Supramolecular transition metal catalysis

Effector controlled catalysis and supramolecular substrate preorganization

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Summary

Control over the selectivity and reactivity in transition metal catalysis is a major challenge and important for applications in both fine and bulk chemical industries. Traditionally, variation of ligands that coordinate to the metal center has been widely applied and explored to optimize the properties of transition metal catalysts. Despite many breakthroughs, the selectivity and reactivity that are generally dictated by the intrinsic properties of the substrate cannot always meet the requirements for applications. Nature serves as the master of making superior catalysts for versatile transformations. Inspired by nature, we explored supramolecular tools, i.e. effector controlled catalysis and supramolecular substrate preorganization, to control the selectivities and reactivities in hydroformylation reactions, asymmetric hydrogenation reactions and C-H activation reactions. These achievements reported in this thesis demonstrate the power of supramolecular interactions in controlling challenging selectivity and reactivity in transition metal-catalyzed transformations.

Hydroformylation, also known as the oxo-process, enables the addition of a formyl group and a hydrogen atom to a C=C double bond using syngas (H₂/CO) to produce aldehydes with 100% atom economy. Hydroformylation is one of the largest industrially applied homogeneous catalytic transformations with a total production capacity of 107 ton/year. Therefore, developing catalysts for regio- and enantioselective hydroformylation has received considerable attention over the past decades. Previously, our group reported a supramolecular catalyst that controls the regioselectivity by substrate orientation, reminiscent of enzymes, which was based on ParaDIMphos (L1). Using this catalyst system, carboxylate containing alkene substrates with a suitable span were pre-organized at the metal center via the DIM-receptor for linear selective hydroformylation. However, 3-butenolic acid that cannot be preorganized by the ParaDIMphos-Rh complex showed poor selectivity, indicating the limitation of substrate scope. Inspired by re-engineering of the enzyme to adapt its cavity for new substrates, we report in Chapter 2 the rational redesign of a rhodium catalyst for selective conversion of shorter substrates via supramolecular substrate preorganization (Fig. 1). For this purpose, we developed a new ligand coined OrthoDIMphos (L2). DFT calculations show that the OrthoDIMphos (L2) based rhodium catalyst has a shorter distance between the DIM-receptor and the Rh center for 3-butenolate ditopic binding, as well as well-defined Rh-hydride coordination geometry. As expected, under optimized conditions, the new catalyst displayed the highest regioselectivity in the hydroformylation of 3-butenolic acid reported to date (l/b up to 84, TON up to 630). Furthermore, the internal alkene analogue, 3-pentenoic acid, was also converted with high selectivity.
regioselectivity (o/i 11) whereas without substrate preorganization a 1:1 mixture of these products is obtained. Detailed in situ High-Pressure (HP) spectroscopy characterization of the active species, kinetic studies, and DFT calculations on the selectivity determining step also show the hydride migration towards the linear product is more favourable than the branched product via substrate preorganization in the DIM-receptor.

The mechanistic studies of Chapter 2 reveal that the dimeric rhodium complexes formed are converted to the monomeric complexes for selective hydroformylation reaction via substrate binding to the DIM-receptor. On that basis, we report in Chapter 3 the first supramolecular rhodium catalyst that form dimeric or monomeric Rh-complexes, controlled by the binding of effectors within the integrated DIM-receptor using hydrogen bonding (Fig. 2-3). X-ray crystal structures, in situ (high-pressure (HP)) spectroscopy studies, and molecular modelling studies show that in the absence of effectors, the preferred Rh-species formed is the dimer, in which two ligands coordinate to two rhodium metals. Importantly, the dimeric structures under hydroformylation conditions are stabilized by hydrogen bonding interactions between the carbonyl-O groups of the ligand and the DIM-receptors. As effector binding competes with this hydrogen bonding, the presence of carboxylate containing effectors in solution results in the formation of monomeric complexes with the effector bound in the DIM-receptor. As a consequence, the equilibrium between the dimeric and monomeric rhodium complexes of this [Rh(L2)]n catalyst system can be regulated by binding of effectors in the DIM-receptor. Furthermore, as the monomeric complex has different catalytic properties from the dimeric complex, we effectively generate a catalytic system of which the properties respond to the presence of effectors. Indeed, catalytic and kinetic experiments show that both the selectivity and activity of this supramolecular catalytic system can be regulated in the hydroformylation of 1-octene using acetates as effectors to shift the equilibrium from the dimeric to monomeric species.

Control over the enantioselectivity is extremely challenging in the hydroformylation reaction. Binaphos, Yangphos and bis-3,4-Diazaphospholane are few representative chiral ligands that are successfully used for the enantioselective hydroformylation reaction. However, these ligands are generally tedious to synthesis, and variations of the ligands can be limited. Also, in some reactions the regioselectivity is too low for practical application. Therefore, we report
in Chapter 4 a series of supramolecular rhodium catalysts, of which the DIM-receptor can bind carboxylate containing effectors, thereby controlling the enantioselectivity (Fig. 4). In this case, both chiral and achiral effectors can be bound to modify the coordination environment of the rhodium center. The optimized supramolecular catalyst with an effector bound in the DIM-receptor displayed high regio- and enantioselectivity in the hydroformylation of vinyl acetate and its derivatives. The enantioselectivities increase up to Δ55% ee (from 17% ee to 72% ee for vinyl acetate). Control experiments with chiral enantiomerically pure effectors and achiral effectors show that both chiral and achiral effectors can enhance the enantioselectivity induced by the rhodium metal. Further catalytic experiments show that many of the complexes based on simple amino acids based effectors displayed decent enantioselectivity and excellent regioselectivity in the hydroformylation of vinyl acetate (up to 68% ee, b/l >99).

The rhodium catalyzed enantioselective hydrogenation reaction is a highly efficient and atom economic transformation, and as such it is often used in the production of enantiopure pharmaceuticals and agrochemicals. For this reason, it has received considerable attention both from academia and industry. Over the past decades, many ligands, including diphosphine ligands with a chiral backbone, P-stereogenic diphosphine ligands, and chiral mono-phosphite or phosphoramidite ligands, have been reported for rhodium catalyzed asymmetric hydrogenation reactions. Note that the enantioselectivity is generally controlled by the steric interactions between the catalyst and the substrate. Recently, our group reported an achiral supramolecular rhodium catalyst controlled by a chiral thiourea based effector for enantioselective hydrogenation (up to 99% ee). Importantly, this supramolecular catalyst can also be optimized via a deconvolution approach by the evolution of mixtures of effectors. In Chapter 5, we studied this supramolecular catalyst system in detail and demonstrate that multiple supramolecular interactions between the effector and the complex are required to obtain high enantioselectivity (Fig. 5). And, it also explains why this effector dominates in the presence of a mixture of competing effectors. In situ VCD, NMR spectroscopy and DFT modelling reveal multiple weak interactions form between the effector and the achiral rhodium complex. These weak interactions include the expected four hydrogen bonds between the carboxylate

![Fig. 4. An effector enhanced regio- and enantioselective hydroformylation reaction via tuning the surrounding environment around the chiral metal center.](image)

![Fig. 5. Multiple supramolecular interactions are involved in an effector controlled enantioselective hydrogenation](image)
group and the DIM-receptor, and an Rh-S bond between the thiocarbonyl group of the effector and the Rh center in the precatalyst, the rhodium-substrate and dihydride complexes. It is important to mention that the extra Rh-S bond results in the formation of well-defined supramolecular assembly in contrast to other effectors. Furthermore, DFT calculations on the four unsaturated catalytic pathways show that the H-bond interactions between the substrate and the effector controls the enantioselection step at the octahedral stage by stabilizing the transition state intermediates. DFT calculations also reveal the possible resting state complexes, which are stabilized by the Rh-S bond, formed in the early stage of the unsaturated mechanism, in line with \textit{in situ} spectroscopy. Finally, control and competition experiments with new effectors and substrates confirm the two crucial factors important for achieving highly enantioselective catalysis. These two factors are: 1) A combination of the S-Rh bond and the four H-bonds leads to the formation of the well-defined supramolecular assembly for enhanced chirality transfer; 2) The hydrogen bonding interactions between the effector and the substrate stabilize the catalytic intermediates.

C-H bond activation and subsequent functionalization with transition metal catalysts is undoubtedly one of the most powerful catalytic transformations. As catalytic C-H functionalization directly converts the inert C-H bond to value added moieties, this technology provides endless opportunities for modern synthetic chemistry. Particularly, Iridium-catalyzed C-H borylation is a state-of-art transformation as the boron group installed can be easily converted to a variety of functional groups leading to value added compounds using known chemistry, such as Suzuki coupling, amination, hydroxylation and halogenation. However, the selectivity and reactivity are generally ruled by the substrates in terms of electronic and steric factors, limiting its potential application. As secondary aromatic amides are widely distributed structures among the chemical kingdoms, such as pharmaceuticals, agrichemicals and other high value intermediates, design of catalyst for \textit{ortho}-selective CH-borylation of this class of compound is of high value. Therefore, we report in \textbf{Chapter 6} the first example of iridium catalyzed direct \textit{ortho}-selective C-H borylation of challenging secondary aromatic amides in which the regioselectivity is controlled by hydrogen bond interactions (Fig. 6). The new iridium catalyst displays unprecedented \textit{ortho}-selectivities for a wide variety of secondary amide substrates that differ in electronic and steric properties. Also, the catalyst tolerates various functional groups. The regioselective C-H borylation catalyst is readily accessible and demonstrated
to convert substrates at gram scale with high selectivity and conversion. These experiments show that supramolecular substrate orientation is a powerful approach to control the regioselectivity in challenging C-H borylation reactions.

In conclusion, the successful control over the challenging selectivity and reactivity in hydroformylation reactions, asymmetric hydrogenation reactions and C-H activation reactions using supramolecular tools demonstrate the power of effector controlled catalysis and supramolecular substrate preorganization concepts in transition metal catalysis. Moreover, beyond traditional approaches, new concepts based on supramolecular tools are envisioned to achieve more challenging goals in the future.
Samenvatting

In overgangsmetaal katalyse is het sturen van selectiviteit en reactiviteit belangrijk voor het maken van fijn chemische en bulk chemische producten. Vaak wordt het ligand dat aan het metaal coördineert gevarieerd om zo de gewenste selectiviteit en reactiviteit te verkrijgen. Ondanks dat deze strategie tot veel succesvolle omzettingen heeft geleid, heeft de strategie een aantal intrinsieke tekortkomingen. Een van deze tekortkomingen is dat de strategie niet toepasbaar is voor omzettingen waar het reactiepad naar het gewenste product een soortgelijke reactiebarrière heeft als andere reactiepaden die leiden naar ongewenste producten. Ook schiet deze strategie tekort als reactiepaden naar ongewenste producten een lagere barriere hebben dan het gewenste product. Ook is controle over de reactiviteit met een specifieke overgangsmetaalkatalysator lastig. De natuur is daarentegen zeer effectief in het controleren van de reactiviteit en de selectiviteit voor veel verschillende omzettingen. Geïnspireerd door de natuur hebben wij supramoleculaire interacties gebouwd om controle over selectiviteit en reactiviteit te krijgen over overgangsmetaal gekatalyseerde reacties. Wij hebben deze supramoleculaire interacties gebouwd om met additieve controle over de reactiviteit te krijgen van een overgangsmetaal katalysator. Verder hebben wij supramoleculaire interacties gebouwd om een specifieke substraten te voor-organiseren ten opzichte van de overgangsmetaal katalysator om zo de selectiviteit te controleren van deze substraten in verschillende omzettingen. In dit proefschrift zijn de bovengenoemde strategieën toegepast op hydroformylaties, asymmetrische hydrogenaties en C-H activatiereacties. Deze strategieën zijn toegepast op de voorgenoemde reacties en staan gerapporteerd in dit proefschrift. Wij demonstreren dat ze gebruikt kunnen worden voor het controleren van uitdagende selectiviteit- en reactiviteit-problemen in overgangsmetaalkatalyse.

In de hydroformylaties reactie wordt een alkeen met een syngas(H₂:CO) mengsel gereageerd tot een aldehyde met behulp van een overgangsmetaal katalysator. Het proces is volledig atoom economisch aangezien alle reagentia terechtkomen in het product. In de chemische industrie is deze reactie qua volume een van de grootste homogege gekatalyseerde reacties met een productiecapaciteit van 107 ton per jaar. Om deze reden, is er veel onderzoek gedaan naar het vinden van katalysatoren die alkenen op een chemo-regio- en enantioselectieve manier omzetten. In het verleden heeft onze groep katalysatoren gerapporteerd die de regioselectiviteit van alkenen kunnen controleren door middel van het voor-organiseren van substraten. Deze katalysatoren bevatten een diindole “backbone”, die ook wel de DIMpocket wordt genoemd. Deze DIMpocket kan dienen als een carboxylaat bindend motief (L1). Terminal onverzadigde carboxylaten konden worden gereageerd met behulp van een een rhodi-

![Fig. 1. Rationeel ontwerp van Ortho DimPhos(L2) voor het regioselectief hydroformyleren van 3-buteenzuur en zijn derivaten via substraat preorganisatie door de afstand tussen het rhodium atoom en de DIM-receptor.](image)
Samenvatting

um katalysator gebaseerd op para DIMphos (L1) tot het lineare aldehyde met hoge selectiviteit. Het was echter niet mogelijk om korte substraten te reageren, zoals 3-butenoaat. Dit komt doordat de afstand te kort was voor dit substraat om ditopisch te binden aan de katalysator gebaseerd op L1. Geïnspireerd door het aanpassen van enzymen om zo de substraat scope te vergroten, rapporteren wij in hoofdstuk 2 het rationale herontwerp van een rhodium katalysator voor regioselectieve conversie van kortere substraten met behulp van supramoleculaire substraat preorganisatie (Figuur 1). Om dit doel te bereiken hebben wij een nieuw ligand ontwikkeld, genaamd OrthoDIMphos (L2). DFT berekeningen laten zien dat het Rhodium complex gebaseerd op dit ligand een kortere afstand heeft tussen het bindingssmotief en het Rhodium atoom. Hierdoor is de afstand kort genoeg om 3-butenoaat ditopisch te binden. Consistent met ons ontwerp is de nieuwe katalysator in staat om 3-butenoaat om te zetten naar het linear product met de hoogste selectiviteit die tot nog toe gerapporteerd was. Verder is 3-penteenoaat ook omgezet met een hoge selectiviteit naar de aldehyde die het verst van de carboxylaat is (buitenste/binnenste =11/1), terwijl er een 1/1 mengsel van beide producten gevormd werd onder condities waar substraat preorganisatie niet mogelijk is. Spectroscopie onder syngas druk en DFT berekeningen laten zien dat de barriere van de hydride migratie stap naar het lineaire product lager in energie ligt dan de barriere naar het vertakte product door het binden van het substraat in de DIM receptor. De mechanistische studies van hoofdstuk 2 laten zien dat er dimerische structuren gevormd worden als het ligand L2 wordt gebonden aan rhodium. Deze dimerische structuren worden opgebroken door het binden van een substraat aan de DIM-receptor en vormen zo de selectieve monomerische katalysator. In hoofdstuk 3 rapporteren wij een supramoleculaire rhodium katalysator, gebaseerd op L2, die dimerische en monomerische complexen kan vormen (Figuur 2-3). Wij kunnen het dimer/monomer evenwicht controllen met behulp van het binden van carboxylaat additieven. Kristalstructuren, hogedruk spectroscopie en DFT berekeningen laten zien dat zonder carboxylaat additieven het dimer het meest stabiel is, waarin twee liganden gebonden zijn aan twee rhodium atomen. Cruciaal is dat deze dimerstructuren gestabiliseerd worden door waterstofbruginteracties tussen de zuurstof atomen van de carbonylen en de NH groepen van de DIM pocket. Aangezien de carboxylaten ook kunnen binden in de DIM pocket, verbreken zij deze waterstofbruggen. Hierdoor wordt het dimer/monomer evenwicht beïnvloed en wordt er meer monomer gevormd bij het toevoegen van carboxylaat "effectoren".
carboxylaat “effectoren”. De monomeer en de dimeer hebben andere katalytische eigenschappen, waardoor we de katalyse kunnen sturen door het binden van effectoren. Dit is aangetoond door katalytische experimenten waarin de activiteit over tijd gevolgd werd gecombineerd met verschillende spectroscopische technieken.

In de hydroformylerings reactive is het extreem lastig om prochirale substraten op een enantioselectieve manier om te zetten. Binaphos, Yanphos en bis-3,4-diazaphospholane zijn een aantal liganden die gebruikt zijn voor het enantioselectief hydroformyleren van substraten. Deze liganden zijn succesvol toegepast op veel prochirale substraten. Echter zijn er ook substraten die niet omgezet kunnen worden met deze liganden en het is vervolgens lastig om op een simpele manier modificaties toe te passen aan deze liganden meer substraten op een enantioselectieve manier om te zetten. Supramoleculaire chemie is echter bij uitstek geschikt hiervoor aangezien er combinaties van chirale katalysatoren en chirale additieven tot een enorme hoeveelheid aan combinaties kan leiden. Zo kan er door het grote aantal gegevene combinaties makkelijk een chirale katalysator gevonden worden. In hoofdstuk 4 rapporteren wij een aantal chirale, supramoleculaire rhodium katalysatoren die de DIM pocket bevatten (Figuur 4). Door het binden van verschillende chirale en achirale carboxylaten in de DIM receptor kan de enantioselectiviteit gevarieerd worden. Onder geoptimaliseerde condities kon vinylacetaat en derivaten hiervan omgezet worden op een enantioselectieve manier. Een verschil in enantioselectiviteit kan gehaald worden tot Δ55% ee door het binden van een chirale thioureum carboxylaat effector (van 17% ee tot 72% ee for vinyl acetaat). Controle experimenten met chirale enantiomerisch zuivere additieven en achirale additieven laten zien dat chirale en achirale effectoren ervoor kunnen zorgen dat de enantioselectiviteit verhoogd wordt. Verder laten katalytische experimenten zien dat er een enantiomere exces van tot 68% ee gehaald kan worden met simpele aminozuren.

De rhodium gekatalyseerde enantioselectieve hydrogenering is een zeer efficiënte en atoom economische transformatie. Het is een vaak gebruikte transformatie voor het maken van enantiozuivere medicijnen en landbouw chemicaliën. Veel verschillende bidentaat phosphine, chirale mono-phosphiet of phosphoramidiet liganden zijn gebruikt voor de asymmetrische hydrogenering van een grote hoeveelheid substraten. Vaak vormen sterische interacties tussen katalysator en het substraat de basis van de chirale transformaties. Recent heeft onze groep een achiraal DIMphos ligand (L1) gebruikt in combinatie met een chirale thioureum carboxylaat effector die kon binden in de DIM pocket aangezien. Deze combinatie zorgde voor een zeer enantioselectieve hydrogeneringskatalysator voor van methyl 2-acetamidoacrylaat (tot wel 99% ee). Noemenswaardig is dat een deconvolutie van een mengsel van additieven ervoor kon zorgen dat dit additief uit een mengsel gevonden kon worden. In hoofdstuk 5 hebben wij deze
supramoleculaire katalysator be-studeerd en laten zien dat meerdere supramoleculaire interacties tussen het thioureum additief en het complex aan de basis staan voor de hoge selectiviteit (Figuur 5). Deze mechanistische studies laten ook zien waarom deze katalysator de transformaties domineert als een mengsel van additieven gebruikt worden. In situ VCD, NMR spectroscopie en DFT studies laten zien dat meerdere zwakke interacties ontstaan tussen het chirale additief en het achirale rhodium complex. Ten eerste worden er vier waterstofbruggen gevormd worden tussen de carboxylaten de DIM-receptor. Ook wordt er een Rh-S binding gevormd tussen het thiocarbonyl van het chirale additief en het rhodium atoom. De aanwezigheid van een Rh-S binding zorgt ervoor dat er gedefinieerde complexen gevormd worden. De andere geteste additieven vormen geen gedefinieerde complexen, wat de basis vormt van de dominantie van dit complex in mengsels. Verder laten DFT berekeningen zien dat waterstofbruggen tussen het substraat en het thioureumadditief de enantioselectiviteit controleren. Ook laten DFT berekeningen structuren zien die mogelijk staten van de katalysator in “rust toestand” zijn, die gestabiliseerd zijn door de Rh-S binding. Deze resultaten leidde tot het gebruik van nieuwe additieven, die lieten zien dat de rhodium-zwavel binding en waterstofbrugmotieven allebei cruciaal waren voor het bereiken van een hoge enantioselectiviteit.

C-H activatie en functionalisatie met overgangsmetaalkatalysatoren is zonder twijfel een van de meest veelbelovende methodologieën die in de afgelopen jaren is ontwikkeld. De reden hiervoor is dat katalytische C-H functionalisatie direct een inerte C-H binding convierteert naar een functionele groep, waardoor het aantal stappen naar het gewenste product drastisch kan worden verminderd. De iridium gekatalyseerde boryleringsreactie is de afgelopen jaren ontwikkeld tot een veelgebruikte transformatie aangezien de boorverbinding gebruikt kan worden voor veel vervolgreacties zoals Suzuki koppelingen, aminieringen, hydroxyleringen en halogeneringen. Echter is het control-
eren van selectiviteit lastig en wordt het gevormde product meestal bepaald door sterische factoren. Dit is echter niet altijd het gewenste product. Secundaire aromatische amiden zijn veel voorkomende motieven in medicijnen en agro chemicaliën en natuurstoffen en als deze geboryleerd worden met een iridium katalysator, worden meestal mengsels van het meta en het para product gevormd. In Hoofdstuk 6 rapporteren wij het eerste voorbeeld van een selectieve ortho-borylering van secundaire aromatische amiden (Figuur 6). Deze selectiviteit is gecontroleerd door waterstofbrug interacties met een supramoleculaire bipyridine katalysator die gefictionaliseerd is met een amidoindool groep. Deze amidoindoolgroep kan de carbonyl van de substraten invangen. Tegelijkertijd laten DFT berekeningen zien dat de NH groep van de secundaire amiden een waterstofbrug kunnen vormen met de boorgroep in de overgangstoestand. Deze 2 effecten gecombineerd zorgen voor efficiënte ortho-boryleringen. Er zijn een groot aantal secundaire aromatische amiden die omgezet kunnen worden met deze katalysator. Ook kan de reactie worden uitgevoerd op gram schaal.

Samengevat laat dit proefschrift zien dat uitdagende transformaties gecontroleerd worden met behulp van waterstofbruginteracties. Zo presenteren wij voorbeelden waarin de (enanti)o-selectiviteit en de reactiviteit gecontroleerd kunnen worden in de hydroformylering reactie, asymmetrische hydrogeneringen en C-H activatie reacties met behulp van supramoleculaire interacties. Wij zijn van mening dat zulke katalysatoren meer en meer uitdagende transformaties mogelijk zullen maken.
Samenvatting
List of Publications during my PhD study

Chapter 1


S.-T. Bai and J.N. H. Reek conceived the projects; S.-T. Bai collected the literature, designed the figures and wrote the articles under the guidance of J.N. H. Reek.

Chapter 2


S.-T. Bai and J. N. H. Reek conceived the project and wrote the article together; S.-T. Bai prepared the catalyst, characterized the complexes, performed catalytic experiments, and collected the data under the guidance of J. N. H. Reek; S.-T. Bai and J. N. H. Reek did the interpretation of the data; S.-T. Bai and V. Sinha performed the DFT calculations under the guidance of B. de Bruin; S.-T. Bai, Z. Abiri and A. M. Kluwer performed the gas uptake experiments; P. R. Linnebank gave valuable suggestions and comments on the article.

Chapter 3


S.-T. Bai and J. N. H. Reek conceived the project and wrote the article together; S.-T. Bai prepared the catalyst, characterized the complexes, performed catalytic experiments, and collected the data under the guidance of J.N. H. Reek; S.-T. Bai and J. N. H. Reek did the interpretation of the data; S.-T. Bai and V. Sinha performed the DFT calculations under the guidance of B. de Bruin; S.-T. Bai, Z. Abiri and A. M. Kluwer performed the gas uptake experiments; P. R. Linnebank and P. Dydio gave valuable suggestions and comments on the article; M. Lutz and P. Dydio provided the X-ray crystal data.

Chapter 4


S.-T. Bai and J. N. H. Reek conceived the project, did the interpretation of the data and wrote the article together; S.-T. Bai prepared the catalysts and effectors and performed catalytic experiments and data interpretation and wrote the article under the guidance of J.N. H. Reek.
Chapter 5
S.-T. Bai and J. N. H. Reek conceived the project and designed the experiments; S.-T. Bai and B. H. Strudwick performed the VCD experiments and data interpretation under the guidance of S. Woutersen; S.-T. Bai performed the DFT calculations and in situ HP NMR experiment under the guidance of J. N. H. Reek; M. A. J. Koenis and W. J. Buma performed the VCD calculations; S.-T. Bai wrote the article under the guidance of J. N. H. Reek.

Chapter 6
S.-T. Bai initiated the project, prepared catalyst, performed the DFT calculations and catalytic experiments, and collected the data; S.-T. Bai and J.N. H. Reek did the interpretation of the data and wrote the article; S.-T. Bai and C. B. Bheeter purified the ortho-C-H borylation compounds and the substrates.

Publications outside of this thesis


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Shaotao (绍涛)
Gent, 17th, October 2019
Shaotao Bai was born in 1988 in Zhen’an, Shaanxi, China. He spent his childhood in the mountainous region with poor living and education conditions. After succeeding in China national exam (top 200 out of 440,000 in Shaanxi), he was admitted by Peking University and studied pharmacy from 2009 to 2013. During that period, he spent time on the topic of preparation of arabino- derived building blocks for high stereoselective synthesis of polysaccharides in the carbohydrate chemistry and chemical biology lab of State Key Laboratory of Natural and Biomimetic Drugs (SKLNBD). After obtaining his bachelor’s degree with honors in 2013, he started his master’s research training in September 2013 at Peking University. With the supervision of Prof. dr. Xin-Shan Ye, Prof. dr. De-Cai Xiong and Prof. dr. Yan-Fen Wu, he learned organic synthesis, carbohydrate chemistry, glycobiology, photo- and palladium catalysis, and published one peer-reviewed paper during that period. He supervised two third year bachelor students and taught third year medicinal chemistry course. Also, he organized ‘volunteer high school education program’, which was aimed to boost the high school education of Zhen’an with the help of the students from Peking University. He got his master degree in chemical biology in July 2013 with honors. Meanwhile, he successfully got a PhD scholarship from the Chinese Scholarship Council (CSC) to join the group of Prof. dr. Joost Reek at the University of Amsterdam to expand my expertise in the field of supramolecular (transition metal) catalysis. As demonstrated by the outcome of the efforts made to the end of his PhD research, he gained fundamental knowledge and advanced training in (homogeneous) catalysis, spectroscopy, supramolecular chemistry, DFT calculations and kinetic studies in the context of many (applied) processes, such as hydroformylation, hydrogenation and CH activations. He initiated and managed five research projects in three different directions using supramolecular concepts to control over selectivity and reactivity in collaboration with colleagues both within and outside the research group, including Dr. A.M. (Sander) Kluwer of InCatT B.V. During this period, he published three papers in ChemCatChem, Chemical Science and Angewandte Chemie, and five more papers are in preparation. Next to publications, he gave many oral and poster presentations in (inter) national conferences. Besides chemistry, he also enjoys running, reading, and hiking, and organizing trips for family and friends.