Novel Metal Amido-Complexes – Syntheses, Reactivity and Asymmetric Catalysis

DISSERTATION

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Abbreviations

Ar	aryl
Å	Ångström
Bn	benzyl
Bu	butyl
br	broad
Cy	cyclohexyl
°C	degree celsius
cod	cis-1,5-cyclooctadiene
d	doublet
δ	chemical shift (ppm)
Et	ethyl
equiv.	equivalents
FDA	U.S. Food and Drug Administration
g	gram
GC	gas chromatography
h	hours
HPLC	high performance liquid chromatography
Hz	Hertz
J	coupling constant (Hz)
K	Kelvin
m	multiplet
Me	methyl
min	minute
mL	milliliter
mmol	millimol
MS	mass spectrometry
NMR	nuclear magnetic resonance
Ph	phenyl
Pr	propyl
q	quartet
(*R*)	rectus (right)
rt	room temperature
s	singlet
(*S*)	sinister (left)
t	triplet
µL	microliter

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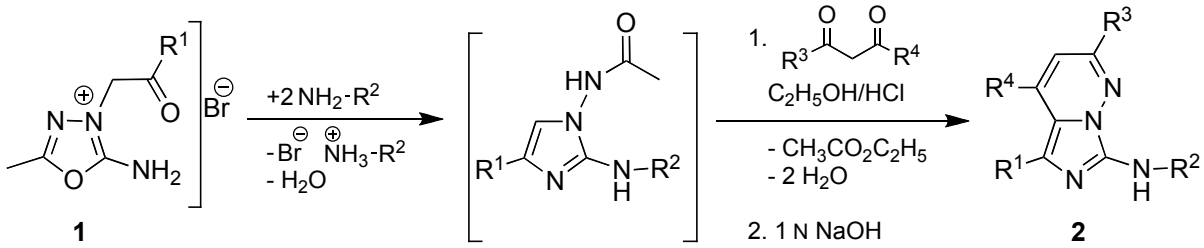
1. Summary / Zusammenfassung

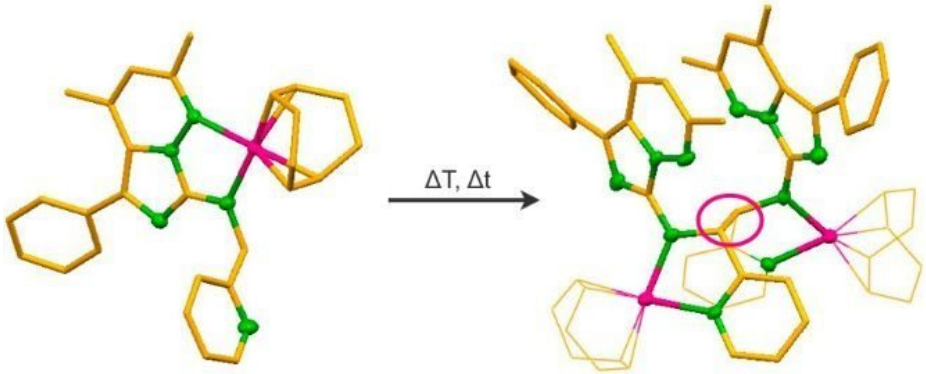
1.1 Summary

In the context of this thesis two classes of novel imidazo[1,5-*b*]pyridazine-substituted amines **2** were developed. Imidazo[1,5-*b*]pyridazine-substituted amines can be synthesized in high purity and good yields *via* the nucleophilic ring transformation of oxadiazolium halides **1** and *N*-nucleophiles, followed by deacetylation and cyclocondensation with 1,3-diketones. The deprotonated amines can act as monoanionic amido-ligands.



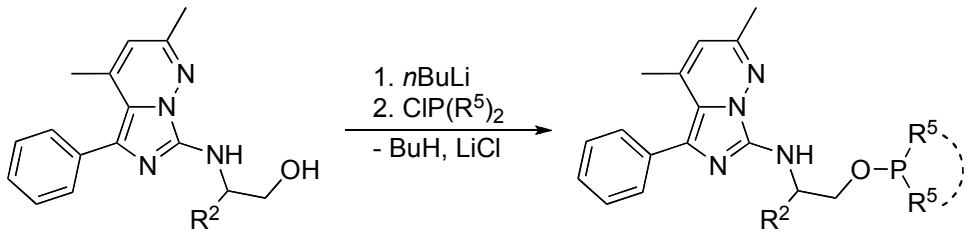
1 **2**

Previous results regarding diamine-bridged imidazo[1,5-*b*]pyridazines have shown, that the deprotonated compounds are suitable for the stabilization of early as well as late transition metal complexes. Since only dinuclear group 9 metal complexes could be obtained, one objective of this work was to enable the synthesis of mononuclear amido-complexes by means of a novel ligand structure. Thus, a series of imidazo[1,5-*b*]pyridazine-substituted (pyridylmethyl)amines was synthesized *via* a one-pot approach. Salt metathesis or alcohol elimination route were chosen for the synthesis of the iridium amido-complexes. The (2-pyridylmethyl)amine-derived complexes exhibited an unusual reactivity in solution. An intermolecular C-C coupling reaction of the mononuclear complexes was observed, yielding a dimeric species.



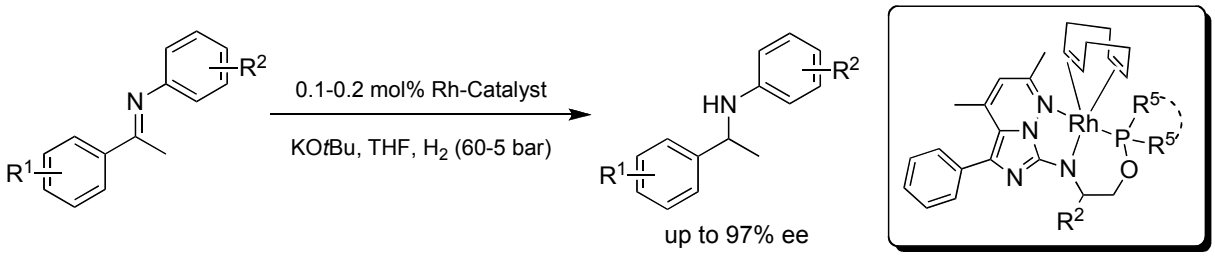
Based on mechanistic and kinetic investigations, it was postulated that the coupling reaction is due to tautomerization yielding an enamido hydrido complex, which subsequently undergoes an intermolecular attack. This gives rise to the dimeric species with iridium mediated hydrogen evolution.

Because of the modular ligand design, optically active imidazo[1,5-*b*]pyridazine-substituted amines can easily be obtained *via* the utilization of chiral *N*-nucleophiles such as amino alcohols. Motivated by previous results regarding chiral imidazo[1,5-*b*]pyridazine-stabilized iridium amido-complexes, which exhibit high selectivities and good activities in the asymmetric hydrogenation of ketones, the development of amido-complex catalysts for the enantioselective hydrogenation of imines represents a major focus of this work. A library of novel amines **4** was synthesized by deprotonation of the hydroxyl function of **3** with *n*BuLi followed by the addition of chlorophosphines or chlorophosphite.



3 **4**

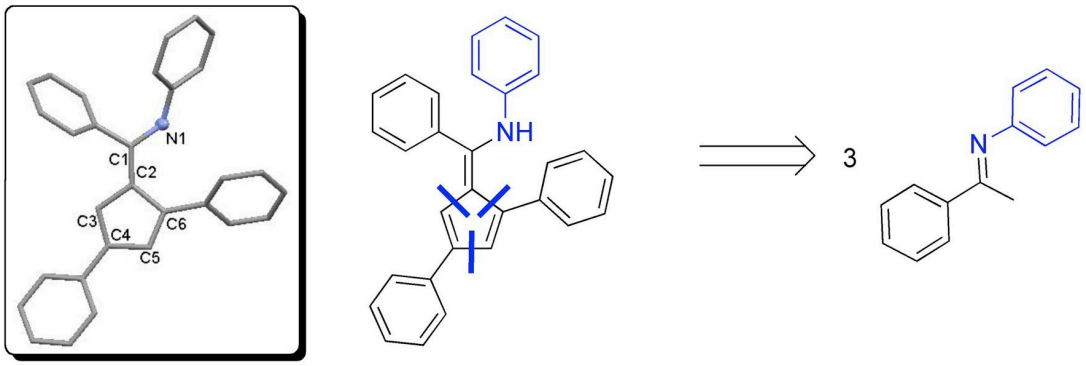
Alcohol elimination reaction of **4** with 0.5 equiv. of $[MOCH_3(cod)]_2$ (M= Ir, Rh) gave rise to transition metal amido-complexes, which were applied to the asymmetric hydrogenation of *N*-aryl imines.



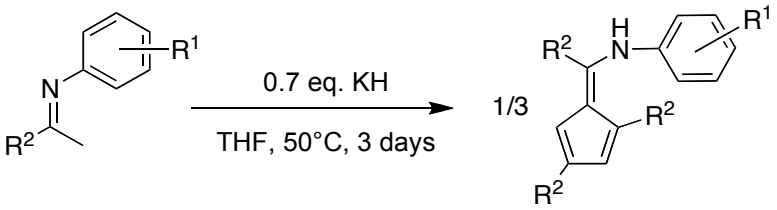
Upon activation with KO*t*Bu moderate initial selectivities and good activities were obtained for rhodium amido-complexes. Following the optimization of the reaction conditions (temperature, pressure, base) a ligand screening was performed. The highest activities and selectivities in the asymmetric hydrogenation of various imines were obtained by combining electron donating P-substituents (*i*Pr) and amino alcohols (*i*Bu). Additionally, the catalyst loading was reduced from 1 mol%, which represents the common usage, to only 0.1-0.2 mol%.

Thus, a novel ligand motif, based on chiral imidazo[1,5-*b*]pyridazines, was established for the efficient rhodium-catalyzed asymmetric hydrogenation of *N*-aryl imines.

In the third section of this thesis a novel potassium-mediated synthesis of 6-aminofulvenes from *N*-aryl imines is introduced. During the hydrogenation experiments regarding the optimization of the added base, the formation of a by-product was observed, if potassium hydride was utilized as a base. The by-product could be identified as novel 6-aminofulvene, namely [(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-phenyl-amine.



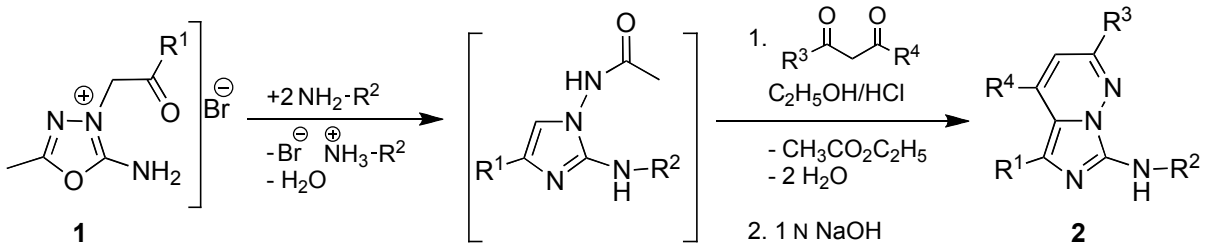
Upon this exciting discovery, the reaction conditions leading to fulvene formation were explored by means of reaction stoichiometry and added base. The resulting novel synthesis route was applied to various *N*-aryl imines.



Mechanistic as well as kinetic investigations indicated, that the reaction is based on the formation of the metalated enamine, which nucleophilicly attacks the imine-carbon. The herein reported new synthesis method provides an easy access to novel 6-aminofulvenes.

1.2 Zusammenfassung

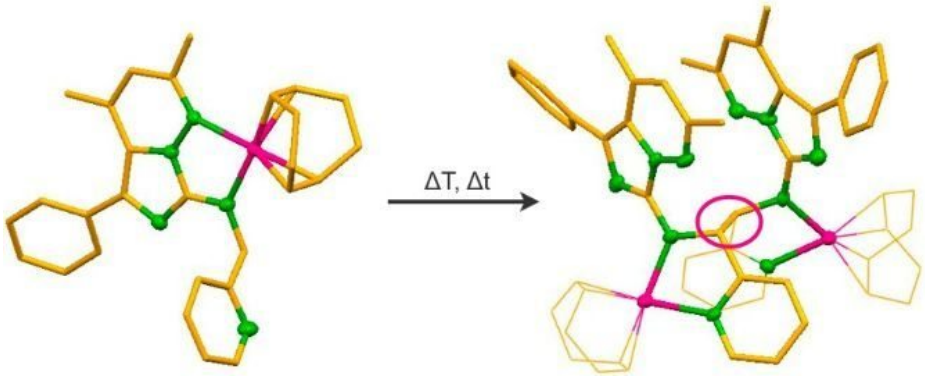
Im Rahmen der vorliegenden Arbeit wurden zwei Klassen neuartiger Imidazo[1,5-*b*]pyridazin-substituierter Amine **2** dargestellt. Imidazo[1,5-*b*]pyridazin-substituierte Amine können durch nukleophile Ringtransformation von Oxadiazoliumhalogeniden **1** mit *N*-Nukleophilen und anschließender mit Entacetylierung gekoppelter Cyclokondensation mit 1,3-Diketonen in hoher Reinheit und guter Ausbeute erhalten werden. Die deprotonierten Amine können als monoanionische Amido-Liganden aufgefasst werden.



1 **2**

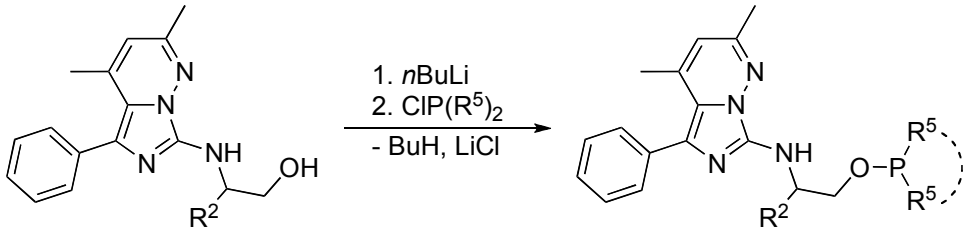
Frühere Arbeiten zu diamin-verbrückten Imidazo[1,5-*b*]pyridazinen haben gezeigt, dass diese in deprotonierter Form hervorragend zur Stabilisierung von frühen und späten Übergangsmetallkomplexen geeignet sind. Da jedoch für Metalle der Gruppe 9 lediglich zweikernige Komplexe erhalten werden konnten, war ein Ziel dieser Arbeit den Übergang zu mononuklearen Komplexen durch eine neuartige Ligandenstruktur zu ermöglichen. Hierzu wurden in einer Eintopfsynthese verschiedene Imidazo[1,5-*b*]pyridazin-substituierte (Pyridylmethyl)amine in moderater bis guter Ausbeute und hoher Reinheit dargestellt. Anschließend wurden diese durch Salzmetathese oder Alkoholeliminierung mit einer Iridium-Vorstufe zu den entsprechenden Iridium-Amido-Komplexen umgesetzt. Es wurde dabei für die (2-Pyridylmethyl)-substituierten Komplexe eine außergewöhnliche Reaktivität beobachtet. Eine intermolekulare C-C-Kupplungsreaktion zwischen den mononuklearen Iridium-Amido-Komplexen führte zur Bildung einer zweikernigen Spezies.

Basierend auf mechanistischen und kinetischen Untersuchungen wurde postuliert, dass diese Kupplungsreaktion auf der Tautomerisierung zum Enamido-Hydrido-Komplex beruht. Anschließend bildet sich durch intermolekularen Angriff die zweikernige Spezies, wobei Iridium-vermittelt Wasserstoff freigesetzt wird.



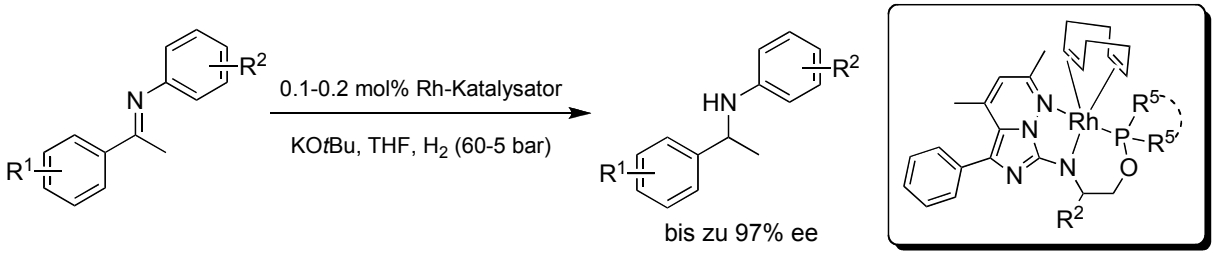
Auf Grund des modularen Liganden-Designs können durch die Verwendung von chiralen *N*-Nukleophilen, wie Aminoalkoholen, optisch aktive Imidazo[1,5-*b*]pyridazin-substituierte Amine erhalten werden. Motiviert durch vorhergehende Arbeiten zu chiralen Imidazo[1,5-*b*]pyridazin-stabilisierten Iridium-Amido-Komplexen, welche hervorragende Aktivitäten und Selektivitäten in der asymmetrischen Hydrierung von Ketonen aufweisen, war die Entwicklung von Amido-Komplexkatalysatoren für die asymmetrische Hydrierung von Iminen ein Schwerpunkt dieser Arbeit.

Durch Lithiierung der Hydroxyfunktion von Imidazo[1,5-*b*]pyridazin-substituierten Aminoalkoholen **3** und anschließender Umsetzung mit Chlorophosphanen oder Chlorophosphit konnten verschiedene neuartige Amine **4** in hohen Ausbeuten und hoher Reinheit erhalten werden.



3 **4**

Diese wurden anschließend durch Alkoholeliminierung zu Amido-Übergangsmetallkomplexen (Ir, Rh) umgesetzt und in der asymmetrischen Hydrierung von *N*-Aryliminen getestet.

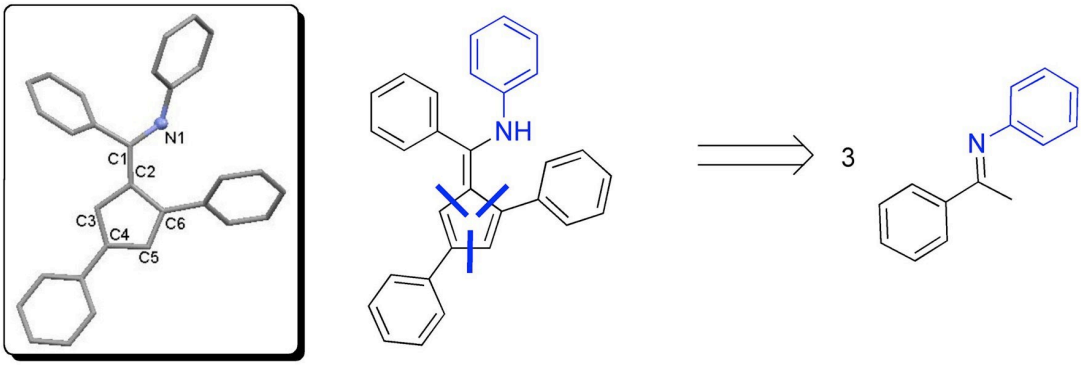


Durch die Zugabe von KO*t*Bu konnten in den ersten Hydrierexperimenten für Rhodium-Amido-Komplexe moderate Selektivitäten und gute Aktivitäten erhalten

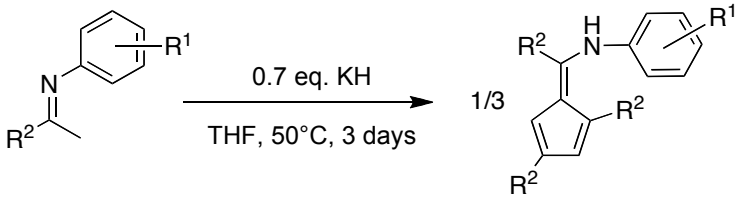
werden. Nach Optimierung der Reaktionsbedingungen (Temperatur, Druck, Base) wurde ein Ligandenscreening durchgeführt. Die höchsten Selektivitäten und Aktivitäten in der enantioselektiven Hydrierung von verschiedenen *N*-Aryliminen wurden mit der Kombination aus elektronenschiebenden P-Substituenten (*i*Pr) und Aminoalkoholen (*i*Bu) erzielt. Die Katalysatorbeladung konnte dabei von in der Literatur üblichen 1 mol% auf 0.1-0.2 mol% gesenkt werden.

Basierend auf chiralen Imidazo[1,5-*b*]pyridazinen wurde somit ein neuartiges Ligandenmotiv für die hoch effiziente Rhodium-katalysierte asymmetrische Hydrierung von Iminen etabliert.

Im dritten Abschnitt der vorliegenden Arbeit wird eine neue Kalium-vermittelte Syntheseroute für 6-Aminofulvene ausgehend von *N*-Aryliminen beschrieben. Bei den Untersuchungen zur Basen-Optimierung in der Hydrierung wurde bei KH-Zugabe die Bildung eines Nebenproduktes beobachtet. Dieses Nebenprodukt konnte als neuartiges 6-Aminofulven, [(2,4-Diphenyl-cyclopenta-2,4-dienyliden)-phenyl-methyl]-phenyl-amin, identifiziert werden.



Anschließend wurden die Reaktionsbedingungen (Stöchiometrie, Base), welche zur Fulvenbildung führen, ermittelt und die neuartige Syntheseroute auf verschiedene *N*-Arylimine angewendet.



Auf Grund mechanistischer und kinetischer Untersuchungen wurde ein Reaktionsmechanismus postuliert. Dieser basiert auf der Bildung von kaliierten Enaminen, welche nukleophil am Imin-Kohlenstoff angreifen. Die hier erstmals vorgestellte Syntheseroute bietet einen einfachen Zugang zu neuen 6-Aminofulvenen.

2. Introduction

Following the pioneering works of Bradley, Lappert and others[1,2], who established the basic structural motifs and synthetic procedures for amido-ligands (NR_2^-) in the 1960's and 1970's, amido-metal chemistry has played a minor role until the mid 1990's.

The search for ligand systems, which allow for reactivity modification of the resulting transition metal complexes e.g. in homogeneous catalysis, is one of the main challenges in today's chemistry. The most important advantage of amido-ligands is the possibility to substitute the amido-N-atom at two positions.[3] Thereby, new functionalities can be introduced, which mask reaction sites due to a hemilabile coordination behavior. This has led to the renaissance of amido-metal chemistry during the last decade.[4]

Recently, we introduced a novel bisamido-ligand system, which is based on diamine-bridged imidazo[1,5-*b*]pyridazines.[5] The deprotonated diamines are suitable for the stabilization of early as well as late transition metal complexes *via* a five-membered chelate. Since the reaction with group 9 metals yielded only dinuclear complexes, we were interested in developing an amido-pincer type of ligand, which allows for the synthesis of mononuclear amido-complexes. Furthermore, the ligand should possess multiple (hemilabile) coordination sites to enable coordination flexibility and reactivity.

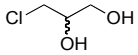
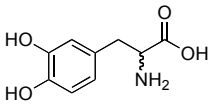
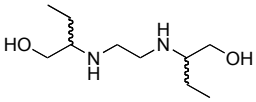
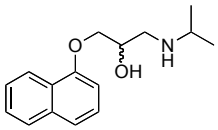
In this work a series of novel imidazo[1,5-*b*]pyridazine-substituted (pyridylmethyl)-amines was developed and applied for the stabilization of iridium complexes, which exhibit an interesting reactivity in solution.

Due to the modular design of imidazo[1,5-*b*]pyridazine-substituted amido-ligands, a wide range of amines can be utilized for their synthesis. This additionally permits the introduction of chirality e.g. *via* the chiral pool approach.

Since nature is based on homochirality[6], many biological processes, for instance enzyme catalysis, signal transduction or molecular recognition, are inherently dissymmetric. Enzymes and receptor sites are capable of differential binding, thereby distinguishing the enantiomers. The biological responses, which are generated upon binding, differ for each enantiomer (Table 1).[7] The undesired enantiomer can either be inactive ('metabolic waste') or have an unwanted, even toxic effect.[8,9] Thus,

certain chiral active pharmaceutical ingredients should be employed as enantiopure compounds.

Table 1: Different biological activities of drug enantiomers.[8,9]

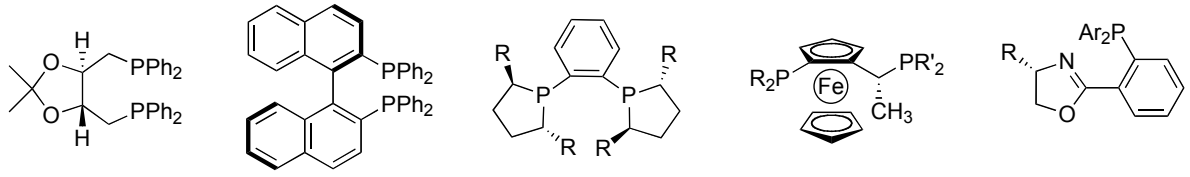
Compound		Absolute Configuration	Biological Activity
1-chloropropane-2,3-diol		*R*	toxic
		S	anti-fertility
dopa		*R*	causes granulocytopenia
		S	anti-parkinson
ethambutol		*R*,*R*	causes blindness
		S,*S*	tuberculostatic
propranolol		*R*	contraceptive
		S	anti-arrhythmic, decrease of blood pressure

Due to the fact that about 80% of the pharmaceuticals in the product pipeline are chiral and furthermore that the FDA is improving the regulations for the launch of chiral pharmaceutical ingredients, there is an increasing demand for optically active intermediates such as amines, alcohols or acids.[10,11] This 'chiral switch' in the pharmaceutical industry has boosted the field of asymmetric catalytic technologies, since these provide excellent access to those substances.

In general asymmetric catalytic technologies are divided into chemocatalysis and biocatalysis. Biocatalysis is based on soluble or immobilized enzymes that are either applied in an isolated form or as whole cell catalysts.[12] Mainly chiral transition metal complexes are applied for asymmetric chemocatalytic reactions, since virtually no restrictions exist regarding their molecular design.[13]

Thus, great efforts have been made to develop novel chiral ligand-systems for asymmetric catalysis. This 'ligand-evolution' is demonstrated through the history of asymmetric hydrogenation technologies. Based on Wilkinson's achiral $[Rh(PPh_3)_3Cl]$ hydrogenation catalyst[14], Horner as well as Knowles utilized butyl-methyl-phenylphosphine as chiral P-ligand.[15] The enantioselectivity in the hydrogenation of olefines was still rather low, but soon more effective P-chirogenic phosphine ligands such as camp[16] (camp = cyclohexyl-*o*-anisylmethylphosphine) and dipamp[17] (dipamp = ethylenebis[(2-methoxyphenyl)phenylphosphine]) were established. Since

the introduction of diop[18] (diop = 4,5-bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane) by Kagan *et al*. the research focused on the development of C_2-symmetric ligands, the most prominent examples being binap[19] (binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) and duphos[20] (duphos = 1,2-bis-[2,5-dialkylphospholano]benzene). More recently additional structural motifs such as the josiphos family[21] and phosphine-oxazolines (phox)[22] were introduced (Figure 1).



(*R,R*)-diop (*R*)-binap (*R,R*)-duphos (*R*)-josiphos (*R*)-phox

Figure 1: Optically active ligands applied in asymmetric hydrogenation reactions.

In general three approaches can be adopted for the synthesis of chiral ligands: the resolution of a racemic mixture, the utilization of chiral building blocks (chiral pool approach) and the conversion of a prochiral substrate via asymmetric (bio)catalysis (amplification of chirality).[23]

Chiral amino acids (chiral pool) and amino alcohols (reduction of amino acids), which are easily accessible, represent ideal building blocks for the synthesis of chiral imidazopyridazine-substituted amines.

Imidazo[1,5-*b*]pyridazine-substituted amino alcohols can be synthesized *via* a one-pot approach in good yields and high purity. Upon deprotonation they can be utilized for the stabilization of iridium amido-complexes, which show excellent activities and selectivities in the asymmetric hydrogenation of ketones.[24]

Based on these promising results, one of the objectives of this work is to find an amido-catalyst system, which is suitable for the asymmetric hydrogenation of imines. Since the hydroxyl function can easily be targeted for functionalization reactions, a novel ligand system was developed by introduction of P-substituents.

Within this work a library of novel amino-P-ligands was synthesized, fully characterized and reacted with metal precursors to yield transition metal amido-complexes. These amido-complexes were tested in the asymmetric hydrogenation of *N*-aryl imines. Upon optimization of the reaction conditions and a catalyst screening, the most promising catalyst system was utilized for the broadening of the substrate scope.

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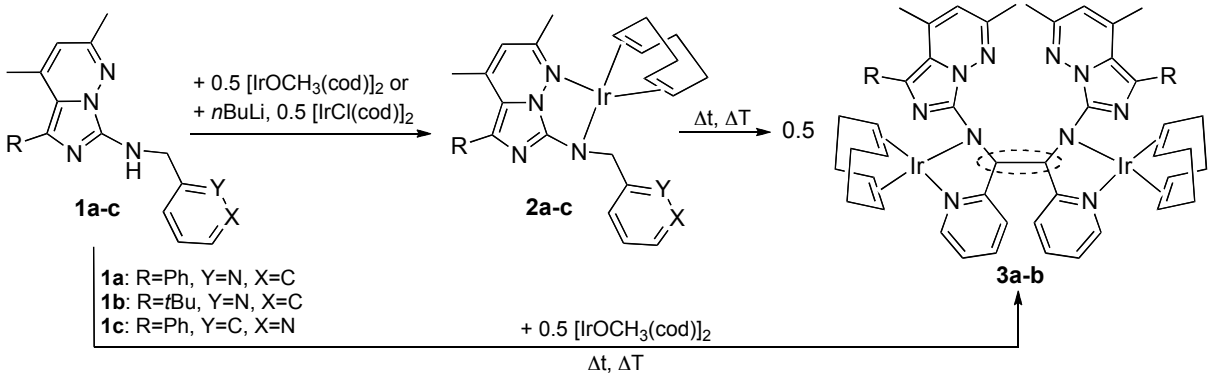
3. Overview of Thesis Results

This thesis comprises 3 publications, which are presented in chapter 4-6.

3.1 An Intermolecular C–C Coupling Reaction of Iridium Complexes

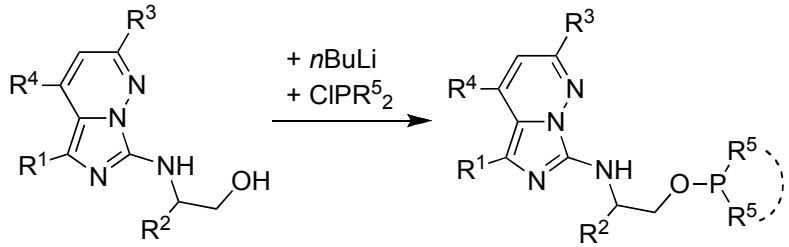
Recently, our group reported the synthesis of novel imidazo[1,5-*b*]pyridazine-substituted bisamido-ligands. Salt metathesis reaction with group 9 metals afforded only dinuclear complexes. We were interested in mononuclear group 9 amido-complexes, which possess coordination flexibility in order to generate reactivity. Thus, a novel amido-pincer type of ligand, namely imidazo[1,5-*b*]pyridazine-substituted (pyridylmethyl)amines **1**, was developed.



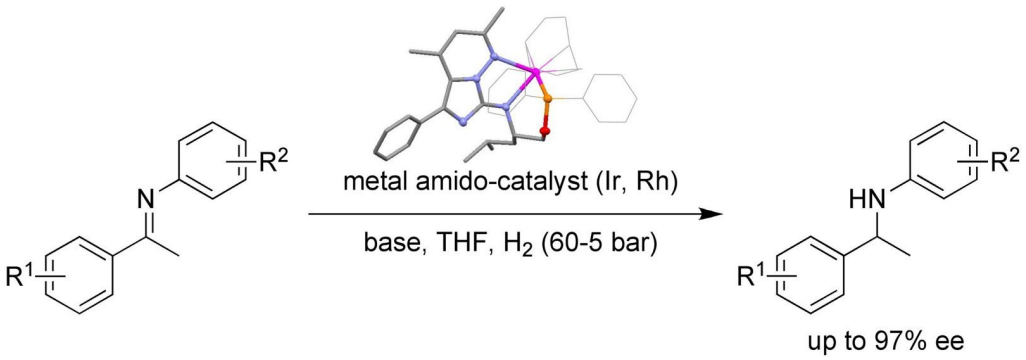
Salt metathesis or alcohol elimination reaction gave rise to mononuclear iridium complexes in good yields. The (2-pyridylmethyl)amine-derived complexes **2a-b** were rather unstable in solution. An intermolecular C-C coupling reaction to dinuclear species, in which another coordination mode is realized, was observed. In order to elucidate the driving force of this coupling reaction, kinetic as well as mechanistic studies were performed. The coupling reaction is not likely to take place *via* a radical based mechanism, because the addition of a radical scavenger does not inhibit the reaction or decrease the rate of dimer formation. Since (3-pyridylmethyl)amine-derived complex **2c** does not perform the C-C coupling reaction, we propose that the mechanism is based on formation of an iridium enamido hydrido complex, intermolecular attack and iridium mediated hydrogen evolution.

3.2 Novel Amido-Complexes for the Efficient Asymmetric Hydrogenation of Imines

Based on previous results regarding the synthesis of chiral imidazo[1,5-*b*]pyridazine-substituted amino alcohols, which are suitable for the stabilization of transition metal amido-complexes, a novel optically active amido-ligand system was developed.
Thereby the hydroxyl function of imidazo[1,5-*b*]pyridazine-substituted amino alcohols was selectively deprotonated with *n*BuLi and subsequently one equiv. of a chlorophosphine or chlorophosphite was added, giving rise to novel amines in high yield and purity.



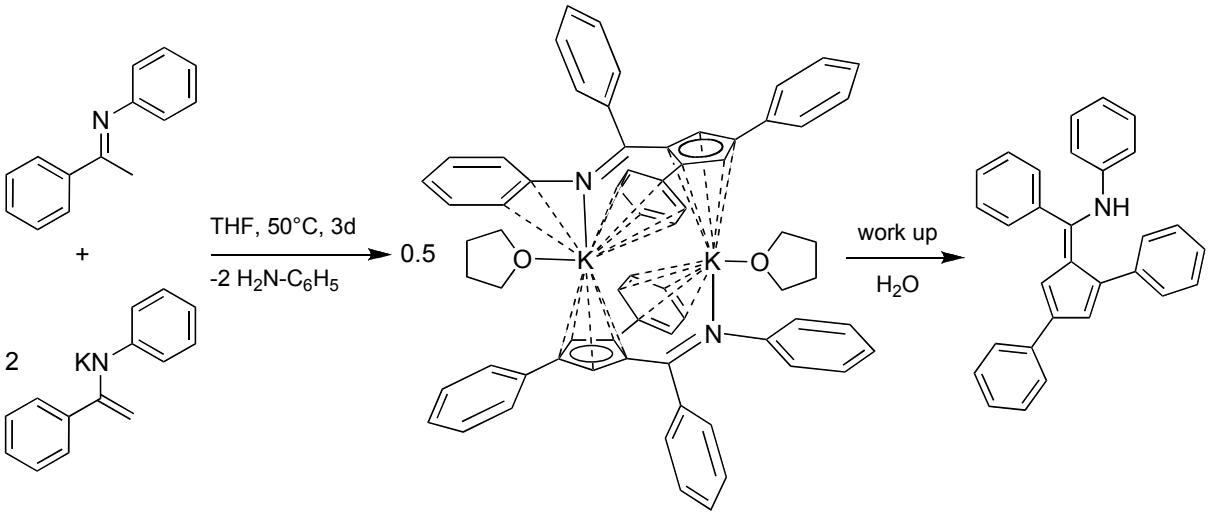
The chiral amines were utilized for the stabilization of group 9 metal complexes (Ir, Rh) *via* alcohol elimination route. The resulting amido-complexes were applied to the asymmetric hydrogenation of various *N*-aryl imines.



Since promising initial selectivities and activities were obtained for rhodium amido-complexes, these were chosen for the optimization of the reaction. Thus, first the ideal reaction conditions by means of reaction temperature, pressure and the added base were determined. Next a ligand screening was conducted to find the best combination of amino alcohol and P-substituent. Therein, the combination of leucinol and -P*i*Pr$_2$ provided the best selectivity and activity in the asymmetric hydrogenation of various *N*-aryl imines.

3.3 The Potassium Hydride Mediated Trimerization of Imines

During the asymmetric hydrogenation of *N*-(1-phenylethylidene)-aniline the formation of a by-product was observed, if potassium hydride was utilized as a base. The by-product could be identified as a novel aminofulvene, namely [(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-phenyl-amine.



In order to reproduce this novel potassium-mediated fulvene synthesis, the ideal reaction-stoichiometry and the utilization of different metal bases was explored. Therein complete conversion of the imine and formation of the fulvene as main product was achieved upon addition of 0.7 equivalents of KH. Based on these results, several *N*-aryl imines were applied to the synthesis of aminofulvenes.

Kinetic and mechanistic experiments were performed to gain insight into the mechanism of the imine trimerization reaction.

It was found that upon base addition the metalated enamine is formed. Experiments regarding the reaction stoichiometry indicated that the imine and its enamine tautomer are involved in the reaction. It was postulated that the reaction is based on the nucleophilic attack of the enamine at the imine-carbon, thus potassium-anilide is eliminated. A second nucleophilic attack gives rise to the trimerization product, which subsequently cyclizes yielding the aminofulvene.

3.4 Individual Contribution to Joint Publication

The results presented in this thesis were obtained in collaboration with others and are published, submitted or are to be submitted as indicated below. In the following, the contributions of all the co-authors to the publications are specified. The asterisk denotes the corresponding authors.

3.4.1 Chapter 4

This work was published in *New J. Chem.* **2010**, *34*, 1954-1960 with the title **'An Intermolecular C–C Coupling Reaction of Iridium Complexes'**
K. Kutlescha, Torsten Irrgang and Rhett Kempe*

I synthesized and characterized all complexes and ligands presented in this work, carried out the NMR-experiments and wrote the publication. Torsten Irrgang carried out previous experiments regarding the synthesis of imidazopyridazine-substituted amido-ligands and was involved in scientific discussions and corrections of the manuscript. Rhett Kempe supervised this work and was involved in scientific discussions and correction of the manuscript.

3.4.2 Chapter 5

This work has been accepted for publication in *Adv. Synth. Catal.* with the title **'Novel Amido-Complexes for the Efficient Asymmetric Hydrogenation of Imines'**
K. Kutlescha, Torsten Irrgang and Rhett Kempe*

I synthesized and characterized all complexes, ligands and imines presented in this work, carried out the NMR- and hydrogenation experiments and wrote the publication. Torsten Irrgang carried out previous experiments regarding the synthesis of imidazopyridazine-substituted amido-ligands and was involved in scientific discussions and corrections of the manuscript. Rhett Kempe supervised this work and was involved in scientific discussions and correction of the manuscript.

3.4.3 Chapter 6

This work has been submitted to *Chem. Commun.* with the title **'The Potassium Hydride Mediated Trimerization of Imines'**
K. Kutlescha, G.T. Venkanna and Rhett Kempe*

I established the synthesis of novel fulvenes, carried out NMR-, GC-MS- and kinetic experiments in order to propose the mechanism and wrote the publication. G. T. Venkanna utilized this methodology for the synthesis of various fulvenes, thereby demonstrating the applicability of this novel synthesis route towards other imines. Rhett Kempe supervised this work and was involved in scientific discussions and correction of the manuscript.

4. An Intermolecular C–C Coupling Reaction of Iridium Complexes

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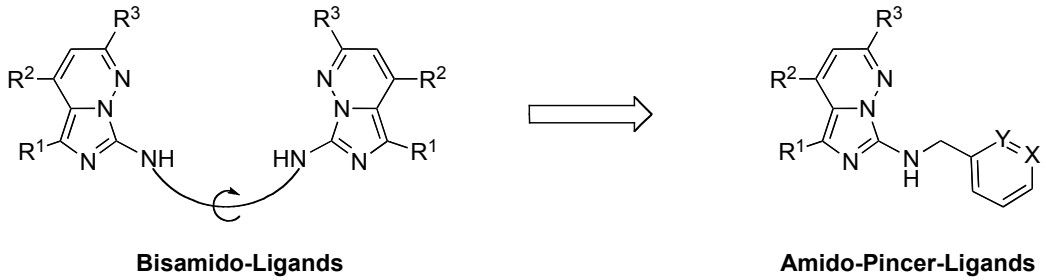
Keywords: Amido-Ligands, C-C Coupling, C-H Activation, Imidazo[1,5-*b*]pyridazines, Iridium, N-Ligands

Published in: *New. J. Chem.* **2010**, *34*, 1954-1960.

Abstract: Novel imidazo[1,5-*b*]pyridazine-substituted (pyridylmethyl)amines were synthesized *via* the nucleophilic ring transformation of oxadiazolium halides and (pyridylmethyl)amines, followed by a cyclocondensation reaction with 1,3-diketones. After deprotonation, these monoanionic amido-pincer-ligands are suitable for the stabilization of mononuclear iridium complexes. For (2-pyridylmethyl)amine-derived complexes, we observed the formation of dimers *via* an intermolecular C-C coupling reaction, whilst the (3-pyridylmethyl)amine-derived complex did not react. We propose that enamine tautomerization plays an important role in the C-C coupling reaction.

4.1 Introduction

Recently, we described a novel ligand system for the stabilization of early and late transition metal complexes- imidazopyridazine-substituted bisamido-ligands (Scheme 1).[1] Since salt metathesis reactions with group 9 metals (Ir, Rh) yielded only dinuclear amido-complexes with *trans* binding modes, we were interested in developing an amido-pincer type of ligand[2] that allows for the synthesis of mononuclear complexes (Scheme 1).



Scheme 1: Imidazo[1,5-*b*]pyridazine-substituted bisamido-ligands and amido-pincer-ligands ($R^{1–3}$ = aryl or alkyl substituents; Y, X = C or N).

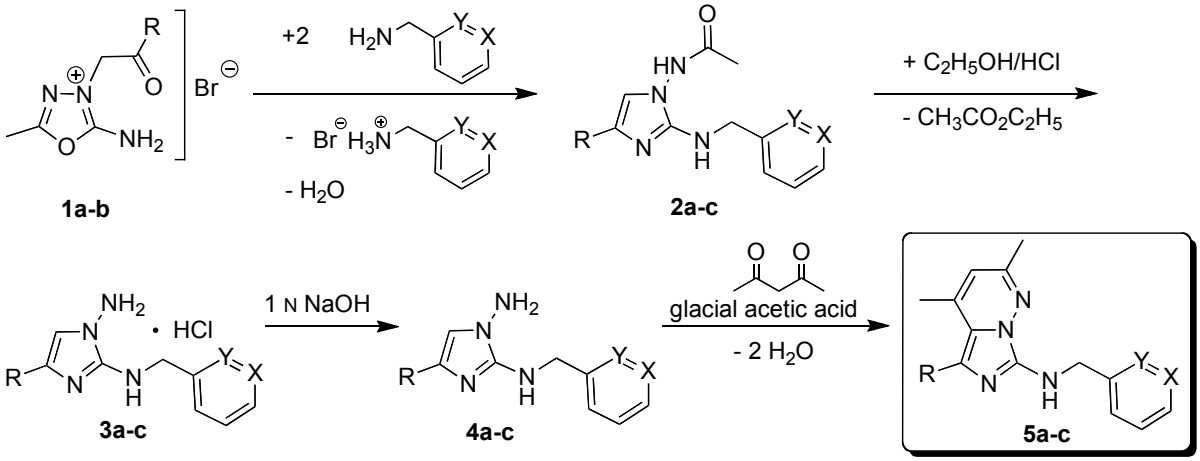
Our approach towards these novel amido-pincer-ligands is based on classical bench-top chemistry, realizing a large variety of substitution patterns. Aryl amines are substantially synthesized *via* palladium-catalyzed aryl amination, which is efficient for the formation of C–N bonds but often employs rather expensive catalysts.[3]

Herein, we report the synthesis of imidazo[1,5-*b*]pyridazine-substituted (pyridylmethyl)amines **5** and their application as monoanionic ligands for the stabilization of iridium complexes **6**. For **6a** and **6b**, we observed an unusual intermolecular C–C coupling reaction, giving rise to dinuclear complexes **7**.

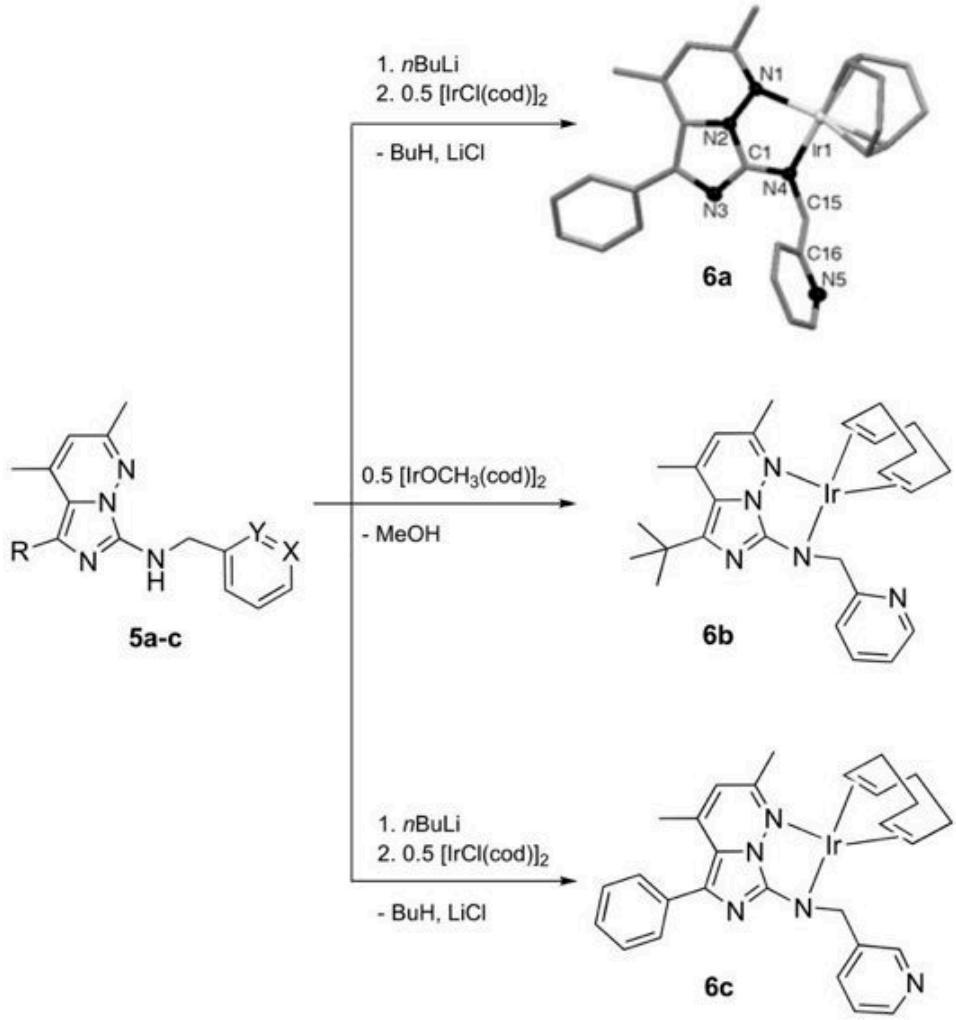
4.2 Results and Discussion

2-Amino-5-methyl-1,3,4-oxadiazolium halides[4] **1a** and **1b** (Scheme 2) react with a large variety of *N*-nucleophiles, such as primary and secondary amines, to yield 2-amino-substituted 1-acetylamino-imidazoles *via* a nucleophilic ring transformation.[5,6] Thus, the reaction with (pyridylmethyl)amines affords *N*-{4-alkyl/aryl-2-[(pyridin-2/3-ylmethyl)-amino]-imidazo-1-yl}-acetamides **2a-c**.

Deacetylation by refluxing **2** in EtOH/HCl, followed by neutralization, gives rise to **4a-c** (Scheme 2). It is known that 1-amino-4-aryl-imidazoles[7] react with 1,3-diketones to yield imidazo[1,5-*b*]pyridazines.[6] Analogously, **4** can be converted into imidazo[1,5-*b*]pyridazine-substituted (pyridylmethyl)amines **5a-c** (Scheme 2) *via* a cyclo-condensation with acetylacetone in moderate yields and high purity. The molecular structure of **5a** was confirmed by X-ray crystal structure analysis.[8] The lithiation of **5a** at −78 °C using one equiv. of *n*butyllithium and the addition of 0.5 equiv. of $[IrCl(cod)]_2$ (cod = 1,5-cyclooctadiene), afforded **6a** as a dark green crystalline material in moderate yield (Scheme 3).



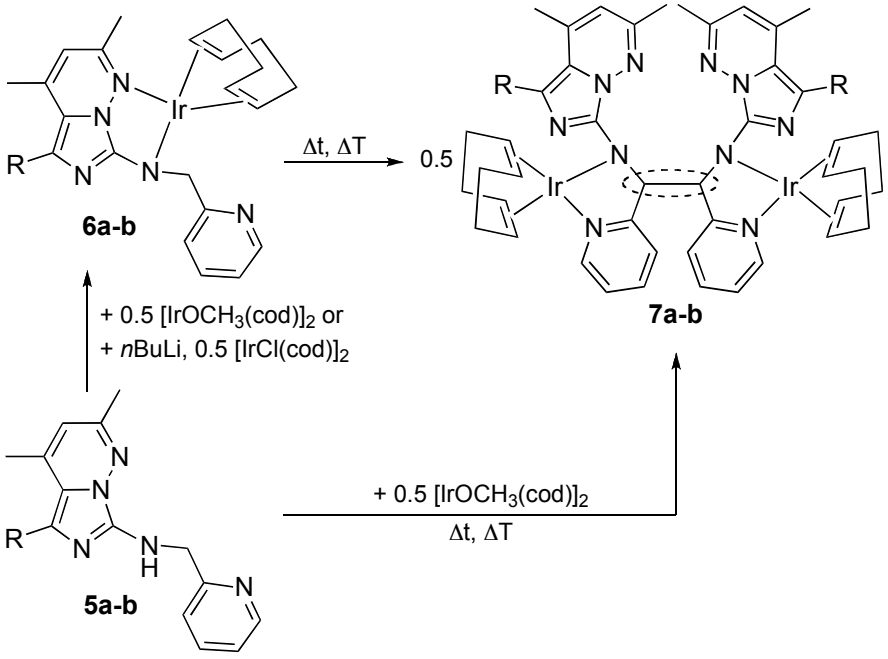
Scheme 2: Ring transformation with (pyridylmethyl)amines [R = C_6H_5 (**1a**), R = *t*butyl (**1b**); R = C_6H_5, Y = N, X = C (**2a-5a**); R = *t*butyl, Y = N, X = C (**2b-5b**); R = C_6H_5, Y = C, X = N (**2c-5c**)].



Scheme 3: Synthesis of iridium complexes **6a-c** [R = C_6H_5, Y = N, X = C (**5a/6a**); R = *t*butyl, Y = N, X = C (**5b/6b**); R = C_6H_5, Y = C, X = N (**5c/6c**)] and molecular structure of **6a**. Selected bond lengths [Å] and angles [°]: Ir1-N1 2.143(3), Ir1-N4 2.050(3), C1-N2 1.360(4), C1-N3 1.341(5), C1-N4 1.351(5), N1-N2 1.393(4); N1-Ir1-N4 80.61(11), Ir1-N1-N2 106.87(19), C1-N2-N1 121.50(3).

An X-ray crystal structure analysis[9] of **6a** was performed to determine the molecular structure (Scheme 3). The monoanionic ligand coordinates the iridium atom via the amido N atom (N4) and N1, forming a five-membered chelate. Since the Ir1-N4 bond (2.050 Å) is significantly shorter than the Ir1-N1 bond (2.143 Å), we propose that the anionic charge of the ligand is localized at the amido N atom. The standard deviation of the imidazopyridazine plane is 0.010 Å. The deviation of the N_{amido} atom out of this plane is 0.043 Å and for Ir it is 0.054 Å. The 2-pyridylmethyl moiety is bent out of the imidazopyridazine plane (N4-C15-C16 116.6°) and coordination by the pyridine nitrogen does not occur. The NMR spectra of **6a** show a single signal set of deprotonated **5a** and a double-coordinated cod ligand.

While compound **6a** is stable as a solid, in solution we observed the formation of the orange-red crystalline material **7a** (Scheme 4) after a few weeks at room temperature. We were able to synthesize **7a** in moderate yields through the reaction of **5a** with 0.5 equiv. of $[IrOCH_3(cod)]_2$[10]. The resulting green solution was heated at 50 °C for 2 weeks and the precipitated red crystalline material isolated (30%). An X-ray crystal structure analysis[11] of **7a** (Figure 1) revealed that intermolecular C-C bond formation between the 2-pyridylmethyl-substituents of two amido-ligands had occurred.



Scheme 4: Evolution of C-C coupled dimers **7a** and **7b**. A dashed line highlights the newly formed C-C bond.

The two imidazopyridazine planes of **7a** are orientated nearly parallel (dihedral angle 2.24°) to each other. The deviation of the N_{amido} atom out of this plane (0.085 Å for

N7 and 0.113 Å for N2) is larger than in **6a**, which is due to the altered coordination mode. In contrast to **6a**, the iridium in **7a** is coordinated by the N_{amido} atom and the $N_{pyridine}$ *via* a five-membered chelate, leading to smaller N-Ir-N angles than in **6a** of 78.7° (N7-Ir2-N6) and 79.5° (N2-Ir1-N1), respectively. The Ir-N bond lengths of 2.019 (Ir2-N7), 2.084 (Ir2-N6), 2.013 (Ir1-N2) and 2.088 (Ir1-N1) Å indicate a rather localized bonding mode. No solution NMR data could be obtained for **7a**, since it is insoluble in common solvents. MAS-NMR data are in accordance with the signals expected for the C-C-coupled deprotonated ligand and cod.

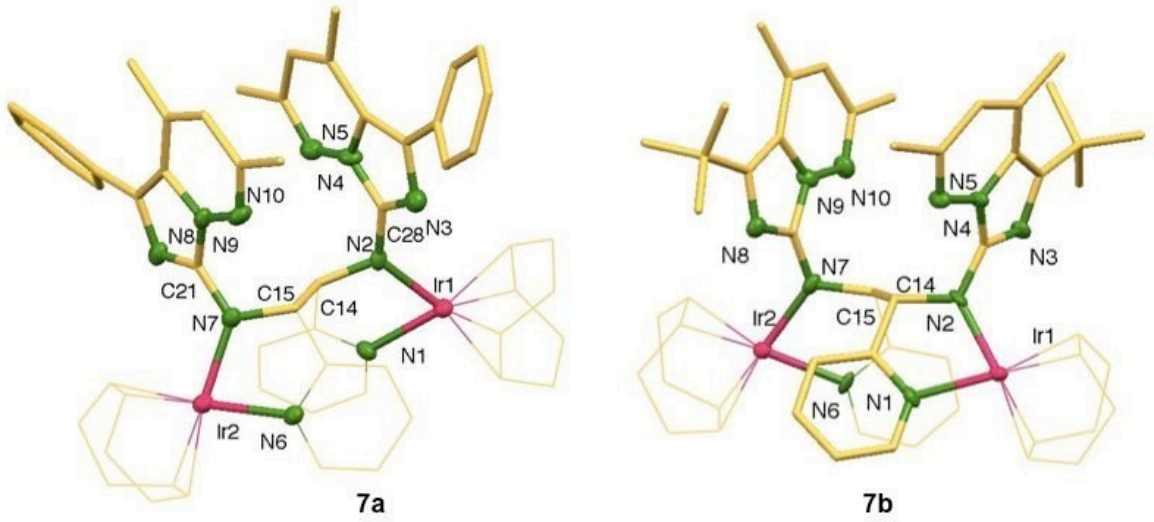


Figure 1: The molecular structures of **7a** and **7b**; selected bond lengths [Å] and angles [°]: **7a** (the asymmetric unit contained two independent molecules of **7a**, one molecule is omitted for clarity): Ir1-N1 2.088(8), Ir1-N2 2.013 (8), Ir2-N6 2.084(8), Ir2-N7 2.019(8), C14-C15 1.589(11), C14-N2 1.448(13), C15-N7 1.432(13); N2-Ir-1-N1 79.5(3), N7-Ir2-N6 78.7(3), N2-C14-C15 111.7(8), N7-C15-C14 112.2(7), C14-N2-Ir1 115.6(6), C15-N7-Ir2 117.2(6); **7b**: Ir1-N1 2.084(5), Ir2-N6 2.090(4), Ir1-N2 1.992(6), Ir2-N7 1.983(7), C15-N7 1.447(8), C14-N2 1.468(8), C14-C15 1.597(8); N2-Ir1-N1 79.1(2), N7-Ir2-N6 79.0(2), C14-N2-Ir2 117.4(3), C6-N2-Ir2 117.7(5), N2-C14-C15 112.4(5), N7-C15-C14 112.0(5).

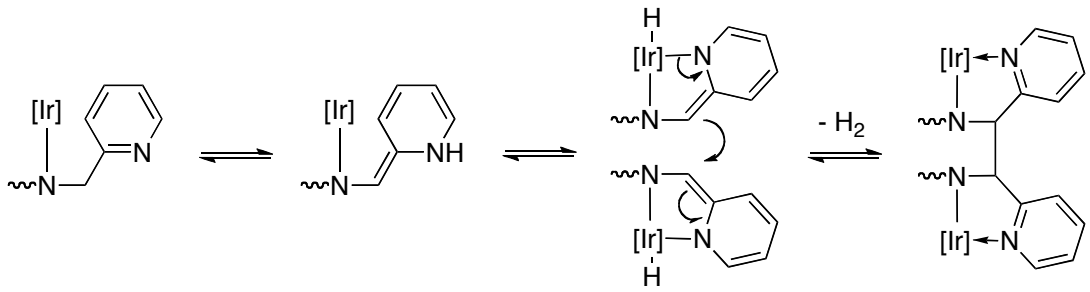
Due to the insolubility of **7a**, we were interested in synthesizing a more soluble derivative, namely *t*butyl-substituted **7b**. When we tried to synthesize **6b** via salt metathesis from lithiated **5b** and $[Ir(cod)Cl]_2$ using the same protocol as for **6a**, we observed that C-C coupling took place more rapidly. Thus, we chose an alcohol elimination reaction. The addition of 0.5 equiv. of $[IrOCH_3(cod)]_2$ to a solution of **5b** in THF gave rise to a dark green material **6b** in quantitative yield (Scheme 3). The NMR spectra show a single signal set for deprotonated **5b** and the signals for a double-coordinated cyclooctadiene. The C-C coupling product **7b** was isolated in moderate yield (28%) using the same protocol as for **7a** (Scheme 4). An X-ray crystal structure analysis[12] of **7b** was performed to determine its molecular structure (Figure 1). The bond length of the new C-C bond (C14-C15) is 1.597 Å. Due to the bulky *t*butyl

substituents, the dihedral angle between these planes is extended to 24.84° (2.24° in **7a**). This also has an effect on the deviation of the N_{amido} atom out of the imidazopyridazine plane (0.252 Å for N2 and 0.055 Å for N7). The iridium is coordinated by the N_{amido} and the $N_{pyridine}$ *via* a five-membered chelate, resulting in N-Ir-N angles of 78.99° (N7-Ir2-N6) and 79.09° (N2-Ir1-N1). Since the Ir-N_{amido} bond lengths of 1.984 Å (N7-Ir2) and 1.991 Å (N2-Ir1) are similar to the Ir-$N_{pyridine}$ bond lengths (2.090 Å (N6-Ir2); 2.085 Å (N1-Ir1)), the bonding mode is localized. The NMR spectra of **7b** show a single signal set for the deprotonated ligand and two double-coordinated cyclooctadiene molecules. The new CH group, which was formed due to the C-C coupling, is characterized as a doublet (^{1}H NMR) at 5.75 ppm with a coupling constant of 4.7 Hz.

Regarding C-C coupling reactions with pyridines, the reactivity of the carbon atom can arise from the enamine tautomer. This is reinforced by the fact that pyridines (or unsubstituted aromatics), which are unable to tautomerize into enamines, do not participate in the reactions.[13]

Therefore, we additionally synthesized the (3-pyridylmethyl)amine derivative of ligand **5c**; herein, the formation of an enamine tautomer is not possible. Complex **6c** was obtained *via* salt metathesis upon deprotonation with *n*BuLi. Since the formation of a C-C coupling product could not be detected *via* NMR for **6c**, we propose a coupling mechanism based on the formation of the enamine tautomer, followed by an intermolecular attack of the carbon atom next to the pyridine moiety (Scheme 5). The altered coordination mode in **7** cannot be realized in ligand **5c**, which might additionally hinder the C-C coupling reaction.

The iridium is thought to mediate the reaction *via* activation of the enamine and hydride transfer, thereby generating molecular hydrogen. Hydrogen evolution could be detected *via* NMR studies; a small singlet appeared at 4.21 ppm ([d_8]THF).



Scheme 5: The proposed mechanism based on tautomerization into an enamine and iridium-mediated hydride transfer.

Regarding the mechanism, double C-H activation followed by an intermolecular dehydrogenative C-C coupling reaction of the two iridium complexes **6a** and **6b** cannot be ruled out completely. The addition of a radical scavenger does not inhibit the formation of dimer **7b** and does not decrease the rate of dimer formation significantly. Thus, radical-based C-C coupling reactions are not very likely.
The reaction does not proceed completely, yielding only 19% of **7b** in 24 h and about 35% in 8 days.
The closest reactivity pattern we could find is the coupling reaction of zinc complexes of *N*-substituted (2-pyridylmethyl)amines *via* oxidative pathways due to addition of white phosphorous or dimethylzinc by Westerhausen *et al*.. Since no radicals were observed by ESR, they propose that the reaction is strongly based on the redox potential of the metal, and that the driving force of the reaction is the regeneration of aromaticity after metalation of the methylene group and charge migration to the pyridine nitrogen.[14]

4.3 Conclusions

In conclusion, imidazo[1,5-*b*]pyridazine-substituted (pyridylmethyl)amines can be synthesized *via* the nucleophilic ring transformation of oxadiazolium halides **1** with (2/3-pyridylmethyl)amine, followed by deacetylation and cyclocondensation with 1,3-diketones, in moderate yields and high purity. The deprotonated amines can act as amido-ligands, binding transition metals as five-membered chelates *via* the amido *N*-atom and N-1 of the imidazopyridazine.
An unusual intermolecular C-C coupling reaction for (2-pyridylmethyl)amine derived complexes **6a** and **6b** takes place in solution, giving rise to dinuclear complexes **7**. We have proposed a mechanism based on enamine tautomerization, and intermolecular attack accompanied by iridium-mediated activation and hydride transfer, thereby evolving molecular hydrogen.

4.4 Experimental Section

4.4.1 General procedures

Syntheses of the starting materials and ligands were performed under standard conditions. Complex syntheses were conducted in an oven (95 °C) and in vacuum dried glassware under an inert atmosphere of dry argon 5.0 *via* standard Schlenk or

glove box techniques. NMR spectra were recorded on a Bruker ARX 250/300 (250 or 300 MHz) or a Varian Inova 300/400 (300/400 MHz) NMR spectrometer. Chemical shifts are reported in ppm from tetramethylsilane, with the solvent resonance resulting from incomplete deuteration as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet or combinations thereof), integration and coupling constant. Mass spectra were recorded on a Finnigan MAT 8500 spectrometer *via* electron ionization (70 eV). Melting points were determined in sealed capillaries by using a Stuart SMP3 melting point apparatus. Elemental analysis was performed with a Vario Elementar EL III or Leco CHN-932 elemental analyzer. Non-halogenated solvents were distilled from sodium benzophenone ketyl and halogenated solvents from P_2O_5. Deuterated solvents were obtained from Cambridge Isotope Laboratories and were degassed, dried and distilled prior to use. All chemicals were purchased from commercial vendors and used without further purification.

4.4.2 Ligand Synthesis

N-{4-phenyl-2-[(pyridin-2-ylmethyl)-amino]imidazo-1-yl}acetamide monohydrate **2a**: 2.00 g (6.71 mmol) 2-amino-5-methyl-3-phenacyl-1,3,4-oxadiazoliumbromide and 1.37 mL (1.45 g; 13.43 mmol) (2-pyridylmethyl)amine were stirred for 1 min on a hot plate (250 °C). Then, the reaction mixture was allowed to cool to room temperature. Water (20 mL) was added and colorless crystals formed after several hours. After recrystallization from ethanol-water (1 : 1 ratio) **2a** (1.95 g, 89%) was obtained. M.p. 180 °C (decomposition). Found: C, 62.3; H, 5.7; N, 21.5. Calc. for $C_{17}H_7N_5O_2$ (307.33 + 18.02): C, 62.8; H, 5.9; N, 21.5%. δ_H (400.13 MHz, [d_6]DMSO, 298 K, TMS) 10.94 (s, 1H, N*H*, acetylamino), 8.58–8.56 (m, 1H, pyridine), 7.80-7.15 (m, 8H, C_6H_5/pyridine), 7.23 (s, 1H, H-5, imidazole), 6.77-6.74 (t, 1H, N*H*-CH_2, J = 6.1), 4.66-4.65 (d, 2H, CH_2-NH, J = 6.1) and 2.08 (s, 3H, CH_3); δ_C (100.63 MHz, [d_6]DMSO, 298 K, TMS) 169.53 (*C*═O), 160.34 (C-2'', pyridine), 149.43 (C-2, imidazole), 148.97 (C-6'', pyridine), 136.82 (C-4'', pyridine), 135.12 (C-1', C_6H_5), 133.85 (C-4, imidazole), 128.57, 124.08 ($C_{o,m}$, C_6H_5), 125.99 (C_p, C_6H_5), 122.23 (C-3'', pyridine), 121.28 (C-5'', pyridine), 112.60 (C-5, imidazole), 47.87 (CH_2) and 21.16 (CH_3); m/z = 307 (M^+), 249, 118, 93 and 43.

4-phenyl-N^2-pyridin-2-ylmethyl-imidazol-1,2-diamine dihydrochloride dihydrate **3a**: To a suspension of 3.00 g (9.22 mmol) of **2a** in 20 mL ethanol, 2 mL of concentrated HCl was added. The reaction mixture was refluxed for 1 h, during which a precipitate was formed after 30 min. After cooling to room temperature and evaporation of the solvent, the colorless product was recrystallized from water-ethanol (1 : 4 ratio) to yield **3a** (2.17 g, 63%). Found: C, 48.1; H, 5.8; N, 18.7. Calc. for $C_{15}H_{21}N_5O_2Cl_2$ (265.31 + 36.03 + 72.90): C, 48.1; H, 5.7; N, 18.7%. δ_H (400.13 MHz, [d_6]DMSO, 298 K, TMS) 8.91-8.89 (m, 1H, H-6'', pyridine), 8.71-8.68 (t, 1H, N*H*-CH_2, *J* = 5.9), 8.39-7.48 (m, 8H, C_6H_5/pyridine), 7.79 (s, 1H, H-5, imidazole) and 5.34-5.32 (d, 2H, CH_2-NH, *J* = 5.9); δ_C (100.63 MHz, [d_6]DMSO, 298 K, TMS) 154.85 (C-2'', pyridine), 147.51 (C-2, imidazole), 144.64 (C-6'', pyridine), 143.19 (C-4'', pyridine), 135.63 (C-1', C_6H_5), 129.16, 125.13 ($C_{o,m}$, C_6H_5), 128.47 (C_p, C_6H_5), 127.80 (C-4, imidazole), 124.97, 124.10 (C-3'', C-5'', pyridine), 115.97 (C-5, imidazole) and 45.54 (CH_2); *m*/*z* = 265 (M^+), 249, 118, 93, 77 and 36.

4-phenyl-N^2-pyridin-2-ylmethyl-imidazol-1,2-diamine semihydrate **4a**: 2.12 g (5.66 mmol) of **3a** was dissolved in water (10 mL) and 1 N NaOH was added until a weak basic reaction (pH 8) occurred. The white precipitate was washed with water and was recrystallized from water-ethanol (1 : 4 ratio) yielding **4a** (1.55 g, 100%). M.p. 152 °C (decomposition). Found: C, 65.7; H, 5.9; N, 25.5. Calc. for $C_{15}H_{16}N_5O_{0.5}$ (265.31 + 9.01): C, 65.6; H, 5.7; N, 25.2%. δ_H (400.13 MHz, $CDCl_3$, 298 K, TMS) 8.72-8.70 (m, 1H, H-6'', pyridine), 7.94-7.23 (m, 8H, C_6H_5/pyridine), 7.32 (s, 1H, H-5, imidazole), 6.36-6.33 (t, 1H, N*H*–CH_2, *J* = 6.2), 5.83 (s, 2H, NH_2) and 4.77-4.76 (d, 2H, CH_2, *J* = 6.2); δ_C (100.63 MHz, $CDCl_3$, 298 K, TMS) 159.80 (C-2'', pyridine), 150.01 (C-2, imidazole), 149.01 (C-6'', pyridine), 136.86 (C-4'', pyridine), 135.67 (C-1', C_6H_5), 132.79 (C-4, imidazole), 128.2, 123.87 ($C_{o,m}$, C_6H_5), 125.52 (C_p, C_6H_5), 122.31, 121.67 (C-3'', C-5'', pyridine), 113.83 (C-5, imidazole) and 48.14 (CH_2).

(2,4-dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine **5a:** To a suspension of 1.10 g (4.01 mmol) of **4a** in 7 mL glacial acetic acid, 0.40 g (0.41 mL; 4.01 mmol) acetylacetone was added. The reaction mixture was refluxed for 2 h. Afterwards, the solvent was evaporated and 20 mL of water was added. After a few days, orange needles were obtained. Recrystallization from water-ethanol (1 : 2 ratio) yielded **5a** (0.55 g, 42%). M.p. 110 °C. Found: C, 73.2; H, 5.8; N, 21.4. Calc. for

$C_{20}H_{19}N_5$ (329.39): C, 72.9; H, 5.8; N, 21.3%. δ_H (400.13 MHz, $CDCl_3$, 298 K, TMS) 8.51-8.50 (d, 1H, H-6'', pyridine), 7.57-7.06 (m, 8H, C_6H_5/pyridine), 5.82-5.81 (d, 1H, H-3, imidazopyridazine, *J* = 1.2), 5.76-5.73 (t, 1H, N*H*-CH_2, *J* = 5.8), 4.84-4.82 (d, 2H, C*H*$_2$-NH, *J* = 5.8), 2.23 (s, 3H, C*H*$_3$-C-2) and 2.08-2.07 (d, 3H, C*H*$_3$-C-4, ^4J = 1.2); δ_C (100.61 MHz, $CDCl_3$, 298 K, TMS) 158.59 (C-2'', pyridine), 152.00 (C-7, imidazopyridazine), 149.52 (C-6'', pyridine), 143.68 (C-2, imidazopyridazine), 139.30 (C-4, imidazopyridazine), 136.94 (C-4'', pyridine), 136.44 (C-1', *C*$_6$H$_5$), 130.70, 128.24 (C$_{o,m}$, *C*$_6$H$_5$), 128.91 (C-4a, imidazopyridazine), 127.38 (C$_p$, *C*$_6$H$_5$), 122.55, 122.50 (C-3'', C-5'', pyridine), 118.18 (C-5, imidazopyridazine), 112.01 (C-3, imidazopyridazine), 48.14 (*C*H$_2$), 21.85 (*C*H$_3$-C-2) and 19.86 (*C*H$_3$-C-4).

The ligands' synthesis was simplified for **5b** and **5c** by sparing the characterization and purification of the intermediates.

(5-*t*-butyl-2,4-dimethyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine hydrate **5b**: 4.00 g (14.38 mmol) 2-amino-3-(3,3-dimethyl-2-oxo-butyl)-5-methyl-1,3,4-oxadiazolium bromide and 3.23 mL (31.68 mmol; 3.42 g) (2-pyridylmethyl)amine were stirred for 1 min on a hot plate (250 °C) and allowed to cool to room temperature. Next, the reaction mixture was extracted with $CHCl_3$ (20 mL) to separate the insoluble (2-pyridylmethyl)amine hydrobromide by-product. After filtration, the solvent was evaporated, the residue was dissolved in 20 mL of ethanol, and 1.49 mL (1.44 g; 14.38 mmol) acetylacetone and 2 mL concentrated HCl were added. After refluxing the orange solution for 2 h, the solvent was evaporated, the red-orange product was dissolved in water (20 mL) and filtered. Then, 1 N NaOH was added to the filtrate until a weak basic reaction was observed and no more product precipitated. Afterwards, the red viscid product **5b** (1.10 g, 25%) was dried *in vacuo*. Found: C, 65.75; H, 7.2; N 21.85. Calc. for $C_{18}H_{25}N_5O$ (309.41 + 18.02): C, 65.9; H, 7.7; N 21.4%. δ_H (250.13 MHz, $CDCl_3$, 298 K, TMS) 8.47-8.44 (d, 1H, H-6'', pyridine, *J* = 4.9), 7.51-7.47 (t, 1H, H-5'', pyridine, *J* = 7.7), 7.36-7.33 (d, 1H, H-3'', pyridine, *J* = 7.8), 7.07-7.04 (m, 1H, H-4'', pyridine), 5.71-5.70 (d, 1H, H-3, imidazopyridazine, ^4J = 1.1), 5.43-5.38 (t, 1H, N*H*-CH_2, *J* = 6.2), 4.75-4.72 (d, 2H, C*H*$_2$-NH, *J* = 6.2 Hz), 2.43-2.32 (d, 3H, C*H*$_3$-C-4, ^4J = 1.1), 2.13 (s, 3H, C*H*$_3$-C-2) and 1.32 (s, 9H, C(C*H*$_3$)$_3$); δ_C (62.89 MHz, $CDCl_3$, 298 K, TMS) 158.91 (C-2'', pyridine), 150.45 (C-7, imidazopyridazine), 148.88 (C-6'', pyridine), 140.63 (C-2, imidazopyridazine), 138.16

(C-4, imidazopyridazine), 137.81 (C-4a, imidazopyridazine), 136.25 (C-4'', pyridine), 122.11, 121.83 (C-3'', C-5'', pyridine), 116.37 (C-5, imidazopyridazine), 110.34 (C-3, imidazopyridazine), 48.31 (*C*H_2), 33.00 (*C*$(CH_3)_3$), 32.24 (C(*C*$H_3)_3$), 23.09 (*C*H_3-C-4) and 20.95 (*C*H_3-C-2); *m*/*z* = 309 (M^+), 294, 218, 203, 93, 65 and 41.

(2,4-dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)-pyridin-3-ylmethyl-amine **5c:**

2.50 g (8.39 mmol) 2-amino-5-methyl-3-phenacyl-1,3,4-oxadiazolium bromide and 1.88 mL (2.0 g; 18.46 mmol) (3-pyridylmethyl)amine were stirred for 1 min on a hot plate (250 °C) and allowed to cool to room temperature. Next, water was added and the white precipitate recrystallized from water-ethanol (1 : 2). 3.00 g (9.76 mmol) *N*-{4-phenyl-2-[(pyridin-3-ylmethyl)amino]imidazo-1-yl}acetamide was dissolved in 10 mL of ethanol and 2–3 mL concentrated HCl was added. The solution was refluxed for 1 h and afterwards the solvent was evaporated. The residue was dissolved in water and 1 N NaOH was added until a weak basic reaction occurred and no more product precipitated. The white product was filtered off and dried. To a suspension of 1.48 g (5.58 mmol) 4-phenyl-N^2-pyridine-3-ylmethyl-imidazol-1,2-diamine in 7 mL glacial acetic acid was added 578 µL (5.58 mmol) acetylacetone and the reaction mixture refluxed for 2 h. Afterwards, the solvent was evaporated and 20 mL of water was added. After a few days, orange needles of **5c** (0.66 g, 24%) were obtained. Found: C, 72.7; H, 6.05; N, 21.7. Calc. for $C_{20}H_{19}N_5$ (329.39): C, 72.9; H, 5.8; N, 21.3%. δ_H (250.13 MHz, $CDCl_3$, 298 K, TMS) 8.65 (s, 1H, C-2'', pyridine), 8.46-8.45 (d, 1H, C-6'', pyridine, *J* = 3.8), 7.75-7.62 (d, 1H, C-4'', pyridine, *J* = 7.8), 7.52-7.40 (d, 2H, C_o C_6H_5, *J* = 7.0), 7.36-7.30 (m, 4 H, C-5'', pyridine/C_6H_5), 5.86 (s, 1H, H-3, imidazopyridazine), 4.98-4.94 (t, 1H, N*H*, *J* = 5.8), 5.21-5.16 (d, 2H, CH_2, *J* = 5.8), 2.23 (s, 3H, CH_3-C-2) and 2.12 (s, 3H, CH_3-C-4); δ_C (75.39 MHz, $CDCl_3$, 298 K, TMS) 151.22 (C-7, imidazopyridazine), 148.87 (C-2'', pyridine), 148.11 (C-6'', pyridine), 142.34 (C-2, imidazopyridazine), 138.53 (C-4, imidazopyridazine), 135.33 (C-3'', pyridine), 135.20 (C-5'', pyridine), 134.70 (C-1', *C*$_6H_5$), 129.72, 127.36 ($C_{o,m}$, *C*$_6H_5$), 128.04 (C-4a, imidazopyridazine), 126.55 (C_p, *C*$_6H_5$), 122.92 (C-4'', pyridine), 117.27 (C-5, imidazopyridazine), 111.15 (C-3, imidazopyridazine), 44.20 (*C*H_2), 20.86 (*C*H_3-C-2) and 18.94 (*C*H_3-C-4).

4.4.3 Complex Synthesis

Preparation of **6a:** To an orange solution of 0.55 g (1.66 mmol) (2,4-dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine **5a** in THF (20 mL) were added carefully (at −78 °C) 1.0 mL (1.66 mmol) *n*butyllithium (1.6 M in *n*hexane). The purple reaction mixture was stirred at −78 °C for another 30 min and was then allowed to warm to room temperature. At room temperature, an orange solution of 0.56 g (0.83 mmol) chloro-1,5-cyclooctadiene iridium(I) dimer in THF (10 mL) was added. The green solution was stirred for 16 h. Next, the solvent was evaporated and the residue dissolved in toluene, filtered and washed with ether. A dark green crystalline product **6a** (0.45 g, 44%) was obtained at −30 °C from the combined filtrates. Found: C, 53.2; H, 5.1; N, 10.7. Calc. for $C_{28}H_{30}IrN_5$ (628.79): C, 53.5; H, 4.8, N, 11.1%. δ_H (300.13 MHz, CD_2Cl_2, 298 K, TMS) 8.03-8.02 (d, 2H, H-6'', pyridine, *J* = 5.5), 7.72-7.67 (t, 1H, pyridine, *J* = 7.7), 7.50-7.45 (t, 2H, C_6H_5, *J* = 8.0), 7.35-7.21 (m, 3H, C_6H_5/pyridine), 7.12–7.10 (m, 2H, C_6H_5), 5.93, 5.90 (2 s, 1H, H-3, imidazopyridazine), 5.24, 5.22 (2s, 2H, CH_2-NH), 3.97 (br s, 2H, C*H*, cod), 3.17 (br s, 2H, C*H*, cod), 2.26 (s, 3H, CH_3-C-2/4), 2.13 (s, 3H, CH_3C-4/2), 2.25–2.09 (br m, 4H, CH_2, cod) and 1.60–1.57 (br d, 4H, CH_2, cod); δ_C (75.48 MHz, CD_2Cl_2, 298 K, TMS) 146.60, 139.35, 137.22, 136.91, 134.38, 130.57, 130.42, 128.75, 128.04, 127.06, 122.22, 121.07 ($C_{o,m,p}$, C_6H_5, pyridine, imidazopyridazine), 118.64 (C-5, imidazopyridazine), 112.20, 111.93 (C-3, imidazopyridazine), 66.83 (4 x *C*H, cod), 55.14 (*C*H_2-N), 31.77 (4 x *C*H_2, cod), 21.70, 21.31 (*C*H_3-C-2/4) and 19.84 (*C*H_3-C-4/2).

Preparation of **6b:** To an orange solution of 0.20 g (0.65 mmol) (5-*t*-butyl-2,4-dimethyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine **5b** in THF (5 mL) was added a yellow solution of 0.21 g (0.32 mmol) 1,5-cyclooctadiene-methoxy iridium(I) dimer in THF (10 mL). The dark green solution was immediately concentrated to dryness *in vacuo*, yielding **6b** (0.39 g, 100%). Found: C, 51.5; H, 6.1; N, 11.2. Calc. for $C_{26}H_{34}IrN_5$ (608.80): C, 51.3; H, 5.6; N, 11.5%. δ_H (250.13 MHz, [d_8]THF, 298 K, TMS) 8.15-8.13 (d, 1H, H-6'', pyridine, *J* = 4.7), 7.59-7.53 (t, 1H, H-5'', pyridine, *J* = 7.4), 7.39-7.36 (d, 1H, H-3'', pyridine, *J* = 7.8), 7.07-7.02 (t, 1H, H-4'', pyridine, *J* = 8.3), 5.76 (s, 1H, H-3, imidazopyridazine), 5.08 (s, 2H, CH_2-N), 4.12 (br s, 2H, C*H*, cod), 3.55-3.49 (m, 2H, C*H*, cod), 2.49 (d, 3H, CH_3-C-2), 2.22 (s, 3H, CH_3-C-4), 2.03 (br s, 4H, CH_2, cod), 1.59 (br s, 4H, CH_2, cod) and 1.24 (s, 9H, C(CH_3)$_3$); δ_C (75.39

MHz, C_6D_6, 298 K, TMS) 147.42, 139.91, 139.00, 136.33, 121.71, 121.18, 118.53 (C-5, imidazopyridazine), 110.04 (C-3, imidazopyridazine), 68.15 (*C*H_2-N), 57.04, 53.35, 52.33 (*C*H cod), 34.78 (*C*$(CH_3)_3$), 32.77 (C(*C*$H_3)_3$), 32.46, 31.95, 26.17 (*C*H_2 cod), 23.22 (*C*H_3-C-2) and 21.00 (*C*H_3-C-4). Even though different solvents, such as C_6D_6, [d_8]THF and CD_2Cl_2, were tested and up to 10 000 scans performed, not all of the quaternary C atoms could be detected.

Preparation of **6c**: To an orange solution of 0.56 g (1.70 mmol) (2,4-dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-3-ylmethyl-amine **5c** in THF (15 mL) was added carefully (at −78 °C) 1.06 mL (1.70 mmol) *n*butyllithium (1.6 M in *n*hexane). The purple reaction mixture was stirred at −78 °C for another 30 min and then allowed to warm to room temperature. At room temperature, an orange solution of 0.57 g (0.85 mmol) chloro-1,5-cyclooctadiene iridium(I) dimer in THF (10 mL) was added. The green solution was stirred for 16 h, the solvent was evaporated, and the residue was dissolved in toluene, filtered and washed with ether. From the combined filtrates in toluene, a dark green crystalline product **6c** (0.33 g, 32%) was obtained at −30 °C. Found: C, 53.25; H, 5.3; N, 10.7. Calc. for $C_{28}H_{30}IrN_5$ (628.79): C, 53.5; H, 4.8; N 11.1%. δ_H (250.13 MHz, $CDCl_3$, 298 K, TMS) 8.61 (s, 1H, pyridine), 8.41-8.39 (d, 1H, pyridine, *J* = 4.3), 7.69-7.66 (d, 1H, pyridine, *J* = 5.5), 7.51-7.12 (m, 6H, pyridine, C_6H_5), 5.75 (s, 1H, H-3, imidazopyridazine), 4.95 (s, 2H, C*H*$_2$), 4.41 (br s, 2H, C*H*, cod), 4.08 (br s, 2H, C*H*, cod), 2.48 (s, 3H, C*H*$_3$-C-2), 2.28 (s, 3H, C*H*$_3$-C-4), 2.33-2.16 (m, 4H, C*H*$_2$, cod) and 1.82-1.61 (m, 4 H, C*H*$_2$, cod); δ_C (62.89 MHz, $CDCl_3$, 298 K, TMS) 160.41 (C-7, imidazopyridazine), 156.86 (C-3'', pyridine), 148.78, 147.52 (C-2'', C-6'', pyridine), 141.90 (C-2, imidazopyridazine), 138.11 (C-4'', pyridine), 136.15 (C-1', *C*$_6$H$_5$), 134.54 (C-5'', pyridine), 130.02, 127.94 (C$_{o,m}$, *C*$_6$H$_5$), 128.98 (C-4a, imidazopyridazine), 127.52 (C$_p$, *C*$_6$H$_5$), 119.20 (C-5, imidazopyridazine), 110.17 (C-3, imidazopyridazine), 62.86, 53.12 (*C*H, cod), 46.03 (*C*H_2), 31.65, 30.40 (*C*H_2, cod), 20.29 (*C*H_3-C-2) and 19.03 (*C*H_3-C-4).

Preparation of **7a:** Into a pressure tube containing an orange solution of 0.21 g (0.65 mmol) (2,4-dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine **5a** in THF (10 mL) was added 0.21 g (0.32 mmol) 1,5-cyclooctadiene-methoxy iridium(I) dimer. The solution immediately changed its color to dark green. The solution was heated at 50 °C for several days, while its color changed to brown and

red crystals formed. The crystalline material **7a** (0.12 g, 30%) was filtered off and washed three times with THF. Found: C, 53.2; H, 4.8; N, 10.8. Calc. for $C_{56}H_{58}Ir_2N_{10}$ (1255.56): C, 53.6; H, 4.7; N, 11.2%. (**7a** is insoluble in all common solvents, such as methanol, isopropanol, CH_2Cl_2, THF, toluene, benzene and DMSO; due to this, no solution NMR data is available.) MAS solid state ^{13}C NMR: δ_C 166.31, 149.78, 148.29, 143.20, 137.02, 128.51, 122.91 (imidazopyridazine, pyridine, C_6H_5), 118.08 (C-5, imidazopyridazine), 110.73 (C-3, imidazopyridazine), 75.37 (*C*H), 67.64, 63.00, 54.69 (*C*H, cod), 32.85, 26.28 (CH_2, cod) and 21.84 (CH_3-C-2/4).

Preparation of **7b**: Into a pressure tube containing an orange solution of 0.20 g (0.65 mmol) (5-*t*-butyl-2,4-dimethyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine **5b** in hexane (10 mL) was added 0.21 g (0.32 mmol) 1,5-cyclooctadiene-methoxy iridium(I) dimer. The solution immediately changed its color to dark green. After several weeks, a red crystalline material, **7b** (0.11 g, 28%) was obtained. Found: C, 51.2; H, 5.7; N, 11.2. Calc. for $C_{52}H_{66}Ir_2N_{10}$ (1215.58): C, 51.3; H, 5.5; N, 11.5%. δ_H (250.13 MHz, [d_8]THF, 298 K, TMS) 9.38-9.35 (d, 1H, pyridine, *J* = 7.8), 8.14-8.11 (t, 1H, pyridine, *J* = 8.3), 7.59-7.57 (d, 1H, pyridine, *J* = 5.6), 7.19–7.14 (t, 1H, pyridine, *J* = 7.1), 5.75–5.74 (m, 2H, C*H*-N, H-3, imidazopyridazine), 2.69 (m, 2H, C*H* cod), 2.37–2.33 (m, 2H, C*H* cod), 2.59 (s, 3H, CH_3-C-2/4), 1.79 (s, 3H, CH_3-C-4/2), 1.99-1.86 (m, 4H, CH_2 cod), 1.49-1.28 (m, 4H, CH_2 cod) and 1.53 (s, 9H, C(CH_3)$_3$); δ_C (62.89 MHz, [d_8]THF, 298 K, TMS) 166.67, 148.12, 144.90, 136.04, 127.78 (C-7, C-2, C-4, C-4a, imidazopyridazine; C-1'', pyridine), 143.56, 134.74, 126.71, 121.46 (pyridine), 116.59 (C-5, imidazopyridazine), 109.85 (C-3, imidazopyridazine), 74.88 (*C*H), 65.56, 67.96, 54.03, 52.08 (*C*H, cod), 33.42, 33.11, 30.17, 28.82 (CH_2, cod), 32.71 (*C*(CH)$_3$), 31.98 (C(*C*H)$_3$), 22.40 and 20.55 (CH_3-C-2/4).

Supporting Information available

X-Ray Crystal Structure Data are available.

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4.5 References

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[9] X-ray crystal structure analysis of **6a**, crystal size 0.38 x 0.10 x 0.05 mm, symmetry space group P-1, triclinic, a = 7.9017(4), b = 8.9335(6), c = 16.8930(10) Å, ß= 80.191(6)°, V = 1174.39(12) Å^3, Z = 2, $\rho_{cald.}$ = 1.778 g/cm^3, 14134 reflections, 4192 independent reflections, R = 0.0200 [I > 2σ(I)], wR2 (all data) = 0.0487, 620 parameters, CCDC-729910 contains the supplementary crystallographic data for this publication.

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[11] X-ray crystal structure analysis of **7a**, crystal size 0.26 x 0.20 x 0.20 mm, symmetry space group P21/n, monoclinic, a = 15.5840(7), b = 22.6799(8), c = 26.5520(12) Å, ß= 98.245(3)°, V = 9287.6(7) Å^3, Z = 8, $\rho_{cald.}$ = 1.796 g/cm^3, 17540 reflections, 9598 independent reflections, R = 0.0501 [I > 2σ(I)], wR2 (all data) = 0.0924, 1233 parameters. CCDC-729911 contains the supplementary crystallographic data for this publication.

[12] X-ray crystal structure analysis of **7b**, crystal size 0.64 x 0.53 x 0.19 mm, symmetry space group P21/n, monoclinic, a = 14.2110(6), b = 23.5720(10), c = 14.6060(6) Å, ß = 103.436(3)°, V = 4758.8(3) Å^3, Z = 4, $\rho_{cald.}$ = 1.697 g/cm^3, 8987 reflections, 6493 independent reflections, R = 0.0361 [I > 2σ(I)], wR2 (all data) = 0.0764, 587 parameters. CCDC-729912 contains the supplementary crystallographic data for this publication.

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5. Novel Amido-Complexes for the Efficient Asymmetric Hydrogenation of Imines

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Abstract: Novel N,N,P-ligand stabilized rhodium complexes exhibiting high activities and enantioselectivities in the asymmetric hydrogenation of N-aryl imines are introduced. The ligands were synthesized from inexpensive starting materials and their modular design allows for the introduction of a broad variety of substitution patterns. Additionally, a rather low catalyst loading could be employed.

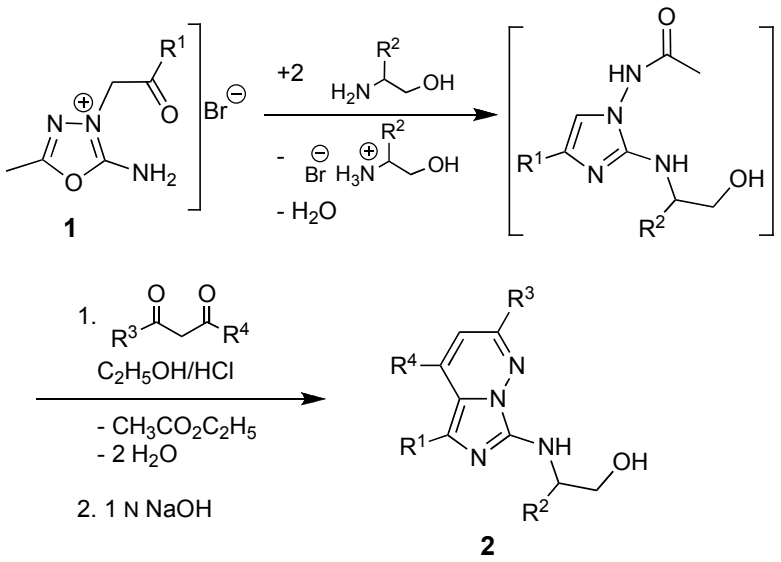
5.1 Introduction

Given that 80% of the pharmaceuticals in the product-pipeline are chiral and that the launch of enantiopure drugs will be facilitated, there is an increasing demand for chiral intermediates such as amines, alcohols or acids.[1] Asymmetric hydrogenation technologies, which are (atom)economic and easily upscalable, provide an excellent access to those substances.[2] During the last decade various enantioselective imine hydrogenation catalysts were introduced,[3-7] most of them being cationic iridium complexes based on neutral P,N- ligands, for instance phosphino-oxazolines or P,N-ferrocenyles.[3] Neutral ligands might be easier replaced by strongly coordinating substrates like imines and consequently we became interested in developing anionic ligands for the enantioselective hydrogenation of imines.

Recently, we introduced imidazo[1,5-*b*]pyridazine- substituted amido-ligands, which stabilize late and early transition metal complexes.[8] Chiral imidazo[1,5-*b*]pyridazine-substituted amino alcohols **2** are of special interest therein. They can be synthesized in a one-pot approach via the nucleophilic ring transformation of oxadiazolium halides **1** with amino alcohols followed by a cyclocondensation reaction with 1,3-diketones (Scheme 1).

The resulting iridium amido-complexes exhibit good activities and excellent enantioselectivities in the asymmetric ketone hydrogenation.[9]

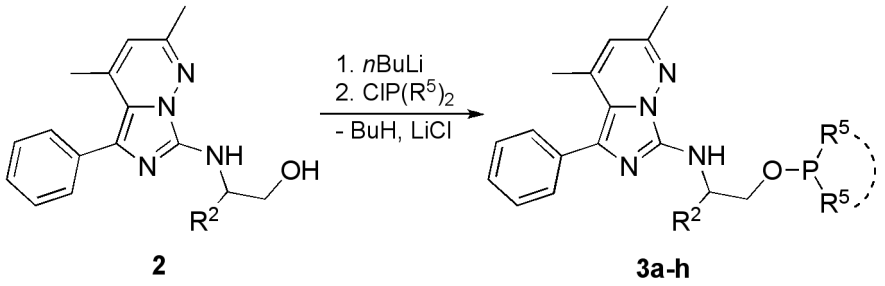
Herein, the synthesis of novel imidazo[1,5-*b*]pyridazine-substituted amines **3** is reported. Upon deprotonation they act as monoanionic tridentate amido-ligands and are suitable for the stabilization of group 9 metal complexes. The chiral amido-complexes **4** show high efficiency and very good enantioselectivity in the asymmetric hydrogenation of imines.[10]



Scheme 1: One-pot synthesis of **2**.

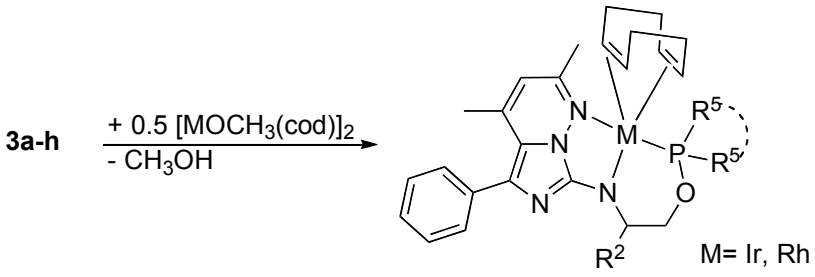
5.2 Results and Discussion

The novel amines **3** can be synthesized via P-functionalization of **2** in good to excellent yields and high purities (Scheme 2). Lithiation with *n*BuLi selectively occurs at the O-atom of the hydroxyl group. Subsequently one equivalent of dialkyl-, diaryl-chlorophosphine or ethylene chlorophosphite is added, giving rise to **3a-h** as orange viscous products.



Scheme 2: Synthesis of **3a-h (3a:** R^2=*i*Bu, R^5=Ph; **3b:** R^2=*i*Bu, R^5=*i*Pr**; 3c:** R^2=*i*Bu, $R^5 \cap R^5$= OCH_2-CH_2O; **3d:** R^2=Me, R^5=*i*Pr; **3e:** R^2=Bn, R^5=*i*Pr; **3f:** R^2=*i*Bu, R^5=Et; **3g:** R^2=*i*Bu, R^5=*t*Bu; **3h:** R^2=*i*Bu, R^5=Cy).

The amido-complexes **4a-j** can be obtained via alcohol elimination route with $[MOCH_3(cod)]_2$[11] (M=Ir, Rh) (Scheme 3). Addition of 0.5 equiv. of the metal precursor to a solution of **3a-h** in THF gives rise to **4a-j**, which is accompanied by a color change to blue/green. The NMR spectra show a single signal set for the deprotonated ligand and 1,5-cyclooctadiene. The Rh(I)-P-coupling constant of 158.40 Hz (**4a**) is in accordance with the literature.[12]



Scheme 3: Synthesis of amido-complexes **4a-j (M=Rh: 4a:** R^2=*i*Bu, R^5=Ph; **4b:** R^2=*i*Bu, R^5=*i*Pr; **4c:** R^2=*i*Bu, $R^5 \cap R^5$= OCH_2-CH_2O; **4d:** R^2=Me, R^5=*i*Pr; **4e:** R^2=Bn, R^5=*i*Pr; **4f:** R^2=*i*Bu, R^5=Et; **4g:** R^2=*i*Bu, R^5=*t*Bu; **4h:** R^2=*i*Bu, R^5=Cy; **M=Ir: 4i:** R^2=*i*Bu, R^5=*i*Pr; **4j:** R^2=*i*Bu, $R^5 \cap R^5$= OCH_2-CH_2O).

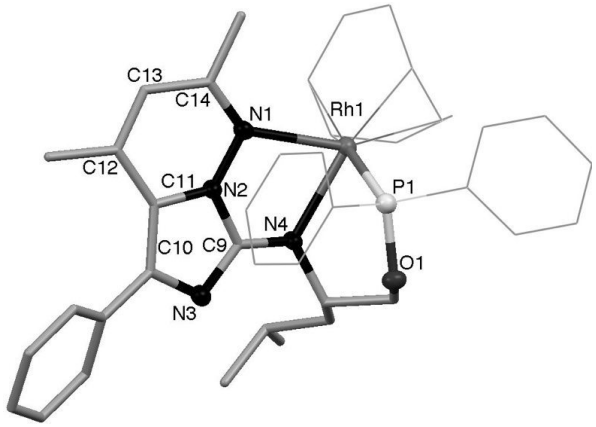


Figure 1. Molecular structure of **4a**; selected bond lengths [Å] and -angles [°]: N4-Rh1 2.233(2), N1-Rh1 2.349(2), P1-Rh1 2.2423(8), O1-P1 1.608(2); N1-Rh1-N4 74.02(8), N4-Rh1-P1 79.67(7), N2-N1-Rh1 107.84(16), C9-N4-Rh1 113.83(18), O1-P1-Rh1 112.30(8).

An X-ray crystal structure analysis of **4a** was performed to determine the molecular structure (Figure 1). The monoanionic ligand coordinates the Rh-atom via a five-membered chelate (Rh, N4, C9, N2, N1). The complex is further stabilized by coordination of the P-atom (P1-Rh1). Since the N4-Rh1 bond length of 2.233 Å is significantly shorter than the N1-Rh1 bond length (2.350 Å), the anionic charge of the ligand is localized at the amido-N-atom. The phenyl substituents of the P-atom are orientated 93.16° to each other and point away from the imidazopyridazine plane.

Complexes **4b-c** (Rh) and **4i-j** (Ir) (Scheme 3) were utilized for the asymmetric hydrogenation of *N*-(1-phenylethylidene)aniline **5a** at 40 °C and 60 bar H_2-pressure (Table 1). Herein, the dialkyl-phosphine- substituted rhodium amido-complex **4b** was the most promising catalyst system. Upon addition of KO*t*Bu complete conversion and 82% ee could be achieved in 24 h with a catalyst loading of only 0.1 mol%.

Table 1: Results of the asymmetric hydrogenation of **5a** with **4**.

No.	Catalyst	Base	Yield[a] [%]	ee[b] [%]
1	**4b**	-	0	-
2	**4b**	KO*t*Bu	>99	82
3	**4c**	-	46	rac
4	**4c**	KO*t*Bu	41	21
5	**4i**	-	0	-
6	**4i**	KO*t*Bu	37	17
7	**4j**	-	0	-
8	**4j**	KO*t*Bu	98	30

0.1 mol% **4**, 24 h, 40 °C, 60 bar H_2; [a] determined *via* GC; [b] determined *via* HPLC

The selectivity in the asymmetric hydrogenation of **5a** with **4b** could be increased from 82% (40°C, 60 bar) to 90% (rt, 20 bar) by optimization of the reaction conditions. A pressure dependence of the selectivity was not observed (5-60 bar). The addition of an excess of KO*t*Bu (see Supporting Information) generates the best activity and enantioselectivity.

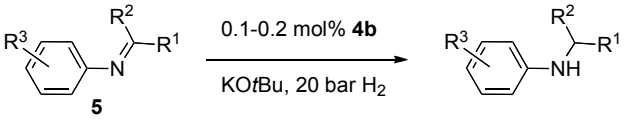
Due to the modular design of **4**, the steric and electronic properties of the ligand can easily be fine tuned towards the substrate. Herein the influence of amino alcohol- and P-substituents on the activity and enatioselectivity was investigated (Table 2). The combination of electron-donating phosphine substituents (*i*Pr, Cy) and amino alcohols (*i*Bu) gave the best results in the hydrogenation of **5a** (Table 2, entry: 2, 7).

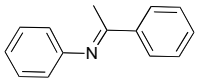
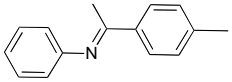
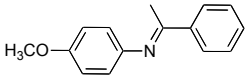
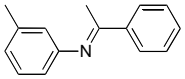
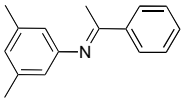
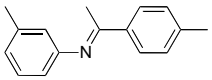
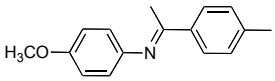
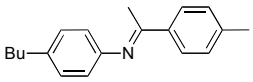
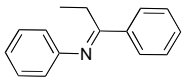
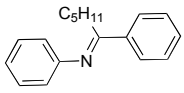
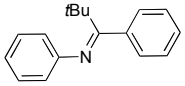
Table 2: Catalyst screening for the hydrogenation of **5a** with 0.1 mol% **4**.

No.	Catalyst	Yield[a] [%]	ee[b] [%]
1	**4a**	62	70
2	**4b**	>99	90
3	**4d**	79	81
4	**4e**	63	84
5	**4f**	85	85
6	**4g**	88	86
7	**4h**	96	90

KO*t*Bu, 24 h, 20 °C, 20 bar H_2; [a] determined *via* GC; [b] determined *via* HPLC

Table 3: Hydrogenation of *N*-aryl imines with **4b**.



No.	Imine		Yield[a] [%]	ee[b] [%]	Lit. ee [%]
1#	**5a**		>99	90	95[4e]
2	**5b**		97	86	94[3f]
3	**5c**		>99	82	97[4e]
4	**5d**		>99	89	91[3f]
5*#	**5e**		98	90	99[4d]
6	**5f**		>99	87	no data
7#	**5g**		>99	75	97[4e]
8#	**5h**		>99	83	no data
9	**5i**		>99	76	78[3e]
10*#	**5j**		>99	74	no data
11*	**5k**		>99	57	no data

0.1 mol% (*0.2 mol%) **4b**, KO*t*Bu, 48 h (#24 h), rt, 20 bar H_2; [a] determined *via* GC; [b] determined *via* HPLC. [3e]0.5 mol% Ir-complex, 25°C, 20 bar H_2. [3f]1 mol% Ir-complex, 10°C, 1 bar H_2.[4d]1 mol% $[Ir(cod)_2]$BArF, 2 mol% (*S*)-PipPhos, rt, 1 bar H_2. [4e]1mol% Ir-complex, 20°C, 20 bar H_2.

High enantioselectivities, which are similar to the best known literature systems[4d,e;3e,f], could be obtained in the asymmetric hydrogenation of various *N*-aryl imines **5** with **4b** (Table 3).

Due to the anionic nature of the supporting ligand a higher hydrogenation efficiency in comparison to most of these literature systems was observed. The catalyst loading could be reduced to 0.1-0.2 mol% (typically 1 mol% in the literature).

The high efficiency and enantioselectivity could furthermore be verified in a preparative experiment. Therein 2.5 g of **5a** was isolated (83% yield and 89% ee).

5.3 Conclusions

In conclusion the reported amido-complexes represent a novel class of efficient and easily accessible catalysts for the asymmetric hydrogenation of imines. Due to the modular ligand design, broad substitution patterns can be realized. The high efficiency and good selectivity combined with the novel structural motif opens up new prospects for the enantioselective hydrogenation of imines.

5.4 Experimental Section

5.4.1 General Procedure for the asymmetric hydrogenation

Stock solutions of the pre-catalysts (3.01 µmol/mL) were prepared in THF via alcohol elimination reaction of the ligand (stock solution in THF) and 0.5 equiv. of $[MOCH_3(cod)]_2$ (M= Rh, Ir). Stock solutions of the imines (1.51 mmol/mL) were prepared in THF. The solutions were prepared and stored in a glove box. A high-pressure steel autoclave (Parr Instruments; 300 mL, 200bar, 350 °C) with an aluminum insert for multiple reaction tubes (5 or 20) was taken into a glove box. Then the reaction tube (placed in a 20- or 5-well insert for the autoclave, equipped with a magnetic stir bar) was loaded with additive (base if required), the pre-catalyst-solution (e.g. 200µL = 0.1 mol%) and 400 µL (0.60 mmol) of the substrate solution. Then the autoclave was sealed and taken out of the glove box. The autoclave was attached to a high-pressure hydrogen line and purged with H_2. The autoclave was sealed under the appropriate H_2 pressure and the mixture was stirred for e.g. 24 h at the appropriate pressure at room temperature or at the appropriate temperature (external heating mantle). In order to stop the hydrogenation reaction, the pressure was released and water and dodecane (standard for GC) were added to the reaction

solution. The samples were extracted with diethyl ether (3 mL) and the organic phase was centrifugalized at 12.000 rpm and filtered through 0.2 µm PTFE-syringe filters. This solution was directly used for determination of the conversion (GC, Lipodex E or Chirasil-DEX column). For HPLC (Chiralpak IB column) purposes the samples were diluted (40x) with diethyl ether (determination of ee).

Supporting Information available

Supporting information including detailed experimental section and crystallographic data is available (Refer to 5.6).

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5.5 References

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5.6 Supporting Information

5.6.1 General

Syntheses of the starting materials and ligands were performed under standard conditions. Complex syntheses were conducted in oven (95 °C) and in vacuum dried glassware under an inert atmosphere of dry argon 5.0 *via* standard Schlenk or glove box techniques. NMR spectra were recorded on a Bruker ARX 250 (250 MHz) or on a Varian Inova 300/400 (300 or 400 MHz) NMR-spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance resulting from incomplete deuteration as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet or combinations thereof), integration and coupling constant. Elemental analysis was performed with a Vario elementar EL III elemental analyzer. Non-

halogenated solvents were distilled from sodium benzophenone ketyl and halogenated solvents from P_2O_5. Deuterated solvents were obtained from Cambridge Isotope Laboratories and were degassed, dried and distilled prior to use. All chemicals were purchased from commercial vendors and used without further purification.

5.6.2 Ligand Synthesis

N-(1-((diphenylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3a:** 0.87 g (2.57 mmol) of 2-((2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-yl)amino)-4-methylpentan-1-ol was dried *in vacuo* and dissolved in 30 mL of dry diethyl ether/THF (1:1). The orange solution was cooled to -78 °C, then 1.61 mL (2.57 mmol) of *n*BuLi (1.6 M in hexane) was added cautiously. Thereby, the solution changed its color to dark brown. The solution was stirred at -78 °C for another 30 minutes and warmed to room temperature. Then 0.48 mL (2.57 mmol) of chlorodiphenylphosphine was added and the solution was stirred for 12 h at room temperature (color changes again to orange). The orange solution was evaporated to dryness and the orange residue was extracted with 15 mL of diethyl ether (2x), the combined filtrates were evaporated to dryness yielding **3a** (0.78 g, 58%) as an orange viscous product. Found: C, 72.6; H, 7.7; N, 9.2. Calc. for $C_{32}H_{35}N_4OP*C_4H_8O$ (522.62 + 72.11): C, 72.7; H 7.3; N 9.4%. δ_H (250.13 MHz, CD_2Cl_2, 298 K, TMS) 7.50-7.25 (m, 15H, 3 x C_6H_5), 5.95-5.94 (d, 1H, H-3, imidazopyridazine, *J* = 1.2), 4.84-4.81 (d, 1H, N*H*, *J* = 9.5), 4.40-4.28 (m, 1H, HN-C*H*), 4.11-3.93 (m, 2H, CH_2O), 2.31 (s, 3H, CH_3-C-2), 2.20-2.19 (d, 3H, CH_3-C-4, *J* = 1.1), 1.85-1.48 (m, 3H, CH_2C*H*$(CH_3)_2$) and 0.98-0.95 (dd, 6H, CH(CH_3)$_2$), *J* = 6.6, 1.4); δ_C (62.90 MHz, CD_2Cl_2, 298 K, TMS) 151.81 (C-7, imidazopyridazine), 143.29 (C-2, imidazopyridazine), 139.19 (C-4, imidazopyridazine), 130.62, 130.61, 130.51, 130.27, 129.49, 129.45, 128.59, 128.49, 128.03, 127.08 (C-4a, imidazopyridazine, 3 x *C*$_6$H$_5$), 117.81 (C-5, imidazopyridazine), 111.67 (C-3, Imidazopyridazine), 72.41, 72.14 (*C*H$_2$O), 68.13 (THF), 52.39, 52.26 (*C*H-NH), 41.72 (CH*C*H$_2$CH), 25.96 (THF), 25.28 (*C*H$(CH_3)_2$), 23.33, 22.48 (CH(*C*H$_3$)$_2$), 21.58 (*C*H$_3$-C-2) and 19.68(*C*H$_3$-C-4); δ_P (101.26 MHz, CD_2Cl_2, 298 K, TMS) 113.19.

N-(1-((diisopropylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3b**: 1.00 g (2.95 mmol) of 2-((2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-yl)amino)-4-methylpentan-1-ol was dried *in vacuo*

and dissolved in 30 mL of dry diethyl ether/THF (1:1). The orange solution was cooled to -78 °C, then 1.84 mL (2.95 mmol) of *n*BuLi (1.6 M in hexane) was added cautiously. Thereby, the solution changed its color to dark brown. The solution was stirred at -78 °C for another 30 minutes and warmed to room temperature. Then 0.47 mL (2.95 mmol) of chlorodiisopropylphosphine was added and the solution was stirred for 12 h at room temperature (color changes again to orange). The orange solution was evaporated to dryness and the orange residue was extracted with 15 mL of hexane (2x), the combined filtrates were evaporated to dryness yielding **3b** (1.19 g, 89%) as an orange viscous product. Found: C, 69.6; H, 9.7; N, 11.75. Calc. for $C_{26}H_{39}N_4OP$*0.5 C_6H_{14} (454.59 + 43.09): C, 69.9; H 9.3; N, 11.3%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.47-7.45 (d, 2H, C_6H_5, *J* = 8.4), 6.99-6.94 (t, 2H, C_6H_5, *J* = 7.8), 6.86-6.83 (m, 1H, C_6H_5), 5.01-5.01 (d, 1H, H-3, imidazopyridazine, *J* = 0.6), 4.81-4.77 (d, 1H, N*H*, *J* = 9.3), 4.29-4.25 (m, 1H, C*H*-NH), 3.76-3.58 (m, 2H, CH_2O), 1.72 (s, 3H, CH_3-C-2), 1.59 (s, 3H, CH_3-C-4), 1.33-1.22 (m, 5H, $CH_2CH(CH_3)_2$, $P(CH(CH_3)_2)_2$), 0.91-0.80 (m, 6H, $CH(CH_3)_2$) and 0.73-0.60 (m, 12H, $P(CH(CH_3)_2)_2$); δ_C (75.39 MHz, $CDCl_3$, 298 K, TMS) 152.02 (C-7, imidazopyridazine), 143.91 (C-2, imidazopyridazine), 139.68 (C-4, imidazopyridazine), 137.09 (C1', C_6H_5), 131.11, 128.69 ($C_{o,m}$, C_6H_5), 129.47 (C-4a, imidazopyridazine), 127.66 (C_p, C_6H_5), 118.26 (C-5, imidazopyridazine), 112.01 (C-3, imidazopyridazine), 74.80, 74.58 (CH_2O), 52.91, 52.79 (*C*H-NH), 42.46 (CH_2), 32.44 (CH_2, hexane), 29.10, 29.08, 28.88, 28.86 ($P(CH(CH_3)_2)_2$), 25.80 ($CH(CH_3)_2$), 24.05, 23.49 ($CH(CH_3)_2$, hexane), 22.19 (CH_3-C-2), 20.33 (CH_3-C-4), 18.99, 18.96, 18.72, 18.69, 17.90, 17.84, 17.79, 17.73 ($P(CH(CH_3)_2)_2$) and 14.98 (CH_3 hexane); δ_P (121.37 MHz, $CDCl_3$, 298 K, TMS) 152.61.

N-(1-((1,3,2-dioxaphospholan-2-yl)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3c**: 0.57 g (1.68 mmol) of 2-((2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-yl)amino)-4-methylpentan-1-ol was dried *in vacuo* and dissolved in 30 mL of dry diethyl ether/THF (1:1). The orange solution was cooled to -78 °C, then 1.05 mL (1.68 mmol) of *n*BuLi (1.6 M in hexane) was added cautiously. Thereby, the solution changed its color to dark brown. The solution was stirred at -78 °C for another 30 minutes and warmed to room temperature. Then 0.15 mL (1.68 mmol) of ethylene chlorophosphite was added and the solution was stirred for 12 h at room temperature (color changes again to orange). The orange solution was evaporated to dryness and the orange residue was extracted with 20 mL of

diethyl ether (2x), the combined filtrates were evaporated to dryness yielding **3c** (0.58 g, 81%) as an orange viscous product. Found: C, 61.5; H, 7.2; N, 12.0. Calc. for $C_{22}H_{29}N_4O_3P$*0.5 $C_4H_{10}O$ (428.46 + 37.06): C, 61.9; H, 7.4; N, 12.0%. δ_H (250.13 MHz, CD_2Cl_2, 298K, TMS) 7.47-7.43 (m, 2H, H_o, C_6H_5), 7.34-7.22 (m, 3H, $H_{m,p}$, C_6H_5), 5.89-5.88 (d, 1H, H-3, imidazopyridazine, *J* = 1.1); 4.86 (br s, 1H, N*H*), 4.25-3.76 (m, 11H, THF/C*H*$_2$O/O-C*H*$_2$-C*H*$_2$-O), 2.25 (s, 3H, C*H*$_3$-C-2), 2.10-2.09 (d, 3H, C*H*$_3$-C-4, *J* = 1.1), 1.62-1.36 (m, 7H, THF/C*H*$_2$C*H*$(CH_3)_2$) and 0.88-0.84 (dd, 6H, CH(C*H*$_3)_2$, *J* = 3.2); δ_C (62.90 MHz, CD_2Cl_2, 298K, TMS) 151.97 (C-7, imidazopyridazine), 142.79 (C-2, imidazopyridazine), 139.05 (C-4, imidazopyridazine), 130.73 (C-1´, *C*$_6H_5$), 130.34, 127.91 ($C_{o,m}$, *C*$_6H_5$), 128.17 (C-4a, imidazopyridazine), 127.09 (C_p, *C*$_6H_5$), 117.67 (C-5, imidazopyridazine), 111.85 (C-3, imidazopyridazine), 67.93 (THF), 65.20, 65.06 (*C*H_2O), 64.58, 64.53, 64.44, 64.39 (O-*C*H_2-*C*H_2-O), 51.41, 51.35 (*C*H-NH), 41.17 (CH-*C*H_2-CH), 25.76 (THF), 24.99 (*C*H$(CH_3)_2$), 23.13, 22.24 (CH(*C*$H_3)_2$), 21.39 (*C*H_3-C-2) and 19.46 (*C*H_3-C-4); δ_P (101.26 MHz, CD_2Cl_2, 298 K, TMS) 132.92.

N-(1-((diisopropylphosphino)oxy)propan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3d**: 1.00 g (3.37 mmol) of 2-((2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-yl)amino)propan-1-ol was dried *in vacuo* and dissolved in 30 mL of dry diethyl ether/THF (1:1). The orange solution was cooled to -78 °C, then 2.10 mL (3.37 mmol) of *n*BuLi (1.6 M in hexane) was added cautiously. Thereby, the solution changed its color to dark brown. The solution was stirred at -78 °C for another 30 minutes and warmed to room temperature. Then 0.53 mL (3.37 mmol) of chlorodiisopropylphosphine was added and the solution was stirred for 12 h at room temperature (color changes again to orange). The orange solution was evaporated to dryness and the orange residue was extracted with 15 mL of hexane (2x), the combined filtrates were evaporated to dryness yielding **3d** (1.17 g, 84%) as an orange viscous product. Found: C, 66.9; H, 8.9; N, 11.8. Calc. for $C_{23}H_{33}N_4OP$*C_4H_8O (412.51 + 72.11): C, 66.9; H, 8.5; N, 11.6%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.57-7.54 (d, 2H, H_o, C_6H_5), 7.41-7.27 (m, 3H, $H_{m,p,}$ C_6H_5), 5.91-5.91 (d, 1H, H-3, imidazopyridazine, *J* = 0.9), 5.02-4.99 (d, 1H, N*H*, *J* = 8.7), 4.33-4.28 (m, 1H, C*H*-NH), 3.93-3.78 (m, 2H, C*H*$_2$O), 2.32 (s, 3H, C*H*$_3$-C-2), 2.19-2.18 (d, 3H, C*H*$_3$-C-4, *J* = 0.9), 1.81-1.70 (m, 2H, P(C*H*$(CH_3)_2)_2$), 1.41-1.39 (d, 3H, CH-C*H*$_3$, *J* = 6.6) and 1.16-1.01 (m, 12H, P(CH(C*H*$_3)_2)_2$); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 151.24 (C-7, imidazopyridazine), 142.84 (C-2, imidazopyridazine), 138.82 (C-4,

imidazopyridazine), 136.14 (C-1', C_6H_5), 130.24, 127.73 ($C_{m,o}$, C_6H_5), 128.63 (C-4a, imidazopyridazine), 126.82 (C_p, C_6H_5), 117.38 (C-5, imidazopyridazine), 111.22 (C-3, imidazopyridazine), 75.45, 75.22 (CH_2O), 49.75, 49.64 (*C*H-NH), 28.26, 28.16, 28.04, 27.94 (P(*C*H(CH_3)$_2$)$_2$), 21.31 (CH_3-C-2), 19.40 (CH_3-C-4), 18.39 (CH-CH_3) and 18.07, 17.81, 16.91 (P(CH(*C*H_3)$_2$)$_2$); δ_P (121.37 MHz, C_6D_6, 298 K, TMS) 153.42.

N-(1-((diisopropylphosphino)oxy)-3-phenylpropan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3e**: 0.60 g (1,61 mmol) of 2-((2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-yl)amino)-3-phenylpropan-1-ol was dried *in vacuo* and dissolved in 30 mL of dry diethyl ether/THF (1:1). The orange solution was cooled to -78 °C, then 1.00 mL (1.61 mmol) of *n*BuLi (1.6 M in hexane) was added cautiously. Thereby, the solution changed its color to dark brown. The solution was stirred at -78 °C for another 30 minutes and warmed to room temperature. Then 0.26 mL (1.61 mmol) of chlorodiisopropylphosphine was added and the solution was stirred for 12 h at room temperature (color changes again to orange). The orange solution was evaporated to dryness and the orange residue was extracted with 15 mL of hexane (2x), the combined filtrates were evaporated to dryness yielding **3e** (0.71 g, 90%) as an orange viscous product. Found: C, 70.4; H, 8.7; N, 10.0. Calc. for $C_{29}H_{37}N_4OP*C_4H_{10}O$ (488.60 + 74.12): C, 70.4; H, 8.4; N, 10.0%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.74-7.71 (m, 2H, H_o, C_6H_5), 7.31-6.97 (m, 8H, C_6H_5), 5.32-5.30 (d, 1H, N*H*, *J* = 8.8), 5.32-5.30 (s, 1H, H-3, imidazopyridazine, *J* = 1.2), 4.65-4.63 (m, 1H, C*H*-NH), 3.92-3.85 (m, 2H, CH_2-C_6H_5), 3.29-3.01 (m, 2H, CH_2O), 1.96-1.95 (d, 3H, CH_3-C-4, *J* = 1.2), 1.84 (s, 3H, CH_3-C-2), 1.69-1.60 (m, 2H, P(C*H*(CH_3)$_2$)$_2$) and 1.24-0.91 (m, 12H, P(CH(C*H*$_3$)$_2$)$_2$); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 150.90 (C-7, imidazopyridazine), 143.33 (C-2, imidazopyridazine), 139.19 (C-4, imidazopyridazine), 138.89 (C-1', C_6H_5), 137.29 (C-1'', C_6H_5), 130.75, 129.89, 128.58, 127.86 ($C_{m,o}$, C_6H_5), 129.61 (C-4a, imidazopyridazine), 126.90, 126.44 (C_p, C_6H_5), 117.84 (C-5, imidazopyridazine), 111.01 (C-3, imidazopyridazine), 72.76, 72.41 (CH_2O), 55.95, 55.84 (*C*H-NH), 38.28 (CH-CH_2-C_6H_5), 28.68, 28.44, 28.40 (P(*C*H(CH_3)$_2$)$_2$), 21.08 (CH_3-C-2), 19.41 (CH_3-C-4) and 18.36, 18.29, 18.09, 18.01, 17.34, 17.22 (P(CH(*C*H_3)$_2$)$_2$); δ_P (121.37 MHz, C_6D_6, 298 K, TMS) 152.39.

N-(1-((diethylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3f**: 1.00 g (2.95 mmol) of 2-((2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-yl)amino)-4-methylpentan-1-ol was dried *in vacuo* and dissolved in 30

mL of dry diethyl ether/THF (1:1). The orange solution was cooled to -78 °C, then 1.84 mL (2.95 mmol) of *n*BuLi (1.6 M in hexane) was added cautiously. Thereby, the solution changed its color to dark brown. The solution was stirred at -78 °C for another 30 minutes and warmed to room temperature. Then 0.36 mL (2.95 mmol) of chlorodiethylphosphine was added and the solution was stirred for 12 h at room temperature (color changes again to orange). The orange solution was evaporated to dryness and the orange residue was extracted with 15 mL of hexane (2x), the combined filtrates were evaporated to dryness yielding **3f** (1.09 g, 86%) as an orange viscous product. Found: C, 67.35; H, 8.7; N, 12.2; Calc. for $C_{24}H_{35}N_4OP$*0.5 $C_4H_{10}O$ (426.53 + 37.06): C, 67.4; H, 8.7; N, 12.1%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.74-7.71 (m, 2H, H_o, C_6H_5), 7.25-7.08 (m, 3H, $H_{m,p}$, C_6H_5), 5.26-5.25 (d, 1H, H-3, imidazopyridazine, *J* = 0.9), 5.04-5.01 (d, 1H, N*H*, *J* = 9.0), 4.55-4.50 (m, 1H, C*H*-NH), 3.94-3.78 (m, 2H, CH_2O), 1.96 (s, 3H, CH_3-C-2), 1.85 (d, 3H, CH_3-C-4, *J* = 0.9 Hz), 1.66-1.42 (m, 3H, $CH_2CH(CH_3)_2$), 1.33-1.21 (m, 4H, $P(CH_2CH_3)_2$) and 1.06-0.85 (m, 12H, $P(CH_2CH_3)_2$, $CH_2CH(CH_3)_2$); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 150.96 (C-7, imidazopyridazine), 143.73 (C-2, imidazopyridazine), 138.96 (C-4, imidazopyridazine), 137.29 (C-1', C_6H_5), 130.73 (C_p, C_6H_5), 129.56 (C-4a, imidazopyridazine), 127.91, 126.86 ($C_{m,o}$, C_6H_5), 117.80 (C-5, imidazopyridazine), 110.91 (C-3, imidazopyridazine), 72.23 (CH_2O), 52.34, 52.24 (*C*H-NH), 41.82 (CH-CH_2-CH), 25.20 ($CH(CH_3)_2$), 25.01, 24.98 ($P(CH_2CH_3)_2$), 23.39, 22.50 ($CH(CH_3)_2$), 21.06 (CH_3-C-2), 19.42 (CH_3-C-4) and 8.22, 8.15, 8.04, 7.96 ($P(CH_2CH_3)_2$); δ_P (121.37 MHz, C_6D_6, 298 K, TMS) 138.69.

N-(1-((di-*t*-butylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3g**: 0.50 g (1.48 mmol) of 2-((2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-yl)amino)-4-methylpentan-1-ol was dried *in vacuo* and dissolved in 30 mL of dry diethyl ether/THF (1:1). The orange solution was cooled to -78 °C, then 0.92 mL (1.48 mmol) of *n*BuLi (1.6 M in hexane) was added cautiously. Thereby, the solution changed its color to dark brown. The solution was stirred at -78 °C for another 30 minutes and warmed to room temperature. Then 0.28 mL (1.48 mmol) of chlorodi-*t*-butylphosphine was added and the solution was stirred for 48 h at room temperature (color changes again to orange). The orange solution was evaporated to dryness and the orange residue was extracted with 15 mL of hexane (2x), the combined filtrates were evaporated to dryness yielding **3g** (0.47 g,

66%) as an orange viscous product. Found: C, 70.0; H, 9.3; N, 11.4. Calc. for $C_{28}H_{43}N_4OP$ (482.64): C, 69.7; H, 9.0; N, 11.6%. δ_H (299.83 MHz, $CDCl_3$, 298 K, TMS) 7.48-7.45 (d, 2H, H_o, C_6H_5, J = 1.5), 7.32-7.29 (t, 2H, H_m, C_6H_5, J = 7.2), 7.23-7.19 (m, 1H, H_p, C_6H_5), 5.81 (s, 1H, H-3, imidazopyridazine), 4.87-4.84 (d, 1H, N*H*, J = 9.9), 4.22-4.20 (m, 1H, C*H*-NH), 3.91-3.69 (m, 2H, CH_2O), 2.23 (s, 3H, (CH_3-C-2/4), 2.10 (s, 3H, (CH_3-C-4/2), 1.81-1.74 (m, 1H, CH(CH_3)$_2$), 1.69-1.47 (m, 2H, CH_2CH(CH_3)$_2$), 1.17-1.13 (d, 3H, CH(CH_3)$_2$, J = 12.0), 1.04-1.01 (d, 3H, CH(CH_3)$_2$, J = 11.4) and 0.95-0.90 (m, 18H, P(C(CH_3)$_3$)$_2$); δ_C (75.39 MHz, $CDCl_3$, 298 K, TMS) 151.39 (C-7, imidazopyridazine), 143.31 (C-2, imidazopyridazine), 139.48 (C-4, imidazopyridazine), 136.48 (C1', C_6H_5), 130.52, 128.01 ($C_{o,m}$, C_6H_5), 128.92 (C-4a, imidazopyridazine), 127.06 (C_p, C_6H_5), 117.63 (C-5, imidazopyridazine), 111.39 (C-3, imidazopyridazine), 75.36, 75.12 (*C*H_2O), 52.38, 52.25 (*C*H-NH), 35.74, 35.67, 35.43, 35.35 (P(*C*(CH_3)$_3$)$_2$), 28.19, 27.97, 27.77, 27.69, 27.58, 27.50 (P(C(*C*H_3)$_3$)$_2$), 25.22 (*C*H(CH_3)$_2$), 23.47, 22.87 (CH(*C*H_3)$_2$) and 21.58, 19.73 (*C*H_3-C-2/4 imidazopyridazine); δ_P (121.37 MHz, $CDCl_3$, 298 K, TMS) 157.29.

N-(1-((dicyclohexylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3h**: 0.77 g (2.30 mmol) of 2-((2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-yl)amino)-4-methylpentan-1-ol was dried *in vacuo* and dissolved in 30 mL of dry diethyl ether/THF (1:1). The orange solution was cooled to -78 °C, then 1.44 mL (2.30 mmol) of *n*BuLi (1.6 M in hexane) was added cautiously. Thereby, the solution changed its color to dark brown. The solution was stirred at -78 °C for another 30 minutes and warmed to room temperature. Then 0.51 mL (2.30 mmol) of chlorodicyclohexylphosphine was added and the solution was stirred for 24 h at room temperature (color changes again to orange). The orange solution was evaporated to dryness and the orange residue was extracted with 15 mL of hexane (2x), the combined filtrates were evaporated to dryness yielding **3h** (1.06 g, 86%) as an orange viscous product. Found: C, 71.1; H, 9.1; N, 9.3. Calc. for $C_{32}H_{47}N_4OP*C_4H_8O$ (534.72 + 72.11): C, 71.25; H, 9.1; N, 9.2%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.75-7.73 (m, 2H, H_o, C_6H_5), 7.26-6.07 (m, 3H, $H_{m,p}$, C_6H_5), 5.30 (s, 1H, H-3, imidazopyridazine, J = 1.2), 5.09-5.06 (d, 1H, N*H*, J = 9.6), 4.58-4.53 (m, 1H, C*H*-NH), 4.06-3.81 (m, 2H, CH_2O), 2.01 (s, 3H, CH_3-C-2), 1.88-1.87 (d, 3H, CH_3-C-4, J = 1.2), 1.72-1.50 (m, 14H, CH_2C*H*(CH_3)$_2$, cyclohexyl), 1.29-1.12 (m, 11H, cyclohexyl), 0.99-0.97 (d, 3H, CH(CH_3)$_2$, J = 6.3) and 0.89-0.87 (d, 3H, CH(CH_3)$_2$, J = 6.6); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 151.33 (C-7, imidazopyridazine), 144.18 (C-

2, imidazopyridazine), 139.42 (C-4, imidazopyridazine), 137.74 (C-1', C_6H_5), 131.15, 128.31 ($C_{m,o}$, C_6H_5), 130.05 (C-4a, imidazopyridazine), 127.27 (C_p, C_6H_5), 118.18 (C-5, imidazopyridazine), 111.24 (C-3, imidazopyridazine), 74.96 (CH_2O), 52.95 (CH-NH), 42.31 (CH-CH_2-CH), 39.09, 38.84 (CH, cyclohexyl), 29.16, 28.91, 27.83, 27.78, 27.73, 27.68, 27.59, 27.50, 27.27, 27.21 (CH_2, cyclohexyl), 25.65 ($CH(CH_3)_2$), 23.75, 22.98 ($CH(CH_3)_2$), 21.54 (CH_3-C-2) and 19.84 (CH_3-C-4); δ_P (121.37 MHz, C_6D_6, 298 K, TMS) 147.73.

5.6.3 Complex Synthesis

[1,5-cyclooctadien-*(N*-(1-((diphenylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amido) rhodium (I)] **4a**: To an orange solution of 0.50 g (0,96 mmol) *N*-(1-((diphenylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3a** in 20 mL of THF 0.23 g (0.47 mmol) 1,5-cyclooctadien-methoxy-rhodium (I) dimer was added, accompanied by a color change to blue/ dark green. The reaction solution was stirred at room temperature for 16 h. Then the THF volume was reduced *in vacuo* to 10 mL. At -30 °C green crystals of **4a** (0.26 g, 37%) were obtained. Found: C, 64.4; H, 6.7; N, 7.3. Calc. for $C_{40}H_{46}N_4OPRh*CH_3OH$ (732.70 + 32.04): C, 64.4; H, 6.6; N, 7.3%. δ_H (299.83 MHz, CD_2Cl_2, 298 K, TMS) 7.62-7.56 (m, 2H, 3 x C_6H_5), 7.40-7.30 (m, 7H, 3 x C_6H_5), 7.26-7.15 (m, 3H, 3 x C_6H_5), 7.03-6.95 (m, 3H, 3 x C_6H_5), 5.82 (br s, 1H, cod), 5.52 (s, 1H, H-3, imidazopyridazine), 4.92 (br s, 1H, cod), 4.77-4.61 (m, 2H, CH_2O), 4.33-4.26 (m, 1H, CH-N), 2.81 (s, 3H, CH_3-C-2), 2.65-2.53 (m, 2H, cod), 2.40-2.22 (m, 4H, cod), 2.02-1.30 (m, 4H, cod), 1.84 (d, 3H, CH_3-C-4), *J* = 0.9), 1.67-1.58 (m, 2H, $CH_2CH(CH_3)_2$), 1.42-1.39 (m, 1H, $CH_2CH(CH_3)_2$), 1.23-1.22 (d, 3H, $CH(CH_3)_2$, *J* = 6.6) and 1.07-1.05 (d, 3H, $CH(CH_3)_2$, *J* = 6.6); δ_C (75.39 MHz, CD_2Cl_2, 298 K, TMS) 155.98 (C-7, imidazopyridazine), 151.38 (C-2, imidazopyridazine), 139.55 (C-4, imidazopyridazine), 138.22, 136.64, 135.93 (C1', 3 x C_6H_5), 130.38 (C-4a, imidazopyridazine), 130.22, 129.44, 129.29, 128.70, 128.65, 128.62, 128.57, 128.48, 128.31, 128.26, 127.91, 127.47, 127.33, 126.37 ($C_{o,m,p}$, 3 x C_6H_5), 115.02 (C-5, imidazopyridazine), 110.00 (C-3, imidazopyridazine), 76.67 (CH_2O), 57.80 (CH-N), 55.12, 45.33 (CH, cod), 44.34 (CH-CH_2-CH), 38.28, 33.59, 29.27, 28.56 (CH_2, cod), 28.27 ($CH(CH_3)_2$), 25.81, 24.39 (2 x CH_3, $CH(CH_3)_2$) and 23.80, 19.23 (CH_3-C-2/4); δ_P (121.37 MHz, CD_2Cl_2, 298K, TMS): 112.94 and 111.64; *J* = 158.4.

Details for X-ray crystal structure analysis of **4a**, STOE-IDPS II equipped with an Oxford Cryostream low-temperature unit, graphite monochromatized MoKα-radiation, λ=0.71069 Å, structure solution and refinements were accomplished with SHELXL-97 (G. M. Sheldrick, SHELXL-97, Program for Crystal Structure Analysis Release 97-2, Institut für Anorganische Chemie der Universität Göttingen, Germany, **1998**), WinGX (L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837-838) and SIR97 (A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori and R. Spagna, *J. Appl. Cryst.* **1999**, *32*, 115-119), crystal size 0.35 x 0.28 x 0.22 mm, symmetry space group R3, trigonal, a = 25.3240(8), b = 25.3240(8), c = 13.5100(7) Å, ß= 90.00°, V = 7503.3(5) $Å^3$, Z = 3, $\rho_{cald.}$ = 1.459 g/cm^3, 6257 reflections, 5601 independent reflections, R = 0.0251 [I > 2σ(I)], wR2 (all data) = 0.0532, 426 parameters. CCDC-782981 contains the supplementary crystallographic data for this publication. These data can be obtained at www.ccdc.cam.ac.uk/data_request/cif free of charge (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk).

[1,5-cyclooctadien-(*N*-(1-((diisopropylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amido) rhodium (I)] **4b**: To an orange solution of 0.35 g (0,76 mmol *N*-(1-((diisopropylphosphino)oxy)-4-methylpentan-2-yl)-2,4-dimethyl-5-phenylimidazo[1,5-*b*]pyridazin-7-amine **3b** in 20 mL of THF 0.19 g (0.38 mmol) 1,5-cyclooctadien-methoxy-rhodium (I) dimer was added, accompanied by a color change to blue/ dark green. The reaction solution was stirred at room temperature for 16 h. Then the THF volume was reduced to dryness *in vacuo* and (hot) hexane was added. The black-green solution was filtered off and reduced to dryness yielding **4b** (0.18g, 36%). Found: C, 60.1; H, 7.7; N, 7.7. Calc. for $C_{34}H_{50}N_4OPRh*CH_3OH$ (664.76 + 32.04): C, 60.3; H, 7.8; N, 8.0%. δ_H (250.13 MHz, [d_8]THF, 298 K, TMS) 7.55-7.52 (d, 2H, H_o, C_6H_5, *J* = 7.0), 7.25-7.20 (t, 2H, H_m, C_6H_5, *J* = 7.8), 7.14-7.08 (m, 1H, H_p, C_6H_5), 5.60 (s, 1H, H-3), 5.49 (br s, 1H, C*H*, cod), 4.33-4.15 (m, 3H, CH_2O, C*H*-N), 3.78-3.70 (m, 2H, C*H*, cod), 3.36 (br s, 1H, C*H*, cod), 2.58 (s, 3H, CH_3-C-2/4), 2.32-2.17 (m, 4H, CH_2, cod), 2.08 (s, 3H, CH_3-C-4/2), 1.91-1.77 (m, 7H, CH_2, cod, $CH_2CH(CH_3)_2$), 1.31-1.13 (m, 8H, $P(CH(CH_3)_2)_2$, $PCH(CH_3)_2$), 1.06-1.01 (t, 6H, $CH(CH_3)_2$, *J* = 6.3), 0.95-0.87 (dd, 3H, $PCH(CH_3)_2$, *J* = 7.3) and 0.76-0.67 (dd, 3H, $PCH(CH_3)_2$, *J* = 7.3); δ_C (75.39 MHz, [d_8]THF, 298 K, TMS) 155.51 (C-7, imidazopyridazine), 151.66 (C-2, imidazopyridazine), 140.17 (C-

4, imidazopyridazine), 139.14 (C1', C_6H_5), 132.16 (C-4a, imidazopyridazine), 130.76, 128.02, 126.46 ($C_{o,m,p}$, C_6H_5), 116.34 (C-5, imidazopyridazine), 110.11 (C-3, imidazopyridazine), 105.14 (*C*H, cod), 97.91 (*C*H, cod), 76.64 (CH_2O), 66.43, 57.66 (*C*H, cod), 56.65 (*C*H-N), 44.70 (CH-CH_2-CH), 37.13, 33.41, 29.53, 28.83 (CH_2, cod), 30.48, 30.10, 29.40, 29.15, 29.09 (P(*C*H$(CH_3)_2$), 27.13 (*C*H$(CH_3)_2$), 24.84, 23.85 (2xCH_3, CH(*C*H$_3)_2$), 23.13, 20.07 (*C*H$_3$-C-2/4) and 18.18, 18.15, 17.95, 17.04, 16.96, 16.68, 16.62 (P(CH(*C*H$_3)_2)_2$); δ_C (101.26 MHz, [d_8]THF, 298 K, TMS) 141.15 and 139.57; *J* = 160.9.

4c-j: not isolated, precatalyst-solution prepared *via* alcohol elimination (refer to 5.5).

5.6.4 Synthesis of Imines

N-Aryl imines were synthesized according to Taguchi[1] *et al.* – a solution of 0.1 mol amine, 0.1 mol ketone and 40 g of molecular sieves (4 Å) in 20 mL of diethyl ether was stirred for 24 hours. The molecular sieves were filtered off and washed with ether. The combined filtrates were evaporated to dryness and the residue was purified *via* vacuum distillation (liquid residue) or recrystallization.

N-(1-phenylethylidene)aniline **5a**: yielded as a pale yellow solid (14.66 g, 75 %). M.p. 37 °C. Found: C, 86.0; H, 6.9; N, 7.3. Calc. for $C_{14}H_{13}N$ (195.26): C, 86.1; H, 6.7; N, 7.2%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.97-7.94 (m, 2H, C_6H_5), 7.21-7.14 (m, 5H, C_6H_5), 6.69-6.91 (t, 1H, C_6H_5, *J* = 7.2), 6.78-6.74 (m, 2H, C_6H_5) and 1.82 (s, 3H, CH_3); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 164.34 (C=N), 152.45, 139.69 (C_q, C_6H_5), 130.40, 129.14, 128.31, 127.54, 123.20, 119.58 ($C_{o,m,p}$, C_6H_5) and 16.63 (CH_3).

N-(1-(*p*-tolyl)ethylidene)aniline **5b**: yielded as a pale yellow solid (14.51 g, 70%). M.p. 62 °C. Found: C, 85.7; H, 7.5; N, 6.8. Calc. for $C_{15}H_{15}N$ (209.29): C, 86.1; H, 7.2; N, 6.7%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.94-7.91 (d, 2H, aryl C*H*, *J* = 8.1), 7.21-7.14 (m, 4H, aryl C*H*), 7.02-6.99 (d, 2H, aryl C*H*, *J* = 8.1), 6.96-6.91 (t, 1H, aryl C*H*, *J* = 7.2), 6.78-6.75 (d, 2H, aryl C*H*, *J* = 7.2), 2.09 (s, 3H, CH_3) and 1.86 (s, 3H, CH_3); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 164.00 (C=N), 152.41, 140.30, 137.00 (aryl C_q), 128.96, 128.92, 127.44, 122.92, 119.53 (aryl *C*H) and 21.00, 16.47 (CH_3).

[1] K. Taguchi, F. H. Westheimer*, J. Org. Chem.* **1971**, 1570-1572.

4-methoxy-*N*-(1-phenylethylidene)aniline **5c**: yielded as a pale yellow solid (19.40 g, 86%). M.p. 86 °C. Found: C, 79.5; H, 6.7; N, 6.1. Calc. for $C_{15}H_{15}NO$ (225.29): C, 80.0; H, 6.7; N; 6.2%. δ_H (399.80 MHz, [d_6]DMSO, 298 K, TMS) 8.00-7.97 (m, 2H, C_6H_5), 7.48-7.45 (m, 3H, C_6H_5), 6.95-6.93 (d, 2H, $C_6H_4OCH_3$, J = 8.4), 6.76-6.74 (d, 2H, $C_6H_4OCH_3$, J = 8.4), 3.75 (s, 3H, OCH_3) and 2.21 (s, 3H, CH_3); δ_C (100.53 MHz, [d_6]DMSO, 298 K, TMS) 165.59 (C=N), 156.15, 144.94, 139.87, 131.02, 128.94, 127.70, 121.40, 114.86 (aryl C_q, aryl *C*H), 55.82 (OCH_3) and 17.64 (CH_3).

3-methyl-*N*-(1-phenylethylidene)aniline **5d**: yielded as a pale yellow solid (11.00 g, 53%). M.p. 34 °C. Found: C, 85.8; H, 7.4; N, 6.8. Calc. for $C_{15}H_{15}N$ (209.29): C, 86.1; H, 7.2; N, 6.7%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.99-7.96 (m, 2H, aryl C*H*); 7.18-7.12 (m, 4H, aryl C*H*); 6.80-6.78 (d, 1H, aryl C*H*, J = 7.5), 6.63-6.60 (d, 2H, aryl C*H*, J = 8.7), 2.14 (s, 3H, CH_3) and 1.86 (s, 3H, CH_3); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 164.10 (C=N), 152.54, 139.80, 139.67 (aryl C_q), 130.34, 129.04, 128.31, 127.52, 123.98, 120.22, 116.64 (aryl *C*H), 21.37 (CH_3) and 16.68 (CH_3).

3,5-dimethyl-*N*-(1-phenylethylidene)aniline **5e**: yielded as an orange liquid (14.40 g, 65%). Found: C, 85.6, H, 7.5; N, 6.6. Calc. for $C_{16}H_{17}N$ (223.31): C, 86.05; H, 7.7; N, 6.3%. δ_H (299.83 MHz, [d_6]DMSO, 298 K, TMS) 7.98-7.95 (m, 2H, C_6H_5), 7.48-7.46 (m, 3H, C_6H_5), 6.69 (s, 1H, H_p, $C_6H_3(CH_3)_2$), 6.38 (s, 2H, H_o, $C_6H_3(CH_3)_2$), 2.26 (s, 6H, $C_6H_3(CH_3)_2$) and 2.17 (s, 3H, CH_3); δ_C (75.39 MHz, [d_6]DMSO, 298 K, TMS) 164.40 (C=N), 151.37, 138.98, 137.95, 130.34, 128.23, 127.00, 124.49, 116.74 (aryl C_q, aryl *C*H), 20.92 (2x CH_3, $C_6H_3(CH_3)_2$) and 16.97 (CH_3).

3-methyl-*N*-(1-(*p*-tolyl)ethylidene)aniline **5f**: yielded as an orange liquid (18.20 g, 82%). Found: C, 85.9; H, 8.2; N, 6.6. Calc. for $C_{16}H_{17}N$ (223.31): C, 86.05; H, 7.7; N, 6.3%. δ_H (299.83 MHz, [d_6]DMSO, 298 K, TMS) 7.88-7.86 (d, 2H, aryl C*H*, J = 8.1), 7.29-7.20 (m, 3H, aryl C*H*), 6.89-6.86 (dd, 1H, aryl C*H*, J = 7.8, 0.9), 6.58-6.54 (m, 2H, aryl C*H*), 2.36 (s, 3H, *m*-CH_3), 2.30 (s, 3H, *p*-CH_3) and 2.16 (s, 3H, CH_3); δ_C (75.39 MHz, [d_6]DMSO, 298 K, TMS) 164.37 (C=N), 151.44, 140.20, 138.17, 136.28, 128.89, 128.78, 127.03, 123.60, 119.75, 116.29 (aryl C_q, aryl *C*H), 21.02 (*m*-CH_3), 20.90 (*p*-CH_3) and 16.94 (CH_3).

4-methoxy-*N*-(1-(*p*-tolyl)ethylidene)aniline **5g**: yielded as a pale yellow solid (10.68 g; 45%). M.p. 83 °C. Found: C, 80.2; H, 7.4; N, 5.9. Calc. for $C_{16}H_{17}NO$ (239.31): C,

80.3; H, 7.2; N, 5.85%. δ_H (299.83 MHz, $CDCl_3$, 298 K, TMS) 7.91-7.89 (d, 2H, aryl C*H*, *J* = 8.1), 7.29-7.26 (d, 2H, aryl C*H*, *J* = 8.1), 6.95-6.92 (d, 2H, aryl C*H*, *J* = 9.0), 6.80-6.77 (d, 2H, aryl C*H*, *J* = 9.0), 3.84 (s, 3H, OCH_3), 2.44 (s, 3H, CH_3) and 2.26 (s, 3H, CH_3); δ_C (75.39 MHz, $CDCl_3$, 298 K, TMS): 165.79 (C=N), 156.11, 145.22, 140.79, 137.33, 129.30, 127.36, 121.08, 114.47 (aryl C_q, aryl *C*H), 55.73 (O*C*H_3), 21.64 (*p*-*C*H_3) and 17.49 (*C*H_3).

4-butyl-*N*-(1-(*p*-tolyl)ethylidene)aniline **5h**: yielded as yellow liquid (8.01 g, 60%). Found: C, 85.7; H, 8.9; N, 5.25. Calc. for $C_{19}H_{23}N$ (265.39): C, 86.0; H, 8.7; N, 5.3%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 8.02-7.99 (d, 2H, aryl C*H*, *J* = 8.1), 7.36-7.33 (d, 2H, aryl C*H*, *J* = 8.4), 7.29-7.26 (d, 2H, aryl C*H*, *J* = 8.1), 6.86-6.83 (d, 2H, aryl C*H*, *J* = 7.8), 2.76-2.71 (t, 2H, CH_2Pr, *J* = 7.5), 2.51 (s, 3H, CH_3), 2.32 (s, 3H, *p*-CH_3), 1.81-1.70 (q, 2H, CH_2CH_2Et, *J* = 6.9), 1.55-1.48 (m, 2H, $(CH_2)_2CH_2CH_3$) and 1.11-1.06 (t, 3H, -$(CH_2)_3CH_3$, *J* = 7.5); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 163.36 (C=N), 147.87, 138.87, 135.91, 135.44 (aryl C_q), 127.45, 127.26, 125.61, 117.91 (aryl *C*H), 33.58, 32.28, 20.85 (*C*H_2) 19.79 (*C*H_3), 15.58 (*C*H_3) and 12.51 (*C*H_3).

N-(1-phenylpropylidene)aniline **5i**: yielded as pale yellow solid (12.76 g, 61%). M.p. 49 °C. Found: C, 85.6; H, 7.4; N, 6.9. Calc. for $C_{18}H_{15}N$ (209.29): C, 86.1; H, 7.2; N, 6.8%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.96-7.91 (m, 2H, aryl C*H*), 7.21-7.14 (m, 5H, aryl C*H*), 6.95-6.90 (t, 1H, aryl C*H*, *J* = 7.2), 6.79-6.77 (d, 2H, aryl C*H*, *J* = 7.2), 2.43-2.35 (q, 2H, CH_2, *J* = 7.8) and 0.84-0.79 (t, 3H, CH_3, *J* = 7.8); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 169.45 (C=N), 152.45, 138.20 (C_q, C_6H_5), 130.14, 129.00, 128.30, 127.43, 122.80, 119.03 ($C_{o,m,p}$, C_6H_5), 22.90 (*C*H_2) and 12.67 (*C*H_3).

N-(1-phenylhexylidene)aniline **5j**: yielded as an orange liquid (9.40 g, 47%). Found: C, 85.5; H, 8.9; N, 5.8. Calc. for $C_{18}H_{21}N$ (251.37): C, 86.0; H, 8.4; N, 5.6%. δ_H (299.83 MHz, [d_6]DMSO, 298 K, TMS) 7.94-7.91 (m, 2H, C_6H_5), 7.50-7.46 (m, 3H, C_6H_5), 7.38-7.32 (t, 2H, C_6H_5, *J* = 7.5), 7.09-7.04 (t, 1H, C_6H_5, *J* = 7.5), 6.76-6.73 (d, 2H, C_6H_5, *J* = 7.2), 2.64-2.59 (t, 2H, CH_2, *J* = 7.8), 1.41-1.34 (m, 2H, CH_2), 1.12-1.05 (m, 4H, 2x CH_2) and 0.74-0.69 (t, 3H, CH_3, *J* = 6.9); δ_C (75.39 MHz, [d_6]DMSO, 298 K, TMS) 169.02 (C=N), 151.27, 137.81, 130.36, 128.92, 128.42, 127.44, 122.81, 118.79 (aryl C_q, aryl *C*H), 30.98 (*C*H_2), 29.27 (*C*H_2), 27.05 (*C*H_2), 21.44 (*C*H_2) and 13.57 (*C*H_3).

N-(2,2-dimethyl-1-phenylpropylidene)aniline **5k**: 0.05 mol of the ketone and 0.05 mol of the amine were refluxed in 15mL of benzene, 15.0 g of molecular sieves and catalytic amounts of *p*-toluenesulfonic acid. The yellow solution was filtered off the molecular sieves and distilled (high vacuum) yielding **5n** (1.98 g, 17%) as a light yellow liquid. Found: C, 85.7; H, 8.3; N, 5.9. Calc. for $C_{17}H_{19}N$ (237.34): C, 86.0; H, 8.1; N, 5.9%. δ_H (250.13 MHz, $CDCl_3$, 298 K, TMS) 7.16-7.10 (m, 3H, C_6H_5), 7.07-7.00 (m, 2H, C_6H_5), 6.94-6.90 (m, 2H, C_6H_5), 6.80-6.74 (m, 1H, C_6H_5), 6.56-6.52 (m, 2H, C_6H_5) and 1.27 (s, 9H, $C(CH_3)_3$); δ_C (75.39 MHz, [d_6]DMSO, 298 K, TMS) 179.83 (C=N), 152.07, 137.27, 135.38, 129.48, 128.85 128.75, 128.34, 128.30, 127.99, 120.39, 114.66, (aryl C_q, aryl *C*H), 40.38 ($C(CH_3)_3$) and 28.44 ($C(CH_3)_3$).

N-(1-(4-bromophenyl)ethylidene)aniline **5l**: yielded as pale yellow solid (24.80 g, 90%). M.p. 87 °C. Found: C, 61.2; H, 4.5; N, 5.0. Calc. for $C_{14}H_{12}BrN$ (274.16): C, 61.3; H, 4.4; N, 5.1%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.57-7.54 (d, 2H, aryl C*H*, *J* = 8.7), 7.27-7.24 (d, 2H, aryl C*H*, *J* = 8.7), 7.18-7.12 (m, 2H, aryl C*H*), 6.94-6.89 (t, 1H, aryl C*H*, *J* = 7.5), 6.70-6.67 (d, 2H, aryl C*H*, *J* = 8.1) and 1.66 (s, 3H, CH_3); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 163.16 (C=N); 151.81, 138.20, 124.96 (aryl C_q); 131.29, 128.96, 128.91, 124.96, 123.24, 119.30 (aryl *C*H) and 16.21 (CH_3).

N-(1-(3,4-dimethoxyphenyl)ethylidene)aniline **5m**: yielded as pale yellow solid (10.55 g, 41%). M.p. 115 °C. Found: C, 74.8; H, 7.2; N, 5.1. Calc. for $C_{16}H_{17}NO_2$ (255.31): C, 75.3; H, 6.7; N, 5.5%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.75-7.74 (d, 1H, H-2, $C_6H_3(OCH_3)_2$, *J* = 1.8), 7.48-7.44 (dd, 1H, H-5, $C_6H_3(OCH_3)_2$, *J* = 8.4, 2.1), 7.36-7.34 (t, 2H, H_m, C_6H_5, *J* = 7.5), 7.12-7.07 (t, 1H, H_p, C_6H_5, *J* = 7.5), 6.92-6.90 (d, 1H, $C_6H_3(OCH_3)_2$, *J* = 8.4), 6.83-6.80 (d, 2H, H_o, C_6H_5, *J* = 8.7), 3.98-3.95 (m, 6H, 2x OCH_3) and 2.22 (s, 3H, CH_3); δ_C (100.53 MHz, [d_6]DMSO, 298 K, TMS) 164.70 (C=N), 152.22, 151.75, 149.11, 132.18, 129.60, 123.51, 121.61, 120.10, 111.43, 110.23 (aryl C_q, aryl *C*H), 56.23 (OCH_3), 56.07 (OCH_3) and 17.52 (CH_3).

N-(1-(naphthalen-2-yl)ethylidene)aniline **5n**: yielded as a pale yellow solid (10.07 g, 60%). M.p. 140 °C. Found: C, 88.0; H, 6.1; N, 5.8. Calc. for $C_{18}H_{15}N$ (245.32): C, 88.1; H, 6.2; N, 5.7%. δ_H (299.83 MHz, [d_6]DMSO, 298 K, TMS) 8.51 (s, 1H, 2-naphtyl), 8.23-8.20 (dd, 1H, 2-naphtyl, *J* = 1.8), 8.09-8.06 (m, 1H, 2-naphtyl), 8.00-7.97 (m, 2H, 2-naphtyl), 7.61-7.58 (m, 2H, 2-naphtyl), 7.42-7.36 (t, 2H, H_m, C_6H_5), 7.13-7.08 (t, 1H, H_p, C_6H_5), 6.86-6.83 (d, 2H, H_o, C_6H_5) and 2.33 (s, 3H, CH_3); δ_C

(75.39 MHz, [d_6]DMSO, 298 K, TMS): 164.83 (C=N), 151.36, 136.21, 133.90, 132.54 (aryl C_q), 128.97, 127.90, 127.68, 127.52, 127.36, 126.51, 123.94, 123.12, 119.30 (aryl *C*H) and 17.09 (CH_3).

5.6.5 Optimization of Reaction Conditions

Reaction conditions were optimized for the asymmetric hydrogenation of imine **5a** with **4b**. Conversion and enantioselectivity were determined *via* GC and HPLC. Based on these results (Tables 4-7) it was chosen to use 20 °C (rt), a large excess of KO*t*Bu and 20 bar of H_2 pressure as standard reaction conditions.

Table 4: Base Screening, 48h, 0.1 mol% **4b**, rt, 20 bar.

No.	Base	Conv. [%]	ee [%]
1	-	37	-
2	$NaNH_2$	25	66
3	NaO*t*Bu	44	80
4	LiO*t*Bu	34	43
5	KO*t*Bu	>99	90
6	KOH	>99	90
7	$KOSiMe_3$	38	31
8	$KN(SiMe_3)_2$	96	86
9	K_2CO_3	27	86
10	NEt*i*Pr_2	-	-

Table 5: Screening – Amount of Base, 24h, 0.1 mol% **4b**, rt, 20 bar.

No.	Base : Catalyst	Conv. [%]	ee [%]
1	1 : 100	-	-
2	1 : 10	-	-
3	1 : 1	-	-
4	4 : 1	-	-
5	6 : 1	51	89
6	8 : 1	>99	90
7	10 : 1	>99	90
8	100 : 1	>99	89
9	1000 : 1	>99	90

Table 6: Pressure Screening, 24h, 0.1 mol% **4b**, rt, KO*t*Bu.

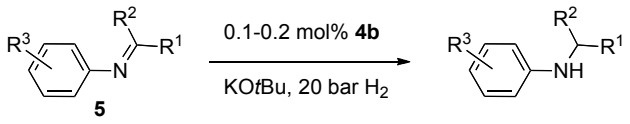
No.	p [bar]	Conv. [%]	ee [%]
1	60	>99	88
2	40	98	90
3	30	>99	90
4	20	>99	90
5	10	62	89
6	5	46	87

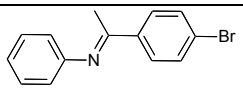
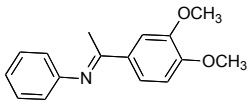
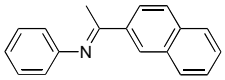
Table 7: Temperature Screening, 48h, 0.1 mol% **4b**, KO*t*Bu, 20 bar.

No.	T [°C]	Conv. [%]	ee [%]
1	40	>99	84
2	20	>99	90
3	10	>99	92
4	0	92	93
5	-20	64	95

5.6.6 Hydrogenation of Miscellaneous Imines

Table 8: Hydrogenation of miscellaneous *N*-aryl imines with **4b**.



No.	Imine		Yield[a] [%]	ee[b] [%]	Lit. ee [%]
1*	**5l**		35.2	97	91[3f]
2*	**5m**		74	89	97[4e]
3#	**5n**		57	91	95[4e]

0.1 mol% (*0.2 mol%) **4b**, KO*t*Bu, 48 h (#24 h), rt, 20 bar H_2; [a] determined *via* GC; [b] determined *via* HPLC.

5.6.7 Characterization (HPLC, GC)

Conversion:

The conversion (*and ee) was determined with dodecane as internal standard *via* gas chromatography.

5a-e,f,i-l: *Instrument setup:* Thermo Focus GC, column: Chirasil-DEX (Varian), Split flow 60.8 mL/min, Carrier He 3.4 mL/min, Inlet 250 °C; *GC program:* 105 °C hold 1', heat 30 °C/min till 150 °C (hold 3'), heat 6 °C/min until 215 °C (hold 12').

Retention Times:

5a:	Dodecane: 7.2 min	Amine: 16.8 min	Imine: 7.3 min
5b:	Dodecane: 7.3 min	Amine: 18.8 min	Imine: 9.7 min
5c:	Dodecane: 7.2 min	Amine: 22.6 min	Imine: 23.4 min
5d:	Dodecane: 7.2 min	Amine: 18.2 min	Imine: 18.7 min
5e:	Dodecane: 7.4 min	Amine: 24.8 min	Imine: 21.0 min
5f:	Dodecane: 7.3 min	Amine: 20.3 min	Imine: 19.5 min
5i:	Dodecane: 7.2 min	Amine: 17.9 min	Imine: 16.8 min
5j:	Dodecane: 7.3 min	Amine: 22.5 min	Imine: 24.8 min
5k*:	Dodecane: 7.4 min	Amine: 18.9, 19.1 min	Imine: 15.7 min
5l:	Dodecane: 7.3 min	Amine: 17.3 min	Imine: 26.1 min

5g: *Instrument setup:* Thermo Focus GC, column: Chirasil-DEX (Varian), Split flow 60.8 mL/min, Carrier He 3.4 mL/min, Inlet 250 °C; *GC program:* 105 °C hold 1', heat 30 °C/min till 150 °C (hold 3'), heat 25 °C/min till 200 °C (hold 2'), heat 5 °C/min until 215 °C (hold 18').

Retention Times:

5g:	Dodecane: 6.9 min	Amine: 22.0 min	Imine: 24.4

5h,m,n:*Instrument setup:* Agilent 6890N Network GC, column: Lipodex-E (Machery-Nagel), Split flow 61.0 mL/min, Carrier He 1.0 mL/min, Inlet 250 °C; *GC program:* 110 °C hold 5', heat 20 °C/min till 215 °C (hold 30').

Retention Times:

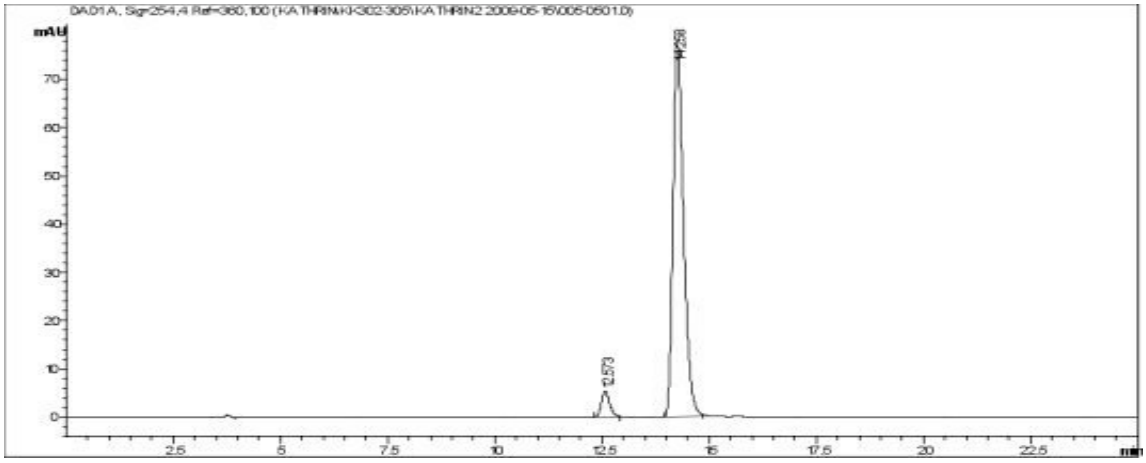
5h:	Dodecane: 3.8 min	Amine: 18.0 min	Imine: 19.4 min
5m:	Dodecane: 4.3 min	Amine: 22.1 min	Imine: 19.5 min
5n:	Dodecane: 3.8 min	Amine: 24.5 min	Imine: 25.7 min

Enantiomeric excess:

The enantiomeric excess was determined *via* HPLC (Agilent 1200) with a Chiralpak IB (Daicel) column.

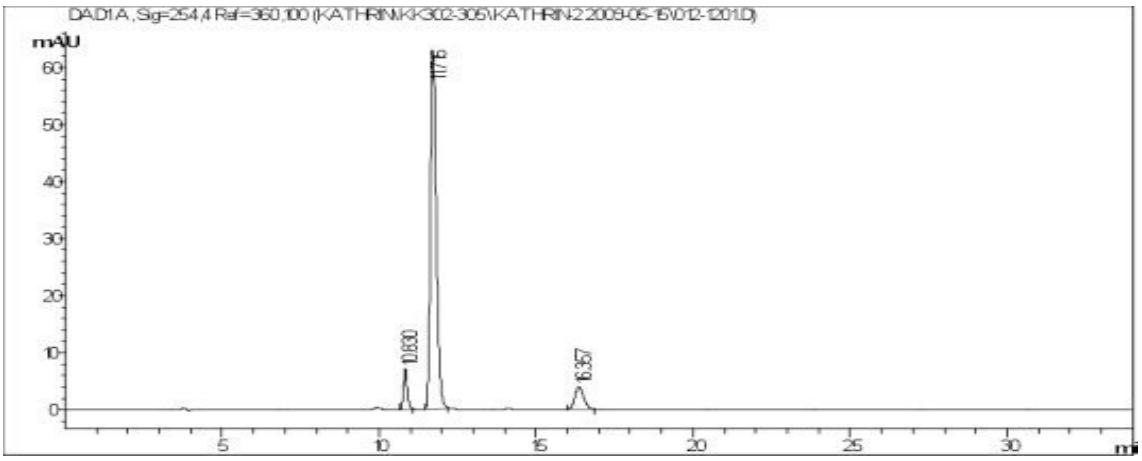
5a: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 12.6 (*S*), 14.3 (*R*) min; (Imine: 15.7 min)



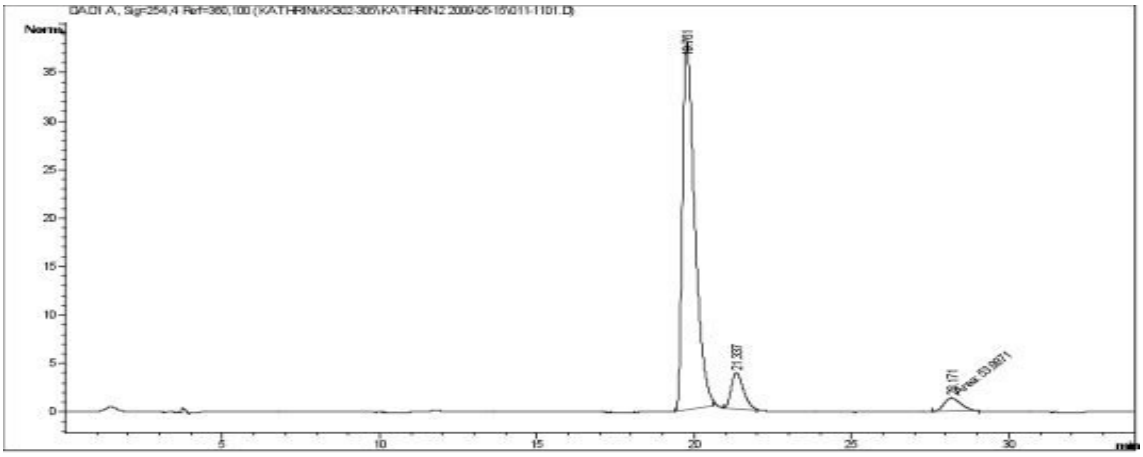
5b: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 10.8, 11.8 min; (Imine: 16.4 min)



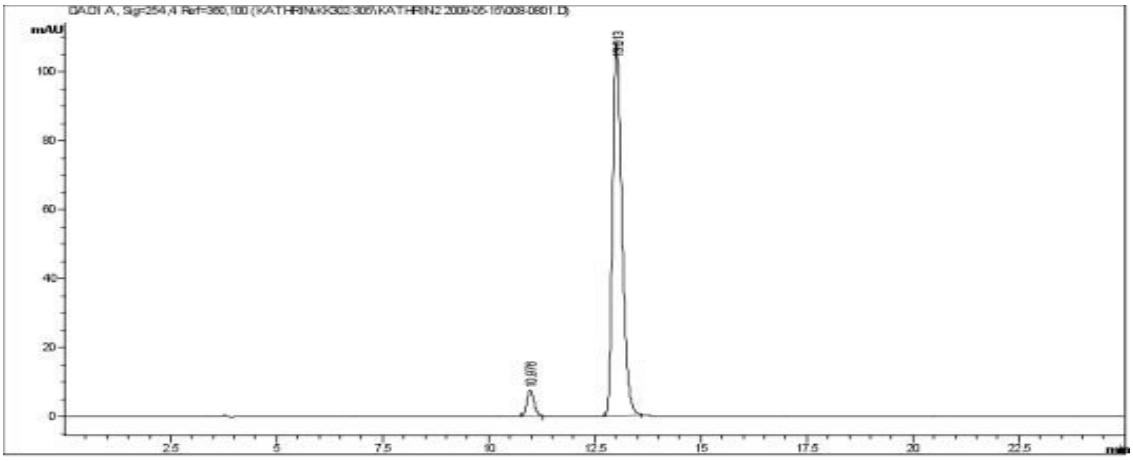
5c: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 20.8, 21.4; Imine: 28.2



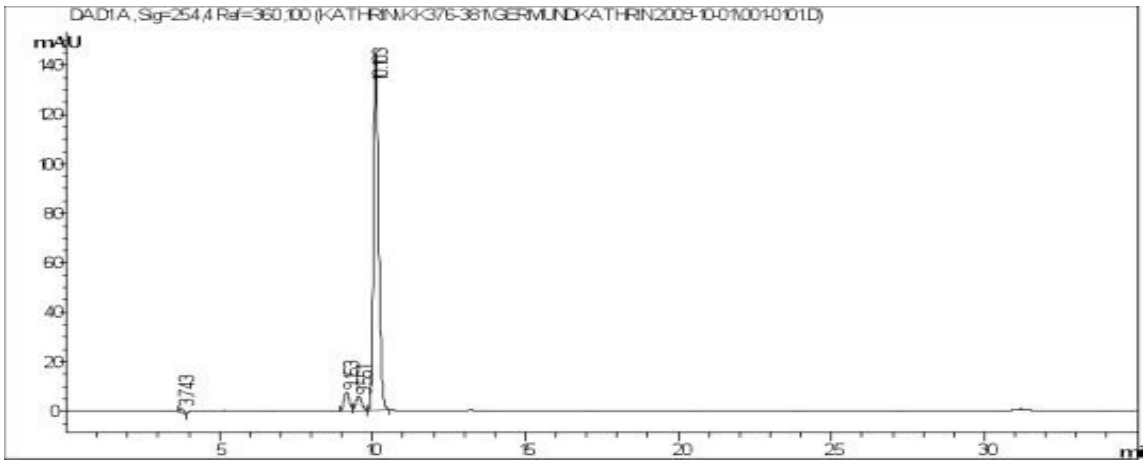
5d: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 11.0 (-), 13.0 (+)



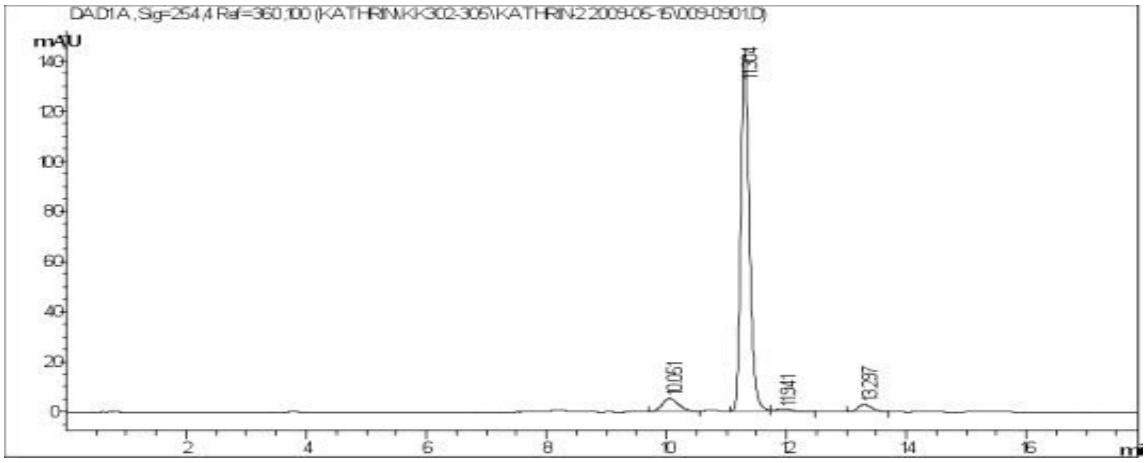
5e: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 9.2, 10.1 min; Imine: 9.6 min



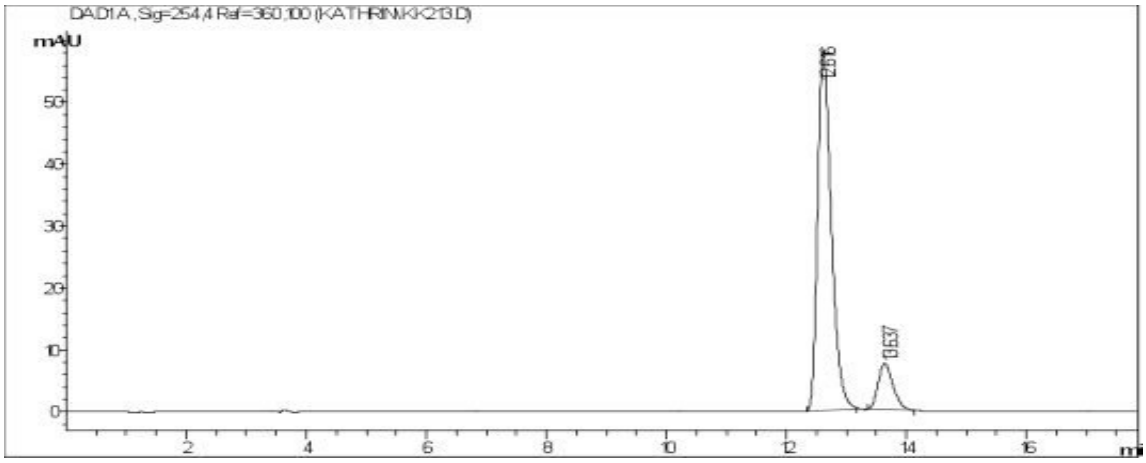
5f: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 10.1, 11.3 min; Imine: 13.3 min



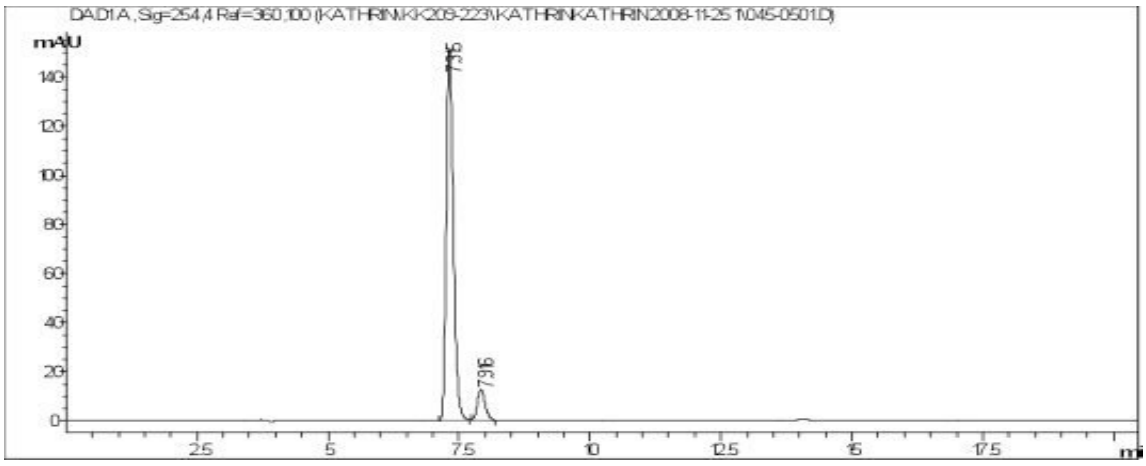
5g: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.5:0.5 Hexane: 2-Propanol

Retention Times: Amine: 12.7, 13.6 min



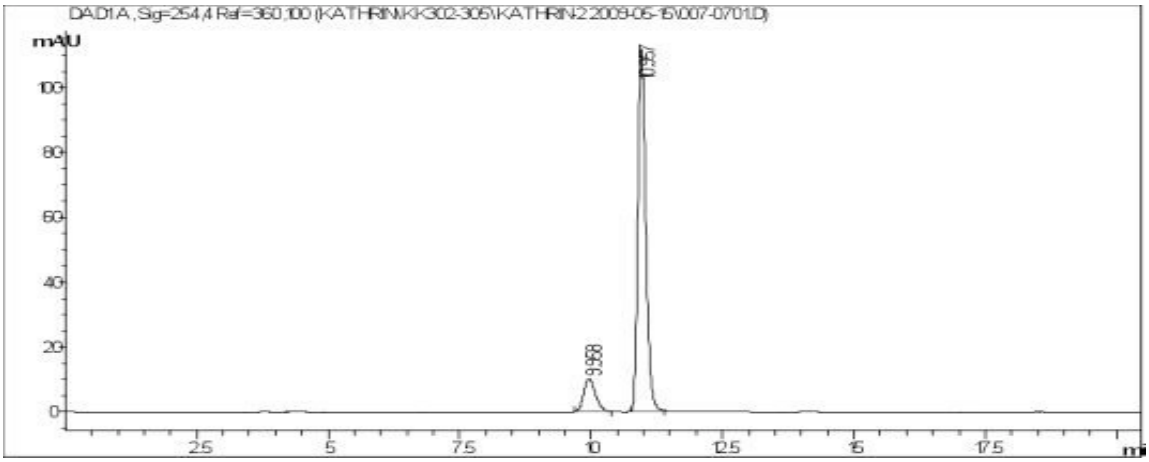
5h: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 7.4, 7.9 min



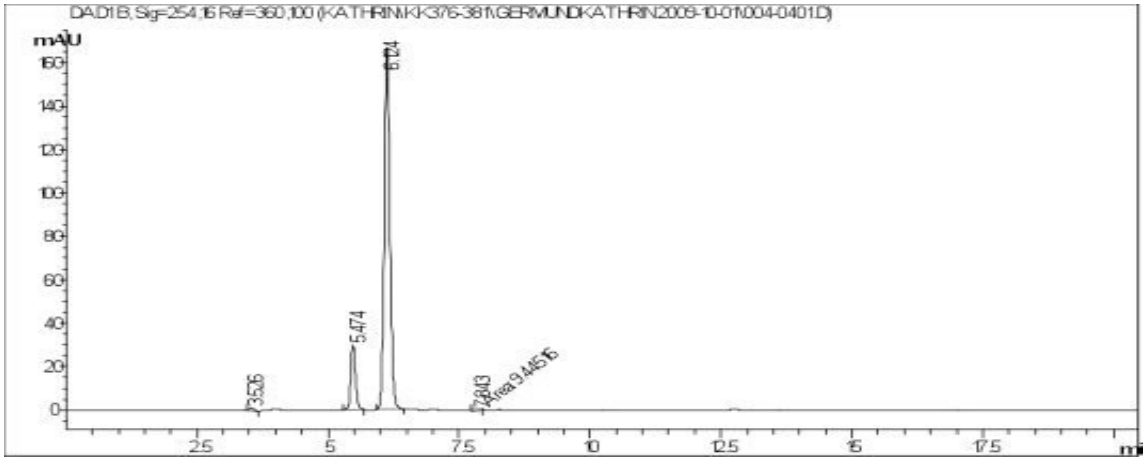
5i: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 10.0, 11.0 min



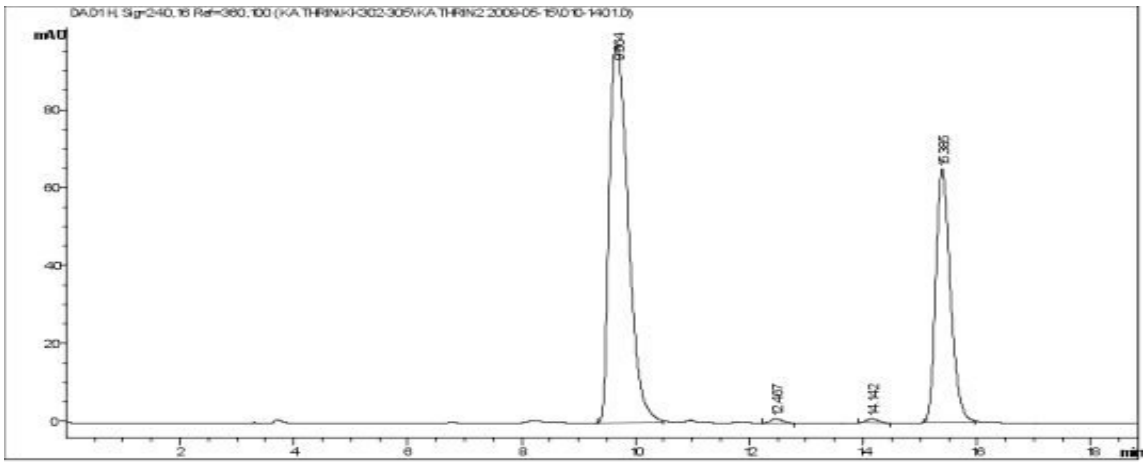
5j: 30 °C, 254 nm, Flow 1 mL/min, 99:1 Hexane: 2-Propanol

Retention Times: Amine: 5.5, 6.1 min; Imine: 22.3 min



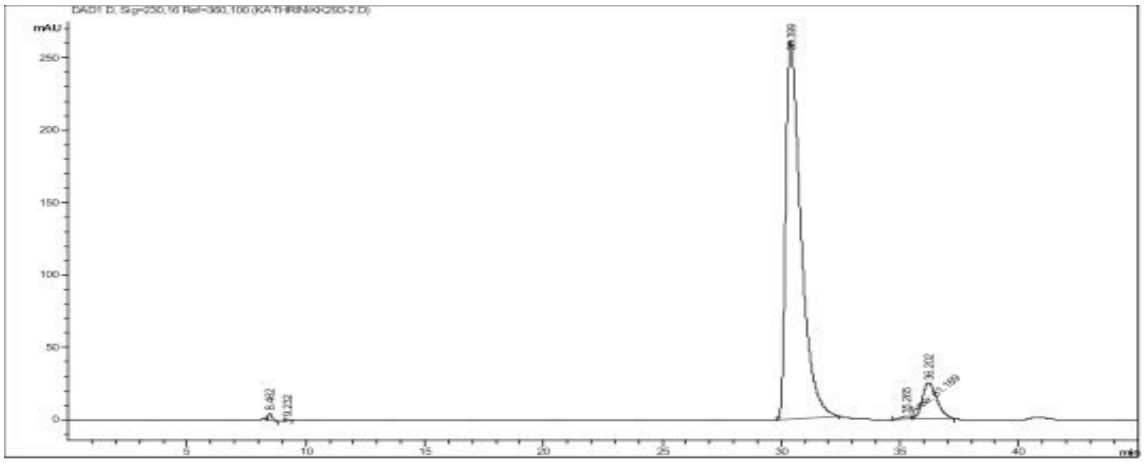
5l: 30 °C, 240 nm, Flow 1 mL/min, 99.7:0.3 Hexane: 2-Propanol

Retention Times: Amine: 12.5, 15.4 Amin; Imine: 9.7 min



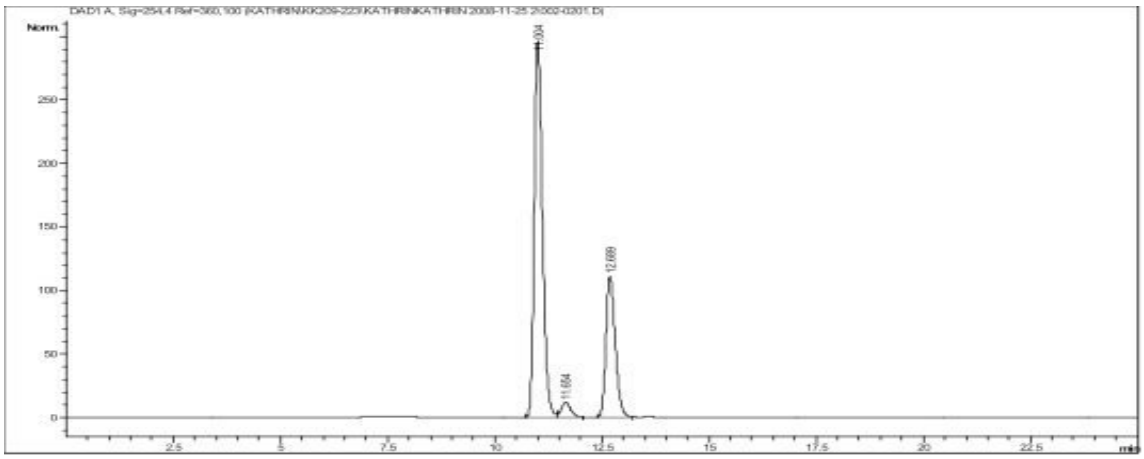
5m: 30 °C, 240 nm, Flow 0.4 mL/min, 97:3 Hexane: 2-Propanol

Retention Times: Amine: 35.3, 36.2 min; Imine: 30.4 min



5n: 30 °C, 254 & 240 nm, Flow 1 mL/min, 99:1 Hexane: 2-Propanol

Retention Times: Amine: 11.0, 11.7; Imine: 12.7



6. The Potassium Hydride Mediated Trimerization of Imines

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Keywords: Aminofulvenes, Fulvene Synthesis, Imines, Potassium Hydride

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Abstract: A novel reaction, the potassium hydride mediated synthesis of fulvenes, is described. The synthesis utilizes *N*-aryl imines as inexpensive starting material affording novel substituted aminofulvenes. It is proposed that the presence of the metalated enamine as well as the imine (ratio 2:1) leads to the formation of an initial trimerization product, which cyclizes, giving rise to the aminofulvene.

6.1 Introduction

Pentafulvenes, first described by Thiele at the beginning of this century,[1] attracted much interest due to their color,[2] reactivity (especially cycloadditions[3]), dipole moment[4] and questions regarding their aromatic or anti-aromatic[5] character. Furthermore they represent a class of very interesting organic ligands. Various organometallic compounds, being applied for instance as polymerization catalysts[6] or anticancer agents,[7] have been synthesized *via* fulvene routes.[8] Fulvenes can be obtained by condensation reaction[9] of aldehydes or ketones with cyclopentadienyl. Additionally, a few other methods can be utilized.[10] Herein we report a novel potassium hydride mediated approach towards 1,3,6-substituted 6-aminofulvenes. The imine trimerization reaction is based on tautomerization into metalated enamines and proceeds *via* C-H activation and multiple C-C bond formation steps.

6.2 Results and Discussion

Within the base optimization experiments for the enantioselective hydrogenation[11] of **1a** (Fig. 1), the formation of a by-product was observed if KH was utilized as a base. A dark red material crystallized in one of the catalysis samples. It was identified as [(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-phenyl-amine **2a** (Fig. 1).

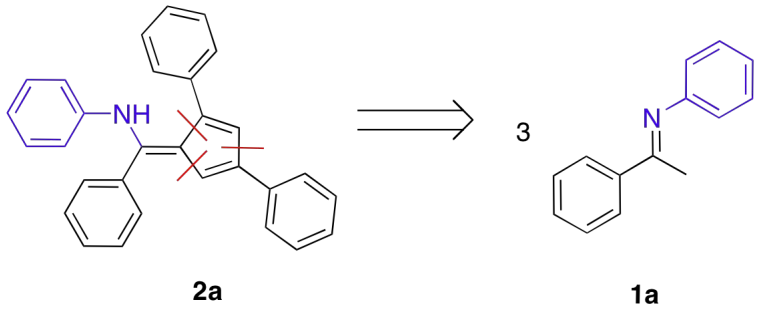

Figure 1: Retrosynthetic approach towards novel fulvenes.

Upon this discovery, we were interested in understanding and using the side reaction. A precise reaction stoichiometry (imine : KH ratio) is crucial to yield fulvenes as main product. Addition of a large excess of potassium hydride (3 eq.) led to amine formation, whilst using one equivalent mainly yielded the imine starting material (after workup). Upon utilization of 0.7 equivalents of potassium hydride, complete conversion of the imine to the corresponding 6-aminofulvene as main product was observed (Fig. 2). The addition of several metal bases was investigated. Only the utilization of potassium hydride gave rise to fulvene **2a** with complete conversion of the starting material.

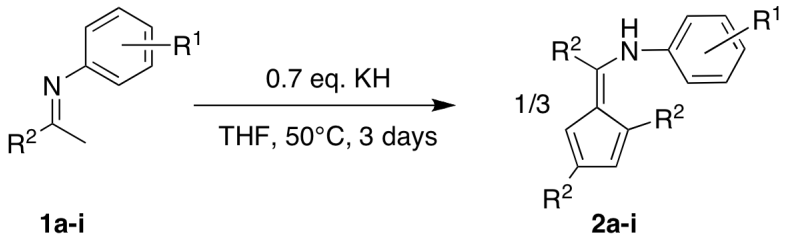

Figure 2: Synthesis of fulvenes from *N*-aryl imines.

Upon the addition of potassium hydride to imines **1a-i** the color of the reaction solution changed quickly to green and then dark red, accompanied by hydrogen evolution. The corresponding fulvenes **2a-i** were obtained as dark red materials in moderate yields (Fig. 3).

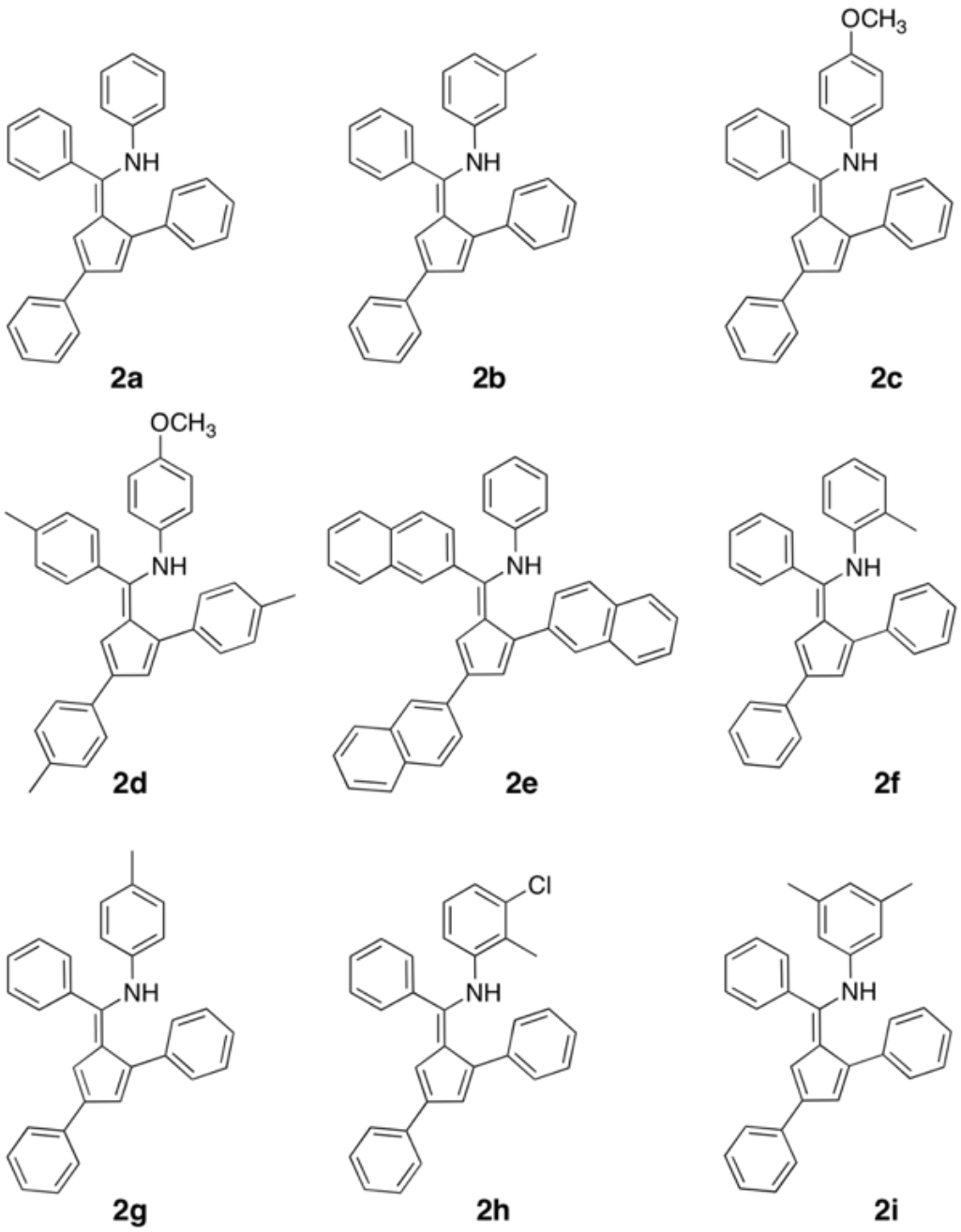

Figure 3: 6-aminofulvenes **2a-i**.

A time-conversion plot was realized to gain additional insight into mechanistic details of this novel reaction (Fig. 4). The isolated yield of the fulvene is consistent with the GC-yield, which was obtained in the kinetic experiment. Additionally, the formation of an intermediate (**3a**) and a by-product (**4a**) could be observed as well as the formation of aniline. The key intermediate (1,3-diphenyl-but-3-enylidene)-phenyl-amine (**3a**) was independently synthesized. Reduction of **3a** gives rise (after aqueous work up) to the by-product (1,3-diphenyl-butylidene)-phenyl-amine (**4a**), which could be isolated from the reaction mixture and was characterized *via* NMR spectroscopy and EA.

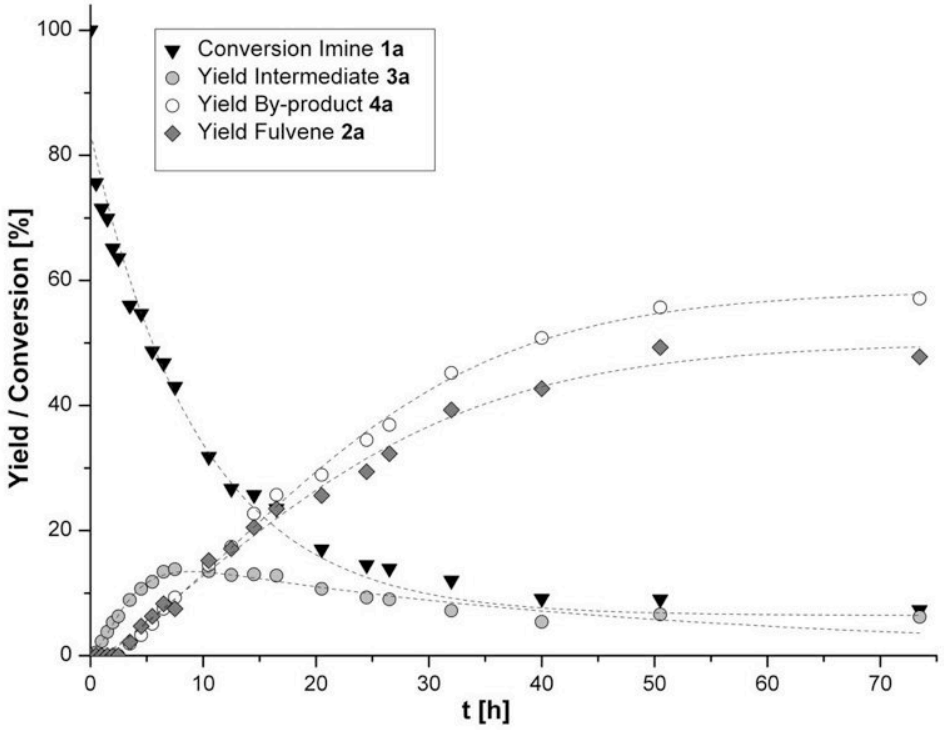

Figure 4: Time-conversion plot; determined *via* GC with dodecane as internal standard.

The potassium cyclopentadienylimine complex **5a** was crystallized from the reaction mixture and was analyzed *via* X-Ray crystal structure analysis to determine the molecular structure (Fig. 5).

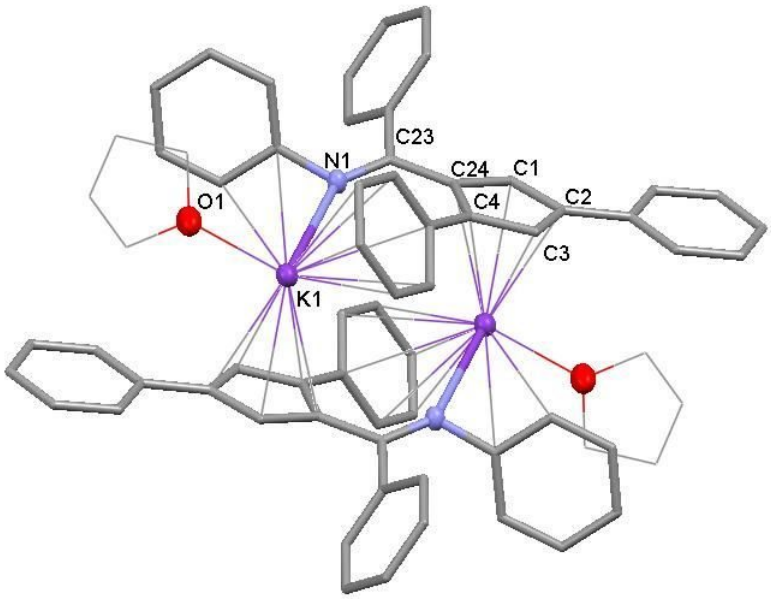

Figure 5: Molecular structure of **5a**; selected bond lengths [Å] and angles [°]: C1-C2, 1.404(5); C1-C24, 1.416(6); C2-C3, 1.409(6); C3-C4, 1.386(6); C4-C24, 1.425(6); C17-K1, 3.208(4); C22-K1, 3.229; C23-N1, 1.304(5); C23-C24, 1.458(6); N1-K1, 2.814(4); N1-C22-K1, 60.4(2); N1-C23-C24, 120.1(4); N1-C23-C25, 122.5(4); C23-N1-C22, 121.4(4).

In the dimeric complex **5a**, the potassium is coordinated by the N-atom and further stabilized by π-coordination of the electron rich phenyl substituents of **5a** and the cyclopentadienyl moiety of a second ligand molecule. The bond lengths of **5a** differ significantly from the bond lengths of the isolated fulvene **2a**. Whereas in **2a** the three double bonds (1.36-1.38 Å) are notably shorter than the sigma-bonds (1.45-1.47 Å), in **5a** only the C3-C4 bond length (1.39 Å) is in the supposed range. The other C-C bond lengths vary between 1.40 and 1.46 Å. The C-N bond length of only 1.304 Å indicates a C-N double bond. These data provide a consistent picture of the coordinated ligand as a cyclopentadienylimine rather than an amidofulvene. The standard deviation of the cyclopentadienyl plane is 0.005 Å. The nitrogen atom is out of this plane (distance 0.41 Å), because it coordinates the potassium atom.

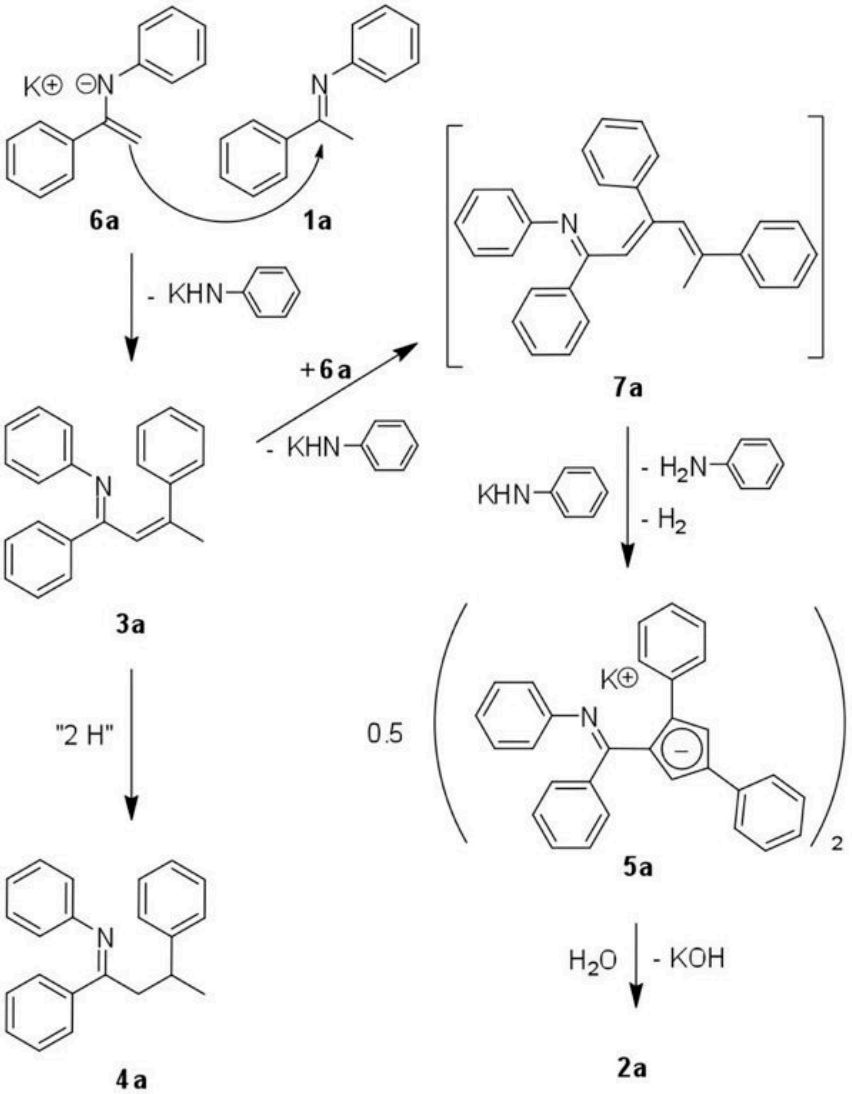

Figure 6: *Proposed reaction mechanism.*

Since Knorr *et al.*[12] reported the formation of metastable secondary enamines *via* lithiation of imines with lithium diisopropylamide, we assumed that enamine-formation

upon potassium hydride addition is a crucial reaction step in fulvene formation. The two olefinic hydrogen-atoms of the enamine **6a** were detected as doublets (J = 1.4 Hz) at 4.29 and 4.12 ppm (solvent C_6D_6:THF-d_8 10:1).

The presence of the imine as well as the enamine is necessary for the reaction to take place, which is supported by the results of the KH : imine ratio screening. As indicated in Figure 6, the enamine species **6a** attacks the C-atom of the C=N bond[13] of **1a** to yield (1,3-diphenyl-but-3-enylidene)-phenyl-amine **3a**, thereby potassium anilide is eliminated. A second attack of **6a** at the imino-group of **3a** occurs and subsequently the trimerization product **7a** cyclizes to **5a**. The proposed mechanism is summarized in Figure 6.

The reaction of *N*-alkyl imines, *N*-phenyl-(1-phenyl-propylidene)-amines, or *N*-phenyl-(1-alkyl-ethylidene)-amines with potassium hydride did not yield the corresponding fulvenes. NMR-experiments upon KH addition suggested that the tautomerization to aldimines or isomerization of the double bond into the alkyl-chain prevents the initial attack.

6.3 Conclusions

In conclusion, a novel reation was discovered. A series of novel 1,3,6-substituted 6-aminofulvenes was synthesized by a facile approach, which utilizes inexpensive and readily available imines as starting material. Furthermore, the mechanism of the reaction was investigated. We propose that the potassium-mediated trimerization reaction of *N*-aryl imines proceeds *via* an observed dimerization and transient trimerization product, which subsequently cyclizes, thereby giving rise to novel fulvenes.

Supporting Information available

Supporting information including crystallographic data, characterization data, and detailed experimental procedures is available (Refer to 6.6).

Acknowledgments

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6.4 Experimental Section

General procedure for the synthesis of fulvenes: In a pressure tube 20.0 mmol of the imine **1** were dissolved in about 10.0 mL of THF. Then 0.57 g (14.0 mmol) of potassium hydride were added, immediately the color changed from orange to green and a second color change to dark red, accompanied by hydrogen evolution, took place. The dark brown solution was heated under slight reflux for three to four days. Then it was cooled to room temperature and water (about 5 mL) was added. The solution was extracted with diethyl ether (10 mL), the organic phase was dried over Na_2SO_4 and evaporated to dryness by rotary evaporation. The dark red product was purified via column chromatography (*n*-hexane/ ethyl acetate) or recrystallized.
Synthesis of [(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-phenyl-amine ***2a****:* yielded as red crystalline product (1.18 g, 45%). M.p. 160-170 °C. Found: C, 90.3; H, 5.7; N, 3.6. Calc. for $C_{30}H_{23}N$ (397.51): C, 90.6; H, 5.8; N, 3.5%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.34-7.27 (m, 5H), 7.15-7.14 (d, 1H, *J* = 1.5), 7.13-7.12 (d, 1H, *J* = 2.1), 6.92-6.67 (m, 9H), 6.43-6.39 (m, 4H), 6.29-6.24 (t, 1H, *J* = 7.5) and 5.90-5.87 (d, 2H, *J* = 7.5); δ_C (63,89 MHz, $CDCl_3$, 298 K, TMS) 154.51, 141.83, 140.68, 139.21, 138.75, 136.85, 136.46, 124.25 (C_q fulvene, aryl C_q), 133.08, 130.85, 130.80, 130.73, 130.39, 130.21, 127.17, 122.86 ($C_{o,m}$, aryl *C*H), 132.06, 129.02, 128.59, 127.87, 125.27 and 121.95 (C_p, aryl *C*H, *C*H fulvene).

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6.6 Supporting Information

6.6.1 General

Syntheses of the imine starting materials were performed under standard conditions. Fulvene syntheses were conducted in oven (95 °C) and vacuum dried glassware under an inert atmosphere of dry argon 5.0 via standard Schlenk or glove box techniques. NMR spectra were recorded on a Bruker ARX 250 (250 MHz) spectrometer or on a Varian Inova 300 or 400 (300 or 400 MHz). Chemical shifts are reported in ppm from TMS with the solvent resonance resulting from incomplete deuteration as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant. Melting points were determined in sealed capillaries with a Stuart SMP3 melting point apparatus. Elemental analysis was performed with a Vario elementar EL *III* elemental analyzer. GC-MS analyses were performed on a Thermo Focus GC with DSQ-MS unit equipped with a HP-5-MS column (30m x 0.32mm x 0.25µm). GC analyses were performed with an Agilent 6890 N Network GC-System equipped with a HP-5 column (30m x 0.32mm x 0.25µm). Non-halogenated solvents were distilled from sodium benzophenone ketyl and halogenated solvents from P_2O_5. Deuterated solvents were obtained from Cambridge Isotope Laboratories and were degassed, dried and distilled prior to use. All chemicals were purchased from commercial vendors and used without further purification.

6.6.2 Synthesis of Imines

N-Aryl imines were synthesized according to Taguchi *et al.*[2] – a solution of 0.1 mol amine, 0.1 mol ketone and 40 g of molecular sieves (4 Å) in 20 mL of diethyl ether was stirred for 24 hours. The molecular sieves were filtered off and washed with ether. The combined filtrates were evaporated to dryness and the residue was purified *via* vacuum distillation (liquid residue) or recrystallization.

N-(1-phenylethylidene)aniline **1a**: yielded as a pale yellow solid (14.66 g, 75 %). M.p. 37 °C. Found: C, 86.0; H, 6.9; N, 7.3. Calc. for $C_{14}H_{13}N$ (195.26): C, 86.1; H, 6.7; N, 7.2%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.97-7.94 (m, 2H, C_6H_5), 7.21-7.14 (m, 5H, C_6H_5), 6.69-6.91 (t, 1H, C_6H_5, J = 7.2), 6.78-6.74 (m, 2H, C_6H_5) and 1.82 (s, 3H,

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C*H*$_3$); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 164.34 (C=N), 152.45, 139.69 (C_q, *C*$_6$H$_5$), 130.40, 129.14, 128.31, 127.54, 123.20, 119.58 (*C*$_{o,m,p}$, *C*$_6$H$_5$) and 16.63 (*C*H$_3$).

3-methyl-*N*-(1-phenylethylidene)aniline **1b**: yielded as a pale yellow solid (11.00 g, 53%). M.p. 34 °C. Found: C, 85.8; H, 7.4; N, 6.8. Calc. for $C_{15}H_{15}N$ (209.29): C, 86.1; H, 7.2; N, 6.7%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.99-7.96 (m, 2H, aryl C*H*); 7.18-7.12 (m, 4H, aryl C*H*); 6.80-6.78 (d, 1H, aryl C*H*, *J* = 7.5), 6.63-6.60 (d, 2H, aryl C*H*, *J* = 8.7), 2.14 (s, 3H, C*H*$_3$) and 1.86 (s, 3H, C*H*$_3$); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 164.10 (C=N), 152.54, 139.80, 139.67 (aryl *C*$_q$), 130.34, 129.04, 128.31, 127.52, 123.98, 120.22, 116.64 (aryl *C*H), 21.37 (*C*H$_3$) and 16.68 (*C*H$_3$).

4-methoxy-*N*-(1-phenylethylidene)aniline **1c**: yielded as a pale yellow solid (19.40 g, 86%). M.p. 86 °C. Found: C, 79.5; H, 6.7; N, 6.1. Calc. for $C_{15}H_{15}NO$ (225.29): C, 80.0; H, 6.7; N; 6.2%. δ_H (399.80 MHz, [*d*$_6$]DMSO, 298 K, TMS) 8.00-7.97 (m, 2H, C$_6$*H*$_5$), 7.48-7.45 (m, 3H, C$_6$*H*$_5$), 6.95-6.93 (d, 2H, C$_6$*H*$_4$OCH$_3$, *J* = 8.4), 6.76-6.74 (d, 2H, C$_6$*H*$_4$OCH$_3$, *J* = 8.4), 3.75 (s, 3H, OC*H*$_3$) and 2.21 (s, 3H, C*H*$_3$); δ_C (100.53 MHz, [*d*$_6$]DMSO, 298 K, TMS) 165.59 (C=N), 156.15, 144.94, 139.87, 131.02, 128.94, 127.70, 121.40, 114.86 (aryl *C*$_q$, aryl *C*H), 55.82 (O*C*H$_3$) and 17.64 (*C*H$_3$).

4-methoxy-*N*-(1-(*p*-tolyl)ethylidene)aniline **1d**: yielded as a pale yellow solid (10.68 g; 45%). M.p. 83 °C. Found: C, 80.2; H, 7.4; N, 5.9. Calc. for $C_{16}H_{17}NO$ (239.31): C, 80.3; H, 7.2; N, 5.85%. δ_H (299.83 MHz, $CDCl_3$, 298 K, TMS) 7.91-7.89 (d, 2H, aryl C*H*, *J* = 8.1), 7.29-7.26 (d, 2H, aryl C*H*, *J* = 8.1), 6.95-6.92 (d, 2H, aryl C*H*, *J* = 9.0), 6.80-6.77 (d, 2H, aryl C*H*, *J* = 9.0), 3.84 (s, 3H, OC*H*$_3$), 2.44 (s, 3H, C*H*$_3$) and 2.26 (s, 3H, C*H*$_3$); δ_C (75.39 MHz, $CDCl_3$, 298 K, TMS): 165.79 (C=N), 156.11, 145.22, 140.79, 137.33, 129.30, 127.36, 121.08, 114.47 (aryl *C*$_q$, aryl *C*H), 55.73 (O*C*H$_3$), 21.64 (*p*-*C*H$_3$) and 17.49 (*C*H$_3$).

N-(1-(naphthalen-2-yl)ethylidene)aniline **1e**: yielded as a pale yellow solid (10.07 g, 60%). M.p. 140 °C. Found: C, 88.0; H, 6.1; N, 5.8. Calc. for $C_{18}H_{15}N$ (245.32): C, 88.1; H, 6.2; N, 5.7%. δ_H (299.83 MHz, [*d*$_6$]DMSO, 298 K, TMS) 8.51 (s, 1H, 2-naphtyl), 8.23-8.20 (dd, 1H, 2-naphtyl, *J* = 1.8), 8.09-8.06 (m, 1H, 2-naphtyl), 8.00-7.97 (m, 2H, 2-naphtyl), 7.61-7.58 (m, 2H, 2-naphtyl), 7.42-7.36 (t, 2H, H$_m$, C$_6$*H*$_5$), 7.13-7.08 (t, 1H, H$_p$, C$_6$*H*$_5$), 6.86-6.83 (d, 2H, H$_o$, C$_6$*H*$_5$) and 2.33 (s, 3H, C*H*$_3$); δ_C

(75.39 MHz, [d_6]DMSO, 298 K, TMS): 164.83 (C=N), 151.36, 136.21, 133.90, 132.54 (aryl C_q), 128.97, 127.90, 127.68, 127.52, 127.36, 126.51, 123.94, 123.12, 119.30 (aryl *C*H) and 17.09 (CH_3).

2-methyl-*N*-(1-phenylethylidene)aniline **1f**: yielded as a pale yellow solid (15.60 g, 75%). M.p. 61 °C. Found: C, 85.7; H, 7.5; N, 6.7. Calc. for $C_{15}H_{15}N$ (209.29): C, 86.1; H, 7.2; N, 6.7%. δ_H (399.83 MHz, [d_6]DMSO, 298 K, TMS) 7.99-7.96 (m, 2H, C_6H_5), 7.48-7.43 (m, 3H, C_6H_5), 7.20-7.18 (d, 1H, aryl C*H*, *J* = 7.6), 7.16-7.12 (t, 1H, aryl C*H*, *J* = 7.6), 6.97-6.93 (t, 1H, aryl C*H*, *J* = 7.6), 6.60-6.59 (d, aryl C*H*, 1H, *J* = 7.6), 2.09 (s, 3H, CH_3) and 1.98 (s, 3H, CH_3); δ_C (100.53 MHz, [d_6]DMSO, 298 K, TMS) 165.31 (C=N), 150.67, 139.50, 131.19, 130.83, 129.02, 127.74, 127.20, 127.05, 123.72, 118.89 (aryl *C*H, aryl C_q), 18.10 (CH_3) and 17.87 (CH_3).

N-(1-(*p*-tolyl)ethylidene)aniline **1g**: yielded as a pale yellow solid (14.51 g, 70%). M.p. 62 °C. Found: C, 85.7; H, 7.5; N, 6.8. Calc. for $C_{15}H_{15}N$ (209.29): C, 86.1; H, 7.2; N, 6.7%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.94-7.91 (d, 2H, aryl C*H*, *J* = 8.1), 7.21-7.14 (m, 4H, aryl C*H*), 7.02-6.99 (d, 2H, aryl C*H*, *J* = 8.1), 6.96-6.91 (t, 1H, aryl C*H*, *J* = 7.2), 6.78-6.75 (d, 2H, aryl C*H*, *J* = 7.2), 2.09 (s, 3H, CH_3) and 1.86 (s, 3H, CH_3); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 164.00 (C=N), 152.41, 140.30, 137.00 (aryl C_q), 128.96, 128.92, 127.44, 122.92, 119.53 (aryl *C*H) and 21.00, 16.47 (CH_3).

3-chloro-2-methyl-*N*-(1-phenylethylidene)aniline **1h**: yielded as pale yellow solid (17.80 g, 73%). M.p. 80 °C. Found: C, 73.8, H, 5.9; N, 5.7. Calc. for $C_{15}H_{17}ClN$ (243.73): C, 73.9; H, 5.8; N, 5.75%. δ_H (299.83 MHz, [d_6]DMSO, 298 K, TMS) 8.03-8.01 (d, 2H, C_6H_5, *J* = 7.6), 7.53-7.49 (m, 3H, C_6H_5), 7.19-7.16 (m, 2H, aryl C*H*), 6.65-6.63 (d, 1H, aryl C*H*, *J* = 7.6), 2.15 (s, 3H, CH_3) and 2.07 (s, 3H, CH_3); δ_C (100.53 MHz, [d_6]DMSO, 298 K, TMS) 166.18 (C=N), 151.86, 138.83, 134.35, 125.11 (aryl C_q), 131.17, 128.77, 127.70, 127.55, 123.89, 117.74 (aryl *C*H), 17.79 (CH_3) and 14.72 (CH_3).

3,5-dimethyl-*N*-(1-phenylethylidene)aniline **1i**: yielded as an orange liquid (14.40 g, 65%). Found: C, 85.6, H, 7.5; N, 6.6. Calc. for $C_{16}H_{17}N$ (223.31): C, 86.05; H, 7.7; N, 6.3%. δ_H (299.83 MHz, [d_6]DMSO, 298 K, TMS) 7.98-7.95 (m, 2H, C_6H_5), 7.48-7.46 (m, 3H, C_6H_5), 6.69 (s, 1H, H_p, $C_6H_3(CH_3)_2$), 6.38 (s, 2H, H_o, $C_6H_3(CH_3)_2$), 2.26 (s,

6H, $C_6H_3(CH_3)_2$) and 2.17 (s, 3H, CH_3); δ_C (75.39 MHz, [d_6]DMSO, 298 K, TMS) 164.40 (C=N), 151.37, 138.98, 137.95, 130.34, 128.23, 127.00, 124.49, 116.74 (aryl C_q, aryl *C*H), 20.92 (2 x CH_3, $C_6H_3(CH_3)_2$) and 16.97 (CH_3).

6.6.3 Synthesis of Fulvenes

General procedure: In a pressure tube 20.0 mmol of the imine **1** were dissolved in about 10.0 mL of THF. Then 0.57 g (14.0 mmol) of potassium hydride were added, immediately the color changed from orange to green and a second color change to dark red, accompanied by hydrogen evolution, took place. The dark brown solution was heated under slight reflux for three to four days. Then it was cooled to room temperature and water (about 5 mL) was added. The solution was extracted with diethyl ether (10 mL), the organic phase was dried over Na_2SO_4 and evaporated to dryness by rotary evaporation. The dark red product was purified via column chromatography (*n*-hexane/ ethyl acetate) or recrystallized.

[(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-phenyl-amine **2a**: yielded as red crystalline product (1.18 g, 45%). M.p. 160-170 °C. Found: C, 90.3; H, 5.7; N, 3.6. Calc. for $C_{30}H_{23}N$ (397.51): C, 90.6; H, 5.8; N, 3.5%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.34-7.27 (m, 5H), 7.15-7.14 (d, 1H, *J* = 1.5), 7.13-7.12 (d, 1H, *J* = 2.1), 6.92-6.67 (m, 9H), 6.43-6.39 (m, 4H), 6.29-6.24 (t, 1H, *J* = 7.5) and 5.90-5.87 (d, 2H, *J* = 7.5); δ_C (63,89 MHz, $CDCl_3$, 298 K, TMS) 154.51, 141.83, 140.68, 139.21, 138.75, 136.85, 136.46, 124.25 (C_q fulvene, aryl C_q), 133.08, 130.85, 130.80, 130.73, 130.39, 130.21, 127.17, 122.86 ($C_{o,m}$, aryl *C*H), 132.06, 129.02, 128.59, 127.87, 125.27 and 121.95 (C_p, aryl *C*H, *C*H fulvene).

[(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-*m*-tolyl-amine **2b**: at -20 °C a red crystalline material (1.52 g, 57%) was obtained. M.p. 181-185 °C. Found: C, 90.4; H, 6.05; N, 3.35. Calc. for $C_{31}H_{25}N$ (411.54): C, 90.5; H, 6.1; N, 3.4%. δ_H (299.83 MHz, C_6D_6, 298 K, TMS) 7.62-7.60 (d, 4H, *J* = 8.1), 7.45-7.44 (d, 1H, *J* = 1.5), 7.43-7.42 (d, 1H, *J* = 2.1), 7.20-6.94 (m, 11H), 6.73-6.72 (d, 1H, *J* = 1.8), 6.67-6.62 (t, 1H, *J* = 7.8), 6.43-6.40 (d, 1H, *J* = 7.5), 6.08-6.06 (d, 1H, *J* = 7.8), 5.99 (s, 1H) and 1.79 (s, 3H, CH_3); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 151.32, 140.36, 139.27, 138.50, 138.13, 137.21, 135.60, 135.01, 123.71 (aryl C_q, C_q fulvene), 131.34,

129.74, 128.77, 128.60, 126.27, 125.29, 125.36, 123.80, 121.72, 120.51, 117.99 (aryl *C*H, *C*H fulvene) and 20.86 (CH_3).

[(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-*p*-methoxy-phenyl-amine **2c**: yielded as red crystalline product (0.77 g, 37%). M.p. 199 °C. Found: C, 87.4; H, 5.9; N, 3.2. Calc. for $C_{31}H_{25}NO$ (427.54): C, 87.1; H, 5.9; N, 3.3%. δ_H (399.83 MHz, $CDCl_3$, 298 K, TMS) 7.63-7.58 (m, 6H), 7.52 (s, 1H), 7.48-7.17 (m, 9H), 7.19-7.15 (t, 1H, *J* = 7.2), 6.92 (s, 1H), 6.62-6.60 (d, 2H, *J* = 8.4), 6.47-6.44 (d, 2H, *J* = 8.4), 6.42 (s, 1H) and 3.71 (s, 3H, OC*H*$_3$); δ_C (100.53 MHz, $CDCl_3$, 298 K, TMS) 156.11, 153.88, 138.90, 136.99, 136.44, 134.81, 134.09, 132.93 123.23 (aryl C_q, C_q fulvene), 131.18, 128.89, 128.68, 128.39, 128.10, 125.14, 123.23, 114.11 ($C_{o,m}$, aryl *C*H), 129.92, 126.49, 126.45, 125.69, 120.01 (C_p, aryl *C*H, *C*H fulvene) and 55.33 (O*C*H$_3$).

[(2,4-di-*p*-tolyl-cyclopenta-2,4-dienylidene)-*p*-tolyl-methyl]-*p*-methoxy-phenyl-amine **2d**: In a pressure tube 3.59 g (15.00 mmol) of the imine **1d** were dissolved in about 10 mL of THF. Then 0.42 g (10.50 mmol) of potassium hydride were added, immediately the color changed from orange to green and a second color-change to dark red, accompanied by hydrogen evolution, took place. The dark brown solution was heated under slight reflux for three days, then cooled to room temperature and water (about 5 mL) was added. The solution was extracted with diethyl ether (10 mL) and the organic phase was dried with Na_2SO_4. At -20 °C a red crystalline material **2d** (0.67 g, 29%) was obtained. M.p. 185 °C. Found: C, 86.5; H, 6.75; N, 2.85. Calc. for $C_{34}H_{31}NO$ (469.62): C, 87.0; H, 6.65; N, 3.0%. δ_H (399.83 MHz, $CDCl_3$, 298 K, TMS) 7.47-7.41 (m, 7H), 7.16-7.07 (m, 6H), 6.81 (s, 1H), 6.59-6.57 (d, 2H, *J* = 8.4), 6.44-6.21 (d, 2H, *J* = 8.4), 6.33 (s, 1H), 3.68 (s, 3H, OC*H*$_3$), 2.39 (s, 3H, C*H*$_3$) and 2.31 (s, 6H, 2x C*H*$_3$); δ_C (100.53 MHz, $CDCl_3$, 298 K, TMS) 155.89, 153.71, 139.95, 136.21, 135.90, 135.04, 134.26, 133.86, 133.20, 131.86, 120.82 (aryl C_q, C_q fulvene), 131.12, 129.47, 129.00, 128.73, 128.46, 124.99, 123.27, 113.97 (aryl $C_{o,m}$), 126.13, 119.16 (*C*H fulvene), 55.25 (O*C*H$_3$) 21.44 (*C*H$_3$), 21.11(*C*H$_3$) and 21.08 (*C*H$_3$).

[(2,4-di-naphtalen-2-yl-cyclopenta-2,4-dienylidene)-naphtalen-2-yl-methyl]-phenyl-amine **2e**: yielded as a red solid (0.50 g, 21%). M.p. 202 °C. Found: C, 92.0; H, 5.4; N, 2.4. Calc. for $C_{42}H_{29}N$ (547.59): C, 92.1; H, 5.3; N, 2.6%. δ_H (399.83 MHz, C_6D_6, 298 K, TMS) 8.20 (s, 3H), 7.83-7.7.78 (t, 2H, *J* = 9.2), 7.68-7.43 (m, 11H), 7.27-7.16

(m, 7H), 7.01 (m, 1H), 6.57-6.49 (m, 3H) and 6.16-6.15 (d, 2H, *J* = 7.2). δ_C (100.53 MHz, $CDCl_3$, 298 K, TMS) 152.61, 139.88, 137.46, 135.94, 134.87, 134.06, 134.03, 133.91, 133.89, 132.72, 132.51, 132.22, 132.15, 123.11 (aryl C_q, C_q fulvene), 128.88, 128.84, 128.30, 127.94, 127.88, 127.85, 127.78, 127.65, 127.52, 127.45, 126.71, 126.62, 126.22, 125.91, 125.53, 124.96, 124.44, 123.45, 122.86 and 121.05 (aryl C*H*, C*H* fulvene).

[(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-*o*-tolyl-amine **2f**: yielded as a red solid (0.85 g, 31%). M.p. 165 °C. Found: C, 90.3; H, 6.0; N, 3.6. Calc. for $C_{31}H_{25}N$ (411.54): C, 90.5; H, 6.1; N, 3.4%. δ_H (399.83 MHz, C_6D_6, 298 K, TMS) 7.58-7.54 (m, 6H), 7.44-7.42 (m, 1H), 7.39-7.36 (m, 2H), 7.32-7.28 (m, 4H), 7.24-7.22 (m, 2H), 7.18-7.12 (m, 1H), 6.99-6.97 (d, 1H, *J* = 6.4), 6.91-6.90 (d, 1H, *J* = 1.6), 6.81-6.79 (m, 2H), 6.46-6.45 (m, 1H, *J* = 1.6), 6.37-6.35 (d, 1H, *J* = 6.4) and 1.75 (s, 3H, CH_3); δ_C (100.53 MHz, $CDCl_3$, 298 K, TMS) 153.48, 139.02, 138.40, 137.41, 137.08, 135.19, 134.79, 129.22, 122.52 (aryl C_q, C_q fulvene), 131.21, 130.62, 130.30, 129.16, 129.08, 128.66, 128.42, 127.00, 126.90, 126.39, 126.12, 125.46, 123.74, 122.16, 120.05 (aryl *C*H, *C*H fulvene) and 17.37 (*C*H_3).

[(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-*p*-tolyl-amine **2g**: yielded as a red solid (1.52 g, 57%). M.p. 167 °C. Found: C, 90.2; H, 6.0; N, 3.3. Calc. for $C_{31}H_{25}N$ (411.54): C, 90.5; H, 6.1; N, 3.4%; δ_H (399.83 MHz, $CDCl_3$, 298 K, TMS) 7.55-7.52 (m, 6H), 7.48-7.43 (m, 2H), 7.39-7.24 (m, 6H), 7.21-7.10 (m, 2H), 6.86 (s, 1H), 6.81-6.79 (d, 2H, *J* = 7.6), 6.36 (s, 1H), 6.29-6.27 (d, 2H, *J* = 7.6) and 2.17 (s, 3H, CH_3); δ_C (100.53 MHz, $CDCl_3$, 298 K, TMS) 153.14, 138.76, 137.17, 136.86, 136.72, 134.84, 134.21, 133.14, 121.52 (aryl C_q, C_q fulvene), 131.06, 129.94, 129.38, 128.84, 128.35, 128.12, 126.63, 126.51, 125.72, 125.12, 121.12, 119.94 (aryl *C*H, *C*H fulvene) and 20.66 (*C*H_3).

[(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-2-chloro-3-methyl-amine **2h**: yielded as a red solid (1.30 g, 44%). M.p. 205 °C. Found: C, 83.5; H, 5.0; N, 3.0. Calc. for $C_{31}H_{24}ClN$ (445.98): C, 83.5; H, 5.4; N, 3.1%. δ_H (399.83 MHz, C_6D_6, 298 K, TMS) 7.63-7.61 (d, 2H, *J* = 8.0), 7.49-7.47 (d, 2H, *J* = 8.0), 7.41-7.38 (d, 2H, *J* = 7.2), 7.22-7.20 (m, 2H), 7.10-7.6.91 (m, 9H), 6.77 (s, 1H), 6.72-6.70 (d, 1H, *J* = 7.6), 6.31-6.28 (m, 2H) and 1.68 (s, 3H, CH_3); δ_C (100.53 MHz, $CDCl_3$, 298 K, TMS) 152.34,

139.73, 138.57, 137.86, 136.56, 134.79, 134.78, 134.64, 127.25, 123.19 (aryl C_q, C_q fulvene), 130.93, 130.14, 128.84, 128.42, 128.25, 127.31, 126.83, 126.23, 126.06, 125.23, 124.30, 120.64, 119.72 (aryl *C*H, *C*H fulvene) and 13.65 (CH_3).

[(2,4-diphenyl-cyclopenta-2,4-dienylidene)-phenyl-methyl]-3,5-dimethyl-amine **2i**:
yielded as red solid (1.40 g, 49%). M.p. 214 °C. Found: C, 89.9; H, 6.4; N 3.5. Calc. for $C_{32}H_{27}N$ (425.56): C, 90.3; H, 6.4; N, 3.3%. δ_H (399.83 MHz, C_6D_6, 298 K, TMS) 7.68-7.63 (m, 4H), 7.49-7.48 (d, 2H, *J* = 6.8), 7.29 (s, 1H), 7.20-7.13 (m, 4H), 7.03-7.02 (m, 6H), 6.77 (s, 1H), 6.29 (s, 1H), 5.93 (s, 2H) and 1.83 (s, 6H, 2x CH_3); δ_C (100.53 MHz, $CDCl_3$, 298 K, TMS) 153.09, 139.45, 138.79, 138.36, 136.87, 136.72, 135.02, 134.21, 121.51 (aryl C_q, C_q fulvene), 130.99, 129.88, 128.87, 128.72, 128.36, 128.06, 126.69, 126.47, 125.73, 125.12, 120.01, 118.84 (aryl *C*H, *C*H fulvene) and 21.14 (2x CH_3).

6.6.4 Base optimization experiments

Table 1: Variation of imine - potassium hydride ratio.

No.	Ratio imine : KH	Conv.[a] [%]	Main product[b]
1	1.0 : 0.3	98.3	fulvene
2	1.0 : 0.7	99.9	fulvene
3	1.0 : 1.0	34.0	imine
4	1.0 : 3.0	70.9	amine

50 °C, 72h; [a] determined after workup *via* GC; [b] determined after workup *via* GC-MS

Table 2: Base Screening.

No.	Base (0.7 eq.)	Conv.[a] [%]
1	KH	99.9
2	KOH	22.0
3	KO*t*Bu	90.0
4	LiH	51.0
5	LiO*t*Bu	0
6	$KOSiMe_3$	0
7	$NaNH_2$	70.0
8	K_2CO_3	0

50 °C, 72h; [a] determined after workup *via* GC

6.6.5 Kinetic experiments

In a Schlenk tube 4.0 g (20.48 mmol) of **1a** were dissolved in 25 mL THF, then 0.58 g KH (14.34 mmol) were added carefully. Thereby the color of the orange solution changed to green and later red with hydrogen being evolved. The Schlenk tube was stirred at 50 °C and periodically samples (0.6 mL) were taken. Water (1 mL), dodecane (93.15 µL) and 2 mL of diethyl ether were added to 500 µL of the sample. The organic phase was extracted and analyzed via GC-(MS).

GC-MS analyses of kinetic-samples:

Aniline: MS (70 eV, EI); m/z (%): 93(M^+, 100), 66(54).

Imine: MS (70 eV, EI); m/z (%): 195(M^+, 40), 180(85), 118(20), 77(100).

By-Product: MS (70 eV, EI); m/z (%): 299(M^+, 7), 284(11), 206(7), 194(23), 180(34), 129(6), 105(43), 91(19), 77(100).
Hydrolysis of (1,3-diphenyl-butylidene)-phenyl-amine to aniline and 1,3-diphenyl-butan-1-one [224(M^+, 10)] was observed after some days.

Intermediate: MS (70 eV, EI); m/z (%): 297(M^+, 6), 284(4), 194(6), 180(4), 207(7), 184(7), 194(6), 180(4), 117(19), 91(100), 77(28), 65(10), 51(39).

Fulvene: MS (70 eV, EI); m/z (%): 397(M^+, 47), 319(7), 294(9), 215(14), 180(29), 153(11), 77(10).

Isolation of (1,3-diphenyl-butylidene)-phenyl-amine ("by-product") 4a: In a pressure tube 4.0 g (20.48 mmol) of **1a** were dissolved in 10 mL THF, then 0.58 g KH (14.34 mmol) were added carefully. Thereby the color of the orange solution changed to green and later red with hydrogen being evolved. The Schlenk tube was stirred at 50 °C for 3 days. Then water (10 mL) was added. The organic phase was extracted, dried with Na_2SO_4 and reduced to dryness *in vacuo*. Pentane was added to the residue and red fulvene precipitated. The remaining solution was filtered, reduced to dryness *in vacuo*, and distilled in high vacuum yielding (1,3-diphenyl-butylidene)-phenyl-amine as an orange viscous liquid (0.67 g, 22%). Found: C, 88.0; H, 7.2; N 4.7. Calc. for $C_{22}H_{21}N$ (299.41): C, 88.25; H, 7.1; N, 4.7%. δ_H (250.13 MHz, C_6D_6, 298 K, TMS) 8.03-7.99 (m, 2H, C_6H_5), 7.32-7.10 (m, 9H, C_6H_5), 6.89-6.85 (m, 2H, C_6H_5), 6.67-6.64 (m, 2H), 3.13-3.02 (m, 1H, C*H*), 2.95-2.92 (m, 2H, CH_2) and 1.10-

1.07 (d, 3H, C*H*$_3$, *J* = 7.0); δ_C (62.90 MHz, $CDCl_3$, 298 K, TMS) 166.80 (C=N), 151.25, 145.12, 138.69 (*C*$_q$, C_6H_5), 129.57, 128.35, 127.97, 127.88, 127.50, 126.46, 125.92, 122.33, 118.87 (*C*$_{o,m,p}$, C_6H_5), 38.14 (*C*H$_2$), 37.68 (*C*H) and 20.61 (*C*H$_3$).

Synthesis of (1,3-diphenyl-but-3-enylidene)-phenyl-amine ("intermediate product") 3a: To a solution of 4.00 g (18.00 mmol) of dypnone and 1.97 mL (21.60 mmol) aniline in 15 mL of benzene, 10.0 g molecular sieves (5 Å) and catalytic amounts of *p*-toluene sulfonic acid were added. The solution was refluxed for 5 days. The solution was filtered off the molecular sieves, and washed with diethyl ether. The organic phase was evaporated to dryness via rotary evaporation. Then the aniline and dypnone were removed by vacuum distillation. The remaining orange-brown solid was recrystallized from ether/hexane yielding 1.20 g (22%) of (1,3-diphenyl-but-3-enylidene)-phenyl-amine as orange needles. Found: C, 88.45; H, 6.4; N 4.3. Calc. for $C_{22}H_{19}N$ (297.39): C, 88.85; H, 6.4; N, 4.7%. δ_H (250.13 MHz, C_6D_6, 298 K, TMS) 8.26-8.22 (m, 2H, C_6H_5), 7.33-7.12 (m, 11H, C_6H_5), 7.03-6.97 (m, 2H), 6.43 (s, 1H, C*H*) and 1.76 (s, 3H, C*H*$_3$); δ_C (62.90 MHz, $CDCl_3$, 298 K, TMS) 165.32 (C=N), 151.55, 141.04, 141.01, 138.88 (*C*$_q$, C_6H_5, *C*-CH_3), 130.08, 128.09, 127.97, 127.92, 127.86, 127.40, 125.41, 123.35, 122.65, 120.40 (*C*$_{o,m,p}$, C_6H_5, *C*H) and 18.26 (*C*H$_3$).

6.6.6 X-Ray Crystallographic Data

Molecular Structure of 2a

X-ray crystal structure analysis of **2a**, STOE-IDPS II equipped with an Oxford Cryostream low temperature unit, graphite monochromatized $Mo_{K\alpha}$-radiation, λ=0.71069 Å, structure solution and refinements were accomplished with SHELXL-97 (G. M. Sheldrick, SHELXL-97, *Program for Crystal Structure Analysis* Release 97-2, Institut für Anorganische Chemie der Universität, Göttingen, Germany, **1998**), WinGX (L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837-838) und SIR97 (A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori, R. Spagna, *J. Appl. Cryst.* **1999**, *32*, 115-119), crystal size 0.56 x 0.41 x 0.35 mm, red prisms, symmetry space group $P2_1/n$, monoclinic, *a* = 11.4870(8), *b* = 10.7950(8), *c* = 17.4210(13) Å, *ß*= 101.575(5)°, *V* = 2116.3(2) Å^3 , *Z* = 4, $\rho_{ber.}$ = 1.248 g/cm^3, 3993 measured reflections, 2986 independent reflections, *R* = 0.0330 [$I > 2\sigma(I)$], wR_2 (all data) = 0.0746, 373 parameters. CCDC-782978 contains the supplementary crystallographic data for this publication. These data can be

obtained free of charge at www.ccdc.cam.ac.uk/data_request/cif (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk).

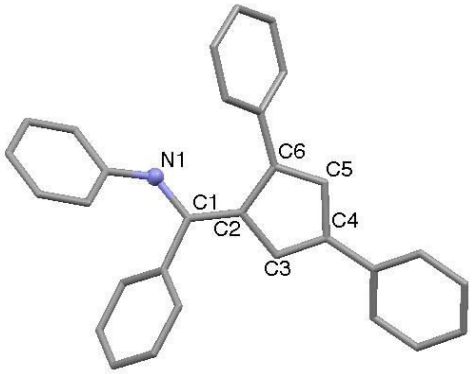

Figure 7: Molecular structure of **2a**; selected bond lengths [Å] and angles [°] for **2a**: C1-N1, 1.3662(15); C1-C2, 1.3751 (16); C2-C3, 1.4483(17); C3-C4, 1.3563(17); C4-C5, 1.4496(17); C5-C6, 1.3587(17); C6-C2, 1.4676(17); N1-C1-C2, 122.19(11); N1-C1-C25, 116.17(10); C1-N1-C19, 128.98(11).

Molecular Structure of 2c

X-ray crystal structure analysis of **2c**, crystal size 0.39 x 0.26 x 0.13 mm, red prisms, symmetry space group $P2_1/n$, monoclinic, a = 10.0630(8), b = 15.9800(13), c = 13.9950(12) Å, ß=93.129(7)°, V = 2247.1(3) Å^3, Z = 4, $\rho_{ber.}$ = 1.264 g/cm^3, 4256 measured reflections, 2494 independent reflections, R = 0.0534 [$I > 2\sigma(I)$], wR_2 (all data) = 0.0880, 303 parameters. CCDC-782980 contains the supplementary crystallographic data for this publication.

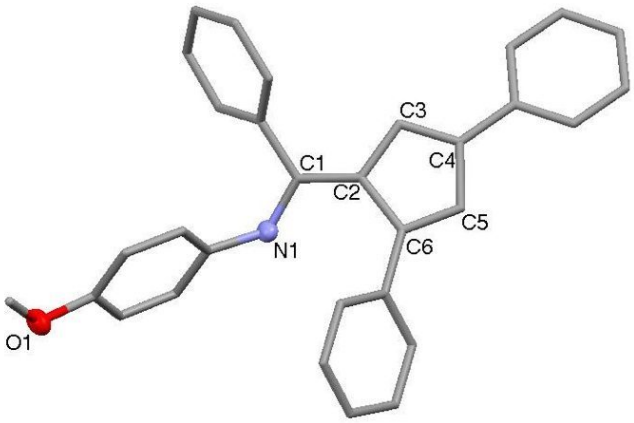

Figure 8: Molecular structure of **2c**; selected bond lengths [Å] and angles [°] for **2c**: C1-N1, 1.362(3); C1-C2 1.378(3); C2-C3, 1.444(3); C3-C4, 1.360(3); C4-C5, 1.451(3); C5-C6, 1.362(3); C6-C2, 1.461(3); N1-C1-C2, 121.5(2); N1-C1-C26, 116.89(19); C1-N1-C19, 127.1(2).

Molecular Structure of 5a

X-ray crystal structure analysis of **5a**, crystal size 0.48 x 0.08 x 0.08 mm, yellow needles, symmetry space group P-1, triclinic, a = 9.2950(11), b = 11.2290(15), c = 13.2300(16) Å, ß= 90.466(10)°, V = 1349.2(3) Å^3, Z = 2, $\rho_{ber.}$ = 1.250 g/cm^3, 5098 measured reflections, 1784 independent reflections, R = 0.0561 [$I > 2\sigma(I)$], wR_2 (all data) = 0.0989, 334 parameters. CCDC-782979 contains the supplementary crystallographic data for this publication.

7. List of Publications

1) T. Irrgang, D. Friedrich, R. Clemente, K. Kutlescha, G. Glatz, R. Kempe, *Z. Kristallogr. NCS* **2007**, *222*, 151-152.
'Crystal structure of 2-amino-5-methyl-1,3,4-oxadiazole, $(CH_3)C_2N_2O(NH_2)$**'**

The following publications have been published, are submitted or are to be submitted during the work on this thesis:

2) K. Kutlescha, T. Irrgang, R. Kempe, *New J. Chem.* **2010**, *34*, 1954-1960.
'An Intermolecular C–C Coupling Reaction of Iridium Complexes'

3) R. Kempe, T. Irrgang, K. Kutlescha, 210ak01.DE (Patent Application)

4) K. Kutlescha, T. Irrgang, R. Kempe; *Adv. Synth. Catal.,* accepted for publication.
'Novel Amido-Complexes for the Efficient Asymmetric Hydrogenation of Imines'

5) K. Kutlescha, G. T. Venkanna, R. Kempe; *submitted to Chem. Commun.*
'The Potassium Hydride Mediated Trimerization of Imines'

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9. Declaration / Erklärung

I hereby declare that I have written this work by myself and that no other sources than those mentioned in this work have been used.

This work has so far neither been submitted to the Faculty of Biology, Chemistry and Earth Sciences at the University of Bayreuth nor to any other scientific institution for the purpose of a doctoral thesis.

Hiermit versichere ich an Eides statt, dass ich die vorliegende Arbeit selbständig und nur unter Verwendung der angegebenen Hilfsmittel und Quellen angefertigt habe.

Diese Arbeit wurde bisher weder an der Fakultät für Biologie, Chemie und Geowissenschaften der Universität Bayreuth noch einer anderen wissenschaftlichen Einrichtung zum Zwecke der Promotion eingereicht.

Kathrin Kutlescha