrogen bond formation increases significantly, which allows for a greater build-up of interaction energy, and induc-

es a reversal of the net bond strength: hydrogen bonds $DH\cdots A^-$ become stronger when the donating atom D is varied from F to I.

In the ninth chapter, halogen bonds are again compared to hydrogen bonds, but for significantly larger complexes. Starting from the hydrogen-bonded Watson-Crick DNA base pairs, the hydrogen bonding N-H moieties are replaced with N-X, where X is one of the halogens F, Cl, Br or I, to obtain the halogen-bonded analogues. We have demonstrated that, again, the hydrogen bonds and halogen bonds in these complexes arise due to a very similar mechanism, which involves charge transfer from the N or O lone pair to the σ^* orbitals on N-H or N-X. The similarities not only showed that the bonding mechanism as described in chapter 8 is equally valid for larger complexes, but also suggested that the cooperative effect, as observed in hydrogen-bonded guanine quartets, might also occur in halogen-bonded *N*-halo-guanine quartets. Our computations show that this is indeed the case, that is, the total bond energy of the *N*-halo-guanine quartets is more stabilizing than four times the bond energy of one *N*-halo-guanine base pair. Interestingly, for the bromine-bonded and iodine-bonded guanine quartets, this cooperative effect is even stronger than for the hydrogen-bonded guanine quartets, due to the larger amount of charge transfer that occurs upon formation of these halogen bonds. These conclusions are supported by multiple independent lines of reasoning, based upon a variety of analysis methods.

One can only hope that in the future the insights obtained from the studies in this thesis will contribute to the achievement of new milestones, based on an improved understanding of the chemistry involved. It is most likely that the concepts presented in this thesis will have to be extended, and, when necessary, even be replaced with superior concepts. This process is one of the fundamental pillars of science, and one of the prime reasons why it is such a powerful tool: the scientific method is the only possible way to improve our understanding of natural phenomena. And it has proven to be a very successful one, although only if applied critically.

