

Summary

This thesis describes the development and application of new diphosphine ligands, based on xanthene-like backbones. These diphosphines lead to unusually large bite angles in transition metal complexes compared to the common diphosphines containing C₁-C₄ bridges. Furthermore, by subtle alterations in the backbone of the ligands, it is possible to fine-tune the chelational characteristics of the ligands. These chelational characteristics can be described by the *natural bite angle* and the *flexibility range* of the ligands, parameters that were introduced by Casey and Whiteker (Casey, C. P.; Whiteker, G. T. *Isr. J. Chem.* **1990**, *30*, 299-304).

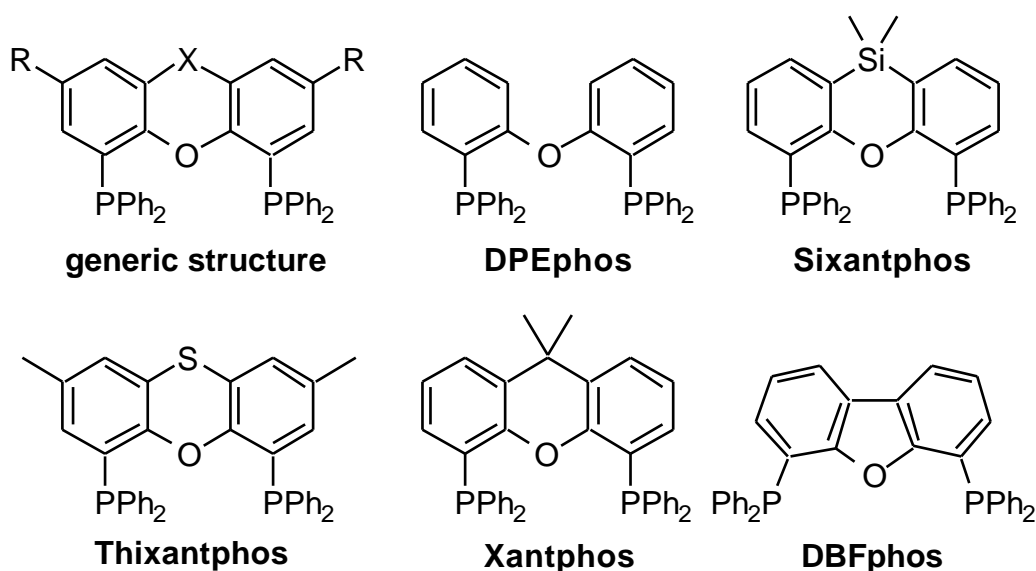
The *natural bite angle* (α_n) is defined as the preferred chelation angle, determined only by ligand backbone constraints and not by metal valence angles. This (hypothetical) natural bite angle is determined by molecular mechanics calculations. The *flexibility range* is defined as the accessible range of bite angles within less than 3 kcal/mol excess strain energy from the calculated natural bite angle.

By substitution of the methylene-bridge in the central ring of the xanthene-backbone with another bridge it is possible to adjust the natural bite angle, whereas changes in steric bulk and electronic properties are virtually absent.

Xantphos, containing a dimethylmethylene bridge has a α_n of 109.8° (in a rhodium-chelate), substitution of this bridge by a sulphur atom (Thixantphos) results in a α_n of 106.7°, substitution by a dimethylsilyl (Sixantphos) results in a α_n of 106.2°, substitution by two H atoms (DPEphos) results in a α_n of 101.6° and substitution by a bond (DBFphos) results in a α_n of 133.9°. The flexibility range calculated for these ligands is approximately 35°.

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In Chapter 1 the synthesis of these ligands is described. An X-ray crystal structure of Xantphos is presented, which clearly shows that the mutual orientation of and the distance between the diphenylphosphine moieties is ideal for chelation to a metal center. By means of semi-empirical quantum-mechanical calculations it is shown that the influence of the various changes in the backbones on the electronic properties of the phosphorus donor atoms is little or none. Furthermore it is shown that the molecular mechanics calculations, which are used throughout this thesis to describe the chelational characteristics of the ligands, offer a better description of the geometry and molecular structure of the ligands than semi-empirical quantum-mechanical calculations.



In Chapter 2 the coordinational behavior of these ligands is investigated by coordination to a palladium-TCNE fragment (TCNE= tetracyano-ethylene). X-ray crystal structures of the complexes of DPEphos, Sixantphos and Xantphos are presented, which show that the geometry of the ligands changes only very little upon complexation. This is most clear when the crystal structures of Xantphos and [Xantphos]Pd[TCNE] are compared, but it is also apparent when the calculated structures of DPEphos and Sixantphos are compared to their respective palladium-TCNE

complexes. For Thixantphos a palladium-TCNE complex was obtained as well (unfortunately not in crystalline form), but attempts with DBFphos to yield the complex failed. Molecular Mechanics calculations indicate that in order to bind to the metal, the geometry of DBFphos must deform very strongly, making the complexation to be energetically unfavourable.

The natural bite angles of the ligands used here make them ideal for stabilization of trigonal geometries. The crystal structures of the different palladium complexes containing the strong acceptor TCNE show that in this type of complexes a small valence angle is preferred. The maximal observed P-Pd-P angle is 104.6°. Increasing the P...P distance in the ligand results in an elongation of the Pd-P bond rather than enlargement of the P-Pd-P angle.

In Chapter 3 the application of the Xantphos-type ligands in the rhodium-catalyzed hydroformylation is described. From the literature it was known that ligands that are able to support a bisequatorial coordination in a (diphosphine)Rh(H)(CO)₂ complex (P-Rh-P= ca. 120°) induce high selectivity to the (industrially more desirable) linear aldehyde in the hydroformylation of 1-alkenes. An important characteristic of the (Xantphos)Rh(H)(CO)₂ catalysts is the absence of hydrogenation and isomerization of the starting alkene. Application of the Xantphos ligand in the hydroformylation of 1-octene resulted in the highest selectivity to 1-nonanal (98.3%) reported for rhodium-phosphine catalysts so far. Comparison of the results obtained for the different ligands reveals a regular increase of selectivity with an increasing bite natural angle. Application of DBFphos results in a decreased selectivity. This ligand is shown not to coordinate in a chelating fashion to the rhodium center; the natural bite angle is consequently no longer a meaningful parameter in this case.

The high selectivity is maintained at higher temperatures (80 °C). This is probably due to the rigidity of the backbones of the ligands that causes the ligands to coordinate in a bisequatorial manner even at higher temperatures, in contrast to most other ligands.

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Therefore high selectivities can be obtained at higher reaction rates.

Even hydroformylation of styrene results in a relatively high selectivity for the linear aldehyde (70.1%). This is remarkable, since styrene is a substrate with a distinct preference for the formation of the branched product.

The palladium-catalyzed cross-coupling and allylic alkylation are two reactions of great synthetic importance. Even though the influence of the ligands used in the catalyst is large, the nature of this influence is not yet fully understood. In Chapter 4 the selectivity and activity of (diphosphine) PdCl_2 catalysts with different diphosphine ligands for the cross-coupling reaction of 2-butyl magnesium chloride and bromobenzene are compared. The natural bite angles range from ca. 78° for dppe (1,2-bisdiphenylphosphino-ethane) to 110° for Xantphos.

A distinct effect of the natural bite angle of the diphosphine used on the activity and especially the selectivity of the catalysts is observed.

The rate of the reaction and the selectivity increase with the natural bite angle up to $\theta_n = 102.7^\circ$, in (DPEphos) PdCl_2 . Application of a catalyst modified with a diphosphine with a larger natural bite angle not only results in a decrease of the reaction rate, but in a decreased selectivity as well.

The formation of side-products is explained by an increasing stabilization of trigonal bipyramidal intermediates (with an increasing bite angle), which are held responsible for the formation of these products.

In the allylic alkylation the rate of the reaction and also the selectivity of the catalyst are determined by the steric hindrance induced by the diphosphine ligand. An increasing natural bite angle of the ligand results in an increased steric hindrance for the substrate upon coordination to the metal center.

This hampers of the reaction of the substrate with the nucleophile, but it also results in a high regioselectivity. The catalyst modified

with the ligand with the largest natural bite angle, Xantphos, is 100 % selective, but also very slow. The best selectivity with reasonably high reaction rates is obtained with DPEphos.

In Chapter 5 the application of the Xantphos-type ligands in the nickel-catalyzed hydrocyanation is described. “Classical” cis-coordinating diphosphines are not able to stabilize the tetrahedral intermediates that occur in the catalytic cycle, which results in the irreversible precipitation of nickel dicyanide complexes from the reaction mixture and conversions of 10% at most. Because of their large natural bite angles, Xantphos-type ligands are able to stabilize tetrahedral geometries. Therefore a virtually complete conversion is obtained in the nickel-catalyzed hydrocyanation of styrene, with high selectivity for the branched product. In this reaction a large effect of small variations in the natural bite angle is observed; when Sixantphos is applied, the best results are obtained.

The application of diphosphines with a large natural bite angle in the synthesis of $(\text{diphosphine})_2\text{Ru}(\text{H})(\text{H}_2)^+$ complexes reveals a large influence of the bite angle of the diphosphine on the properties of the complex. The bond between a metal center with the H_2 ligand is a subtle balance between the H-H σ -donating electrons to the Lewis acidic metal center and backdonation of metal d electrons to the H-H σ^* -orbital.

In Chapter 6 it is shown that the large natural bite angle of the Xantphos-ligands distort the ideal octahedral geometry of the complex, which results in less donation of the phosphines to the ruthenium center. This facilitates the exchange of the H and H_2 ligands (these are indistinguishable in the ^1H NMR), but it results in a low thermostability when compared to other complexes. The complexes lose H_2 easily, yielding a cationic monohydride.

Application of DPEphos results in the (initial) formation of a classical trihydride complex, while Sixantphos and Thixantphos

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yielded unprecedented non-classical *cis* (diphosphine)₂Ru(H)(H₂)⁺ complexes.