TECHNISCHE UNIVERSITÄT WIEN
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DISSERTATION

Catalytic applications of non-precious transition metal complexes with newly designed pincer ligands in organic chemistry

Ausgeführt zum Zweck des akademischen Grades eines Doktors der technischen Wissenschaften unter der Leitung von

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"Es kann gut gehen, wenn es geht!?"

" Der Tag gehört den Mutigen"

Prof. Dr. Christian R. Noe

"Es ist zehn Mal besser nachzudenken, lieber zehn Mal eine Zigarette zu rauchen und einen Kaffee zu trinken, bevor man einen unnötigen Ansatz tätigt"

Dr. Hubert Gstach

for Romana

Abstract

Previous works in the group focus on PNP and PCP pincer complexes with iron, molybdenum and tungsten, based on a limited 2,6-diaminopyridine scaffold featuring different phosphine modifications as two-electron donor groups. During the last years the application of non-precious metals became more relevant instead of the standard costly metals, like Pd, Ru, and Ir, for a high diversity of catalytic reactions.

Two concepts built the main part of this cumulative thesis. The first part focuses on the requirement for more variety on the pyridine backbone that goes from different ring functionalities up to a solid phase linkable ligand. Furthermore, the replacing of the NH linker with a *N,N´*-substitution for new activities and mechanistically studies. After some excurses to other ligand systems, like PSP, the focus was set back to the PNP systems in form of 2,6-diaminopyridines, -pyrimidines and -triazines.

Not only the reactivity, but also the simple modification on the ligand and consequently improvement of properties done in such a brief time was of great advantage. These allowed a direct variation after crude catalytic results and a straight modulation for the required electronic properties in catalysis.

The second part engages in the usage of modified Mn, Fe, Co and Ni complexes as sustainable catalysts for different organic reactions. During this research, the use of different metals with catalytic activity for a Ni Suzuki-Miyaura coupling were found by simple featuring ligand design to a triazine PNP scaffold.
Another powerful reaction was the coupling of alcohols with primary amines to substituted amines or imines. Especially for the PCP-Co complex and the isoelecetronic PNP-Fe/PNP-Mn complexes that allowed a divergent amination or imination formation under different conditions. Two different systems were found for this application, a base free via the hydride complexes at higher temperatures and one with milder temperatures and higher substrate tolerance under basic conditions. Furthermore, the first manganese catalyzed reactions to substituted quinolines and multi component pyrimidines were discovered and assembled on the first amine couplings.
In resume, this thesis demonstrates the way from ligand design beyond to find an efficient catalysis and the enhancement between a benign and simple ligand variety and the commitment as catalyst.

Kurzfassung

Frühere Arbeiten in der Gruppe befassten sich vorwiegend mit PNP und PCP Pincerkomplexen mit Eisen, Molybdän und Wolfram, basierend auf einen eingeschränkten 2,6-Diaminopyridin Grundgerüst substituiert mit unterschiedlichen Phosphinresten als Liganden. Seit einigen Jahren ist die Verwendung dieser Systeme zusammen mit kostengünstigeren Übergangsmetallen in den Fokus gerückt um die bis dato genutzten Edelmetalle wie Pd, Ru oder Ir zu ersetzt.

Diese beiden Konzepte bildeten die Hauptthemen dieser kumulativen Dissertation. Als Erstes wurden unterschiedliche ringfunktionalisierte Pyridine bis hin zu Festphasenlinkern, sowie die *N,N´*-Substitution zur Blockierung der NH Funktionalität, für neue Aktivitäten und mechanistische Studien untersucht. Auf der Suche nach neuen Liganden und einigen Exkursen wie PSP wurde jedoch wieder das ursprüngliche PNP Konzept weiterverfolgt basierend auf 2,6-Diaminopyridinen, -pyrimidinen und -triazinen. Als vorteilhaft zeigte sich die schnelle und effiziente Variation der neuen Liganden innerhalb kürzester Zeit. Welche eine annähernd zeitnahe einfache und schnelle Modellierung basierenden auf den neuesten Katalyse-Ergebnissen zulässt.

Als zweiter Themenschwerpunkt wurde der Einsatz von Mn, Fe, Co und Ni Komplexen mit diesen Liganden für katalysierte organische Reaktionen getestet. Dabei wurde durch einfaches Ligandendesign ein PNP Triazin Ni Komplex für eine Suzuki-Miyaura Kreuzkupplung entdeckt.

Eine der momentan meist genutzten Reaktionen ist die Kupplung von Alkoholen mit primären Aminen zu sekundären Aminen oder Iminen. Die Verwendung von PCP-Co oder den isoelektronischen PNP-Mn/PNP-Fe Komplexen ermöglichte eine divergierende Aminierung oder Iminierung unter diversen Bedingungen. Es wurde hierbei ein bei höheren Temperaturen Hydrid-Komplex basierendes System und ein substrattolerantes System unter basischen Bedingungen entwickelt. Basierend auf diesen Ergebnissen wurde dabei die erste Mangan katalysierte Synthese für mehrfach substituierte Chinoline und multikomponenten Reaktion für Pyrimidine entwickelt.

Im Allgemeinen zeigt diese Arbeit den Weg von einer effizienten Liganden Optimierung bis hin zur katalytischen Anwendung und dessen ideales Zusammenspiel.

Aims and Structure of this Thesis

The essential part of this doctoral research was the efficient and fast modification of new pincer type ligands and a beneficial application of first row transition metal complexes for catalysis. Therefore, the focus of this work was for one side directed towards the synthesis of ligands based on heterocyclices like pyridines, pyrimidines and triazines. The heterocyclic systems were assembled and modified using from all the well-known standard methods up to the new techniques like microwave assisted methods and new synthetic routes. The prepared complexes were synthesized analogously to other published systems with the propose for new catalytic applications, special applying non-precious metals.

This thesis gathers the results from ligand design up to a reactive catalyst and their application in different reactions. In sum, the main part based on "Hydrogen-Borrowing" reactions for amines and imines, furthermore the usage of this effect for multi component heterocyclic synthesis.

This thesis is written as cumulative work and contains:

1) a brief introduction of the overall topic

2) the main part with the results and discussion

The content of the PhD work provides a lot of material for different publication. Only a small associated part of 4 publications was selected (manuscripts 1# and 2#, already published, manuscript 3# and 4# as sent draft). Further important facts from other publications were discussed in the general part, conclusion and outlooks.

The author (Matthias Mastalir) is first author of all of these publications. The design of the ligands and the full organic part was improved by the author. PCP-Co and pyridine based PNP-Fe and PNP-Mn systems were already published but the application for amination reactions was found by the author. The design for the PNP-Fe triazine and the multi-component catalytic reaction were both an idea from the author.

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1 Introduction

1.1 Theoretical background

The design of benign and sustainable catalysts in combination with optimized ligand systems and the application thereof is one of the most important research fields in organic and organometallic chemistry. Currently, almost all the chemical processes in industry and organic synthesis are mediated by catalysts implying and efficient process. On the one hand, standard heterogeneous catalysis has been replaced by a more regio-, chemo- and stereo selective homogeneous catalyst for organic disconnecting reactions. On the other hand, environmentally, benign and "green" reactions as well as catalysts are demanded from industrial and laboratory field.
Formerly, one of the goals in homogeneous catalysis was mostly to use of precious metals such as Pd, Pt, Ru, Rh, Ir, and Os for standard used in cross-couplings up to metathesis or CH activation as powerful synthetic tool. At this time the research for more powerful, selective and convenient systems became more interesting. In the last 10 years, higher requirements for a new age of non-precious transition metals have begun. Reasons for this change were the high costs of noble metals, recycling and especially the toxicity in the pharmaceutical products.[10,14,59]
In combination with these earth abundant metals (V, Cr, Mn, Fe, Co, Ni), ligand design plays a major key role for an efficient usage, packaging and activation.

1.2 Pincer Complexes

The first pincer systems where published by Dahlhoff & Nelson in 1971 as PNP and by Shaw & Moulton in 1976 as PCP type ligand.[1,2] PNP and PCP systems with a meta substituted diamino functionality, like a simple N-P bond formation were described from Dyson and co-workers.[3]
General pincer ligands are tridentate ligands that enforce a meridional coordination geometry, named after their coordination centers and bound to two electron donating groups. This ligand framework became more important for their high stability, easy synthesis and well catalytic applications in small molecule activation. Different linker atoms (C, N, O or S) can be used according to the electron density in the ring and

donor system.

Over the years many pincer ligands have been developed, a small selected overview of them are given with different backbones and donor groups in the following Figure1.

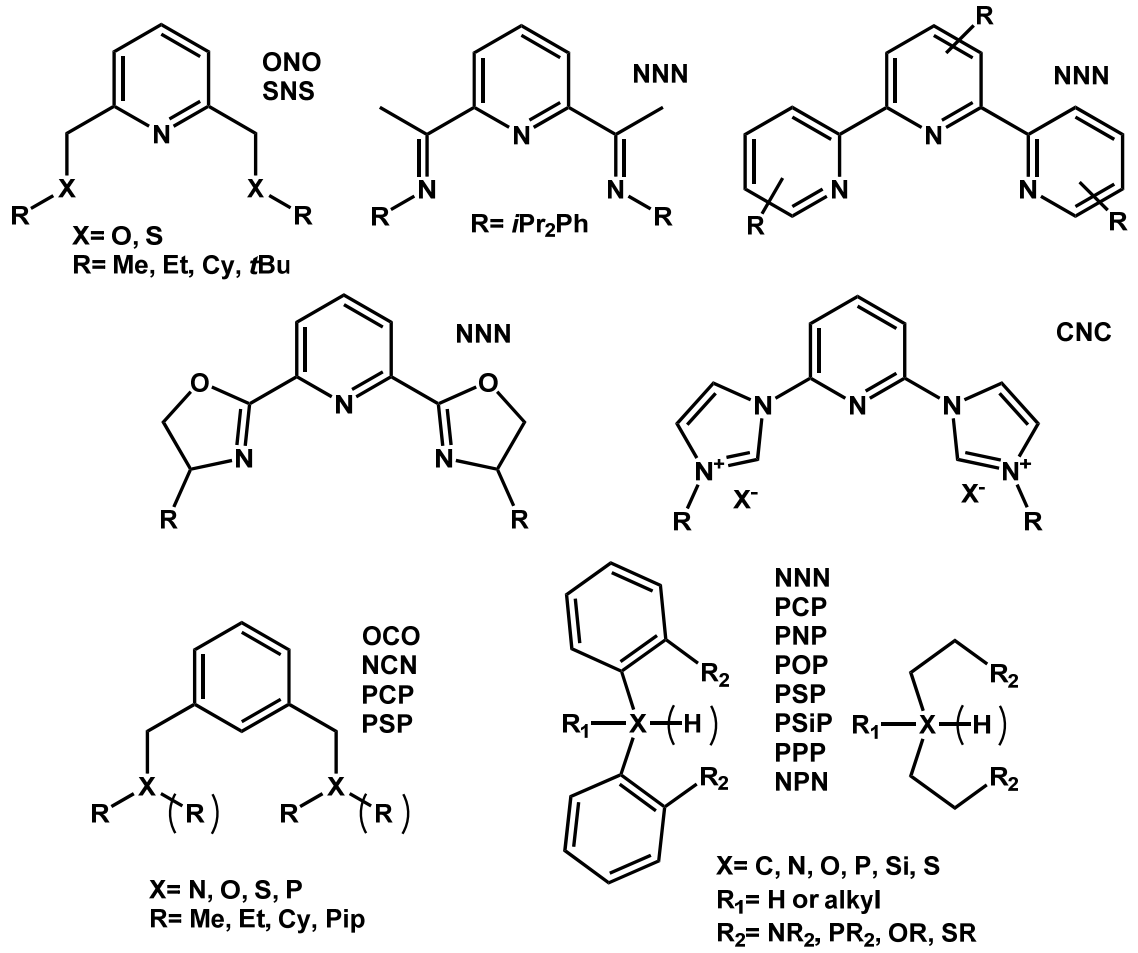


Figure 1: Pincer ligands overview

Phosphines as donors are one of the most useful practiced groups. Beneficial is the easy P-N bond formation starting from R_2PCl and their good donor properties. Furthermore, direct or in situ characterizations via ^{31}P NMR analysis for the ligand synthesis, purity, complexation, reaction control of catalysis are a very helpful tool. Moreover, intermediates can be synthesized, analyzed and characterized supported by direct ^{31}P NMR measurement.

This work based on the classical one from Sacco first published PNP system, substituted to 2,6-diaminopyridine and used in the Kirchner group since 2006 as standard ligand.[4] Some excursions to other systems were done (e.g. triazine, pyrimidine) without further notable usage.[5] 2014 Murugesan published new Ni and

Co PCP systems based on *N,N´*-Dimethyl-1,3-diamonobenzene without any catalytic applications in analogy to the pyridine PNP scaffold.[6]

Primary NH and CH_2 containing backbones are used and they can be easily deprotonated in basic environment, which causes a reversible dearomatization (pyridine vs. triazine) and increase electron density in the backbone.

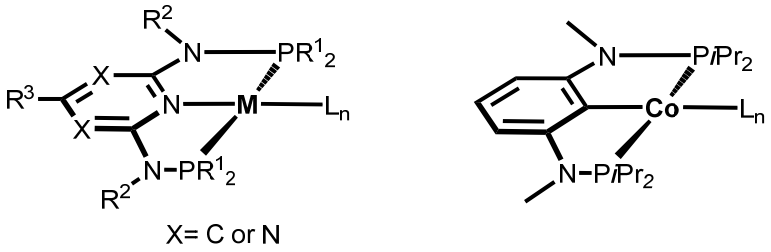


Figure 2: Pincer complexes

1.2.1 Application of pincer complexes

Pincer complexes find one´s way into organic chemistry and exposing a large range of catalytic activities for applied synthesis.

Some of these reactions are shown in Scheme 1 and are described below except hydrogen borrowing methodology that is closer discussed in following chapters.

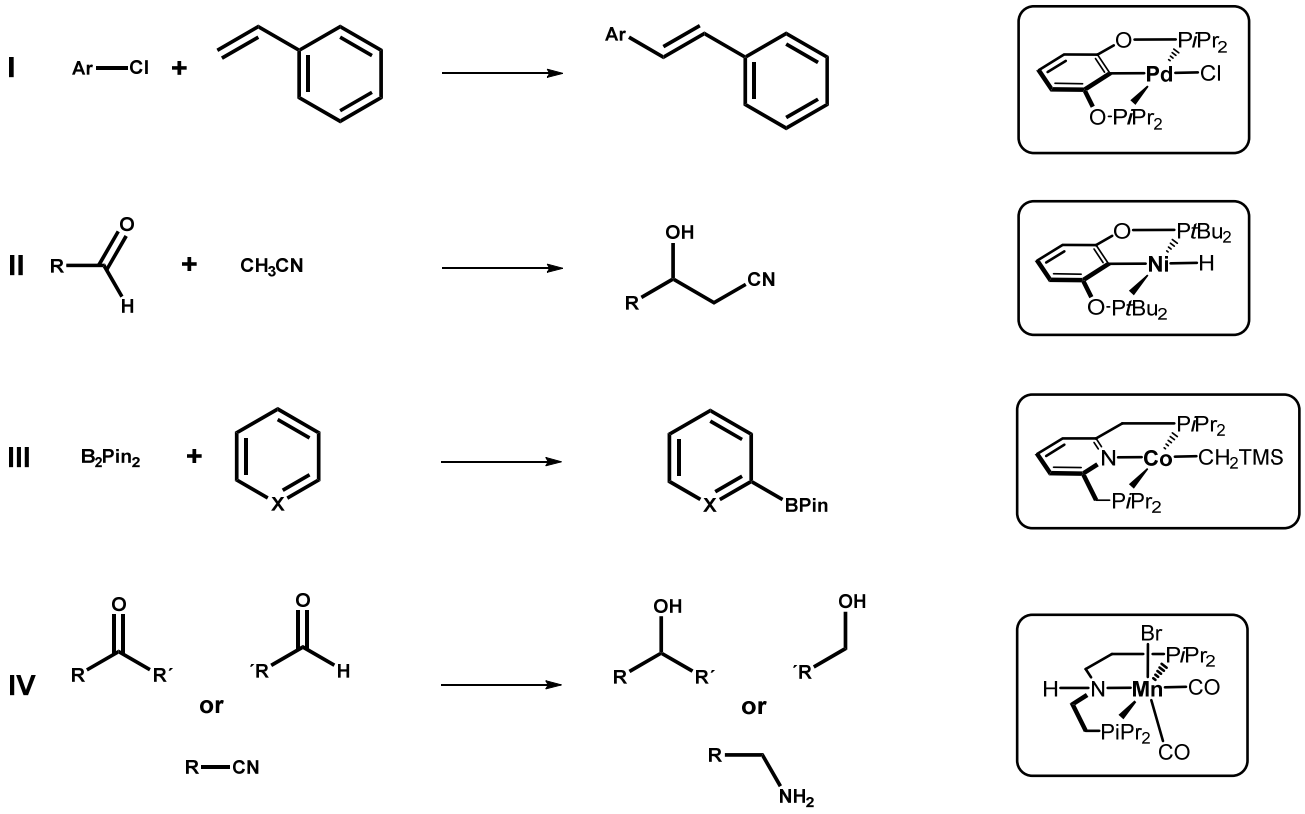
One of the major usage are Ni and Pd systems for different cross couplings like the Suzuki-Miyaura, Heck, Buchwald-Hartwig, Kumada, Negishi or Sonogashira reactions. An applied Heck reaction is shown in **I**, but highly stable tridentate ligands are not successful for this kind of reactions. About their geometry and binding site, one arm must be more labile with a weaker donor (e.g. NR_2) or applied at higher reaction temperatures.

Reaction **II** give one example of CH- acidic systems and Michael-additions, where Ni-H complex release H_2 in contact with the substrate. The alkyl complex was formed and reacts as nucleophile for cyanomethylation.[7]

C-H activations with Ru, Ir, Rh and Co complexes are well known, for example reaction **III** which shows the conversion with pinacol borane. Chirik´s group also used the same system for mono- up to polyborylation of toluene CH_3 group.[8]

Hydrogenation is one of the most used applications (real hydrogenation, transfer hydrogenation and hydrogen borrowing) for keto compounds, double and triple bonds, nitriles and carboxylic systems and their derivatives. The first published base

activated PNP manganese pincer is represented in **IV**, for reduction of ketones, aldehydes and nitriles.[9]



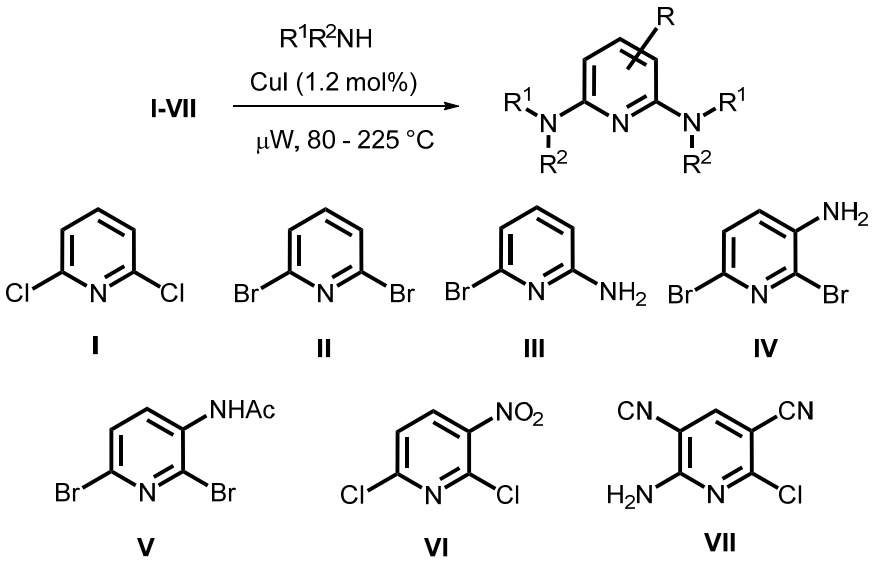
Scheme 1: application of pincer complexes

1.3 Ligand backbone design and modification

1.3.1 *N,N´*-Substitution for 2,6-diaminopyridine

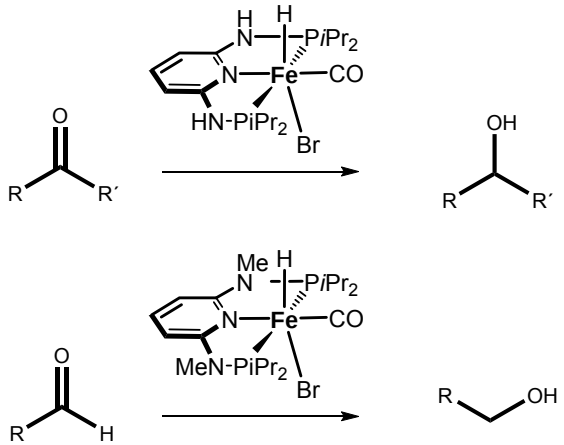
Based on the 2,6-diaminopyridine backbone, no other ring or *N,N´*-substituted precursors are commercial available and published with an efficient synthesis. Further works engaged with this first topic. First of all, a microwave assisted copper-catalyzed amination protocol was reported utilizing a series of 2,6-dihalo- and 2-amino-6-halo pyridine precursors. Using this procedure, selective substitution of one or two halogens by aryl or alkyl amines were achieved in good to excellent isolated yields in relatively short time. The reaction allows easy variation between educts and different N-substitutions. This methodology constitutes a practical alternative to other methods like Buchwald-Hartwig aminations, Ir catalyzed alkylation or amination *via*

N-oxides. A series of 30 different products was synthesized from simple aliphatic systems up to chiral precursors for new *N*-substituted ligands.[10]

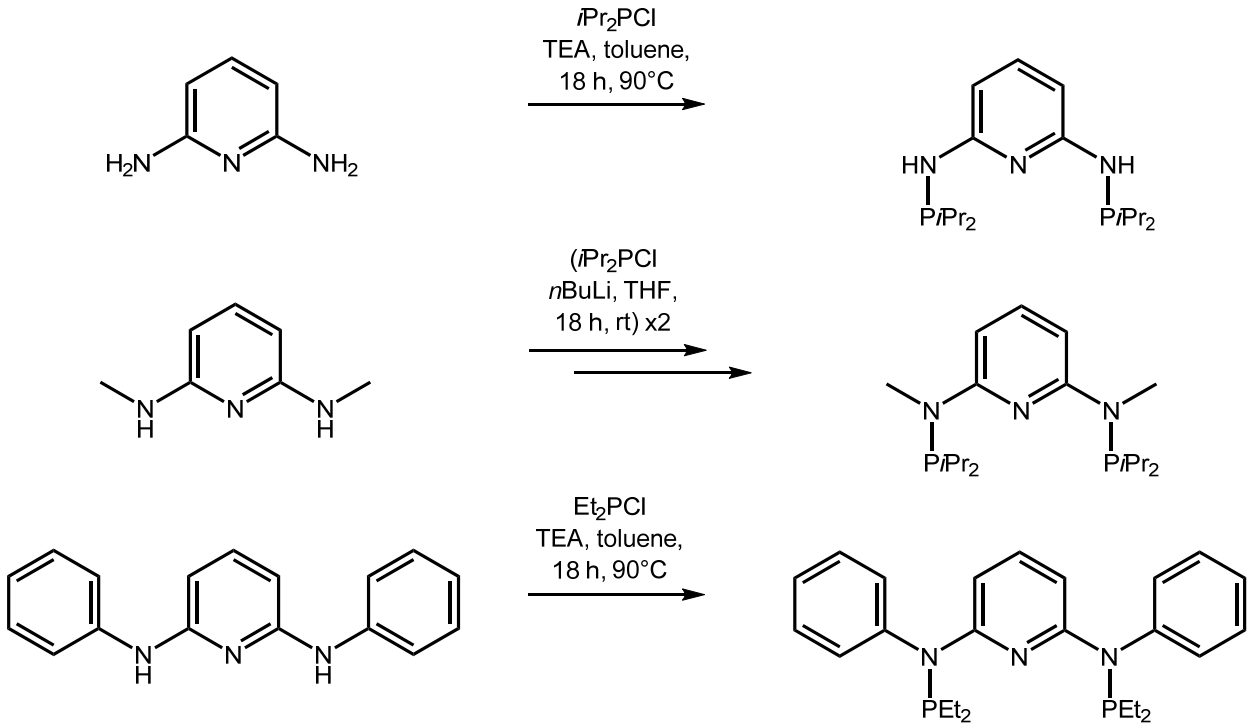


Scheme 2: MW assisted synthesis for N-substituted DAP´s

The importance of this lies in the fact that the NH group can be deprotonated with bases and reacts easier than the classical 2,6-lutidine scaffold. When the NH group was blocked with new substituents, this interaction was not possible anymore and prevent the NH interaction for catalysis. This simple modification plays a key role for mechanistical studies and activity. For example a Fe hydride complex catalyzed chemo selective hydrogenation of aldehydes worked only with N^{Me} and ketones with NH complexes (Scheme 3).[11]



Scheme 3: PNP ligand synthesis



Scheme 4: PNP ligand synthesis

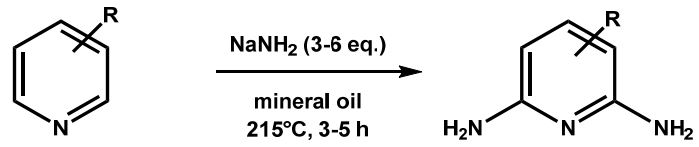
Unsubstituted 2,6-diaminopyridine reacts with R_2P-Cl (except *t*Bu_2PCl with NaH) and weak bases such as TEA to the desired PNP ligands. For *N*-substituted systems in combination with bulky phosphines, *n*BuLi as stronger base is needed. Direct double deprotonation leads to side reactions, a two-step synthesis was afforded.

An interesting combinations were found for *N*-phenylated systems, phosphorylation can be carried out with Et_2PCl under standard conditions. The phenyl group in combination with less bulky groups switched the reactivity and steric properties nearly to the range of *i*Pr-PNP^{Me} ligands.[12]

1.3.2 Ring substitution via Chichibabin reaction

For ring substituted pyridine, classical sodium amide initiated amination of pyridine, known as the Chichibabin reaction.[13] This method is very useful for the preparation of 2-aminopyridine and parent 2,6-diaminopyridine by the reaction of pyridine with sodium amide under heterogeneous conditions, but was hardly applied to ring-substituted pyridines. It has to be noted that the Chichibabin reaction provides an inexpensive and atom economic alternative to other methods. Starting from

halopyridines, via nucleophilic substitutions catalyzed by copper, copper salts or proline and Buchwald-Hartwig aminations or pyridine *N*-oxides.[14] Despite the harsh reaction conditions an useful method was created with a relatively short reaction time and a good handling. The use of 11 different substrates with an overview of substrate limitation, yields more than 63% and mineral oil as medium instead of highly toxic *N,N*-dimethylaniline.



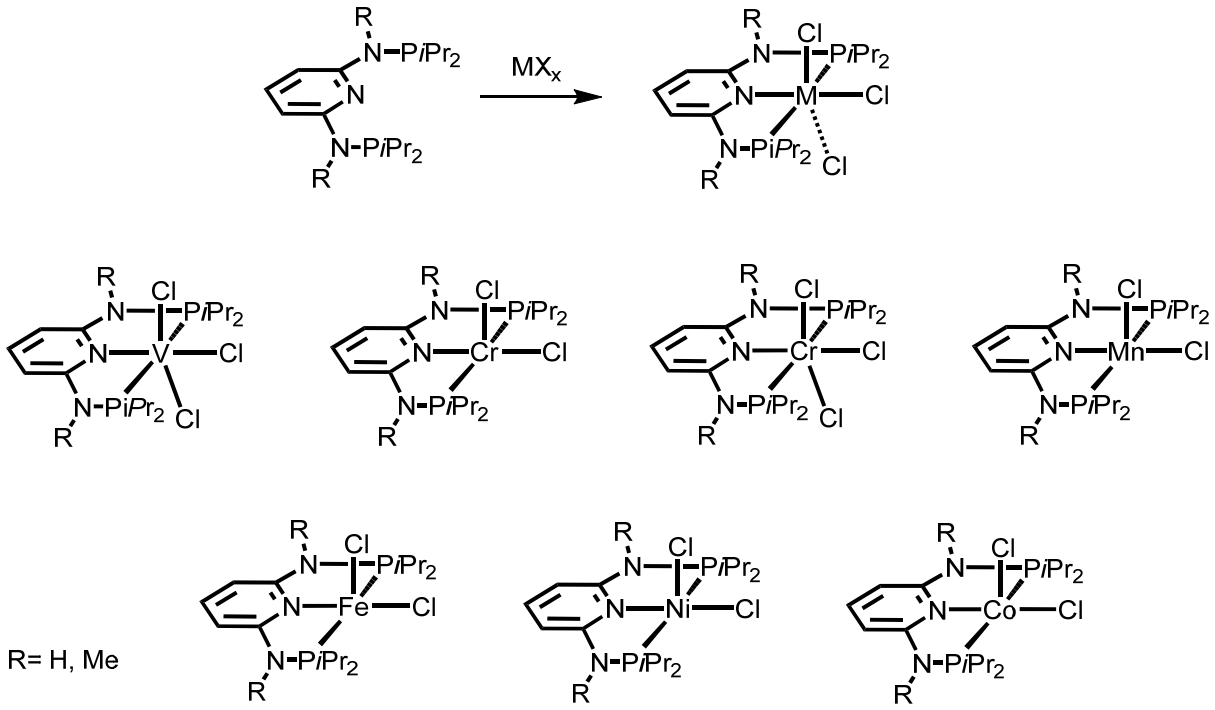
Scheme 5: Chichibabin reaction

Ring substituted DAP´s allowed changes at the electron density, steric effects and a well solubility, especially 4-*tert*-butyl-2,6-diaminopyridine. Furthermore 4-hydroxy-2,6-diaminopyridine was predestinated useful precursor for solid phase immobilization.[15]

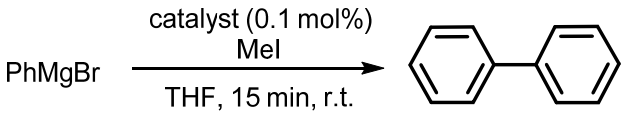
1.4 Catalytic application of PNP complexes

1.4.1 Research for new metal precursor

As far as non-precious first-row transition metals are considered, the chemistry of neutral pyridine-based iron and cobalt PNP complexes experienced an impressive upswing in recent years. Reports on chromium, nickel, and copper PNP pincer complexes are still rare, while vanadium, manganese, and titanium PNP pincer complexes appear to be unknown as yet. Herein the synthesis, characterization and reactivity of a series of new vanadium, chromium, and manganese PNP complexes of the types [M(PNP)Cl_3] (M = V, Cr) and [M(PNP)Cl_2] (M = Cr, Mn) is exhibited. In a preliminary study, these complexes were found to catalyze the homo-coupling of PhMgBr in the presence of MeI or atmospheric oxygen as oxidizing agents. However they were inactive for cross coupling and other reactions. In summery we tried V, Cr, Mn, Fe and Co for the homo-coupling to form biphenyl was not much better than the pure metal salts excepted that Ni formed in moderate yields the cross coupled product.[16]



Scheme 6: PNP metal salt complexation



catalyst	Yield [%]
$V(PNP\text{-}Ph)Cl_3$	81
$V(PNP\text{-}iPr)Cl_3$	85
$V(PNP^{Me}\text{-}iPr)Cl_3$	85
VCl_3	59
$Cr(PNP\text{-}iPr)Cl_3$	82
$Cr(PNP\text{-}Ph)Cl_2$	89
$Cr(PNP\text{-}Cy)Cl_2$	92
$Cr(PNP\text{-}iPr)Cl_2$	91
$Cr(PNP^{Me}\text{-}iPr)Cl_2$	93
$CrCl_2$	73
$Mn(PNP\text{-}iPr)Cl_2$	81
$Fe(PNP\text{-}iPr)Cl_2$	**73**
$Co(PNP\text{-}iPr)Cl_2$	88

Scheme 7: Homo coupling with PNP metal complexes

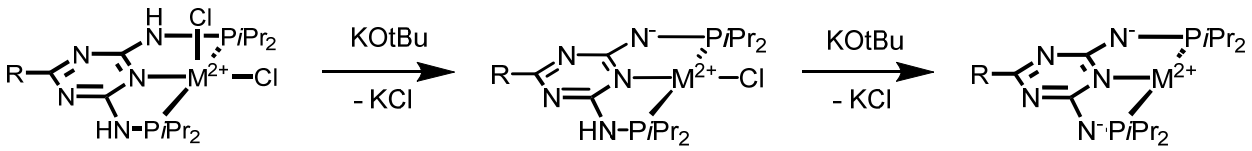
Other catalytic reactivities were not found, except that polymerization reactions initiating with $Cr(PNP)Cl_3$ were published. This kind of application activated the

complex with alkyl aluminum salts and worked under Ziegler-Natter conditions for alkene polymerizations.[17,18]

1.4.2 Metal activation with triazine based ligands

2,6-Diaminotriazine based PNP complexes were first published from Kirchner and co-workers without any specific application. Kempe *et al.* described the activation of triazine PNP-Co for catalytic hydrogenation and alcohol-amine coupling under basic conditions. In 2016, as the third paper an active triazine PNP-Ni complex for Suzuki-Miyaura was published in analogy by their own.[19, 52, 53]

Under normal conditions triazine is an electron poor unimportant and weak coordinative ligand. The NH acidity is higher than in other heterocyclic systems and undergoes smooth deprotonation. This is the main key step for high reactive triazine complexes. Mono- or di-deprotonation forms an anionic ligand and increases the electron density in context with a higher activity for the metal center. Furthermore, the deprotonated species aides the dearomatization in catalytic cycle´s. Comparable activity showed highly instable $Ni^0(COD)_2$ or strong donating NHC ligands as cross-coupling catalyst.



Scheme 8: Triazine ligand deprotonation

In combination with lower metal oxidation states higher catalytic activity can be reached. The air and water stable pre-catalyst can be stored and forms *in-situ* to the active catalytic species. (Scheme 8)

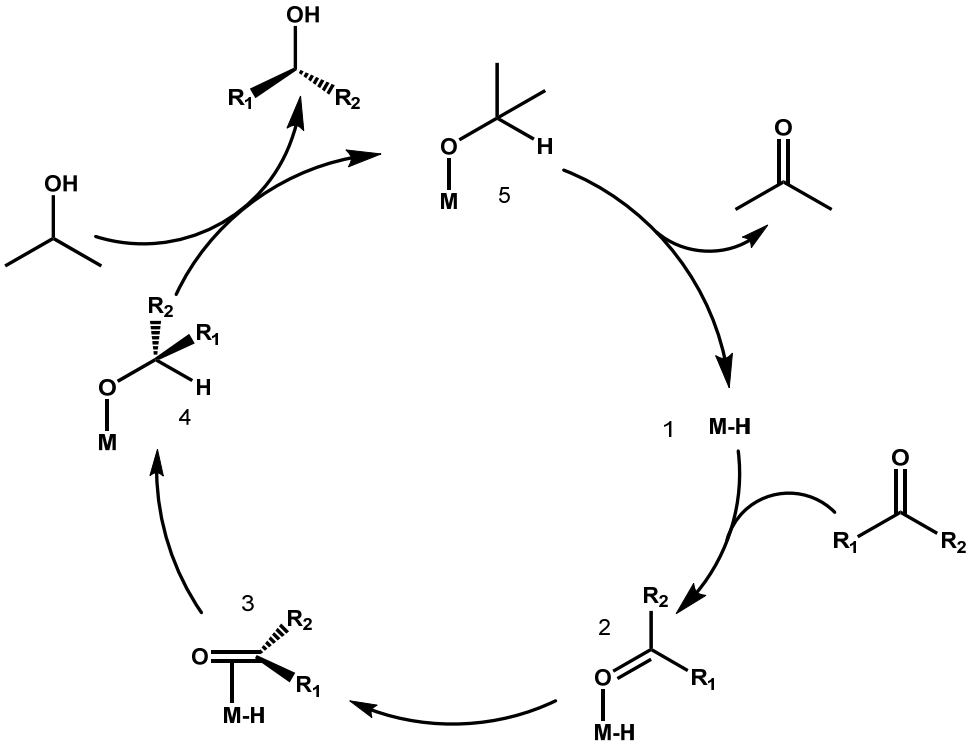
Depending on the metal, substituents and co-ligands, different deprotonated complexes are formed. Only the abstract anionic complex was not stable enough, depending on the deprotonation degree further ligands for stabilization like CO, bipy terpy were needed. For Ni only a mono deprotonated neutral complex was isolated under normal conditions and characterized by NMR and single crystal x-ray

diffraction. Co was isolated as di-deprotonated complex stabilized with bipy as co-ligand and analyzed via x-ray diffraction.[19, 52, 53]

1.5 Hydrogen-Borrowing in catalysis

1.5.1 Hydrogen transfer

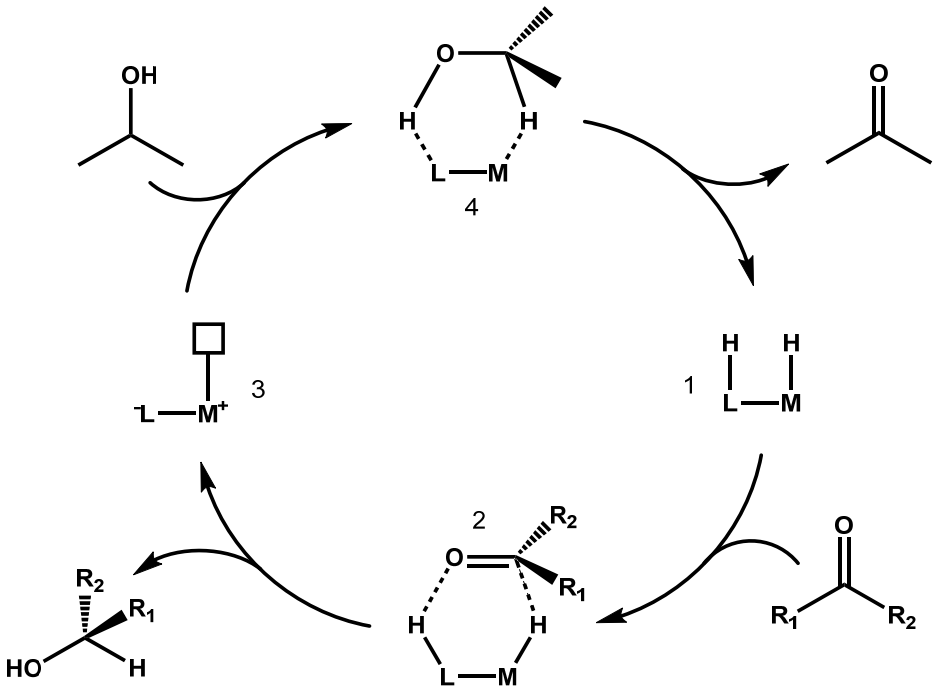
Two of the first classical known direct hydrogen transfer reactions were the equilibria Oppenauer oxidation and Meerwein-Ponndorf-Verley reduction with aluminum-isopropoxide as catalyst. General importance of the reversible storage of hydrogen with transition metal complexes was proposed by Crabtree. In 1996, Noyori disclosed novel ruthenium catalysis in combination with chiral amines and BINAP as ligand system, that enabled a conceptually new enantioselective hydrogenation process for prochiral substrates like ketones and imines via a hydridic pathway.[20, 21, 22]



Scheme 9: inner-sphere mechanism

A coordinated carbonyl **2** inserts into the metal hydride via π-coordination **3** the metal alkoxide **4** is formed, after ligand exchange the product is released. Finally the metal

hydride **1** is regenerated by β-hydride elimination and closes the inner-sphere cycle. (Scheme 9)



Scheme 10: outer-sphere mechanism

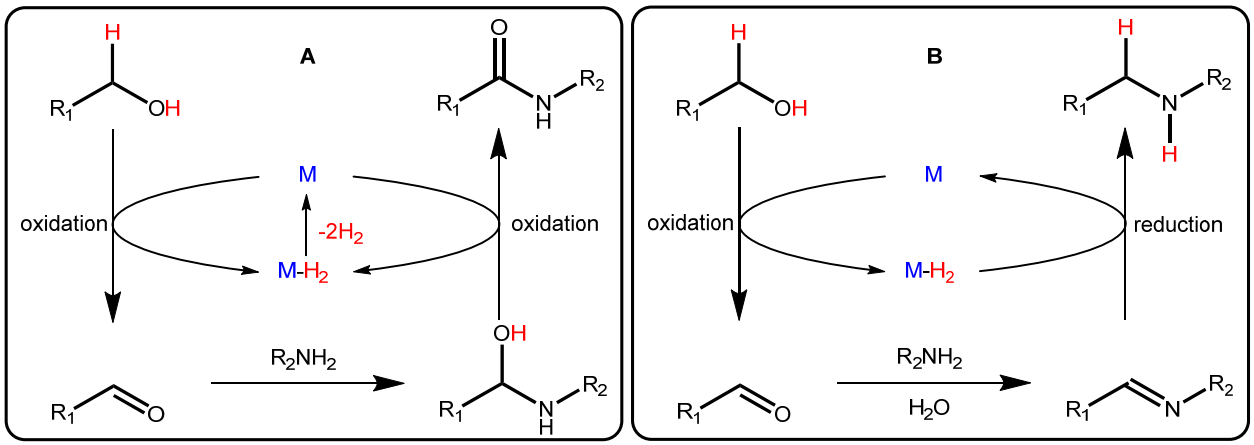
In analogy the outer-sphere- mechanism proposed from Noyori work without coordination of the alcohol to the metal. The keto compound coordinates with the protonated ligand-metal hydride system **2** for a cyclic transfer of protons. A deprotonated catalyst with a free coordination site **3** reacts with a second alcohol. Another cyclic intermediate **4** was formed and after β-hydride elimination the starting hydride catalyst **1** was regenerated.[23] (Scheme 10)

1.5.2 Hydrogen-Borrowing

Instead of wasting the hydrogen donor compound from hydrogen transfer reaction, the Borrowing-Hydrogen methodology formal cleaved hydrogen as source for the catalytic recycling and the reduction step for substrates. This redox neutral approach for C-C or C-N bond formation is potentially of significant interest in synthetic organic chemistry.

General pathways starting with alcohol oxidation to a C=O species, nucleophilic

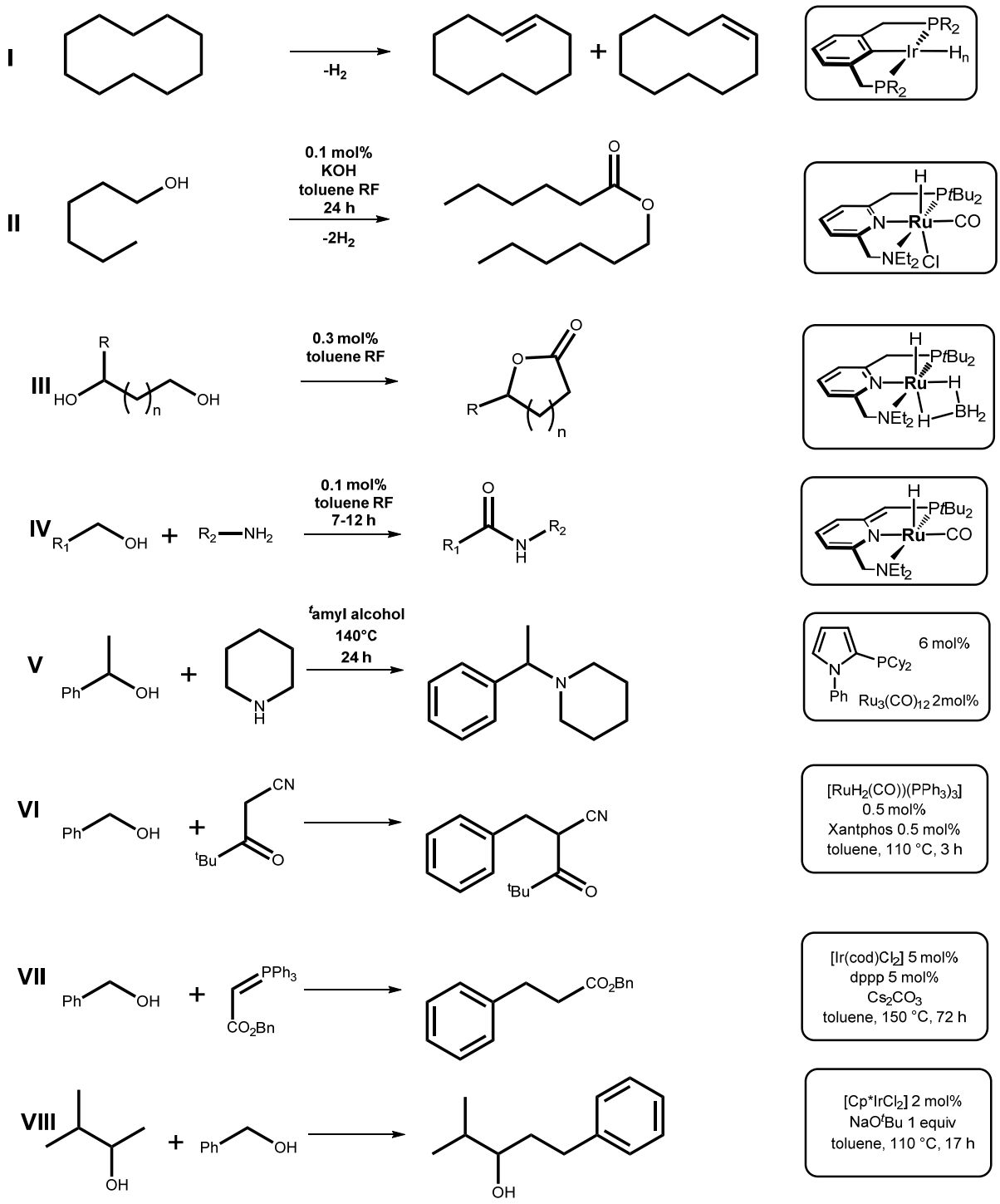
attack from substrate and reduction of the higher sensitive intermediate or second dehydrogenation with a reactivation of the catalyst.



Scheme 11: Hydrogen-Borrowing mechanism

In the literature some different intricacies for the catalyst and the hydrogen bond and cleavage are published.[24, 25, 26] Amides are formed via alcohol oxidation, formation of aldimine as reactive intermediate and second oxidation, instead of a condensation (**A**). Amines are generated by condensation of aldehyde and imine under formation of imine as intermediate. Afterwards reduction of the higher reactive imine instead of aldehyde as reductive-amination follows (**B**). Other pathways react under similar condition with other nucleophiles (Scheme 11).[27]

First of all, exclusive catalyzed AD reactions were published with ruthenium and iridium.[28,29] All used systems were developed at the beginning for single transformations like hydrogenations. Later, the reverse reaction got more interests for keto formations from alcohols with a limited application. In general the corresponding tautomer enole (or enolate) from all CO species is acts as highly reactive nucleophile with a wide spread reactivity.

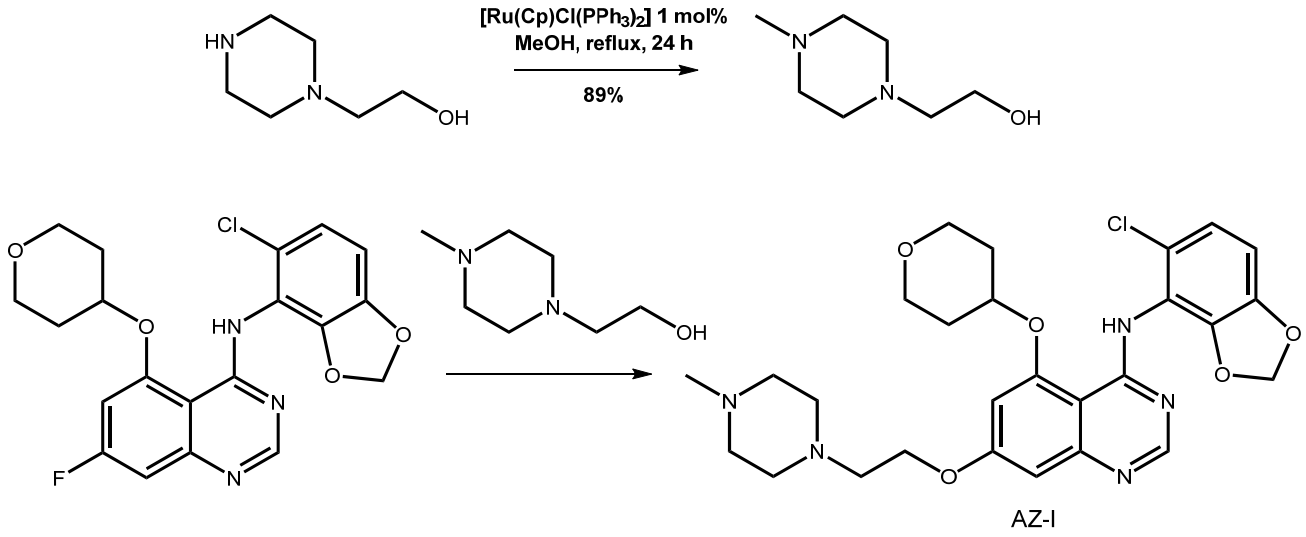


Scheme 12: Hydrogen-Borrowing reactions

Reversible and irreversible iridium catalysis is known for cyclic systems such as cyclodecane, quinolines or isoquinolines to di- or tetrahydro products. All these kinds of reactions worked under harsh conditions with temperatures up to 150 °C and formed the substrate back under hydrogen atmosphere at 120 °C (**I**). The same concept was further published from Xu *et al.* at first with a aliphatic PNP-Co

complex.[30] Moreover, the groups of Jones, Goldman and Miller used the same iridium system for similar reactions like CH activations, C-C formation and electrochemical transformations.[31,32] **II** and **IV** showed the formation of carboxylic species under mechanism **A** e.g. esters are formed with a formal carboxylic acid hydrate intermediate.[33,34,35] Lactones are formed from diols with different OH priorities and thermodynamic ring closing reactions (**III**). Open polymerization systems react similar with primary diols. *Sec.* and *tert.* amines can be formed from pathway **B** depending on the complex system (**V**).[36] **VI-VIII** show a small selection for C-C and C=C couplings with standard organic reactions starting from alcohols. In general the aldehyde reacts with activated CH substrates in a Knövenagel, aldol condensation or Wittig reaction, form the alkene intermediate and reduce in the cycle to the desired alkane. Similar systems with CH acidic system such picolines can be alkylated.[37,38,39]

However, direct alkylation of amines found their way as helpful industrial tool in bulk or pharmaceutical chemistry. Selective amine formation starting from biomass gives them a high benefit for diversity. A small overview was summarized in 2015 from R. Newton´s group for pharmaceutical applications on selected agents. One example was selected of this work for selective piperazine alkylation's for the SRC kinase inhibitor AZ-I. Normal industrial conditions worked with HCHO, H_2 (10 bar), Pd/C (2 w/w), Et_2NH in AcOH/H_2O over two steps yielding 93%.[40]

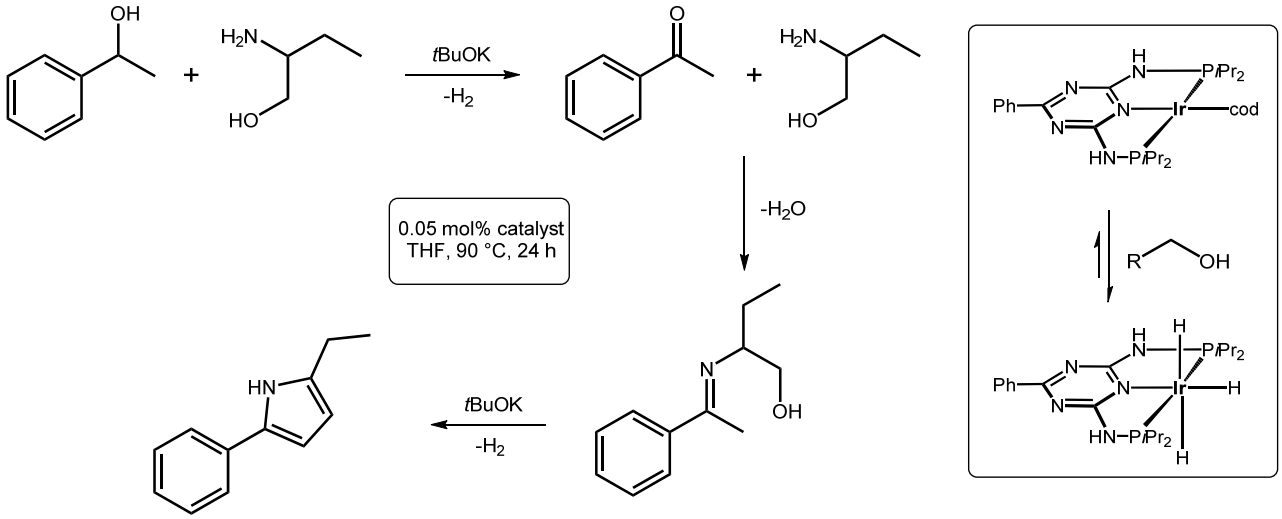


Scheme 13: Hydrogen-Borrowing in drug synthesis

1.5.3 Heterocycles via hydrogen-borrowing methodology

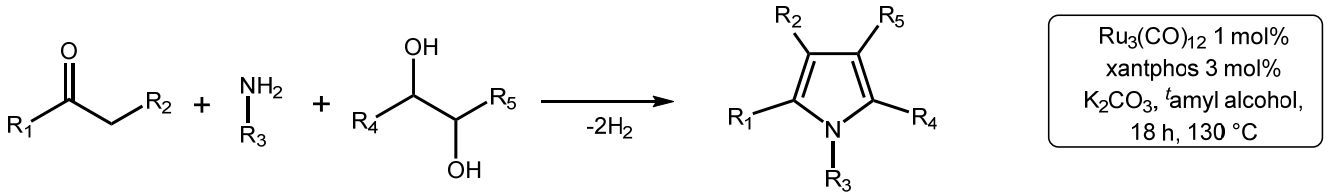
Nitrogen containing heterocycles constitute one of the largest groups of organic compounds and are becoming increasingly more important in all aspects of nature chemistry. Applications as antimalarial, antibacterial and much more agents of them in medicine played a key role in medicinal chemistry. The development of efficient catalysis with highly regioselective conversion from abundant alcohols in different heterocyclic systems via AD methodology has significant importance in synthetically chemistry.

Recently, a 2-component transformation of pyrroles from β-amino-alcohols has been reported by Kempe, Milstein and Saito with iridium and ruthenium catalysts. The shown system published from R. Kempe group used PNP^{Triaz} -Ir-COD as pre-catalyst. At first an active Ir hydride catalyst was formed from an Ir-COD complex and oxidized both alcohols to keto species. After the imine formation and further aldol condensation the desired pyrrole was formed. Based on the same concept diversely functionalized pyridines have been synthesized by the Kempe group.[41,42,43]



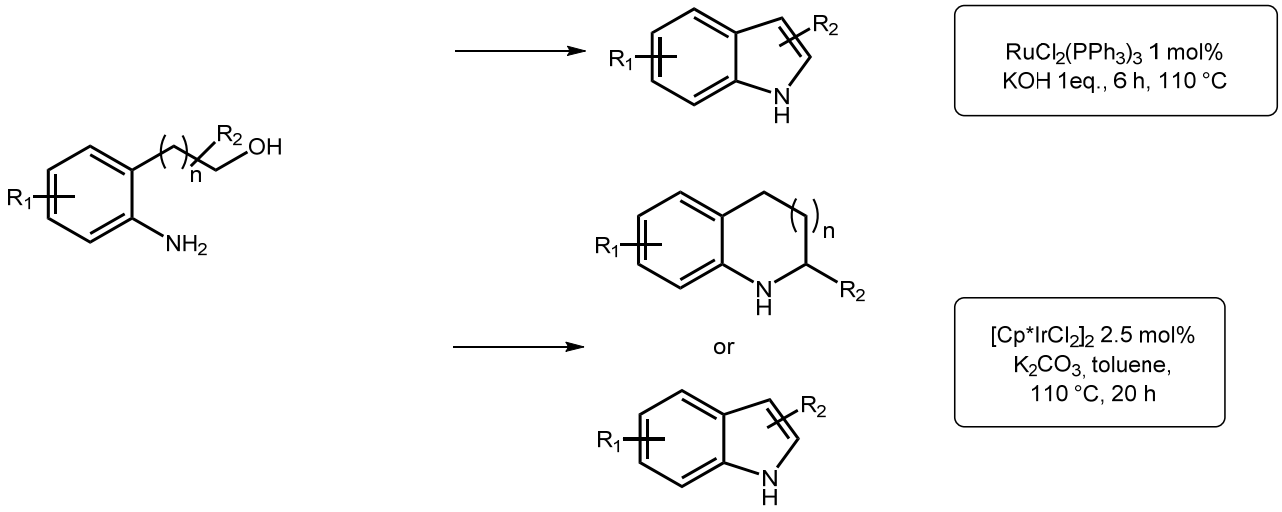
Scheme 14: PNP-Ir catalyzed pyrrole synthesis

Beller *et al.* disclosed in 2013 at first a ruthenium catalyzed 3-component pyrrole method using the similar conceptual approach for higher substituted rings.[44,45] (Scheme 14)



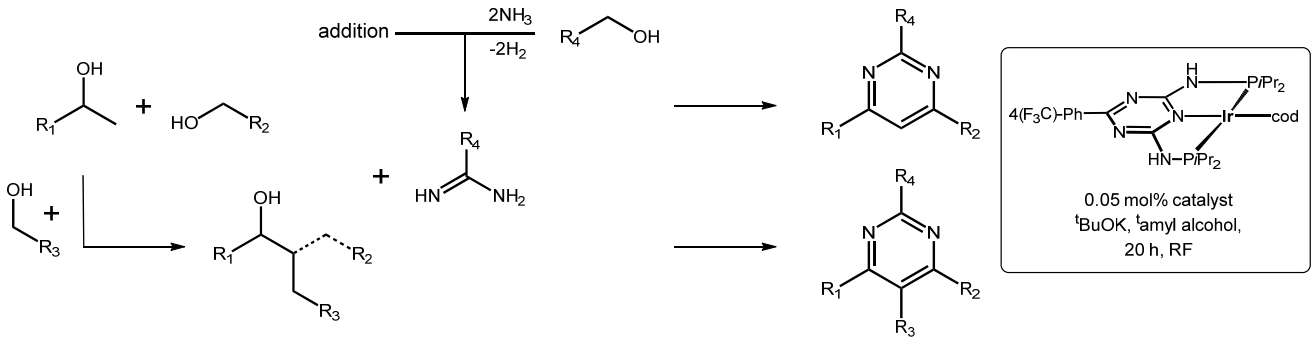
Scheme 15: Ru catalyzed pyrrole synthesis

Watannabe employed already in 1990 a $RuCl_2(PPh_3)_3$ complex catalyzed the cyclic formation of indoles starting from 2-(2-aminophenyl)ethan-1-ol under cleavage of hydrogen.[46] Fujita et al. described further a new Ir-catalyzed method for indoles and 1,2,3,4-tetrahydroquinolines.[47] (Scheme 15)



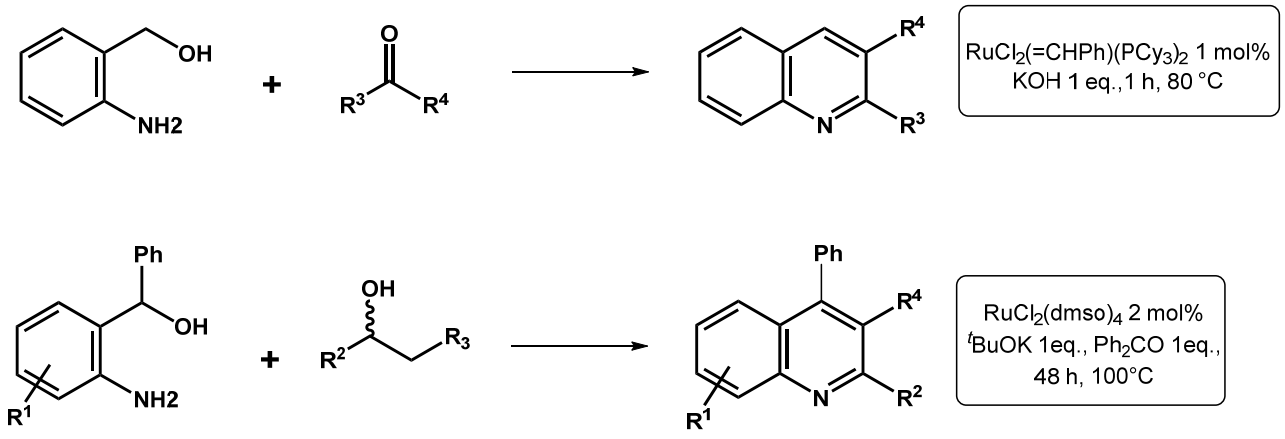
Scheme 16: PNP-Ir multicomponent pyrimidine synthesis

Based on the same scaffold the Kempe group described the first multi component pyrimidine synthesis via PNP^{Triaz}-Ir-COD pre-catalyst. A primary and secondary alcohol was oxidized at first. After the aldol condensation (base catalyzed) the amidine formed the pyrimidine ring. Furthermore as shown in Scheme 17 benzamidine can be formed from alcohol and ammonia, in a one pot reaction. But this reaction wasn´t accurately described in the experimental part as synthetic approach.[48]



Scheme 17: PNP-Ir multicomponent pyrimidine synthesis

One of the first AD methodologies applied a ruthenium catalyst for Friedländer annulation to form substituted quinolines. Shim published already in 2001 the first method based on hydrogen borrowing starting from 2-aminobenzylalcohol and a ketone for double substituted quinolines.[49] Verpoort (2007, 2008) and Yus (2007) applied a transfer hydrogenation approach starting from 2-aminobenzophenone with an equimolar ratio of benzophenone to form a second CH acidic ketone for annulations.[50]



Scheme 18: Ru catalyzed quinoline synthesis

All of these discussed example reactions allowed an atom economic alkylation for C-C or C-N couplings in one step up to more component heterocyclic synthesis. In general Hoffman alkylation or other standard organic reactions with irritating alkyl halides, and less selectivities are used. Depending on the addition of base or additives, borrowing hydrogen reactions have a very low E-factor (= mass of products/mass of non-benign educts) by the formation, reusing of hydrogen, water release and usually nontoxic prosperity of alcohols. In terms of sustainability, the

choice of alcohols as substrates is highly desirable as they are readily available by a variety of industrial processes and can be obtained renewably via fermentation or catalytic conversion of lignocellulosic biomass.

However, in all described and investigated cases only novel metals were used with a high cost factor and toxicity.

1.5.4 Hydrogen-Borrowing with non-precious metal catalysts

During the course of ongoing studies on novel metal catalysts, earth-abundant transition metal catalysis is becoming more powerful over the recent years being equal in C-C and C-N bond formation. Hanson, Zhang and Kempe worked on Co pincer complexes catalyzing alcohol aminations. Depending on the catalyst, amines or imines can be formed. Hanson and Zhang´s system deals with a subtle change of the reaction conditions to readily switch the products. Simple additions of molecular sieve switch with a high chemo selectivity, between amines or imines.[51,52] Furthermore, the D. Jones group used this type of complexes for reversible dehydrogenation and hydrogenation of *N*- heterocycles like quinolines.

PNP^{Triaz}-$CoCl_2$ was used from the Kempe group as pre-catalyst and activated under basic conditions with ^{t}BuOK. After formation of a double deprotonated anionic complex, Co reacts with a similar reactivity like Ir for hydrogenation of ketones and alcohol amine couplings.[53]

The groups of Feringa and Barta, Wills, and Zhao reported the alkylation of amines with alcohols to give amines by utilizing Fe catalysts featuring functionalized cyclopentadienone or hydroxy cyclopentadienyl ligands based upon Knölker's complex or derivatives thereof.[54] With this type of complex aromatic and aliphatic precursors can be coupled. However, highly air sensitive complexes and difficult handling of them impede a useful application.[55, 56]

The newest system was published from Milstein as first PNP-Mn complex for dehydrogenative coupling of alcohols and amines to form imines.[57] Moreover, the first mild catalytic Michael addition of non-activated nitriles with acrylate esters was reported. At this point a big run on new Mn complexes and application was created. Very recently, triazine based PNP manganese complexes were reported from the

Kempe group for hydrogenations of ketones. The pre-catalyst was synthesized in analogy to our systems, being activated with ^{t}BuOK.[58]

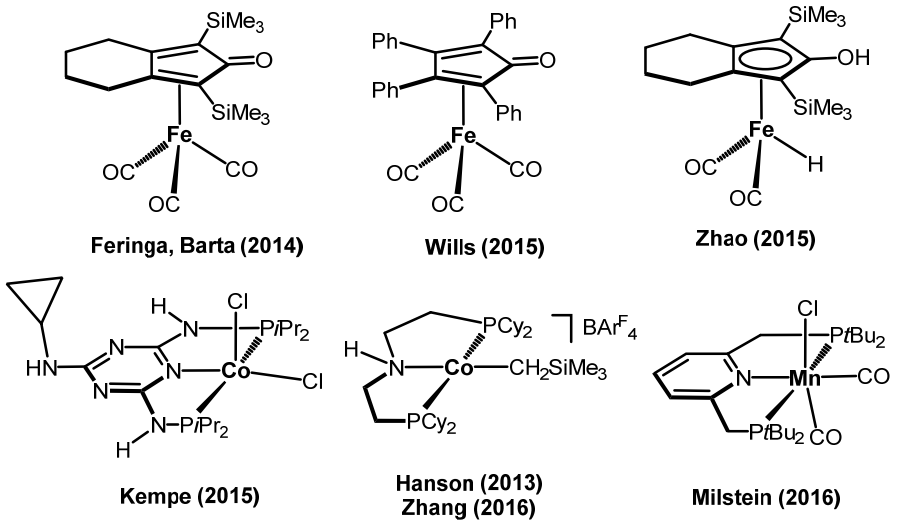


Figure 3: Non-precious pincer metal complexes

Intrigued by all this hitherto discoveries, our group focuses on 2,6-diaminopyridine/triazine or *N,N´*-dimethyl-1,3-diamonobenzene backbones. The broad applicability of this ligand class has been demonstrated recently in the case of Fe, which is highly efficient catalyst for hydrogenation.

This work used the following selected main complex systems for all catalytic manipulations in all tailed publications. Starting from first results of homo coupling up to efficient Ni catalyzed Suzuki cross coupling reactions. Next, new ways for mild and selective catalyzed amination of alcohols were developed towards to polysubstituted pyrimidines and quinolines.

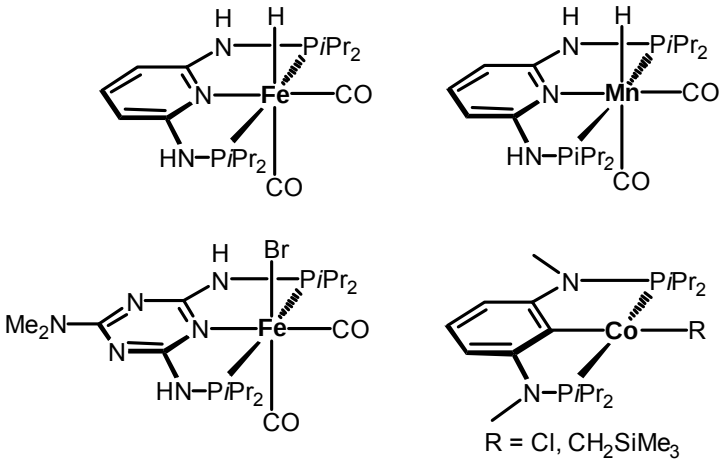


Figure 4: Non-precious pincer metal complexes

2 Results and Discussion

2.1 Overview of Contributions

Manuscript #1:

Co(II) PCP Pincer Complexes as Catalysts for the Alkylation of Aromatic Amines with Primary Alcohols
Mastalir, M.; Tomsu, G.; Pittenauer, E.; Allmaier, G.; Kirchner, K. *Org. Lett.* **2016**, 18, 3462–3465.

Manuscript #2:

Divergent Coupling of Alcohols and Amines Catalyzed by Isoelectronic Hydride Mn (I) and Fe (II) PNP Pincer Complexes
Mastalir, M.; Glatz, M.; Gorgas, N.; Stöger, B.; Pittenauer, E.; Allmaier, G.; Veiros, L.F.; Kirchner, K.
Chem. Eur. J. **2016**, *22*, 12316-12320.

Manuscript #3:

Sent draft to Advanced Synthesis and Catalysis; just accepted

Air Stable Fe(II) PNP Pincer Complexes as Efficient Catalysts for the Selective Alkylation of Amines with Alcohols
Mastalir, M.; Stöger, B.; Pittenauer, E.; Allmaier, G.; Kirchner, K.

Manuscript #4:

Send draft to Journal of the Americal Chemical Society

Sustainable Synthesis of Quinolines and Pyrimidines Catalyzed by Manganese PNP Pincer Complexes

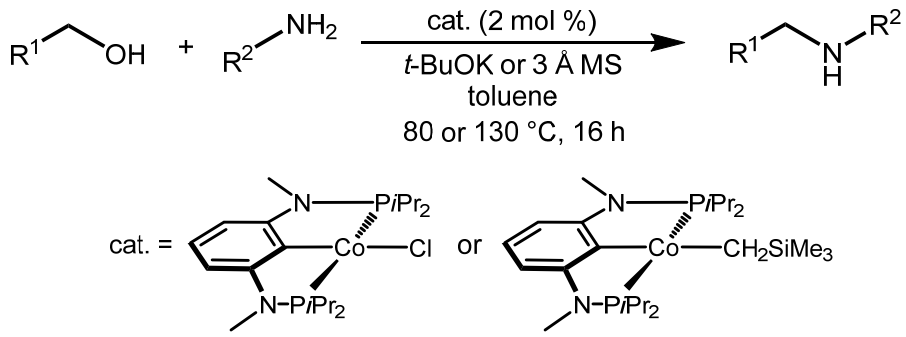
Mastalir, M.; Glatz, M.; Stöger, B.; Pittenauer, E.; Allmaier, G.; Kirchner, K.

2.2 Context of Contributions

In this chapter the context of all the subsequently introduced manuscripts will be outlined. The next passage will briefly dispute the focus of research in the individual topic, refer to theoretical fundamentals and reveal of these contribution to the main topic of this thesis. For detailed background information and respective references see Chapter 2.3.

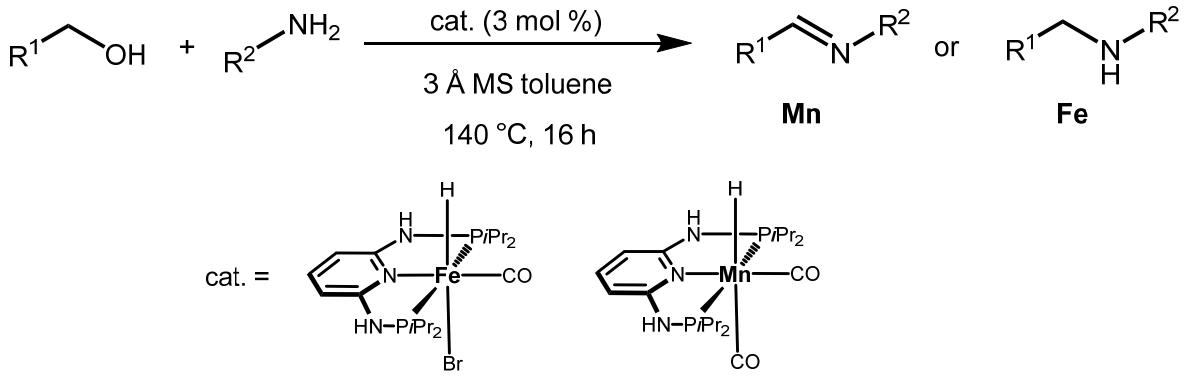
At the research for modified PNP and PCP pincer type ligands in combination with earth abundant transition metals, catalytic activities were found in analogy to known precious catalysts. Starting from simple derivatization of classically used pyridine systems with new *N,N´* disubstituted precursors and new ring modified DAP´s. This was achieved via Chichibabin reactions, a technique already used for modification of other ligand systems. During the ligand design, the selection of metals was extended from Fe, Mo and W up to five more metals (V, Cr, Mn, Co and Ni). At first, all PNP metal complexes were tested for different catalytic organic reactions like e.g. cross couplings, hydrogenations and Michael additions.

Since two years a synthetic hype started for hydrogen borrowing methodology, especially with non-precious metals. Therefore we tried the investigation of our complexes included the existing PCP-Co-Cl system for this kind of reaction.
Manuscript #1 bargain from the first catalytic usage of a PCP-Co complex for amination of alcohols. A range of primary alcohols and aromatic amines were efficiently converted into mono N-alkylated amines with good to excellent isolated yields. The basic version showed higher substrate tolerance instead of the high temperature method.



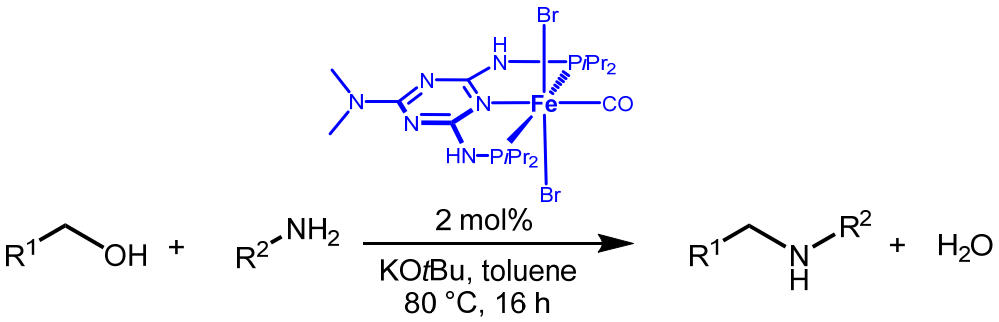
Scheme 19: PCP-Co catalyzed amination of alcohols

During the catalyst screening, the standard PNP-Fe hydride was tried under basic conditions with success. In analogy to the Milstein PNP-Mn work, we synthesized a similar complex with our ligands and applied it for the same procedure. This reaction is an environmentally benign process implementing inexpensive, earth abundant non-precious metal catalysts and is based on the acceptor-less alcohol dehydrogenation concept. A range of alcohols and amines including both, aromatic and aliphatic substrates, were efficiently converted in good to excellent isolated yields. While in the case of Mn selectively imines were obtained, with Fe exclusively mono-alkylated amines were formed. These reactions proceed under base free conditions and require the addition of molecular sieves. (Manuscript #2).



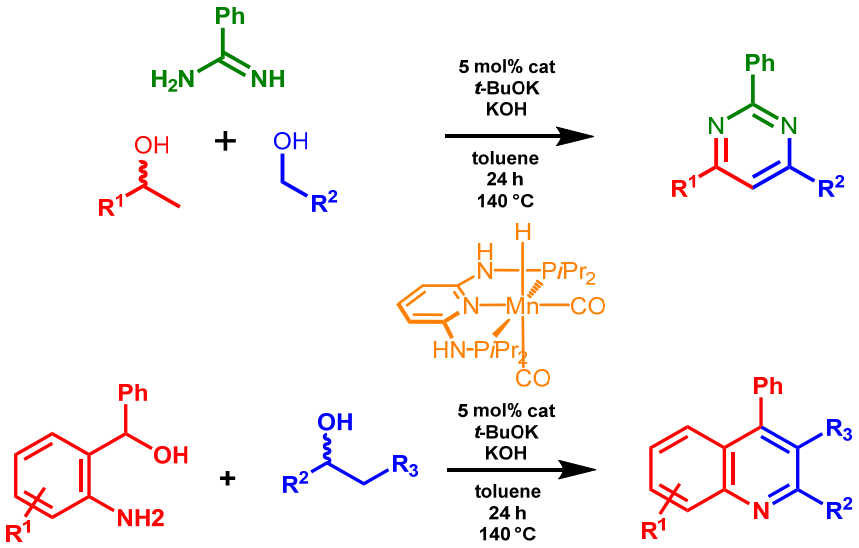
Scheme 20: Divergent amination of alcohols with Mn and Fe

A series of well-defined Fe(II) complexes based on triazine and pyridine backbone due the catalyst screening was found. These complexes were tested as catalysts for amination of alcohols. The catalytic necessity of a stabilizing CO as co-ligand was important instead of the inactive high spin PNP-$FeBr_2$ complex. The low spin complexes [Fe(PNP)(CO)Br_2] bearing a CO co-ligand efficiently and selectively convert primary alcohols and aromatic and benzylic amines into mono N-alkylated amines in good to excellent isolated yields. Beneficial under the basic conditions at milder temperatures conversions of chiral precursors is also possible and higher substrate tolerances are given. (Manuscript #3)



Scheme 21: PNP-Fe catalysed amination of alcohols

In manuscript #4 we applied a sustainable quinoline and multi component pyrimidine synthesis catalyzed by PNP-Mn hydride based on all other former published reactions. In the first step 2-aminobenzhydryl alcohol and a secondary alcohol were oxidized to ketones under hydrogen release. Via the Friedländer annulation the imino species or the aldol adduct was formed. Equally, which mechanism starts at first two equivalents of water were lost and formed the desired substituted quinoline. Pyrimidines were formed from a primary and secondary alcohol oxidization followed by further aldol coupling and cyclization with benzamidine. Here, the first non-precious metal catalyzed reaction for heterocycles was reported by well-defined Mn(I) complexes based on triazine and pyridine backbones.



Scheme 22: PNP-Mn catalysed heterocyclic formation

2.3 Original Works

In this chapter, all published and used manuscripts are included. All permission for reprints are added in the appendix

Manuscript #1:

Reprinted from *Organic Letters* **2016**, 18, 3462–3465 with kind permission from ACS.

Mastalir, M.; Tomsu, G.; Pittenauer, E.; Allmaier, G.; Kirchner, K.

Co(II) PCP Pincer Complexes as Catalysts for the Alkylation of Aromatic Amines with Primary Alcohols

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Co(II) PCP Pincer Complexes as Catalysts for the Alkylation of Aromatic Amines with Primary Alcohols

Matthias Mastalir,[†] Gerald Tomsu,[†] Ernst Pittenauer,[‡] Günter Allmaier,[‡] and Karl Kirchner*[,†]

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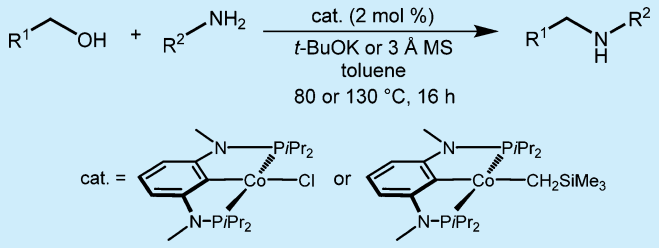
Supporting Information

ABSTRACT: Efficient alkylations of amines by alcohols catalyzed by well-defined Co(II) complexes are described that are stabilized by a PCP ligand (*N*,*N*′-bis-(diisopropylphosphino)-*N*,*N*′-dimethyl-1,3-diaminobenzene) based on the 1,3-diaminobenzene scaffold. This reaction is an environmentally benign process implementing inexpensive, earth-abundant nonprecious metal catalysts and is based on the acceptorless alcohol dehydrogenation concept. A range of primary alcohols and aromatic amines were efficiently converted into mono-*N*-alkylated amines in good to excellent isolated yields.



The catalytic alkylation of amines with alcohols represents an environmentally benign and atom-economic pathway for the synthesis of substituted imines or amines that have important synthetic applications in the synthesis of dyes, fragrances, fungicides, pharmaceuticals, and agricultural chemicals.[1−3] In terms of sustainability, the choice of alcohols as substrates is highly desirable as they are readily available by a variety of industrial processes and can be obtained renewably via fermentation or catalytic conversion of lignocellulosic biomass.[4] The catalytic cycle involves two or three successive steps: (i) acceptorless dehydrogenation (AD) of alcohols,[5] (ii) imine formation, and (iii) in situ hydrogenation of imines (borrowing hydrogen methodology). Key features are that the process is hydrogen neutral and that the only stoichiometric byproduct is water.

Despite the significance of such coupling reactions, homogeneous catalysts mostly employ precious metals such as Ru,[6] Rh,[7] Ir,[8] and Os.[9] In comparison, the same reaction with catalysts that utilize nonprecious, earth-abundant metals[10] is much less developed, although base metals were found to readily oxidize alcohols via AD.[11,12] Kempe and co-workers described for the first time new Co PNP pincer catalysts based on a triazine backbone that was highly active for the alkylation of aromatic amines (Figure 1).[13] This compound was particularly interesting since in the course of the catalytic reaction species with deprotonated, i.e., anionic, triazines seem to play a key role. Hanson[14a] and Zhang[14b] reported a Co catalyst, stabilized by a bis(phosphino)amine (PNP) ligand (Figure 1), which is able to afford imines and/or amines depending on the reaction conditions. The groups of Feringa and Barta,[15a] Wills,[15b] and Zhao[15c] reported the alkylation of amines with alcohols to give amines by utilizing Fe catalysts featuring functionalized cyclopentadienone or hydroxy cyclopentadienyl ligands based upon Knölker's complex or derivatives thereof.[16]

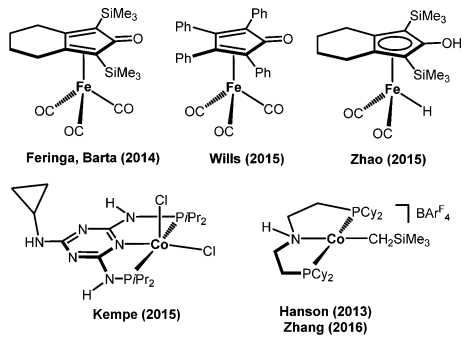


Figure 1. Efficient base metal catalysts for the alkylation of amines with alcohols.

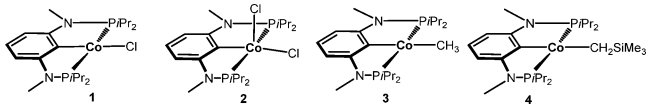


Figure 2. Co(II) and Co(III) PCP pincer complexes tested as catalysts.

Inspired by recent discoveries, we describe here the efficient alkylation of amines with alcohols catalyzed by Co(II) complexes which are stabilized by an anionic PCP ligand based on the 1,3-diaminobenzene scaffold (Figure 2).[17] It has to be noted that Co PCP complexes have as yet not been applied in catalysis.[18]

Co complexes **1** and **2** were screened for the alkylation of aniline with benzyl alcohol (1.4 equiv) in toluene (4 mL) at 80 °C with *t*-BuOK (1.3 equiv) as the additive. Complexes **3** and **4**

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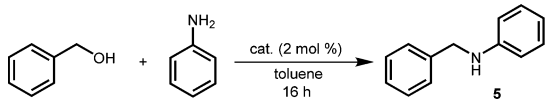
Org. Lett. 2016, 18, 3462−3465

Table 1. Catalyst Screening of the Alkylation of Aniline with Benzyl Alcohol

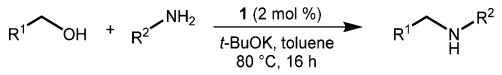


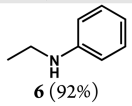
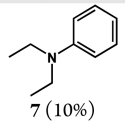
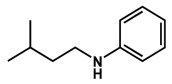
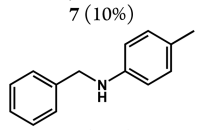
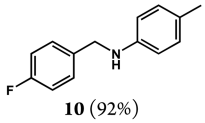
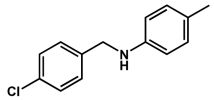
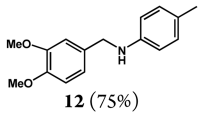
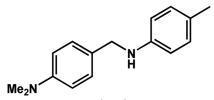
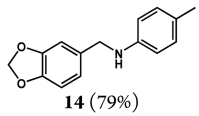
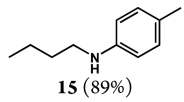
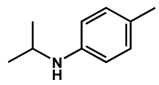
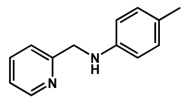
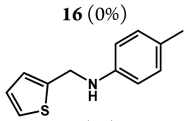
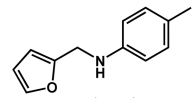
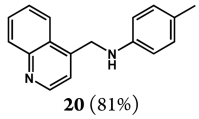
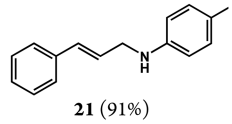
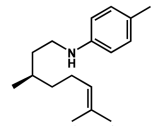
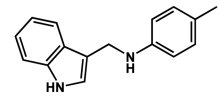
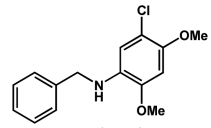
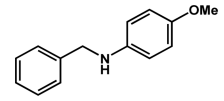
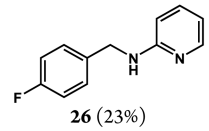
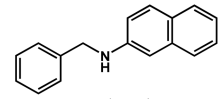
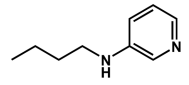
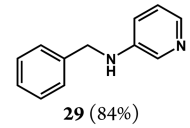
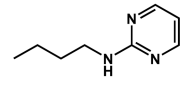
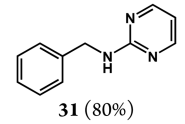
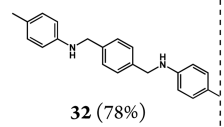
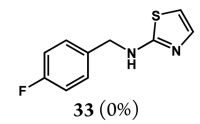
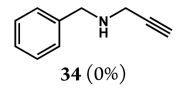
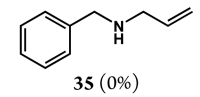
entry	cat.	temp (°C)	additive	yield[a] (%)
1	**1**	80	*t*-BuOK	93
2	**1**[b]	80	*t*-BuOK	84
3[c]	**1**	80	*t*-BuOK	79
4[d]	**1**	80	*t*-BuOK	65
5	**2**	80	*t*-BuOK	30[e]
6	**3**	130	3 Å MS	74
7	**3**	130	none	15
8	**4**	130	3 Å MS	94
9	**4**	130	none	22

[a]Isolated yields. [b]1 mol % of catalyst. [c]8 h. [d]4 h. [e]59% imine.

bearing the strongly basic coligands Me and CH_2SiMe_3 were studied under base-free conditions with the same substrates but with added 3 Å (0.2 g) molecular sieves (MS) in toluene (4 mL). For this methodology, higher reaction temperatures (130 °C) were required. All reactions were performed in a closed vial. The results are summarized in Table 1. The products were analyzed by ^1H and $^{13}C\{^1H\}$ NMR and ESI MS and identified by comparison with authentic samples. All new products were additionally analyzed by HRMS. In general, isolated yields after purification by column chromatography are reported. When **1** (2.0 mol % based on alcohol) was used as precatalyst, *N*-benzylaniline was isolated selectively after 16 h in 93% yield (Table 1, entry 1). Lower catalyst loading (1 mol %) or shorter reaction times (8 and 4 h) resulted in slightly lower yields (Table 1, entries 2–4). Co(III) precatalyst **2** exhibited poor catalytic activity and an in addition to amine formation, large amounts of the corresponding *N*-phenylmethylene benzeneimine were obtained (Table 1, entry 5). With **3** and **4**, in both cases *N*-benzylaniline was formed selectively, but the yield was

Table 2. Coupling of Primary Alcohols and Amines Catalyzed by 1[a]



entry	product (yield)	entry	product (yield)
1	 **6** (92%)	2	 **7** (10%)
3	 **8** (85%)	4	 **9** (94%)
5	 **10** (92%)	6	 **11** (72%)
7	 **12** (75%)	8	 **13** (87)%
9	 **14** (79%)	10	 **15** (89%)
11	 **16** (0%)	12	 **17** (17%)
13	 **18** (59)%	14	 **19** (67%)
15	 **20** (81%)	16	 **21** (91%)
17	 **22** (91%)	18	 **23** (79%)
19	 **24** (72%)	20	 **25** (90%)
21	 **26** (23%)	22	 **27** (93%)
23	 **28** (78%)	24	 **29** (84%)
25	 **30** (75%)	26	 **31** (80%)
27	 **32** (78%)	28	 **33** (0%)
29	 **34** (0%)	30	 **35** (0%)

[a]Isolated yields.

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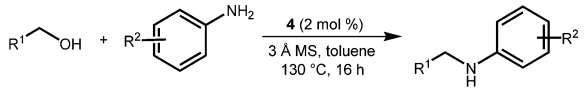
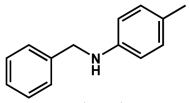
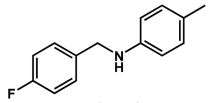
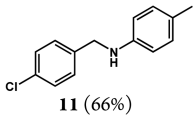
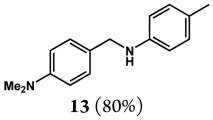
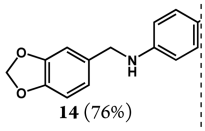
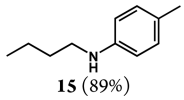
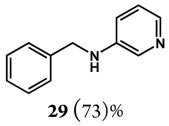
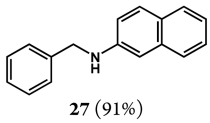
Table 3. Coupling of Primary Alcohols and Anilines Catalyzed by 4[a]



entry	product (yield)	entry	product (yield)
1	 **9** (90%)	2	 **10** (78%)
3	 **11** (66%)	4	 **13** (80%)
5	 **14** (76%)	6	 **15** (89%)
7	 **29** (73)%	8	 **27** (91%)

[a]Isolated yields.

significantly higher in the case of the latter (94%) (Table 1, entries 6 and 8). In the absence of MS, the yields were considerably lower (Table 1, entries 7 and 9).

Having established **1** and **4** as efficient catalysts, the two methodologies were applied to other substrates including substituted benzyl alcohols, aliphatic alcohols such as (*R*)-citronellol, EtOH, and *n*-BuOH as well as aromatic amines. These results are shown in Tables 2 and 3. In most cases, the resulting mono-*N*-alkylated amines were isolated in good to excellent yields. Exceptions are the reactions of 2-propanol with *p*-toluidine (Table 2, entry 7), *p*-fluorobenzylacohol with thiazol-2-amine (Table 2, entry 28), as well as benzyl acohol with allyl- and propargylamine (Table 2, entries 29 and 30) where no product was obtained at all. In the case of the latter, the low yield may be due to polymerization of the amines under these reaction conditions. With 2-pyridinemethanol and *p*-toluidine only 17% of product could be isolated (Table 2, entry 14). It has to be noted that in general dialkylated amines were not formed. This has been tested with EtOH (2.2 mmol), *t*-BuOK (2.6 mmol), and aniline (1.0 mmol) affording only 10% of the dialkylated aniline; the major product is the monoalkylated amine **6** (Table 2, entry 2).

In conclusion, we have reported two examples of efficient alkylations of amines with alcohols catalyzed by well-defined Co(II) complexes which are stabilized by an anionic PCP ligand based on the 1,3-diaminobenzene scaffold. The precatalysts are easily prepared from commercially available reagents in either one- or two-step procedures in high yields. These alkylation reactions are environmentally benign processes, implement inexpensive, earth-abundant nonprecious metal catalysts, and are based on the acceptorless alcohol dehydrogenation concept. A range of substituted benzyl alcohols and aliphatic alcohols ((*R*)-citronellol, EtOH, and *n*-BuOH) and aromatic amines were efficiently converted into mono-*N*-alkylated amines in good to excellent isolated yields. We believe that this work may contribute to the development of waste-free sustainable base metal catalysis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01647.

Synthetic procedures; ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra for all organic products (PDF)

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Notes

The authors declare no competing financial interest.

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Pincer Complexes

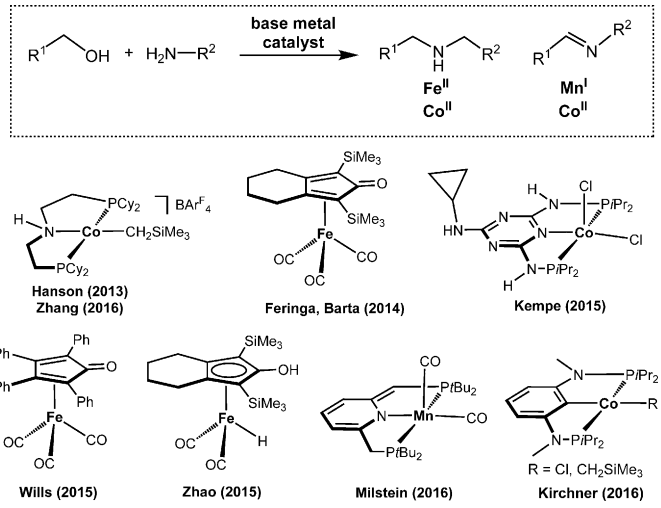
Divergent Coupling of Alcohols and Amines Catalyzed by Isoelectronic Hydride Mn^{I} and Fe^{II} PNP Pincer Complexes

Matthias Mastalir,[a] Mathias Glatz,[a] Nikolaus Gorgas,[a] Berthold Stöger,[b] Ernst Pittenauer,[b] Günter Allmaier,[b] Luis F. Veiros,[c] and Karl Kirchner*[a]

Abstract: Herein, we describe an efficient coupling of alcohols and amines catalyzed by well-defined isoelectronic hydride Mn^{I} and Fe^{II} complexes, which are stabilized by a PNP ligand based on the 2,6-diaminopyridine scaffold. This reaction is an environmentally benign process implementing inexpensive, earth-abundant non-precious metal catalysts, and is based on the acceptorless alcohol dehydrogenation concept. A range of alcohols and amines including both aromatic and aliphatic substrates were efficiently converted in good to excellent isolated yields. Although in the case of Mn selectively imines were obtained, with Fe—exclusively monoalkylated amines were formed. These reactions proceed under base-free conditions and required the addition of molecular sieves.

The catalytic coupling of amines with alcohols represents an environmentally benign and atom-economic pathway for the synthesis of substituted imines or amines that have important synthetic applications in the synthesis of dyes, fragrances, fungicides, pharmaceuticals, and agricultural chemicals.[1–3] In terms of sustainability, the choice of alcohols as substrates is highly desirable, because they are readily available by a variety of industrial processes and can be obtained renewably by fermentation or catalytic conversion of lignocellulosic biomass.[4] The catalytic cycle involves two or three successive steps: 1) acceptorless dehydrogenation (AD) of alcohols;[5] 2) imine formation; and 3) in situ hydrogenation of imines, provided that the hydrogen generated from the first step can be temporarily stored on the metal complex (borrowing hydrogen methodology). Key features are that the process is hydrogen neutral and that the only stoichiometric by-product is water and H_2 (in the case of imines).

Despite the significance of such coupling reactions, homogeneous catalysts mostly employ precious metals, such as Ru,[6] Rh,[7] Ir,[8] and Os.[9] In comparison, the same reaction with catalysts that utilize non-precious, earth-abundant metals[10] is much less developed although base metals demonstrated the ability to oxidize alcohols via AD.[11,12] Recently, Hanson and co-workers[13a] and Zhang and co-workers[13b] reported a Co catalyst, stabilized by a bis(phosphino)-amine (PNP) ligand (Scheme 1), which is able to give imines and/or amines de-



Scheme 1. Efficient base metal catalysts for the coupling of alcohols and amines involving acceptorless dehydrogenation of alcohols.

pending on the reaction conditions. Kempe and co-workers described a new Co PNP pincer catalyst based on a triazine backbone, which was highly active for the alkylation of aromatic amines.[14] The groups of Feringa and Barta,[15a] Wills,[15b] and Zhao[15c] reported the alkylation of amines with alcohols to give amines by utilizing Fe catalysts featuring functionalized cyclopentadienone or hydroxycyclopentadienyl ligands based upon Knölker's complex or derivatives thereof.[16] We described

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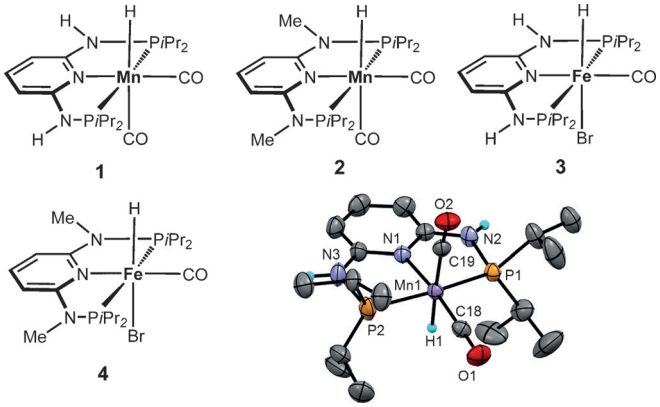
Supporting information for this article and ORCIDs for some of the authors are available on the WWW under http://dx.doi.org/10.1002/chem.201603148. It contains complete crystallographic data, experimental details of the synthesis of all complexes including ^{1}H, $^{13}C\{^{1}H\}$, and $^{31}P\{^{1}H\}$ NMR spectra, computational details, atomic coordinates of optimized species, and technical details in CIF format for **1** (CCDC 1479482 contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre).

the application of well-defined Co^{II} catalysts, which feature a PCP ligand based on the 1,3-diaminobenzene scaffold.[17] Very recently, Milstein and co-workers[18] discovered the first Mn catalyst, which is active for the dehydrogenative coupling of alcohols and amines to form selectively imines. This catalyst features a deprotonated 2,6-bis-(di-*tert*-butylphosphino-methyl)pyridine pincer ligand. Noteworthy, this reaction does not require any additives, such as base or Lewis acids.

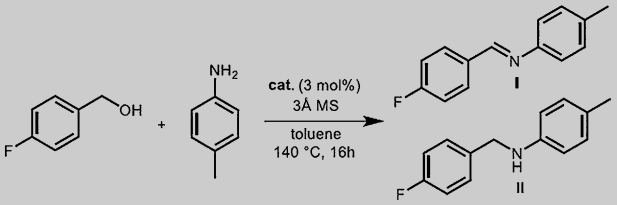
Intrigued by these recent discoveries, we describe herein the efficient coupling of alcohols and amines catalyzed by isoelectronic hydride Mn^{I} and Fe^{II} complexes, which are stabilized by a PNP ligand based on the 2,6-diaminopyridine scaffold. The aromatic pyridine ring and the phosphine P*i*Pr$_2$ moieties are connected by NH or NMe linkers. The broad applicability of this ligand class has been demonstrated recently in the case of Fe, which are highly efficient catalysts for the hydrogenation of ketones, aldehydes and CO_2.[19] New Mn complexes **1** and **2** were synthesized, characterized, and applied in addition to the known Fe complexes **3** and **4**. The molecular structure of **1** was determined by X-ray crystal-structure analysis (Scheme 2).



Scheme 2. Mn and Fe complexes **1**–**4** tested as catalysts, and structural view of **1** showing 30% thermal ellipsoids (most hydrogen atoms omitted for clarity). Selected bond lengths [Å] and angles [°]: Mn1–P1 2.2074(7), Mn1–P2 2.2059(9), Mn1–N1 2.060(2), Mn1–C18 1.747(2), Mn1–C19 1.775(2), Mn1–H1 1.46(2); P1-Mn1-P2 161.00(3), N1-Mn1-C18 171.3(1), N1-Mn1-C19 96.2(1).

First, the Mn and Fe catalysts **1**–**4** were screened for the coupling of 4-fluorbenzyl alcohol with *p*-toluidine (1.4 equiv) in toluene (4 mL) at 140 °C in a closed vial with added 3 Å molecular sieves (MS), and the results are summarized in Table 1. The products were analyzed by ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy and identified by comparison with authentic samples. In general, isolated yields after purification by column chromatography are reported. When **1** (3.0 mol% based on alcohol) was used as catalyst, selectively 1-(4-fluorophenyl)-*N*-(*p*-tolyl)methane imine (**I**) was obtained in 84% yield (entry 1), whereas with **3**, the corresponding amine, *N*-(4-fluorobenzyl)-4-methylbenzene amine (**II**), was isolated in 81% yield (entry 3). Catalysts **2** and **4** bearing NMe linkers were catalytically inactive, and no reaction took place (entries 2 and 4). This emphasizes the importance of the acidic NH moieties for the catalytic reaction. In

Table 1. Screening of Mn and Fe complexes as catalysts for the coupling of *p*-toluidine and 4-fluorobenzyl alcohol.[a]



Entry	Catalyst	Yield [%][b] I	II
1	**1**	84	
2	**2**		
3	**3**		81
4	**4**		
5[c]	**1**	39	
6[c]	**3**		14
7[d]	**3**	45	
8[d]	**1**		22
9[e]	**3**	41	19
10[f]	**1**	70	
11[f]	**3**		73

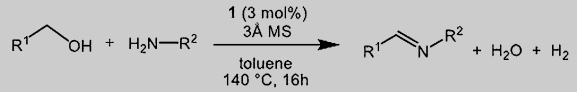
[a] Reaction conditions: 1.0 mmol 4-fluorobenzyl alcohol, 1.4 mmol *p*-toluidine, 0.3 g 3 Å MS, 3.0 mol% catalyst, 4 mL toluene, 140 °C, 16 h. [b] Isolated yields. [c] Without MS. [d] Without MS, 60 h. [e] Open system in *o*-xylene. [f] 1.0 mmol LiOTf.

the absence of MS, even after 60 hours, the yields were considerably lower (entries 5–8). When the reaction with **3** was performed in an open system, a mixture of imine and amine were obtained (entry 9). When the reaction was performed in the presence of LiOTf instead of MS, good yields were also achieved (entries 10 and 11) suggesting that Lewis acid property of these additives may also play a role.

Having established **1** and **3** as active catalysts, this methodology was applied to other substrates including benzyl alcohols and *n*BuOH, as well as aromatic and aliphatic amines. These results are shown in Tables 2 and 3. The resulting imines and *N*-alkylated amines were isolated in good to excellent yields. An exception is the Mn-catalyzed reaction of *n*BuOH and *p*-toluidine were only 17% of the respective imine was obtained (Table 2, entry 6). The low yield was due to polymerization of the product under these reaction conditions. Moreover, in the case of Fe, exclusively monoalkylated amines were formed.

Simplified catalytic cycles with **1** and **3** as catalyst and precatalyst, respectively, are shown in Schemes 3 and 4. Key species are $\mathbf{A}^{Mn}$ and $\mathbf{A}^{Fe}$ with the latter being formed initially from **3** in the presence of base.[19c] Both compounds feature a deprotonated PNP ligand and are coordinatively unsaturated with the important difference that the first contains two, the latter only one inert CO co-ligand, but additionally a hydride ligand, which can participate in the catalytic reaction. Accordingly, the Fe system is capable of performing both alcohol dehydrogenation (oxidation cycle) and imine hydrogenation (reduction cycle) via an insertion mechanism. In the reduction cycle, coordination of dihydrogen ($\mathbf{E}^{Fe}$) and subsequent protonation of

Table 2. Dehydrogenative coupling of alcohols and amines to form imines utilizing catalyst **1**.[a]



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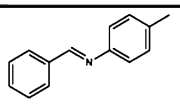
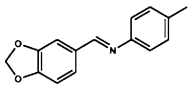
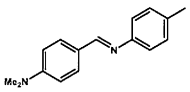
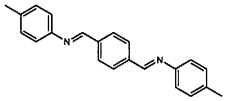
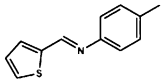
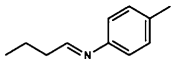
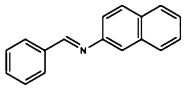
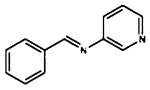
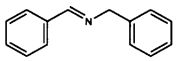
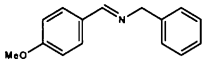
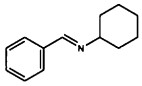
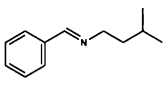
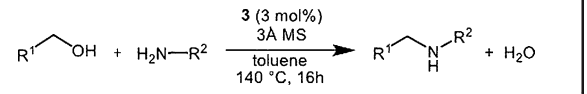
1		90%	2		84%
3		92%	4		71%
5		68%	6		17%
7		90%	8		60%
9		86%	10		92%
11		87%	12		73%

[a] Reaction conditions: 1.0 mmol alcohol, 1.4 mmol amine, 0.3 g 3 Å MS, 3.0 mol% catalyst, 4 mL toluene, 140 °C, 16 h. [b] Isolated yields.

Table 3. Coupling of alcohols and amines catalyzed by **3**.[a]



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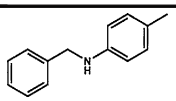
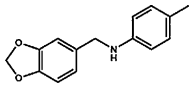
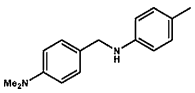
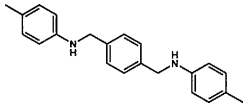
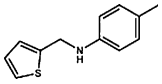
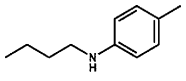
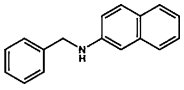
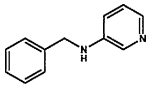
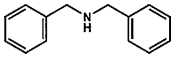
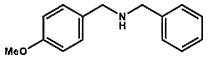
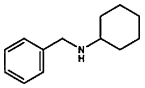
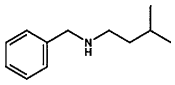
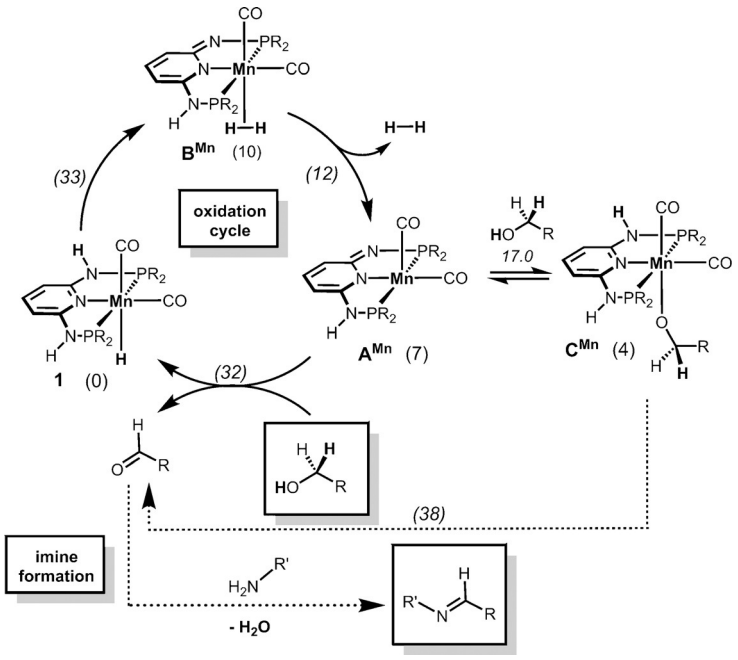
1		91%	2		82%
3		88%	4		67%
5		80%	6		61%
7		93%	8		61%
9		82%	10		89%
11		82%	12		79%

[a] Reaction conditions: 1.0 mmol alcohol, 1.4 mmol amine, 0.3 g 3 Å MS, 3.0 mol% catalyst, 4 mL toluene, 140 °C, 16 h. [b] Isolated yields.

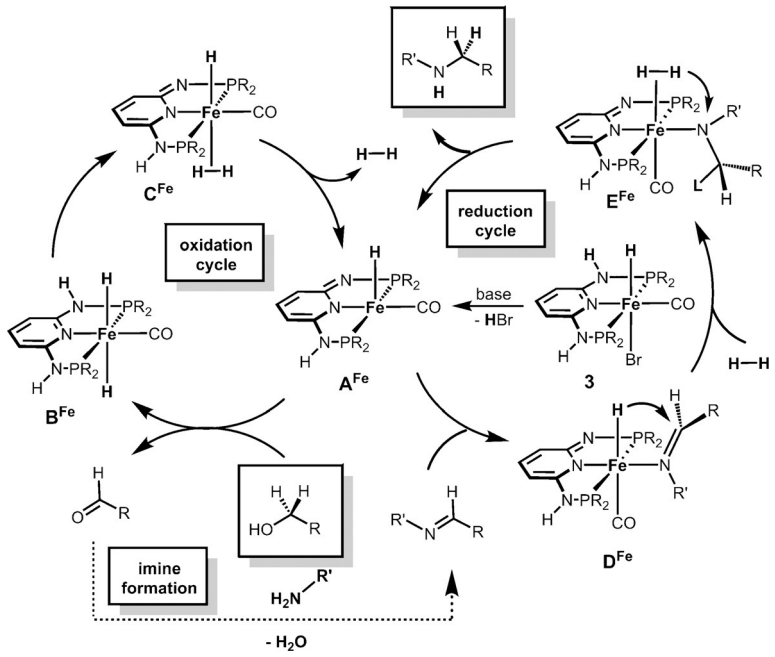
the imine N atom with formation of the amine and regeneration of the hydride ($\mathbf{A}^{Fe}$) is essential. The same mechanism was recently proposed for the hydrogenation of ketones and aldehydes.[19c] The Mn system, on the other hand, is only able to oxidize the alcohol with concomitant irreversible H_2 release.

For the Mn-catalyzed reaction, we carried out preliminary DFT calculations[20] to establish a reasonable mechanism for the dehydrogenation of EtOH as model substrate. A summary of these results with the most relevant points along the catalytic cycle is presented in Scheme 3 (for details, see the Supporting Information). The first step is a proton transfer from the N atom of the PNP ligand to the hydride with formation of dihydrogen complex $\mathbf{B}^{Mn}$. Hydrogen transfer is assisted by a nearby EtOH molecule acting as proton shuttle. This process is endergonic ($\Delta G =$ 10 kcal mol^{-1}) with the highest barrier $\Delta G^{\neq}$ along the path being 33 kcal mol^{-1}. In the next step, H_2 release from $\mathbf{B}^{Mn}$ gives the five-coordinate intermediate $\mathbf{A}^{Mn}$. This occurs easily with a maximum barrier of 12 kcal mol^{-1} in an almost thermoneutral step. In the final step, an EtOH molecule approaches the metal center in outer-sphere fashion and protonates the PNP N atom regenerating **1** and releasing acetaldehyde. This process occurs in a single concerted step with a barrier of 32 kcal mol^{-1}. In a very recent work, a similar mechanism was proposed for the hydrogenation of nitriles with a related Mn PNP complex.[21]

The overall reaction has a high barrier of 33 kcal mol^{-1} in accordance with the experimental conditions, that is, reaction temperature of 140 °C, and a thermodynamically unfavorable free energy balance of 9 kcal mol^{-1}. Thus, the driving force must be provided by the consecutive reaction, that is, condensation between aldehyde and amine and probably by water re-



Scheme 3. Simplified catalytic cycle with **1** as catalyst. Free-energy values ([kcal mol^{-1}], barriers in italic) are referred to **1**.



Scheme 4. Simplified catalytic cycle with **3** as pre-catalyst.

moval by molecular sieves, as was indicated by the experimental observations.

Alternatively, dehydrogenation of EtOH may proceed via the ethoxide complex $\mathbf{C}^{\mathbf{Mn}}$, which undergoes β-elimination with regeneration of **1** and formation of aldehyde. However, this alternative pathway is less favorable than the one calculated for the concerted step.

In conclusion, we have reported two rare examples of an efficient coupling of alcohols and amines catalyzed by well-defined isoelectronic hydride Mn^{I} and Fe^{II} complexes, which are stabilized by a PNP ligand based on the 2,6-diaminopyridine scaffold. The precatalysts were easily prepared from commercially available reagents in a two-step procedure and in high yields. The coupling reactions are environmentally benign processes implementing inexpensive, earth-abundant non-precious metal catalysts and are based on the acceptorless alcohol dehydrogenation concept. A range of alcohols and amines including both aromatic and aliphatic substrates were efficiently converted in good to excellent isolated yields. In the case of Mn—selectively imines, and in the case of Fe—exclusively monoalkylated amines were formed. These reactions proceed under base-free conditions and required the addition of molecular sieves. Detailed mechanistic studies are currently underway. This work contributes to the development of waste-free sustainable base metal catalysis.

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Keywords: alcohols · amination · homogeneous catalysis · iron · manganese

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Air Stable Fe(II) PNP Pincer Complexes as Efficient Catalysts for the Selective Alkylation of Amines with Alcohols

Air Stable Iron(II) PNP Pincer Complexes as Efficient Catalysts for the Selective Alkylation of Amines with Alcohols

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Supporting information for this article is available on the WWW under http:/ xxxxxx

Abstract

A series of well-defined iron(II) complexes of the types [Fe(PNP)Br_2] and [Fe(PNP)(CO)Br_2] with PNP pincer ligands based on triazine and pyridine backbones were prepared and fully characterized. These complexes were tested as catalysts for the alkylation of amines by alcohols. The high spin complexes [Fe(PNP)Br_2] are catalytically inactive. The low spin complexes [Fe(PNP)(CO)Br_2] bearing a carbonyl co-ligand efficiently and selectively convert primary alcohols and aromatic and benzylic amines selectively into mono N-alkylated amines in good to excellent isolated yields. A mechanistic proposal is given.

Keywords: iron complexes; pincer complexes; homogeneous catalysis; alcohols; amines

Introduction

The choice of alcohols as substrates is highly desirable in terms of sustainability as they are readily available by a variety of industrial processes and can be obtained renewably via fermentation or catalytic conversion of lignocellulosic biomass.[1] Accordingly, the catalytic alkylation of amines with alcohols represents an environmentally benign and atom-economic pathway for the synthesis of substituted imines or amines that have important synthetic applications in the synthesis of dyes, fragrances, fungicides, pharmaceuticals, and agricultural chemicals.[2-4] The catalytic cycle involves three successive steps: (i) acceptorless dehydrogenation (AD) of alcohols,[5] (ii) imine formation, and (iii) *in situ* hydrogenation of imines (borrowing hydrogen methodology). Key features are that the process is hydrogen neutral and that the only stoichiometric by-product is water.

Despite the importance of such coupling reactions, homogeneous catalysts mostly employ precious metals such as ruthenium,[6] rhodium,[7] iridium,[8] and osmium,[9] while the same reaction with non-precious, earth abundant metal catalyst[10] is much less developed. This is surprising taken the fact that base metals were found to readily oxidize alcohols via AD.[11,12] Kempe and coworkers described for the first time a new cobalt PNP pincer catalyst based on a triazine backbone, which was highly active for the alkylation of aromatic amines (Figure 1).[13] Hanson[14a] and Zhang[14b] reported a cobalt catalyst, stabilized by a bis(phosphino)amine (PNP) ligand (Figure 1), which is able

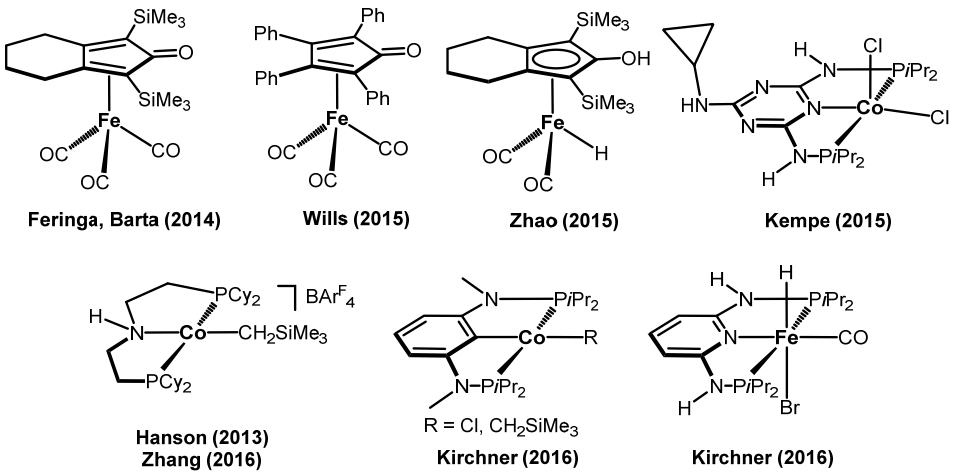


Figure 1. Efficient Base Metal Catalysts for the Alkylation of Amines with Alcohols

to afford imines and/or amines depending on the reaction conditions. As iron catalysts are concerned the groups of Feringa and Barta,[15a] Wills,[15b] and Zhao[15c] reported the alkylation of amines with alcohols to give amines. All these iron catalysts feature functionalized cyclopentadienone or hydroxy cyclopentadienyl ligands based upon Knölker's complex or derivatives thereof.[16] We have prepared the first cobalt(II) PCP pincer complexes with a 1,3-diaminobenzene backbone as well as a hydride iron(II) PNP pincer complex based on the 2,6-diamonopyridine scaffold which are also active catalysts for the alkylation of amines with alcohols to give amines.[17,18] Depending on the co-ligands, *i.e.* chloride vs CH_2SiMe_3, the reaction with cobalt(II) works in the presence of a strong or under base-free conditions with molecular sieve as additive. Very recently, Milstein and coworkers[19] discovered the first manganese catalyst which is active for the dehydrogenative coupling of alcohols and amines to form selectively imines. This catalyst features a deprotonated 2,6-bis-(di-*tert*-butylphosphino-methyl)pyridine pincer ligand.

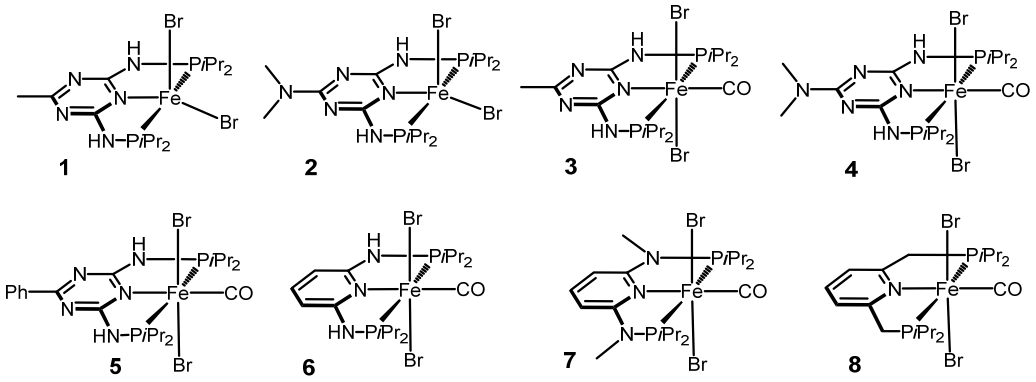


Figure 2. Iron(II) PNP Pincer Complexes Tested as Catalysts

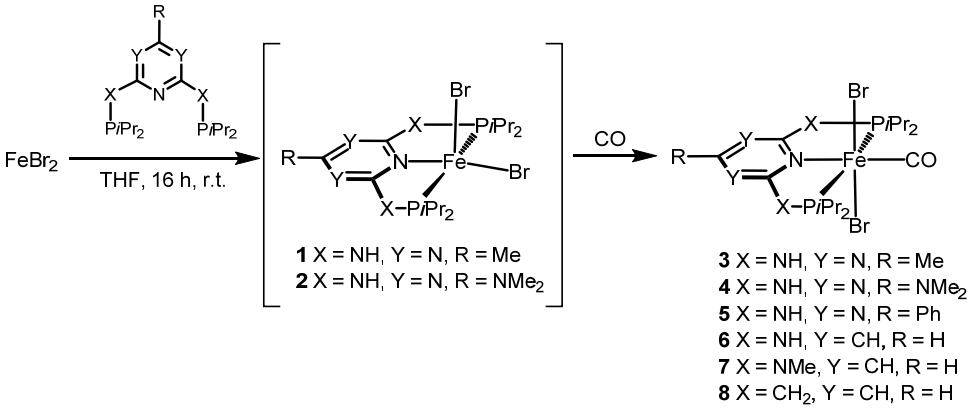
Inspired by these recent discoveries in this area, we describe here an efficient alkylation of amines with alcohols catalyzed by well-defined iron(II) complexes which are stabilized by PNP ligands featuring triazine and pyridine backbones as shown in Figure 2.

Results and Discussion

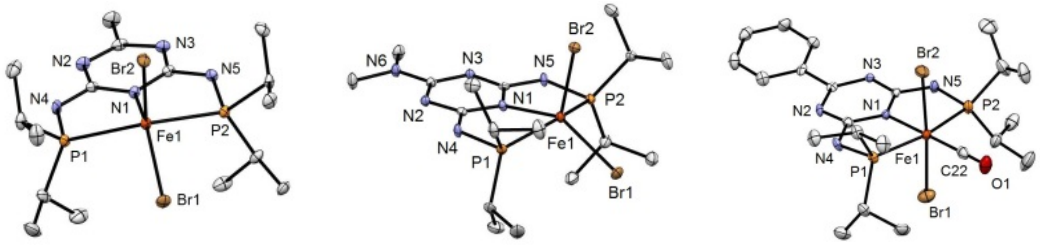
Treatment of anhydrous $FeBr_2$ with 1 equiv of the PNP ligands Triaz^{Me}-*i*Pr and Triaz^{NMe2}-*i*Pr in THF at room temperature afforded the pentacoordinated complexes [Fe(Triaz^{Me}-*i*Pr)Br_2] (**1**) and [Fe(Triaz^{NMe2}-*i*Pr)Br_2] (**2**) in 90 and 93% isolated yields (Scheme 1). These complexes are paramagnetic with an effective magnetic moment of 5.1μ_B as determined in solution (Evans method[20]) corresponding to four unpaired electrons. These type of complexes do not need to be isolated, as the readily react with carbon monoxide to afford the diamagnetic octahedral mono carbon monoxide complexes *trans*-[Fe(Triaz^{Me}-*i*Pr)(CO)Br_2] (**3**) and *trans*-[Fe(Triaz^{NMe2}-*i*Pr)(CO)Br_2] (**4**). Accordingly, all mono carbon monoxide complexes were obtained in an one-step procedure yielding directly *trans*-[Fe(Triaz^{Me}-*i*Pr)(CO)Br_2] (**3**), *trans*-[Fe(Triaz^{NMe2}-*i*Pr)(CO)Br_2] (**4**) and *trans*-[Fe(Triaz^{Ph}-*i*Pr)(CO)Br_2] (**5**) in 89-95% isolated yields (Scheme 1). In all cases, selectively the *trans*-dibromide complexes were obtained as indicated by only one strong ν_{CO} band in the range of 1947 to 1963 cm^{-1}. The

syntheses of complexes *trans*-[Fe(PNP-*i*Pr)(CO)Br_2] (**6**),[21] *trans*-[Fe(PNP^{Me}-*i*Pr)(CO)Br_2] (**7**),[22] and *trans*-[Fe(PNP^{CH2}-*i*Pr)(CO)Br_2] (**8**)[23] were reported elsewhere.

Unlike **5**, complexes **3** and **4** were poorly soluble in all common solvents. All complex were characterized by elemental analysis and IR spectroscopy. Complex **5** was also characterized by solution ^{1}H, $^{31}P\{^{1}H\}$, $^{13}C\{^{1}H\}$ NMR spectroscopy, while **3** and **4** were characterized by solid state ^{13}C and ^{31}P NMR spectroscopy. In addition, the molecular structures of **1, 2** and **5** were determined by X-ray crystallography. Structural views are depicted in Figure 3 with selected bond distances and angles given in caption.



Scheme 1. Synthesis of pre-catalysts **1**-**8**



1 **2** **5**

Figure 3. Structural views of [Fe(Triaz^{Me}-*i*Pr)Br_2]·1THF (**1**·THF), [Fe(Triaz^{NMe2}-*i*Pr)Br_2]·THF (**2**·THF), and *trans*-[Fe(Triaz^{Ph}-*i*Pr)(CO)Br_2]·2THF (**5**·2THF) and showing 50% thermal ellipsoids (H atoms and solvent molecules omitted for clarity). Selected bond lengths (Å) and bond angles (°):**1:** Fe1-N1

2.186(2), Fe1-Br1 2.5338(5), Fe1-Br2 2.4161(5), Fe1-P1 2.4790(9), Fe1-P2 2.4804(9), N1-Fe1-Br1 139.36(6), N1-Fe1-Br2 104.84(5), Br1-Fe1-Br2 115.73(2), P1-Fe1-P2 148.48(3). **2:** Fe1-Br1 2.5196(6), Fe1-Br2 2.4516(6), Fe1-P1 2.482(1), Fe1-P2 2.490(1), Fe1-N1 2.171(3), Br1-Fe1-Br2 111.51(3), P1-Fe1-P2 149.24(2). **5:** Br1-Fe1 2.4517(8), Fe1-Br2 2.4426(8), Fe1-P1 2.266(1), Fe1-P2 2.264(1), Fe1-N1 1.984(3), Fe1-C22 1.782(4), P1-Fe1-P2 165.09(4), Br1-Fe1-Br2. 175.34(3), N1-Fe1-C22 179.5(2).

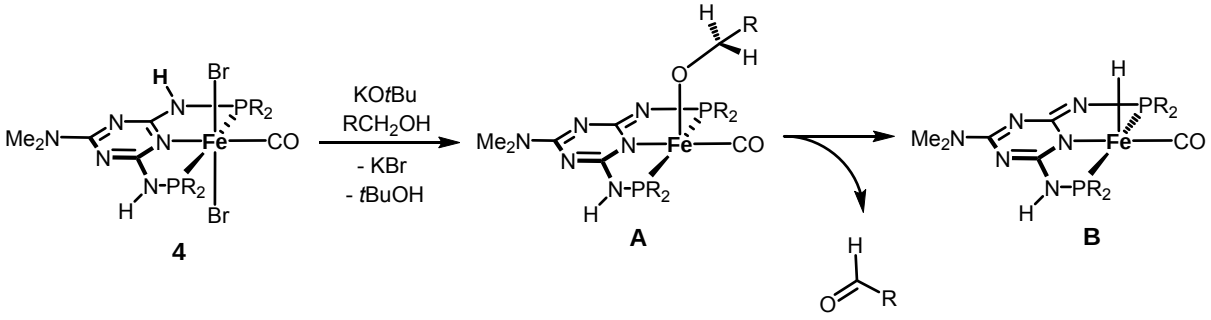
Iron complexes **1** to **8** were screened for the alkylation of aniline (1.2 equiv) with benzyl alcohol (1.0 equiv) in toluene (4 mL) at 80 °C with KO*t*Bu (1.3 equiv) as additive. The role of stoichiometric amounts of base is not fully understood at this stage. One role is the deprotonation of the PNP ligand, but another role may be the facilitation of the condensation reaction, *i.e.*, the liberation of water. All reactions were performed in a closed vial. A mercury poisoning experiment support a homogeneous catalyzed pathway. The results are summarized in Table 1. The products were analyzed by ^{1}H, $^{13}C\{^{1}H\}$ NMR, and ESI MS and identified by comparison with authentic samples reported elsewhere.[17,18] In general, isolated yields after purification by column chromatography are reported.

When **1**, **2** and **7** were used as pre-catalyst no reaction took place (Table 1, entries 1, 4 and 7). In the case of **1** and **2** this may be due to the fact that these complexes, in contrast to all other compounds, contain no carbon monoxide co-ligand and are thus paramagnetic d^6 high spin complexes. Alternatively, these complexes may be also unstable to dehydrogenative deprotonation without the stabilizing carbonyl co-ligand. Complex **7**, on the other hand contains an NMe linker instead of an NH linker and thus deprotonation of the ligand is blocked, a feature which turned out to be very important for these type of complexes in order to exhibit a good catalytic performance. Moreover, the pyridine based complex **8**[23] bearing CH_2 linkers showed only modest activity (Table 1, entry 8). All other complexes other complexes showed excellent to good activities, with **4** being the best catalyst yielding selectively N-benzylaniline in 91 % yield (entry 5). Lower catalyst loading (1 mol %) or shorter reaction times (8 and 4 h) resulted in slightly lower yields (Table 1, entries 12-14). The best solvent for these reactions was

toluene, while in THF or dioxane much lower yields were achieved (Table 1, entries 10 and 11).

Having established **4** as the most efficient catalyst in this series, this methodology was applied to other substrates including substituted benzyl alcohols or furfurylaclohol, aliphatic alcohols such as *R*-citronellol, EtOH, and *n*BuOH as well as aromatic amines. These results are shown in Table 2. In most cases the resulting mono N-alkylated amines were isolated in good to excellent yields. Exceptions are the reactions of isopropanol and 2-pyridinemethanol with *p*-toluidine (Table 2, entries 11 and 21) where no and only 17 % product, respectively, could be isolated. It has to be noted that in general dialkylated amines were not formed. This has been tested with EtOH (2.2 mmol), KO*t*Bu (2.6 mmol) and aniline (1.0 mmol) affording only 7 % of the dialkylated aniline (Table 2, entry 2). The major product is the monoalkylated amine **10** (Table 2, entry 1).

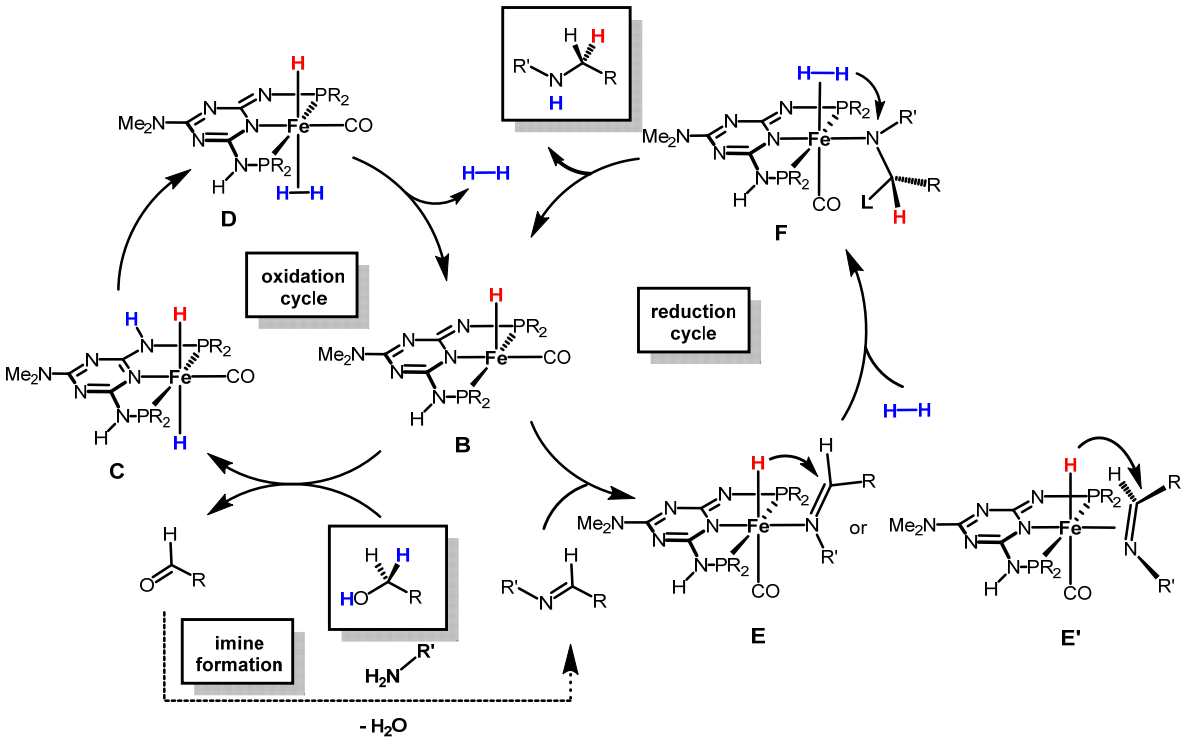
The actual catalyst is presumably formed upon reaction of pre-catalyst **4** with the strong base KO*t*Bu in the presence of a primary alcohol (Scheme 2). Deprotonation of both the triazine ligand and the alcohol affords initially the alkoxide complex **A** which undergoes β-elimination to yield the hydride complex **B** thereby releasing aldehyde.



Scheme 2. Proposal for the Formation of Catalyst **B** (R = *i*Pr).

As recently shown by Kempe[24] and by us,[25] triazine based PNP pincer complexes are indeed readily deprotonated in the presence of strong bases.

A tentative, simplified catalytic cycle with **B** as key species is depicted in Scheme 3. Intermediate **B** can participate in two catalytic reactions performing both alcohol dehydrogenation (oxidation cycle) and imine hydrogenation (reduction cycle) *via* an insertion mechanism. A related oxidation cycle was recently described for a related manganese(I) PNP complex based on DFT calculations.[18] In the reduction cycle coordination of dihydrogen (**F**) and subsequent protonation of the imine N-atom with formation of the amine and regeneration of the hydride **B** is essential. A similar insertion mechanism with complexes of the type **B** as catalyst was recently proposed for the hydrogenation of ketones and aldehydes by an iron(II) PNP pincer complex.[26a] It has to be noted that an outer sphere hydrogenation of imines, as proven recently for the chemoselective hydrogenation of aldehydes,[26b] cannot be fully excluded but appears to be less likely in this particular case.



Scheme 3. Tentative catalytic cycle with **B** as catalyst (R = *i*Pr).

Conclusion

We prepared and fully characterized a series of well-defined iron(II) complexes of the types [Fe(PNP)Br_2] and [Fe(PNP)(CO)Br_2] with PNP pincer ligands based on triazine and pyridine backbones. While complexes with carbon monoxide as co-ligand, which are diamagnetic d6 low spin systems, are catalytically active, paramagnetic d^6-high spin complexes [Fe(PNP)Br_2] are completely inactive. We have described here an example of an efficient alkylation of amines with alcohols catalyzed by well-defined iron(II) complexes which are stabilized by a PNP ligand based on the 4,6-diamino-triazine scaffold. The precatalyst is easily prepared from commercially available reagents in a two-step procedure in high yields. These alkylation reactions are environmentally benign processes and implement inexpensive, earth abundant non-precious metal catalysts and are based on the acceptorless alcohol dehydrogenation concept. A range of substituted benzyl alcohols including heterocyclic systems such as furfuryl alcohol and aliphatic alcohols (*R*-citronellol, EtOH, *n*BuOH) and aromatic amines were efficiently converted into mono N-alkylated amines in good to excellent isolated yields. A mechanistic proposal is presented with a deprotonated hydride iron(II) complex as key intermediate.

Experimental Section

General. All manipulations were performed under an inert atmosphere of argon by using Schlenk techniques or in a MBraun inert-gas glovebox. The solvents were purified according to standard procedures.[27] The deuterated solvents were purchased from Aldrich and dried over 4 Å molecular sieves. The ligands N,N'-bis(diisopropylphosphino)-2,4-diamino-6-methyltriazine (Triaz^{Me}-*i*Pr),[22] N,N'-bis(diisopropylphosphino)-2,4-diamino-6-phenyltriazine (Triaz^{Ph}-*i*Pr),[28] N,N'-bis(diisopropyl-phosphino)-N''-dimethyl-2,4,6-triaminotriazine (Triaz^{NMe2}-*i*Pr),[28] and the complexes *trans*-[Fe(PNP-*i*Pr)(CO)Br_2] (**6**),[21] *trans*-[Fe(PNP^{Me}-*i*Pr)(CO)Br_2] (**7**),[22] and *trans*-[Fe(PNP^{CH2}-*i*Pr)(CO)Br_2] (**8**)[23] were prepared according to literature procedures. All substrates are known compounds and were used as obtained from commercial sources. ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra were recorded on Bruker

AVANCE-250 and AVANCE-400 spectrometers. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were referenced internally to residual protio-solvent, and solvent resonances, respectively, and are reported relative to tetramethylsilane (σ = 0 ppm). $^{31}P\{^{1}H\}$ NMR spectra were referenced externally to H_3PO_4 (85%) (σ = 0 ppm). Room-temperature solution magnetic moments were determined by ^{1}H NMR spectroscopy using the method of Evans (CD_3OD/CH_3OH).[20]

The solid state NMR spectra were measured at room temperature at a Bruker AVANCE 300 spectrometer using a 4 mm MAS broadband probe head. The rotor spinning speed for all performed experiments was 11 kHz. The ^{13}C spectra were measured with ramped-CP/MAS experiments at a resonance frequency of 75.40 MHz. The ^{31}P spectra were measured with high power decoupled (HPDEC) experiments at a resonance frequency of 121.38 MHz and the spectra were referenced externally against phosphoric acid (^{31}P: 0 ppm).

All mass spectrometric measurements were performed on an Esquire 3000*plus* 3D-quadrupole ion trap mass spectrometer (Bruker Daltonics, Bremen, Germany) in positive-ion mode by means of electrospray ionization (ESI). Mass calibration was done with a commercial mixture of perfluorinated trialkyl-triazines (ES Tuning Mix, Agilent Technologies, Santa Clara, CA, USA). All analytes were dissolved in CH_3CN/H_2O/HCOOH “hypergrade for LC-MS Lichrosolv” quality (Merck, Darmstadt, Germany) to form a concentration of roughly 1 mg/mL in order to suppress dehydrogenations of several analytes. Direct infusion experiments were carried out using a Cole Parmer model 74900 syringe pump (Cole Parmer Instruments, Vernon Hills, IL, USA) at a flow rate of 2 μL/min. Full scan and MS/MS (low energy CID)-scans were measured in the range m/z 100-1100 with the target mass set to m/z 1000. Further experimental conditions include: drying gas temperature: 200°C; capillary voltage: -4 kV; skimmer voltage: 40 V; octapole and lens voltages: according to the target mass set. Mass spectra were averaged during data acquisition time of 1 to 2 min and one analytical scan consisted of five successive micro scans resulting in 50 and 100 analytical scans, respectively, for the final full scan mass spectrum.

Synthesis

[Fe(Triaz^{Me}-*i*Pr)Br$_2$] (1). A suspension of anhydrous $FeBr_2$ (1.15 g, 5.3 mmol) and Triaz^{Me}-*i*Pr (2.0 g, 5.6 mmol) in THF (10 mL) was stirred for 16 h at room temperature. The volume of the solvent was then reduced to about 3 mL and the formed solid was collected on glass frit, was washed with *n*-pentane (3 x 7 mL) and dried under vacuum. Yield: 2.74 g (90%), pale yellow solid. Anal. Calcd. for $C_{16}H_{33}Br_2FeN_5P_2$ (573.08): C, 33.53; H, 5.80; N, 12.22. Found: C, 33.40; H, 5.90; N, 12.30. μ_{eff} = 5.1 μ_B. (CD_3OD/CH_3OH).

[Fe(Triaz^{NMe2}-*i*Pr)Br$_2$] (2). This complex was prepared analogously to **1** with $FeBr_2$ (1.06 g, 4.9 mmol) and Triaz^{NMe2}-*i*Pr (2.0 g, 5.2 mmol) as starting materials. Yield: 2.72 g (92%), white solid. Anal. Calcd. for $C_{17}H_{36}Br_2FeN_5P_2$ (602.12): C, 33.91; H, 6.03; N, 13.96. Found: C, 33.90; H, 6.03; N, 13.95. μ_{eff} = 5.1 μ_B. (CD_3OD/CH_3OH)

***trans*-[Fe(Triaz^{Me}-*i*Pr)(CO)Br$_2$] (3).** A suspension of anhydrous $FeBr_2$ (1.15 g, 5.3 mmol) and Triaz^{Me}-*i*Pr (2.0 g, 5.6 mmol) in THF (10 mL) was stirred for 30 min at room temperature. Afterwards CO was bubbled into the clear solution for 5 min and then stirred for additional 16h. The solvent was than reduced to about 3 mL, the formed solid was collected on glass frit, was washed with *n*-pentane (3 x 7 mL) and dried under vacuum. Yield: 2.97 g (93%), red solid. IR (ATR, cm^{-1}): 3166 (m, ν_{NH}), 1947 (m, ν_{CO}). $C_{17}H_{33}Br_2FeN_5OP_2$ (601.09): C, 33.97; H, 5.53; N, 11.65. Found: C, 34.16; H, 5.61; N, 11.58. Solid-state NMR: ^{13}C-CP/MAS (δ, 20°C): 217.2 (CO), 164.3 (C_{Triaz}), 158.5 (C_{Triaz}), 54.8 (d, J = 51.7 Hz, CH), 28.4 (CH_3), 12.2 (d, J = 10.5 Hz, CH_3). ^{31}P-HPDEC NMR (δ, 20ºC): 121.00.

***trans*-[Fe(Triaz^{NMe2}-*i*Pr)(CO)Br$_2$] (4).** This complex was prepared analogously to **3** with $FeBr_2$ (1.06 g, 49 mmol) and Triaz^{NMe2}-*i*Pr (2 g, 5.2 mmol) as starting materials. Yield: 2.94 g (95%), blue solid. IR (ATR, cm^{-1}): 3251 (m, ν_{NH}), 1958 (m, ν_{CO}). $C_{18}H_{36}Br_2FeN_5OP_2$ (630.13): C, 34.31; H, 5.76; N, 13.34; Found: C, 34.42; H, 5.80; N, 13.28. ^{13}C-CP/MAS (δ, 20°C): 219.9 (CO), 168.9 (C_{Triaz}), 165.4 (C_{Triaz}), 62.3 (CH_3), 20.0 (CH), 13.6 (CH_3). ^{31}P-HPDEC NMR (δ, 20ºC): 123.6.

***trans*-[Fe(Triaz^{Ph}-*i*Pr)(CO)Br$_2$] (5).** This complex was prepared analogously to **3** with $FeBr_2$ (0.97 g, 4.5 mmol) and Triaz^{Ph}-*i*Pr (2.0 g, 4.7 mmol) as starting materials. Yield: 2.67 g (89%), green solid. IR (ATR, cm^{-1}): 3257 (m, ν_{NH}), 1963 (m, ν_{CO}). $C_{22}H_{35}Br_2FeN_5OP_2$ (663.16): C, 39.85; H, 5.32; N, 10.56. Found: C, 39.95; H,

5.27; N, 10.60. ^{1}H NMR (δ, d_8-THF, 20°C): 8.76 (s, 2H, NH), 8.32 (d, J = 7.5 Hz, 2H, PhH), 7.43 (t, J = 7.2 Hz, 1H, PhH), 7.36 (d, J = 7.4 Hz, 2H, PhH), 3.19-3.14 (m, 4H, CH), 1.48 (q, J = 6.9 Hz, 12H, CH_3), 1.32 (q, J = 7.2 Hz, 12H, CH_3). ^{13}C{^{1}H} NMR (δ, d_8-THF, 20°C): 226.0 (t, J = 21.6 Hz, CO), 172.8 (t, J = 12.7 Hz, C_{Triaz}), 171.9 (C_{Triaz}), 136.6 (Ph), 132.5 (PhH), 129.0 (PhH), 128.6 (PhH), 27.6 (t, J = 10.0 Hz, CH), 19.0 (t, J = 27.7 Hz, CH_3), 18.0 (t, J = 59.7 Hz, CH_3). ^{31}P{^{1}H} NMR (δ, d_8-THF, 20°C): 120.4.

General Procedure for the Alkylation of Amines. Alcohol (1.0 mmol), aniline (1.2 mmol) and KO*t*Bu (1.3 mmol) were mixed in toluene (4 mL) and catalyst (0.02 mmol, 2 mol%) was added under inert conditions. After stirring for 16 h at 80°C the mixture was quenched with water (ca 2 mL), the organic layer was dried with $MgSO_4$ and purified via silica column chromatography (eluted with toluene and Et_2O). The products were analyzed by ^{1}H, ^{13}C{^{1}H} NMR, and ESI MS and identified by comparison with authentic samples reported elsewhere.[17] In general, isolated are reported.

Crystal Structure Determination

X-ray diffraction data of [Fe(Triaz^{Me}-*i*Pr)Br_2]·THF (**1**·THF), [Fe(Triaz^{NMe2}-*i*Pr)Br_2]·THF (**2**·THF), and [Fe(Triaz^{Ph}-*i*Pr)(CO)Br_2]·2THF (**5**·2THF) were collected at 100 K in a dry stream of nitrogen on a Bruker Kappa APEX II diffractometer system using graphite-monochromatized Mo-*K*α radiation (λ = 0.71073 Å) and fine sliced *φ*- and *ω*-scans.[29] The diffraction spots of **5**·2THF were attributed to two triclinic domains related by twofold rotation about [100]. Data were reduced to intensity values with SAINT (in the case of **5**·2THF with overlap information) and an absorption correction was applied with the multi-scan approach implemented in SADABS or TWINABS.[30] The structures were solved by charge flipping using SUPERFLIP[31] and refined against *F* with JANA2006.[32] Although **1**·THF possessed orthorhombic metrics, the structure is monoclinic and was refined as a twin by pseudo-merohedry. **5**·2THF was refined as a twin with partially overlapping reflections. Non-hydrogen atoms and the C atoms of a disordered THF molecule in **5**·2THF were refined anisotropically. The H atoms connected to C atoms were placed in calculated positions and thereafter refined as riding on the parent atoms. The amine-Hs were located in difference Fourier maps.

The N–H distances were restrained to 0.870(1) Å and the C-C distances of the disordered THF molecule in **5**·2THF to 1.500(1) Å.

Acknowledgements

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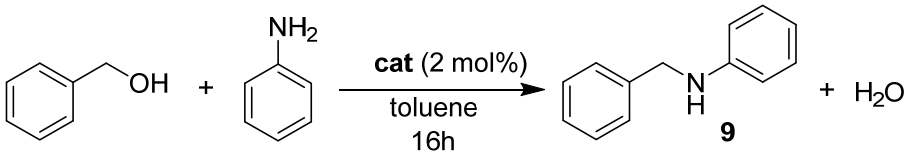
Table 1. Catalyst Screening of the Alkylation of Aniline with Benzyl Alcohol.[a,b]



Entry	Cat.	Solvent	Yield [%]
1	**1**	toluene	0
2	**2**	toluene	0
3	**3**	toluene	80
4	**4**	toluene	91
5	**5**	toluene	51
6	**6**	toluene	84
7	**7**	toluene	0
8	**8**	toluene	24
9	**4**	benzene	90
10	**4**	THF	34
11	**4**	dioxane	28
12[c]	**4**	toluene	79
13[d]	**4**	toluene	69
14[e]	**4**	toluene	54

[a] Reaction conditions: 1.0 mmol benzyl alcohol, 1.2 mmol aniline, 1.3 mmol KO*t*Bu, 2 mol % catalyst, 4 mL toluene, 16 h, 80 °C.

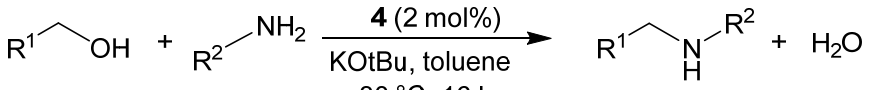
[b] Isolated yields.

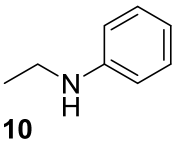
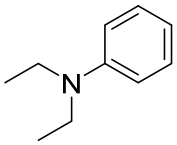
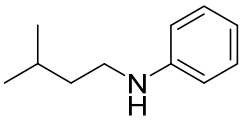
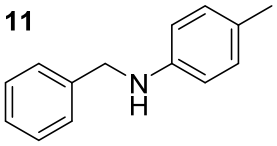
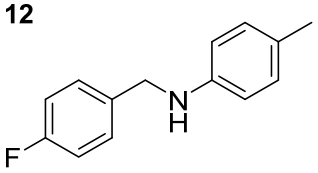
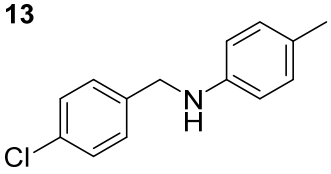
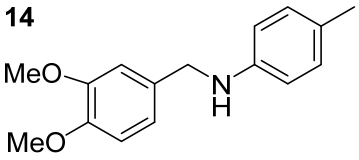
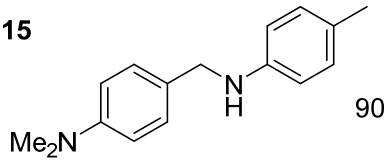
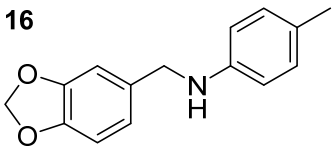
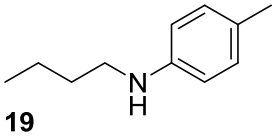
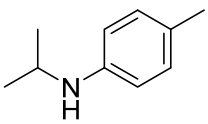
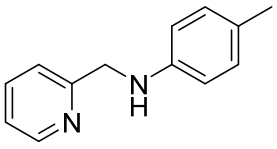
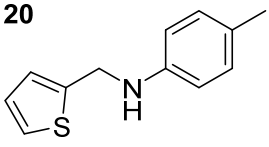
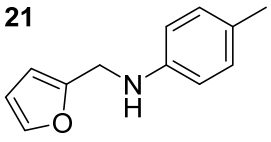
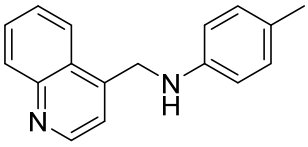
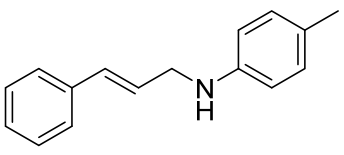
[c] 1 mol % catalyst.

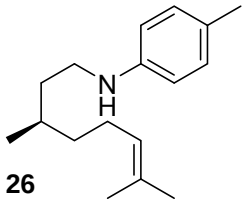
[d] 8 h.

[e] 4 h.

Table 2. Coupling of Primary Alcohols and Amines Catalyzed by **4**.[a, b]



Entry	Product	Yield [%]	Entry	Product	Yield [%]
1	 **10**	88	2	 **11**	4
3	 **12**	63	4	 **13**	93
5	 **14**	82	6	 **15**	71
7	 **16**	86	8	 **17**	90
9	 **18**	85	10	 **19**	87
11	 **20**	0	12	 **21**	34
13	 **22**	81	14	 **23**	87
15	 **24**	82	16	 **25**	91

17  88

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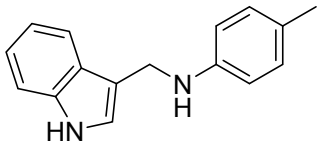
18  73

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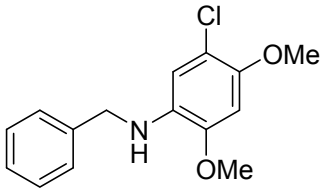
19  74

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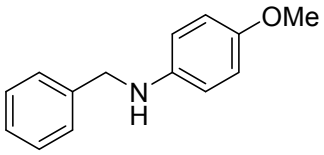
20  87

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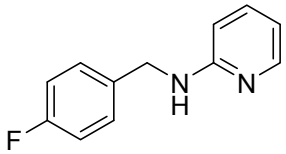
21  21

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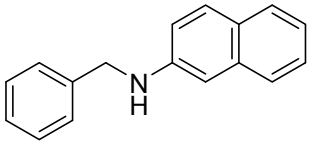
22  90

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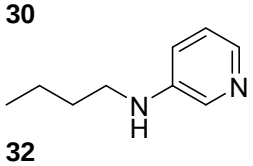
23  71

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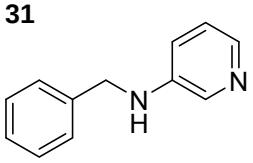
24  74

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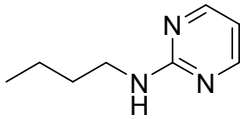
25  62

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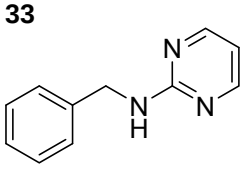
26  76

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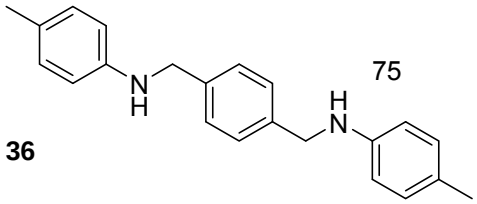
27  75

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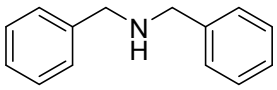
28  81

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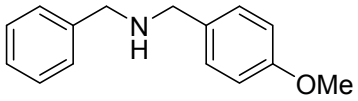
29  88

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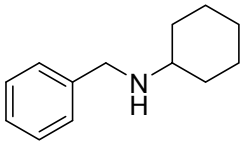
77  62

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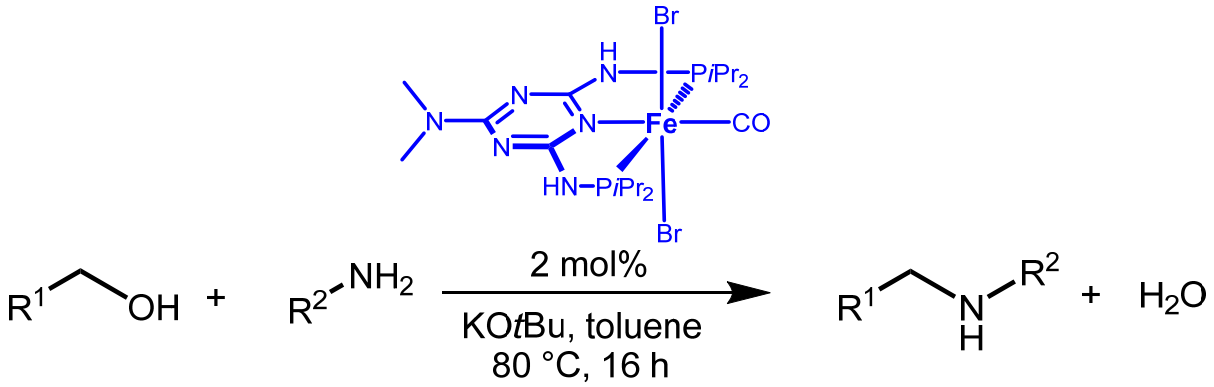
[a] Reaction conditions: 1.0 mmol alcohol, 1.2 mmol amine, 1.3 mmol KO*t*Bu, 2 mol % catalyst, 4 mL toluene, 80 °C, 16 h.

[b] Isolated yields.

[c] 4 mol % catalyst.

For Table of contents use only

An efficient alkylation of amines with alcohols catalyzed by a well-defined iron(II) complex which is stabilized by a PNP ligand based on the 4,6-diaminotriazine scaffold is described. A range of alcohols and amines were efficiently and selectively converted into mono N-alkylated amines in good to excellent isolated yields.



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Manuscript #4:

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Sustainable Synthesis of Quinolines and Pyrimidines Catalyzed by Manganese PNP Pincer Complexes

Mastalir, M.; Glatz, M.; Stöger, B.; Pittenauer, E.; Allmaier, G.; Kirchner, K.

Sustainable Synthesis of Quinolines and Pyrimidines Catalyzed by Manganese PNP Pincer Complexes

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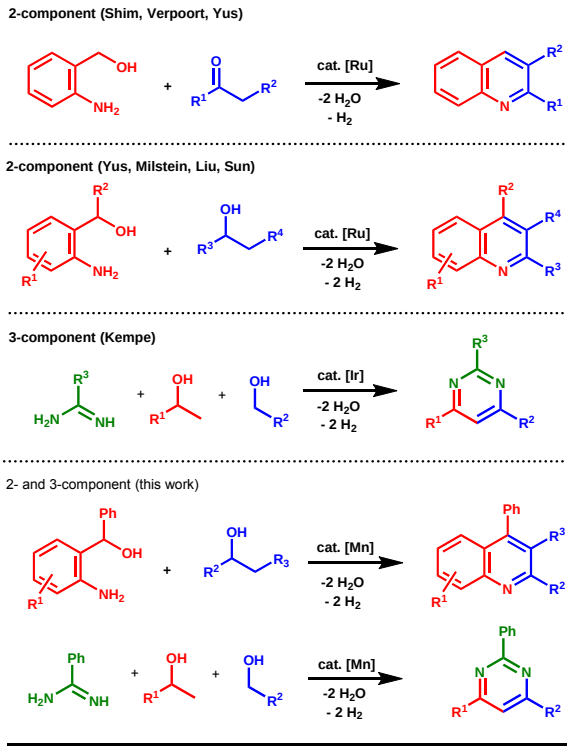
ABSTRACT: This study represents the first example an environmentally benign, sustainable, and practical synthesis of substituted quinolines and pyrimidines using combinations of 2-aminobenzyl alcohols and alcohols as well as benzamidine and two different alcohols, respectively. These reactions proceed with high atom-efficiency *via* a sequence of dehydrogenation and condensation steps which give rise to selective C−C and C−N bond formations, thereby releasing. two equivs of hydrogen and water. A hydride Mn(I) PNP pincer complex, recently developed in our laboratory, catalyzes this process in a very efficient way. A total of 16 different quinolines and 14 different pyrimidines were synthesized in isolated yields of up to 91 and 90%, respectively.

Nitrogen-containing heterocycles such as pyridines, pyrroles, pyrimidines, or quinolines are ubiquitous core structures of many naturally-occurring and biologically active molecules.[1,2] They have found broad applications as pharmaceuticals, flavors, agrochemicals, and dyes,[3,4] and are prominently represented in medicinal chemistry.[5] Accordingly, there is a continuous need for new synthetic processes which allow the preparation of highly functionalized N-heterocycles preferably in an atom economic and sustainable fashion.

During the past decade, the acceptorless dehydrogenation (AD) of alcohols[6] has become a powerful tool for the benign construction of complex organic molecules using sustainable and abundant alcohols as coupling reagents as they are readily available by a variety of industrial processes and can be obtained renewably *via* fermentation or catalytic conversion of lignocellulosic biomass.[7] Catalytic AD of

alcohols is an oxidant-free, atom-economical approach for the oxidation of alcohols to form carbonyl compounds which subsequently can be converted into other useful organic materials such as amines, imines, amides, or esters. In these transformations only dihydrogen and water are generated as nontoxic byproducts in the initial steps. Despite the significance of such C-C and C-N bond forming reactions, homogeneous catalysts mostly employ precious metals such as Ru,[8] Rh, [9] and Ir. [10] In comparison, the same reactions with catalysts that utilize non-precious, earth abundant metals like Mn,[11,12] Fe,[13,14,15] Co,[16,17,18] or Ni [19] are much less developed. Moreover, the preparation of biologically interesting *N*-heterocycles by employing N-H alkylation or C-H alkylation is scarcely explored.

Scheme 1. Examples of the Catalytic Syntheses of Quinolines and Pyrimidines with Alcohols as Key Feedstock

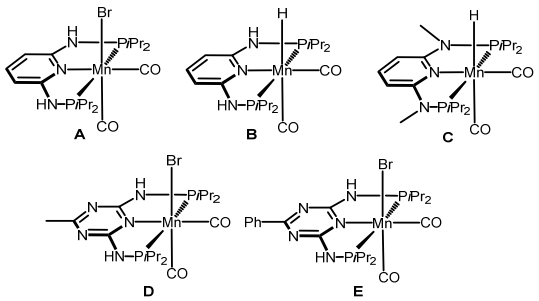


In 2011, Crabtree and coworkers described a Ru-catalyzed formation of pyrroles from 1,4-diols and amines.[20] In 2013, the groups of Beller,[21] Kempe,[22] Milstein[23] and Saito[24] reported efficient Ir- and Ru-catalyzed two- and three-component pyrrole synthesis where secondary alcohols, diols, and primary alcohols were coupled. In the same year Ir- and Ru-catalyzed formations of functionalized pyridines were described by the groups of Kempe,[25] Milstein,[26] Liu and Sun.[27] Later on, Kempe and co-workers

also reported the first multicomponent pyrimidine synthesis from amidines and different alcohols (Scheme 1).[28] The catalytic formation of quinolones was reported by the groups of Shim,[29] Yus,[30] Verpoort,[31] Milstein,[26] Liu and Sun[27] *via* a Ru-catalyzed indirect Friedländer synthesis involving oxidative cyclisation of 2-aminobenzyl alcohol with either ketones or alcohols (Scheme 1). Thus far, however, precious metals were used as catalysts and in terms of sustainability they ought to be replaced by inexpensive and widely abundant first-row base metals.[32] Noteworthy, the first Fe- and Co-catalyzed pyrrole synthesis was reported by Barta *et al* and Milstein and co-workers in 2016.[33]

Intrigued by these recent discoveries in the area of nitrogen-containing heterocycles, we began to explore the potential of well-defined Mn(I) PNP pincer complexes with pyridine and triazine backbones as catalyst for the preparation of N-heterocycles. We describe here an efficient synthesis of substituted quinolines from amino alcohols and alcohols as well as the synthesis of pyrimidine derivatives *via* a three component reaction utilizing benzamidine and two different alcohols as key feedstock. Despite the fact that Mn is the third most abundant transition metal in the Earth's crust, after Fe and Ti, catalytic application of Mn(I) complexes in dehydrogenation/hydrogenation catalysis is still rare. Seminal progress in this area includes the dehydrogenative coupling of alcohols and amines to form selectively imines and the conjugative addition of non-activated nitriles by the group of Milstein[11] and our group,[12] and the hydrogenation of ketones, aldehydes, nitriles, and esters by the groups of Beller[34] and Kempe.[35]

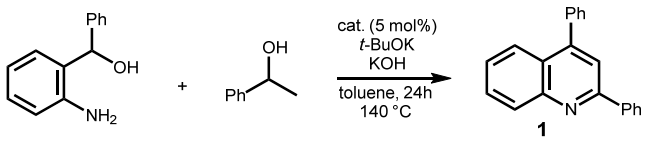
Scheme 2. Mn(I) PNP Pincer Complexes Tested as Catalysts



Initially, the catalysts **A-E**[12,35,36] (5 mol% catalyst loading) were screened for the synthesis of 2,4-diphenylquinoline from (2-aminobenzyl alcohol (1.0 equiv) and 1-phenylethane-1-ol (1.5 equivs) in toluene (4 mL) at 140 °C in a closed vial for 24 h in the presence of base. The results are summarized in Table 1. The products were analyzed by ^{1}H and $^{13}C\{^{1}H\}$ NMR and identified by comparison with authentic

samples. In general, isolated yields after purification by column chromatography are reported. The best results could be achieved with **A** and **B** in the presence of *t*BuOK and KOH in a 4.2:1 ratio (Table 1, entries 1, 2). In the absence of KOH, the yield dropped significantly from 86 to 28 % (Table 1, entry 3). Catalyst **C** bearing NMe linkers was catalytically inactive (entry 4) emphasizing the importance of the acidic NH moieties for the catalytic reaction. Catalysts **D** and **E**, featuring a triazine backbone, turned out to be less active (Table 1, entries 5, 6). Lowering the temperature from 140 to 120 ^{o}C with **B** as catalyst resulted in a lower yield (Table 1, entry 7).

Table 1. Catalyst Screening for the Synthesis of Quinolines from 2-Aminobenzyl Alcohol and 1-Phenylethane-1-ol[a]



1

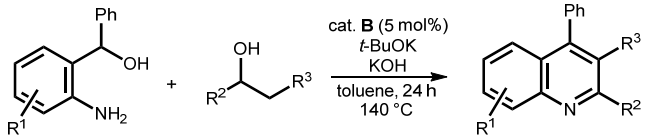
entry	catalyst	T [^{o}C]	yield [%] [b]
1	**A**	140	84
2	**B**	140	86
3[c]	**B**	140	28
4	**C**	140	0
5	**D**	140	67
6	**E**	140	53
7	**B**	120	72

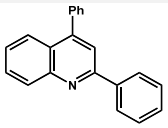
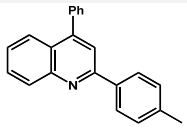
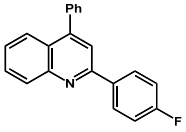
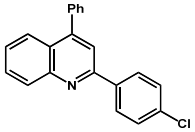
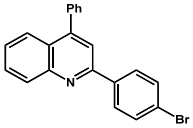
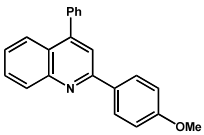
[a] Reaction conditions: Reaction conditions: 1.0 mmol (2-aminobenzyl alcohol, 1.5 mmol 1-phenylethane-1-ol, 2.1 mmol *t*BuOK, 0.5 mmol KOH, 5 mol % catalyst, 4 mL toluene, 140 ^{o}C, 24 h. [b] Yield of pure isolated product after column chromatography. [c] Without KOH.

Having established complex **B** as the most efficient catalysts in the series, this methodology was applied to other substrates utilizing a series of substituted benzyl

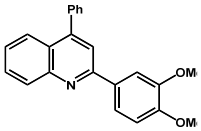
alcohols, cyclic aliphatic alcohols, 1-indanol as well as heterocyclic systems starting from 1-(thiophen-2-yl)ethano-1-ol and 1-(pyridine-4-yl)ethan-1-ol. The reaction is regioselective with regard to the carbonyl component formed *in situ* taking place at its less substituted position. The results are shown in Table 2. All quinoline derivatives were isolated in good to excellent yields (61-91%). The reaction gave good yields not only with 1-phenylethanol (Table 2, entry 1) but also for other related 4-substituted phenyl alcohols (Table 2, entries 1-3) independently of the electronic natures of the substituents (electron-donating group in the methyl and methoxy derivatives (Table 2, entries 2, 6, 7) or electron-withdrawing ones in the halide derivatives (Table 2, entries, 3-5). Yields were also good for heterocyclic derivatives (pyridyl, thienyl) (Table 2, entries 8, 9). In the case of aliphatic alcohols and 1-indanol (entries 12-14) the yields are generally slightly lower than for the benzylic and heterocyclic alcohols (Table 2, entries 1-11,15,16). The reaction involves the *in situ* oxidation of the two alcohols to the corresponding carbonyl compounds thereby releasing dihydrogen, followed by a Friedländer annulation process.

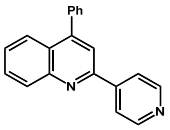
Table 2. Synthesis of Quinolines using 2-Aminobenzyl Alcohol and Secondary Alcohols[a,b]

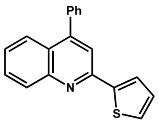


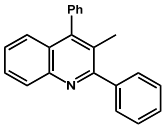
entry	product	entry	product
1	 **1** (89 %)	2	 **2** (91 %)
3	 **3** (84 %)	4	 **4** (67 %)
5	 **5** (64 %)	6	

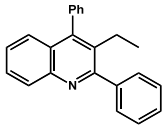
6 (82 %)

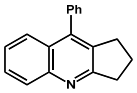
7  **7** (71 %)

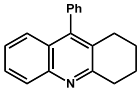
8  **8** (79 %)

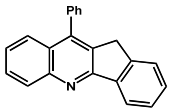
9  **9** (78 %)

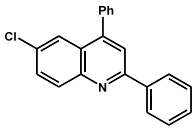
10  **10** (84 %)

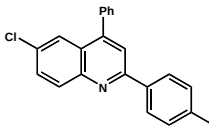
11  **11** (83 %)

12  **12** (61 %)

13  **13** (68 %)

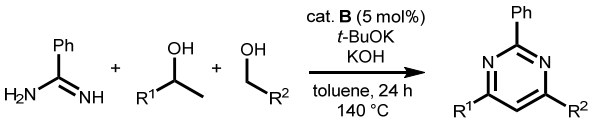
14  **14** (73 %)

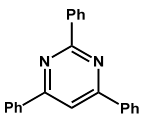
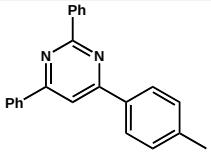
15  **15** (86 %)

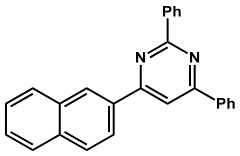
16  **16** (88 %)

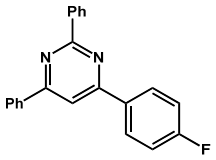
[a] Reaction conditions: 1.0 mmol 2-aminobenzyl alcohol, 1.5 mmol alcohol, 2.1 mmol *t*BuOK, 1 mmol KOH, 5 mol% catalyst, 4 mL toluene, 140 ^{o}C, 24 h. [b] Yield of pure isolated product after column chromatography.

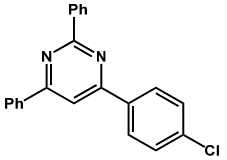
Table 3. Three Component Pyrimidine Syntheses using Benzamidine and Primary and Secondary Alcohols.[a,b]

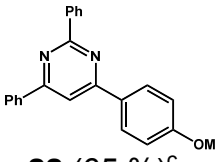


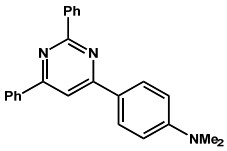
entry	product	entry	product
1	 **17** (86 %)	2	 **18** (90 %)

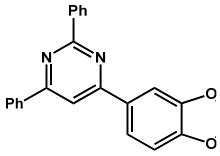
3  **19** (84 %)

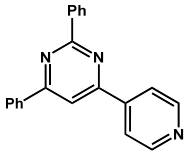
4  **20** (81 %)

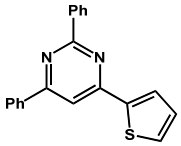
5  **21** (68 %)

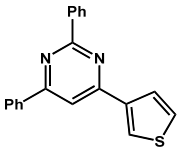
6  **22** (65 %)[c]

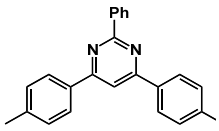
7  **23** (80 %)

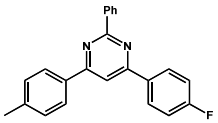
8  **24** (58 %)[c]

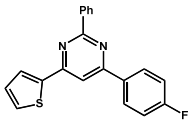
9  **25** (75 %)

10  **26** (74 %)

11  **27** (77 %)

12  **28** (88 %)

13  **29** (79 %)

14  **30** (72 %)

[a] Reaction conditions: 1.0 mmol benzamidine, 1.5 mmol *prim.* alcohol, 1.2 mmol *sec.* alcohol, 1.5 mmol *t*BuOK, 1.5 mmol KOH, 5 mol% catalyst, 4 mL toluene, 140 °C, 24 h. [b] Yield of pure isolated product after column chromatography. [c] 7 mol% catalyst, 130 °C and 16 h.

In order to further demonstrate the potential of Mn(I) catalyst **B** in AD processes combined with condensation reactions, the synthesis of substituted pyrimidines *via* a three component process was also studied. Under similar conditions as described above for the preparation of quinolines, a total of 14 different pyrimidines were synthesized. Variation of the primary and secondary alcohols led to the formation

compounds **17**− **30** in yields between 58 to 90% (Table 3). Aryl chlorides, fluorides, amines, heterocycles like pyridines and thiophenes as well as benzo[d][1,3]dioxole were tolerated. The whole process is an efficient, selective, and high-yielding single-step procedure.

In conclusion, this study represents the first example of an environmentally benign, sustainable, and practical synthesis of both substituted quinolines and pyrimidines catalyzed by a well-defined hydride Mn(I) complex which is stabilized by a PNP ligand, based on the 2,6-diaminopyridine scaffold. Quinolines can be regioselectively assembled from 2-aminobenzyl alcohols and secondary alcohols, while pyrimidines are obtained *via* a three component process utilizing benzamidine and two different alcohols. The selective C−C and C−N bond formations proceed with the liberation of 2 equivs of dihydrogen (acceptor-less dehydrogenation) and the elimination of water (condensation). The optimized reaction conditions allow the presence of a wide range of typical organic functional groups. This work may contribute to the development of waste-free sustainable base metal catalysis.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge on the ACS Publications website at DOI: xxxxx

Synthetic procedures, ^{1}H, and $^{13}C\{^{1}H\}$ NMR spectra of all organic products (PDF).

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Notes

The authors declare no competing financial interest.

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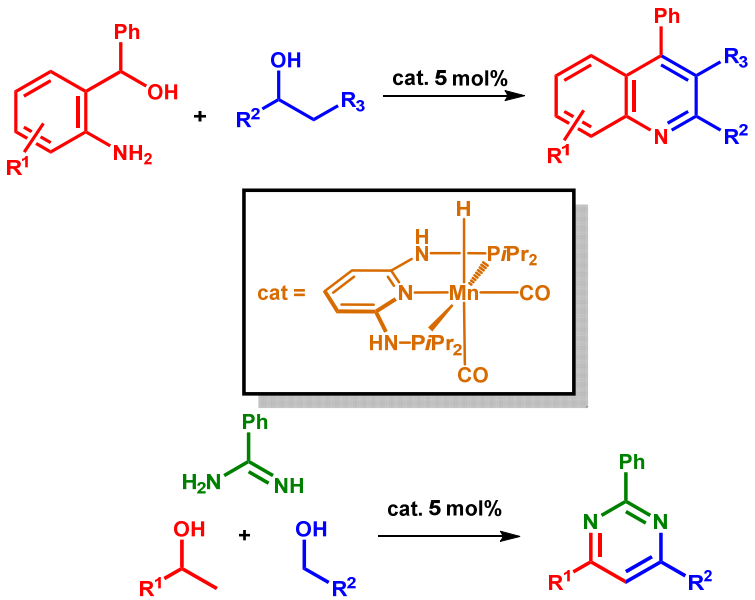
Table of Contents (TOC)

The first quinoline and three-component pyrimidine synthesis with alcohols as key feedstock catalyzed by well-defined Mn(I) PNP complexes is described. A range of different alcohols were efficiently converted into the desired *N*-heterocycles in good isolated yields.



SUPPORTING INFORMATION

Sustainable Synthesis of Quinolines and Pyrimidines Catalyzed by Manganese PNP Pincer Complexes

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1. General Information

2. General Procedure for the Synthesis Quinolines.

3. General Procedure for the Synthesis Pyrimidines.

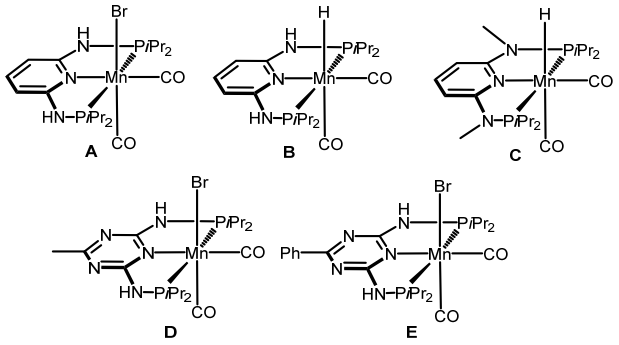
4. Characterization of Organic Products.

5. References

6. ^{1}H and ^{13}C NMR Spectra of Organic Products

1. General Information

All manipulations were performed under an inert atmosphere of argon by using Schlenk techniques or in a MBraun inert-gas glovebox. The solvents were purified according to standard procedures.[1] The deuterated solvents were purchased from Aldrich and dried over 3 Å molecular sieves. Complexes **A-E** were prepared according to the literature.[2,3,4] All substrates are known



compounds and were used as obtained from commercial resources or reduced with $NaBH_4$ to the desired alcohols and purified before usage. ^{1}H and $^{13}C\{^{1}H\}$, $^{19}F\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR spectra were recorded on Bruker AVANCE-250, AVANCE-400 AVANCE-600 spectrometers. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were referenced internally to residual protio-solvent, and solvent resonances, respectively, and are reported relative to tetramethylsilane (σ = 0 ppm). $^{31}P\{^{1}H\}$ NMR spectra were referenced externally to H_3PO_4 (85%) (σ = 0 ppm). $CDCl_3$ was filtered over basic Al_2O_3 for all product NMR´s. As reaction vessel 8 mL microwave vials from Biotage or VWR with aluminium Teflon septum cap were used.

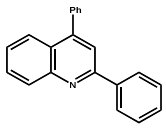
All mass spectrometric measurements were performed on an Esquire 3000*plus* 3D-quadrupole ion trap mass spectrometer (Bruker Daltonics, Bremen, Germany) in positive-ion mode by means of electrospray ionization (ESI) except accurate mass measurements, which were done on a Bruker maXis Q-TOF mass spectrometer (Bruker Daltonics, Bremen, Germany) at a resolution of roughly 20.000 (FWHM) and typical accuracy of better than ± 5 ppm. Mass calibration was done with a commercial mixture of perfluorinated trialkyl-triazines (ES Tuning Mix, Agilent Technologies, Santa Clara, CA, USA). All analytes were dissolved in ACN/H_2O/HCOOH to form a concentration of roughly 1 mg/mL in order to suppress dehydrogenations of several analytes. Direct infusion experiments were carried out using a Cole Parmer model

74900 syringe pump (Cole Parmer Instruments, Vernon Hills, IL, USA) at a flow rate of 2 μL/min. Full scan and MS/MS (low energy CID)-scans were measured in the range m/z 100-1100 with the target mass set to m/z 1000. Further experimental conditions include: drying gas temperature: 200°C; capillary voltage: -4 kV; skimmer voltage: 40 V; octapole and lens voltages: according to the target mass set. Mass spectra were averaged during data acquisition time of 1 to 2 min and one analytical scan consisted of five successive micro scans resulting in 50 and 100 analytical scans, respectively, for the final full scan mass spectrum.

2. General Procedure for the Synthesis Quinolines. 2-amino-benzhydryl alcohol (1.0 mmol), alcohol (1.5 mmol), *t*-BuOK (2.1 mmol) and KOH (1 mmol) were mixed in toluene (4 mL) and the catalyst (0.05 mmol, 5 mol %) was added under inert conditions. After 24 h at 140 °C the mixture was quenched with water (ca. 2 mL), the organic layer was dried with $MgSO_4$ and purified via silica column chromatography (eluted with toluene and DCM).

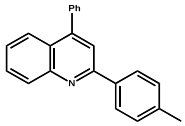
3. General Procedure for the Synthesis Pyrimidines. Benzamidine (1.0 mmol), prim. alcohol (1.5 mmol) sec. alcohol (1.2 mmol), KOH (1.5 mmol) and *t*-BuOK (1.5 mmol) were mixed in toluene (4 mL) and the catalyst (0.05 mmol, 5 mol %) was added under inert conditions. After 16 h at 80 °C the mixture was quenched with water (ca. 2 mL), the organic layer was dried with $MgSO_4$ and purified via silica column chromatography (eluted with toluene and M*t*BE).

4. Characterization of Organic Products.



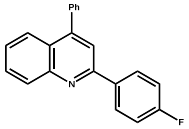
2,4-Diphenylquinoline (1)

fawn solid 250 mg (89%). ^{1}H NMR (δ, d_6-DMSO, 20°C): 8.31 (d, J= 6.5 Hz, 2H, PhH), 8.16 (d, J= 8.2 Hz, 1H, QuiH), 7.99 (s, 1H, QuiH), 7.85-7.75 (m, 2H, QuiH), 7.59-7.50 (m, PhH, QuiH). ^{13}C{^{1}H} NMR (δ, d_6-DMSO, 20°C): 159.2, 152.1, 151.7, 142.1, 141.1, 133.3, 133.3, 133.1, 133.1, 132.3, 132.2, 132.1, 130.3, 128.7, 128.6, 122.3. ESI-MS: $[M+H]^+$, found 282.0. $C_{21}H_{15}N$ requires 281.1, MS-MS: 204.0.



2-(4-Methylphenyl)-4-phenylquinoline (2)

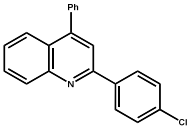
slightly yellow 268 mg (91%). ^{1}H NMR (δ, CD_2Cl_2, 20°C): 8.26 (d, J= 8.5 Hz, 1H, QuiH), 8.19 (d, J= 7.8 Hz, 2H, PhH), 7.96 (d, J= 8.2 hz, 1H, QuiH), 7.90 (s, 1H, QuiH), 7.81-7.77 (m, 1H, QuiH), 7.69-7.56 (m, 5, PhH), 7.55-7.51 (m, 1H, QuiH), 7.39 (d, J= 8.2 Hz, 2H, PhH). ^{13}C{^{1}H} NMR (δ, CD_2Cl_2, 20°C): 156.4, 149.2, 148.6, 139.8, 138.4, 136.4, 129.8, 129.6, 129.5, 128.6, 128.4, 128.0, 127.3, 126.2, 125.7, 125.7, 119.0, 21.1. ESI-MS: $[M+H]^+$, found 296.1. $C_{22}H_{17}N$ requires 295.1, MS-MS: 204.0.



2-(4-Fluorophenyl)-4-phenylquinoline (3)

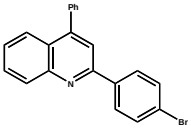
fawn solid 251 mg (84%). ^{1}H NMR (δ, d_6-DMSO, 20°C): 8.41-8.36 (m, 2H), 8.13 (d, J= 8.0, 1H), 8.01 (s, 1H, QuiH), 7.85-7.75 (m, 2H), 7.60 (m, br, 6H), 7.35 (t, J= 8.1 Hz, 2H).

^{13}C{^{1}H} NMR (δ, d_6-DMSO, 20°C): 166.8 (d, J_{CF}= 246.5 Hz), 158.2, 152.2, 151.6, 141.0, 138.6 (d, J_{CF}= 3.0 Hz), 133.4, 133.2, 133.1, 132.2, 132.1, 130.3, 128.7, 128.5, 122.1, 119.1 (d, J_{CF}= 21.6 Hz). ^{19}F{^{1}H} NMR (δ, d_6-DMSO, 20°C): -112.2. ESI-MS: $[M+H]^+$, found 300.0. $C_{21}H_{14}FN$ requires 299.1, MS-MS: 204.0.



2-(4-Chlorophenyl)-4-phenylquinoline (4)

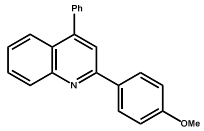
slightly brown solid 211 mg (67%). ^{1}H NMR (δ, d_6-DMSO, 20°C): 8.35 (d, J= 8.7 Hz, 2H, PhH), 8.16 (d, J= 8.7 Hz, 1H, QuiH), 8.04 (s, 1H, QuiH), 7.88-7.77 (m, 2H, QuiH), 7.62-7.55 (m, 8H, PhH, QuiH). ^{13}C{^{1}H} NMR (δ, d_6-DMSO, 20°C): 157.9, 152.6, 151.3, 140.9, 140.6, 138.2, 133.6, 133.1, 133.0, 132.7, 132.3, 132.2, 130.6, 128.8, 128.7, 122.2. ESI-MS: $[M+H]^+$, found 315.9. $C_{21}H_{14}ClN$ requires 315.1, MS-MS: 204.0.



2-(4-Bromophenyl)-4-phenylquinoline (5)

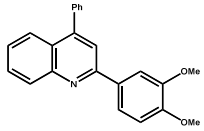
fawn solid 230 mg (64%). ^{1}H NMR (δ, d_6-DMSO, 20°C): 8.29 (d, J= 8.7 Hz, 2H, PhH), 8.16 (d, J= 8.3 Hz, 1H, QuiH), 8.05 (s, 1H, QuiH), 7.88-7.80 (m, 2H, QuiH), 7.73 (d, J= 8.9 Hz, 2H, PhH), 7.65-7.57 (m, 6H, PhH, QuiH). ^{13}C{^{1}H} NMR (δ, d_6-DMSO, 20°C): 154.9, 149.5, 148.3, 138.0, 137.8, 132.2, 130.6, 130.1, 130.0, 129.9,

129.2, 129.1, 127.6, 125.8, 119.1. ESI-MS: $[M+H]^+$, found 359.9. $C_{21}H_{14}BrN$ requires 359.0, MS-MS: 280.0, 204.0.



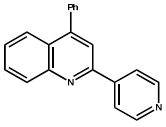
2-(4-Methoxyphenyl)-4-phenylquinoline (6)

slightly yellow solid 255 mg (82%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.61 (d, J= 8.5 Hz, 1H, QuiH), 8.16 (d, J= 7.9 Hz, 2H, PhH), 8.00 (d, J= 7.9 Hz, 1H, QuiH), 7.92-7.85 (m, 2H, QuiH), 7.66-7.60 (m, 6H, PhH, QuiH), 7.05 (d, J= 7.3 Hz, PhH), 3.86 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$, 20°C): 162.9, 155.1, 154.7, 142.5, 136.4, 132.8, 130.7, 129.9, 129.4, 129.1, 128.1, 126.4, 125.6, 125.5, 124.4, 120.3, 114.9, 55.6. ESI-MS: $[M+H]^+$, found 312.1. $C_{22}H_{17}NO$ requires 311.1, MS-MS: 297.0, 269.0.



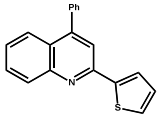
2-(4-Methoxyphenyl)-4-phenylquinoline (7)

yellow solid 242 mg (71%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.67 (d, J= 8.7 Hz, 1H, QuiH), 8.02 (d, J= 8.7 Hz, 1H), 7.98-7.94 (m, 1H), 7.92 (s, 1H, QuiH), 7.85 (d, J= 2.7 Hz, 1H), 7.73-7.69 (m, 2H), 7.67-7.59 (m, 5H), 7.00 (d, J= 8.5 Hz, 1H, PhH). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$, 20°C): 156.2, 154.5, 153.0, 149.9, 141.2, 136.0, 133.5, 130.2, 129.4, 129.2, 128.6, 126.6, 125.6, 124.7, 123.3, 123.1, 120.6, 111.5, 111.4, 56.3, 56.2. ESI-MS: $[M+H]^+$, found 342.1. $C_{23}H_{19}NO_2$ requires 341.4, MS-MS: 326.0.



4-Phenyl-2-(pyridin-4-yl)quinoline (8)

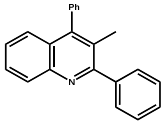
yellow solid 223 mg (xx%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.70 (d, J= 5.4 Hz, 2H, PyH), 8.18 (d, J= 8.3 Hz, 1H, QuiH), 8.01 (d, J= 5.0 Hz, 2H, PyH), 7.86 (d, J= 8.6 Hz, 1H, QuiH), 7.76 (s, 1H, QuiH), 7.69 (t, J= 7.4 Hz, 1H, QuiH), 748-7.18 (m, 6H, PhH, QuiH). $^{13}C\{^1H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 154.0, 150.5, 149.8, 148.8, 146.7, 138.0, 130.4, 130.0, 129.5, 129.1, 128.7, 128.7, 127.3, 126.4, 125.8, 121.7, 118.8. ESI-MS: $[M+H]^+$, found 283.0. $C_{20}H_{14}N_2$ requires 282.1, MS-MS: 256.0, 204.0.



4-Phenyl-2-(thiophen-2-yl)quinoline (9)

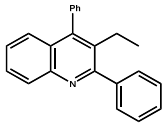
yellow solid 224 mg (78%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.18 (d, J= 8.1 Hz, 1H, QuiH), 7.78 (d, J= 8.1 Hz, QuiH), 7.77-7.67 (m, 3H, QuiH, ThH), 7.59-7.53 (m, 5H, PhH), 7.51-7.52 (m, 2H, ThH), 7.19-7.16 (m, 1H, ThH). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$, 20°C): 151.9, 149.1, 148.7, 145.4, 138.2, 129.7, 129.5, 128.6, 128.5, 128.1, 126.2, 125.9,

125.9, 125.7, 117.9. ESI-MS: $[M+H]^+$, found 288.0. $C_{19}H_{13}NS$ requires 287.1, MS-MS: 204.1.



3-Methyl-2,4-diphenylquinoline (10)

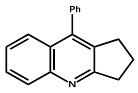
yellow solid 248 mg (84%). ^1H NMR (δ, d_6-DMSO, 20°C): 8.04 (d, J= 6.6 Hz, 1H, QuiH), 7.66-7.34 (m, 13H, PhH, QuiH), 2.01 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (δ, d_6-DMSO, 20°C): 163.6, 150.6, 149.3, 144.5, 140.5, 132.7, 132.6, 132.5, 132.2, 132.2, 131.5, 130.1, 129.8, 129.0, 21.9. ESI-MS: $[M+H]^+$, found 296.0. $C_{22}H_{17}N$ requires 295.1, MS-MS: 218.0, 217.0.



3-Ethyl-2,4-diphenylquinoline (11)

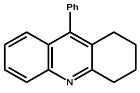
yellow solid 256 mg (83%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.18 (d, J= 8.1 Hz, 1H, QuiH), 7.67 (t, J= 7.4 Hz, 1H, QuiH), 7.62-7.33 (m, 12H, PhH, QuiH), 2.63 (q, J= 7.2 Hz, 2H, CH_2), 0.80 (t, J= 6.9 Hz, 3H, CH_3). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$, 20°C): 161.1, 147.4, 146.0, 141.7, 137.4, 133.1, 129.5, 129.4, 128.7, 128.6, 128.4, 128.3, 128.0, 127.8, 127.5, 126.2, 126.2, 23.5, 15.1. ESI-MS: $[M+H]^+$, found 310.0. $C_{23}H_{19}N$ requires 309.2, MS-MS: 217.0, 294.0.

9-Phenyl-2,3-dihydro-1H-cyclopenta[b]quinoline (12)



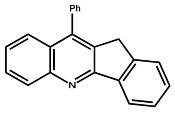
yellow solid 149 mg (61%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.07 (dd, J= 1.7 Hz, J= 8.8 Hz, 1H, QuiH), 7.66-7.59 (m, 2H, QuiH), 7.57-7.47 (m, 3H, PhH, QuiH), 7.41-7.35 (m, 3H, PhH, QuiH), 3.24 (t, J= 7.6 Hz, 2H, CH_2), 2.91 (t, J= 7.4 Hz, 2H, CH_2), 2.15 (q, J= 7.5 Hz, 2H, CH_2). $^{13}C\{^1H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 167.4, 148.0, 142.7, 136.8, 133.7, 129.3, 128.8, 128.5, 128.2, 128.0, 126.2, 125.7, 125.5, 35.2, 30.3, 23.5. ESI-MS: $[M+H]^+$, found 246.1. $C_{18}H_{15}N$ requires 245.1, MS-MS: 230.1, 218.1, 217.1, 204.1.

9-Phenyl-1,2,3,4-tetrahydroacridine (13)



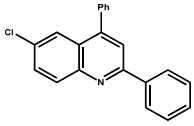
yellow solid 176 mg (68%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.05 (d, J= 7.6 Hz, 1H, QuiH), 7.63-7.60 (m, 1H, QuiH), 7.55-7.52 (m, 2H, QuiH), 7.49-7.47 (m, 1H), 7.35-7.31 (m, 2H), 7.26-7.24 (m, 2H, PhH), 3.23 (t, J= 5.9 Hz, 2H, CH_2), 2.62 (t, J= 5.9 Hz, 2H, CH_2), 2.00-1.96 (m, 2H, CH_2), 1.83-1.78 (m, 2H, CH_2). $^{13}C\{^1H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 159.1, 146.6, 146.3, 137.1, 129.1, 128.6, 128.4, 128.3, 127.8, 126.7, 125.8,

125.4, 34.3, 28.1, 23.0, 22.9. ESI-MS: $[M+H]^+$, found 260.1. $C_{19}H_{17}N$ requires 259.1, MS-MS: 232.1.



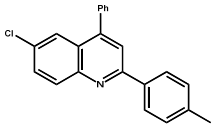
10-Phenyl-11H-indeno[1,2-b]quinoline (14)

yellow solid 214 mg (73%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.39 (d, J= 7.5 Hz, 1H, QuiH), 8.29 (d, J= 8.6 Hz, 1H, PhH), 7.73-7.70 (m, 2H, QuiH), 7.61-7.42 (m, 9H, PhH, QuiH), 3.84 (s, 2H, CH_2). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$, 20°C): 161.1, 148.4, 145.3, 143.8, 140.4, 136.5, 133.0, 130.0, 129.3, 129.1, 128.8, 128.7, 128.3, 127.8, 127.6, 126.4, 125.8, 125.7, 125.4, 122.2, 34.0. ESI-MS: $[M+H]^+$, found 194.0. $C_{22}H_{15}N$ requires 293.1, MS-MS: 217.0, 216.0.



6-Chloro-4-phenyl-2-(p-tolyl)quinoline (15)

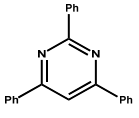
yellow solid 271 mg (86%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.27 (d, J= 7.5 Hz, 2H, PhH), 8.19 (d, J= 9.1 Hz, 1H, QuiH), 7.93 (s, 1H, QuiH), 7.71 (dd, J= 8.8 Hz, J= 1.9 Hz, 1H, QuiH), 7.64-7.51 (m, 8H, PhH). $^{13}C\{^1H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 157.1, 148.4, 147.2, 139.2, 137.8, 132.2, 131.7, 130.5, 129.6, 129.5, 128.9, 128.8, 128.7, 127.6, 126.5, 124.5, 120.1. ESI-MS: $[M+H]^+$, found 316.0 $C_{21}H_{14}ClN$ requires 315.1, MS-MS: 280.0, 238.0, 203.0.



6-Chloro-4-phenyl-2-(p-tolyl)quinoline (16)

yellow solid 290 mg (88%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.18 (d, J= 8.8 Hz, 1H, QuiH), 8.11 (d, J= 8.1 Hz, 2H, PhH), 7.87 (d, J= 2.3 Hz, 1H, QuiH), 7.83 (s, 1H, QuiH), 7.67 (dd, J= 2.3 Hz, J= 8.9 Hz, 1H, QuiH), 7.59-7.56 (m, 5H, PhH), 7.35 (d, J= 7.9 Hz, 2H, PhH).

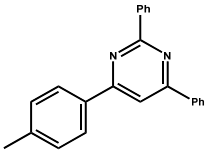
$^{13}C\{^1H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 157.0, 148.3, 147.2, 139.8, 137.8, 136.4, 132.0, 131.6, 130.4, 129.7, 129.5, 128.8, 128.7, 127.4, 126.4, 124.5, 119.9, 21.4. ESI-MS: $[M+H]^+$, found 330.0 $C_{22}H_{16}ClN$ requires 329.1, MS-MS: 238.0, 203.0, 294.0.



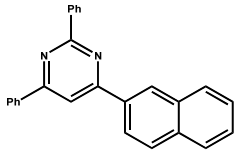
2,4,6-Triphenylpyrimidine (17)

white solid 265 mg (86%). 289 mg (94%) ^1H NMR (δ, $CDCl_3$, 20°C): 8.81-8.79 (m, 2H, PhH), 8.35-8.32 (m, 4H, PhH), 8.04 (s, 1H, PymH), 7.60-7.58 (m, 8H, PhH).

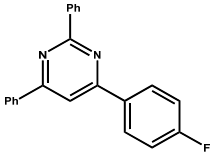
$^{13}C\{^{1}H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 164.8, 164.6, 138.2, 137.6, 130.8, 130.7, 128.9, 128.5, 128.5, 127.3, 110.3. ESI-MS: $[M+H]^+$, found 309.1. $C_{22}H_{16}N_2$ requires 308.1, MS-MS: 231.0, 104.2.

2,4-Diphenyl-6-(p-tolyl)pyrimidine (18) 

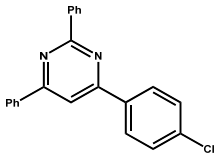
white solid 290 mg (90%). ^{1}H NMR (δ, $CDCl_3$, 20°C): 8.78 (s, 2H, PhH), 8.32 (s, 2H, PhH), 8.23 (d, J= 6.7 Hz), 8.01 (s, 1H, PymH), 7.58 (s, 6H, PhH), 7.39 (d, J= 6.7 Hz, 2H, PhH), 2.49 (s, 3H, CH_3). $^{13}C\{^{1}H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 164.7, 164.6, 164.5, 141.2, 138.3, 137.7, 134.7, 130.7, 130.6, 129.7, 128.9, 128.5, 128.5, 127.3, 127.2, 110.0, 21.5. ESI-MS: $[M+H]^+$, found 323.1. $C_{23}H_{18}N_2$ requires 322.1, MS-MS: 245.0, 220.0, 104.2.

4-(Naphthalen-2-yl)-2,6-diphenylpyrimidine (19) 

white solid 301 mg (84%). ^{1}H NMR (δ, $CDCl_3$, 20°C): 8.83-8.79 (m, 3H, PhH), 8.43-8.35 (m, 3H, PhH), 8.14 (s, 1H, PymH), 8.08-8.02 (m, 2H, PhH), 7.96-7.92 (m, 1H, PhH), 7.61-7.58 (m, 8H, PhH). $^{13}C\{^{1}H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 164.8, 164.6, 164.6, 138.3, 137.6, 134.8, 134.6, 133.3, 130.8, 130.7, 129.1, 129.0, 128.7, 128.6, 127.8, 127.4, 127.4, 126.6, 124.3, 110.5. ESI-MS: $[M+H]^+$, found 359.0. $C_{26}H_{18}N_2$ requires 358.1, MS-MS: 281.0, 256.0, 239.0, 178.0, 104.2.

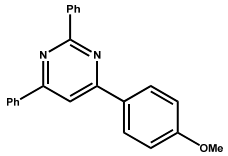
4-(4-Fluorophenyl)-2,6-diphenylpyrimidine (20) 

white solid 264 mg (xx%). ^{1}H NMR (δ, $CDCl_3$, 20°C): 8.74 (dd, J= 1.9 Hz, J= 7.2 Hz, 2H, PhH), 8.34-8.30 (m, 4H, PhH), 7.98 (s, 1H, PymH), 7.61-7.55 (m, 6H, PhH), 7.29-7.25 (m, 2H, PhH). $^{13}C\{^{1}H\}$ NMR (δ, $CDCl_3$, 20°C): 164.8, 164.5, 164.2 (d, J_{CF}= 251.2), 163.6, 138.0, 137.4, 133.6 (d, J_{CF}= 3.0 Hz), 130.9, 130.8, 129.3 (d, J_{CF}= 8.8 Hz), 129.0, 128.5, 128.5, 127.3, 115.9 (d, J= 21.6 Hz), 109.9. $^{19}F\{^{1}H\}$ NMR (δ, $CDCl_3$, 20°C): 109.8. ESI-MS: $[M+H]^+$, found 327.1. $C_{22}H_{15}FN_2$ requires 326.1, MS-MS: 249.0, 224.0, 146.1, 122.1, 104.2.



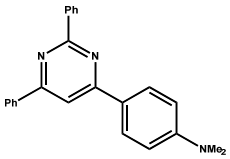
4-(4-Fluorophenyl)-2,6-diphenylpyrimidine (21)

white solid 222 mg (65%). ^{1}H NMR (δ, CD_2Cl_2, 20°C): 8.61-8.56 (m, 2H, PhH), 8.19-8.12 (m, 4H, PhH), 7.87 (s, 1H, PymH), 7.49-7.41 (m, 8H, PhH). $^{13}C\{^{1}H\}$ NMR (δ, CD_2Cl_2, 20°C): 164.8, 164.3, 163.4, 138.0, 137.3, 136.9, 135.9, 130.9, 130.7, 129.1, 128.9, 128.6, 128.5, 128.4, 127.2, 110.0. ESI-MS: $[M+H]^+$, found 343.0. $C_{22}H_{15}ClN_2$ requires 342.1, MS-MS: 265.0, 242.0, 240.0, 138.0, 104.2.



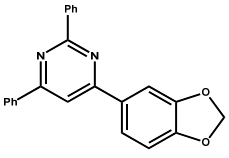
4-(4-Methoxyphenyl)-2,6-diphenylpyrimidine (22)

white solid 219 mg (65%). ^{1}H NMR (δ, $CDCl_3$, 20°C): 8.76 (dd, J= 1.7 Hz, J= 7.7 Hz, 2H, PhH), 8.32-8.29 (m, 4H, PhH), 7.96 (s, 1H, PymH), 7.62-7.53 (m, 6H, PhH), 7.09 (d, J= 8.8 Hz, 2H, PhH), 3.92 (s, 3H, CH_3). $^{13}C\{^{1}H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 164.5, 164.4, 164.2, 161.9, 138.3, 137.7, 130.7, 130.6, 129.9, 128.9, 128.8, 128.5, 128.4, 127.3, 114.3, 109.4, 55.5. ESI-MS: $[M+H]^+$, found 339.1. $C_{23}H_{18}N_2O$ requires 338.1, MS-MS: 324.0, 296.0.



4-(2,6-Diphenylpyrimidin-4-yl)-N,N-dimethylaniline (23)

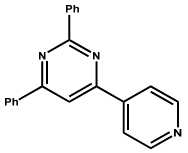
yellow solid 281 mg (80%). ^{1}H NMR (δ, $CDCl_3$, 20°C): 8.78 (dd, J= 1.6 Hz, J= 7.9 Hz, 2H, PhH), 8.32 (dd, J= 1.6 Hz, J= 8.0 Hz, 2H, PhH), 8.27 (d, J= 8.9 Hz, 2H, PhH), 7.93 (s, 1H, PymH), 7.61-7.54 (m, 6H, PhH), 6.84 (d, J= 8.9 Hz, 2H, PhH), 3.08 (s, 6H, CH_3). $^{13}C\{^{1}H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 164.5, 164.2, 164.0, 152.3, 138.7, 138.1, 130.4, 130.4, 128.8, 128.5, 128.4, 127.3, 124.6, 111.8, 108.6, 40.2. ESI-MS: $[M+H]^+$, found 352.1. $C_{24}H_{21}N_3$ requires 351.1, MS-MS: 336.0, 308.0, 274.0, 146.1.



4-(Benzo[d][1,3]dioxol-5-yl)-2,6-diphenylpyrimidine (24)

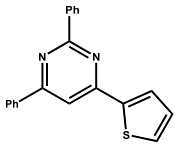
yellow solid 204 mg (58%). ^{1}H NMR (δ, CD_2Cl_2, 20°C): 8.59-8.55 (m, 2H, PhH), 8.16-8.13 (m, 2H, PhH), 7.77 (s, 1H, PymH), 7.8 (s, 1H, PhH), 7.46-7.40 (m, 6H, PhH), 6.82 (d, J = 3.4Hz, 1H, PhH). $^{13}C\{^{1}H\}$ NMR (δ, d_6 CD_2Cl_2, 20°C): 164.4, 164.1, 163.8, 150.1, 148.5, 138.2, 137.5, 131.6, 130.7, 130.6, 128.9, 128.4, 128.3, 127.2,

121.8, 109.5, 108.4, 107.3, 101.9. ESI-MS: $[M+H]^+$, found 353.0. $C_{23}H_{16}N_2O_2$ requires 352.1, MS-MS: 325.0, 323.0, 275.0, 252.0, 128.1, 104.2. HRMS (ESI): $[M+H]^+$ = 353.1285 (calc.); found: 353.1289 (error in ppm 1.3 ppm).



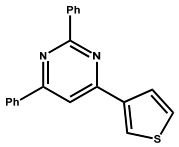
2,4-Diphenyl-6-(pyridin-4-yl)pyrimidine (25)

white solid 232 mg (75%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.86 (d, J= 5.9 Hz, 2H, PyH), 8.77-8.70 (m, 2H, PhH), 8.31-8.29 (m, 2H, PhH), 8.13 (d, J= 5.6 Hz, 2H, PyH), 8.03 (s, 1H, PymH), 7.60-7.56 (m, 6H, PhH). $^{13}C\{^1H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 165.5, 164.8, 162.3, 150.7, 144.8, 137.6, 136.9, 131.2, 131.0, 129.0, 128.6, 128.5, 127.3, 121.2, 110.6. ESI-MS: $[M+H]^+$, found 310.1. $C_{21}H_{15}N_3$ requires 309.1, MS-MS: 232.0, 207.0, 206.0, 105.2, 104.2. HRMS (ESI): $[M+H]^+$ = 310.1339 (calc.); found: 310.1343 (error in ppm 1.3 ppm).



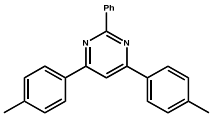
2,4-Diphenyl-6-(thiophen-2-yl)pyrimidine (26)

white solid 232 mg (74%). ^1H NMR (δ, $CDCl_3$, 20°C): 8.72 (dd, J= 1.7 Hz, J= 7.4 Hz, 2H, PhH), 8.29 (dd, J= 1.8 Hz, J= 7.5 Hz, 2H, PhH), 7.94 (dd, J= 0.7 Hz, J= 3.6 Hz, 1H, ThH), 7.87 (s, 1H, PymH), 7.61-7.54 (m, 7H, PhH, ThH), 7.23 (t, J= 4.3 Hz, 1H, ThH). $^{13}C\{^1H\}$ NMR (δ, d_6 $CDCl_3$, 20°C): 164.6, 164.4, 159.7, 143.4, 137.8, 137.3, 130.9, 130.8, 129.8, 128.9, 128.5, 128.3, 127.3, 127.1, 108.4. ESI-MS: $[M+H]^+$, found 315.0. $C_{20}H_{14}N_2S$ requires 314.1, MS-MS: 237.0, 212.0, 128.1, 104.2.

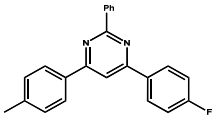


2,4-Diphenyl-6-(thiophen-3-yl)pyrimidine (27).

off white solid 242 mg (77%). ^1H NMR (δ, CD_2Cl_2, 20°C): 8.71 (m, 2H, PhH), 8.34-8.29 (m, 3H, PhH, ThH), 7.92-7.90 (m, 2H, ThH, PymH), 7.69-7.51 (m, 7H, PhH, ThH). $^{13}C\{^1H\}$ NMR (δ, CD_2Cl_2, 20°C): 165.2, 164.9, 161.0, 141.3, 138.7, 137.9, 131.3, 131.2, 129.4, 128.9, 128.8, 127.7, 127.3, 127.2, 126.7, 110.7. ESI-MS: $[M+H]^+$, found 315.0. $C_{20}H_{14}N_2S$ requires 314.1, MS-MS: 237.0, 212.0, 128.1, 104.2. HRMS (ESI): $[M+H]^+$ = 315.0950 (calc.); found: 315.0995 (error in ppm 1.6 ppm).

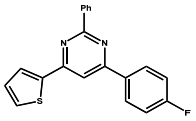
2-Phenyl-4,6-di-p-tolylpyrimidine (28). 

white solid 296 mg (88%). ^{1}H NMR (δ, CD_2Cl_2, 20°C): 8.79-8.8 (m, 2H, PhH), 8.25 (d, J= 7.9 Hz, 4H, PhH), 8.02 (s, 1H, PyrmH), 7.64-7.59 (m, 4H, PhH), 7.42 (d, J= 7.5 Hz, 4H, PhH), 2.5 (s, 6H, CH_3). ^{13}C{^{1}H} NMR (δ, CD_2Cl_2, 20°C): 164.4, 164.1, 141.3, 138.4, 134.7, 130.5, 129.6, 128.4, 128.4, 127.1,109.5, 21.2. ESI-MS: $[M+H]^+$, found 337.1. $C_{19}H_{17}N_2$ requires 336.1, MS-MS: 259.0, 142.1, 118.2.

4-(4-Fluorophenyl)-2-phenyl-6-(p-tolyl)pyrimidine (29) 

white solid 268 mg (79%). ^{1}H NMR (δ, $CDCl_3$, 20°C): 8.73 (dd, J= 1.8 Hz, J= 7.4 Hz, 2H, PhH), 8.32-8.29 (m, 2H, PhH), 8.20 (d, J= 8.1 Hz, 2H, PhH), 7.93 (s, 1H, PymH), 7.60-7.53 (m, 3H, PhH), 7.38 (d, J= 8.0 Hz, 2H, PhH), 7.28-7.23 (m, 2H, PhH), 2.48 (s, 3H, CH_3).

^{13}C{^{1}H} NMR (δ, $CDCl_3$, 20°C): 164.7, 164.6 (d, J_{CF}= 250.9), 164.4, 163.4, 134.1, 133.7 (d, J_{CF}= 3.2 Hz), 130.7, 129.7, 129.5 (d, J_{CF}= 8.5 Hz), 128.5, 127.2, 115.9 (d, J= 21.3 Hz), 109.5, 21.5. ^{19}F{^{1}H} NMR (δ, $CDCl_3$, 20°C): 110.0. ESI-MS: $[M+H]^+$, found 341.1. $C_{23}H_{17}FN_2$ requires 340.1, MS-MS: 263.0, 238.0, 122.2, 118.2, 104.2.

4-(4-Fluorophenyl)-2-phenyl-6-(thiophen-2-yl)pyrimidine (30) 

white solid 262 mg (72%). ^{1}H NMR (δ, $CDCl_3$, 20°C): 8.69-8.67 (m, 2H, PhH), 8.30-8.27 (m, 2H, PhH), 7.92 (dd, J= 1.0 Hz, J= 3.7 Hz, 1H, ThH), 7.80 (s, 1H, PyrmH), 7.59-7.50 (m, 4H, PhH, ThH), 7.36-7.22 (m, 3H, PhH, ThH). ^{13}C{^{1}H} NMR (δ, $CDCl_3$, 20°C): 164.4, 164.6 (d, J_{CF}= 251.5), 163.4, 159.8, 143.3, 137.6, 133.4 (d, J_{CF}= 3.2 Hz), 130.8, 129.9, 129.3 (d, J_{CF}= 8.5 Hz), 128.5, 128.4, 128.3, 127.1, 115.9 (d, J= 21.7 Hz), 108.0. ^{19}F{^{1}H} NMR (δ, $CDCl_3$, 20°C): 109.7. ESI-MS: $[M+H]^+$, found 333.0. $C_{20}H_{13}FN_2S$ requires 332.1, MS-MS: 255.0, 230.0, 122.2, 104.2. HRMS (ESI): $[M+H]^+$ HRMS (ESI): $[M+H]^+$ = 333.0950 (calc.); found: 315.0856 (error in ppm 1.2 ppm).

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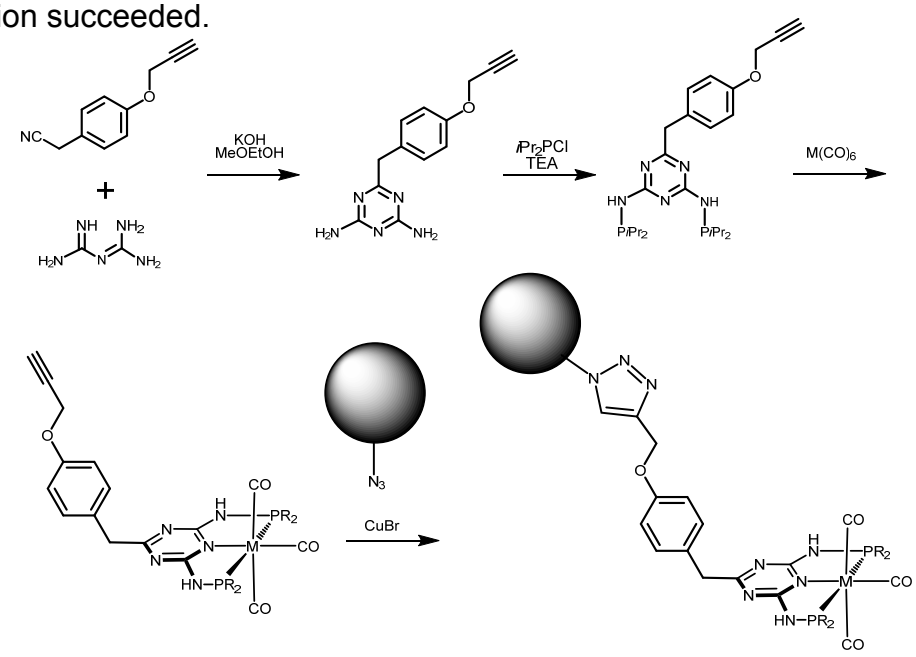
3 Conclusion and Outlooks

In agreement to scientific aims, this work described a successful way for heterocyclic PNP ligand design and modifications on all possible reactive positions. The greatest benefit was the fast and isochronic variation besides the catalyst screenings for the ideal required properties and full synthesis in a few days. All ligands can be mono- or di-substituted at the NH group. Manipulations at this position are helpful for mechanistically studies and induce different catalytic activities (inner- or outer-sphere mechanism).

Based on the research for new ligands, special modifications for solid phase immobilization were started as actual unpublished work. First of all DAP´s featured with ethinyl or propargyloxy spacer were synthesized. High air sensitivity and incompatibility with R_2PCl carried the research to spaced triazine backbones. 4-(Benzyl-4-propargyloxy)-2,4-diaminotriazine was used as final ligand system to form Cr, Mo and W tri-carbonyl complexes. PNP-$M(CO)_3$ complexes are highly stable and simply visible via IR measuring. These properties aided the first research for copper (I) catalyzed “click-reaction” on $–N_3$ loaded surfaces. For the first experiments Merrifield-resin and silicon nano wires were used as solid phase, in both cases the immobilization succeeded.



Scheme 23: PNP complex “Click-Immobilisation”

Further designs opened a new scaffold for pyrimidine based PCP ligands with a higher CH acidity. 2-Methyl or 2-phenyl substitutions delivered mono- or di-nuclear PN complexes. 2-*t*-Butyl substitution on the pyrimidine ring enforces a steric blocking for PN complexes. Subsequent detailed background information will be described in the diploma thesis of Gerald Tomsu.

Systems like PSP were not useful for applications performed due to lack of stability and reactivity with sulphur as main donor and the unfavorable bite angle. Some tests with cobalt and nickel CNC ligands based on *N*- heterocyclic carbenes as donors showed also no results in our applications.

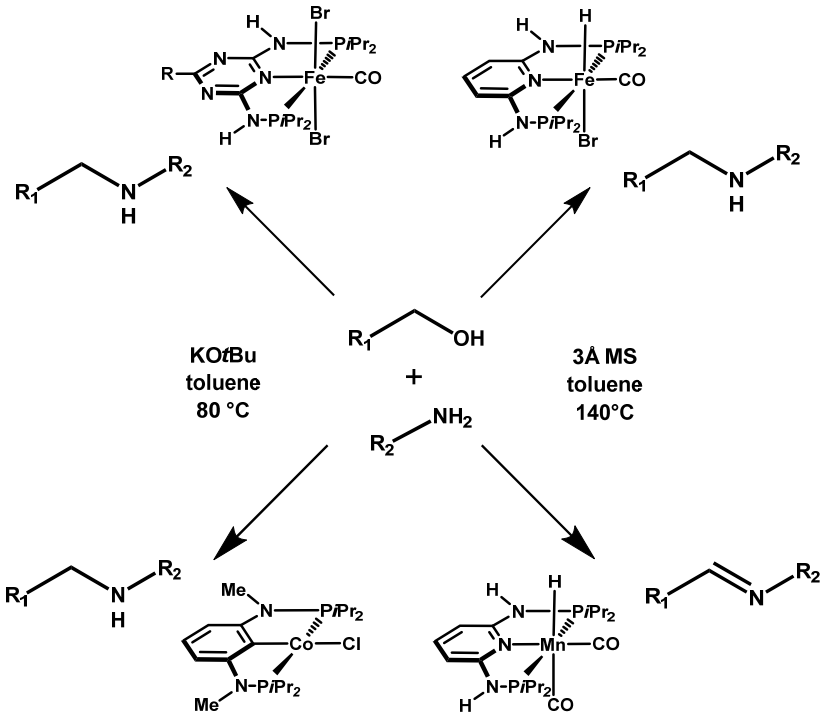
For the catalyst screenings V and Cr showed actual no useful results, grounds by the lack of reactivity of the complexes and modifications of them, inappropriate precursors and wrong applications.
However only pyridine PNP-Ni showed moderate activities for Kumada cross-couplings, all other metals formed homo biphenyls. Air-stable and thermally robust 2,4-diaminotriazine based cationic Ni(II) PNP pincer complexes were synthesized. The cationic Ni(II) complexes are readily deprotonated to give neutral complexes. With these easy to handle Ni(II) complexes, we have developed a protocol for the arylation, alkylation, and vinylation of a wide range of aryl, heteroaryl, alkyl halides and pseudohalides with different organoboronate reagents using the Suzuki Miyaura coupling.

In this work acceptorless dehydrogenation of alcohols was performed catalyzed by Mn, Fe and Co pincer complexes.
Two rare examples of an efficient coupling of alcohols and amines catalyzed by well-defined isoelectronic hydride Mn(I) and Fe(II) complexes which are stabilized by a PNP ligand based on the 2,6-diaminopyridine scaffold were synthesized and applied. In the case of Mn selectively imines, and in the case of Fe exclusively mono-alkylated amines were formed. These reactions proceed under base free conditions at higher temperatures and require the addition of molecular sieves.

Furthermore a series of triazine based PNP-Fe pre-catalysts were easily prepared from commercially available reagents in a two-step procedure and were reported for the same application under basic conditions. The catalyst is presumably formed upon reaction with KO*t*Bu in the presence of a primary alcohol. The most efficient

catalyst in this series was applied to other substrates including substituted benzyl alcohols or furfurylaclohol, aliphatic alcohols such as *R*-citronellol or EtOH as well as aromatic amines. In all cases, exclusively the resulting mono N-alkylated amines were isolated under basic conditions at 80 °C.

At last, two examples of efficient alkylations of amines with alcohols catalyzed by well-defined Co(II) complexes, which are stabilized by an anionic PCP ligand based on the 1,3-diaminobenzene scaffold were published. A range of substituted benzyl alcohols and aliphatic alcohols (R-citronellol, EtOH, n-BuOH) and aromatic amines were efficiently converted into mono N-alkylated amines with good isolated yields. PCP-Co-Cl was screened for the alkylation of anilines with alcohols and as strong base at 80 °C. PCP-Co-Me or CH_2SiMe_3 were applied under base-free conditions with the same substrates. For this methodology, higher reaction temperatures (130 ^{o}C) and addition of 3 Å molecular sieves were required.
In general, depending on the conditions, Mn formed in all cases imines, Co and Fe depending on the conditions, amines.



Scheme 24: Alcohol amination overview

Moreover, manifold contributions to the field of AD with non-precious metals were delivered with this study for amination of alcohols.
In Manuscript #4 we demonstrate the first non-nobel-metal catalyzed reactions for substituted quinolines and multicomponent pyrimidine synthesis based on the previous applied catalysts.

Actually, new applications were investigated among other CH acidic compounds for alkylation reactions, amine-amine couplings, conversions with Wittig-Reagents and crossed aldol couplings. Also combined systems with two different catalysts for more component reactions e.g. amination with following CH activation will be tested.

4 Statement of Contribution

Manuscript #1

The PCP-Co-Cl complex was synthesized and investigated by S. Murugesan in his thesis and publications. In analogy to other Co systems, the author applied this system for amination of alcohols after research for other reactions. Furthermore derivatization and usage of PCP-Co-Me and PCP-CH_2TMS were done. During his diploma thesis, Gerald Tomsu, contributed to this work by performing some of the further complex reaction. All ESI-MS measurements were done together with Dr. Ernst Pittenauer.

Manuscript #2

The PNP-Fe hydride complex was used in the group for hydrogenation reactions and after some other screening reactions for Manuscript #3, activities for alcohol aminations were found by the applicant. PNP-Mn hydride was synthesized together with Mathias Glatz and Nikolaus Gorgas. All catalysis and modification were done from the author. Calculations and DFT calculation were done by Dr. Luis F. Veiros and Dr. Karl Kirchner. All ESI-MS measurements were done together with Dr. Ernst Pittenauer. Singe crystal structures was measured and calculated by Dr. Berthold Stöger.

Manuscript #3

The triazine complexes were synthesized in analogy to pyridine based PNP-$FeBr_2$(CO). All triazine ligands were developed and screened by the applicant. All ESI-MS measurements were done together with Dr. Ernst Pittenauer. Singe crystal structures was measured and calculated by Dr. Berthold Stöger.

Manuscript #4

In analogy to alcohol amination reactions and novel metal catalyzed synthesis for heterocycles a new PNP-Mn hydride application was developed. All complexes were synthesized from Mathias Glatz. The applicant modified all reactions by himself and optimized the reaction conditions. All ESI-MS measuring were done together with Dr. Ernst Pittenauer. Singe crystal structures was measured and calculated by Dr. Berthold Stöger.

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7 Abbreviations

AD	acceptorless dehydrogenation
BINAP	2,2'–Bis(diphenylphosphino)–1,1'–binaphthyl
bipy	2,2´-Bipyridine
^{t}BuOK	Potassium *tert.*-butoxide
cat.	Catalyst
CNC	Pincer with carbene oxygen carbene
cod	1,5-Cyclooctadien
DAP	2,6-Diaminopyridine
EE	Ethylacetate
e.g.	for example
eq. /equiv.	equivalent
M*t*BE	tert-Butylmethylether
MW	microwave
PE	Petrolether
PCP	Pincer with phosphorus carbon phosphorus
Pip	Piperidinyl
PNP	Pincer with phosphorus nitrogen phosphorus
POP	Pincer with phosphorus oxygen phosphorus
PSP	Pincer with phosphorus sulfur phosphorus
RF	reflux
rt	room temperature
terpy	2,2′:6′,2″-Terpyridin
Triaz	1,3,5-Triazine

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Title: Co(II) PCP Pincer Complexes as Catalysts for the Alkylation of Aromatic Amines with Primary Alcohols

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Environmentally benign catalytic reactions based on non-precious transition metal complexes – Divergent coupling of alcohols and amines.

Matthias Mastalir, Mathias Glatz, Ernst Pittenauer, Karl Kirchner

BOSS XV, Antwerp, Belgium, 10.07-15.07.2016

Divergent amination and imination with alcohols based on non-precious transition metal complexes

Matthias Mastalir, Mathias Glatz, Ernst Pittenauer, Berthold Stöger, Karl Kirchner

Tokyo Festa CSJ, Tokyo, Japan, 16.10.2014

Synthesis of Photo-antenna Ligands for Efficient Lanthanide Emission

Matthias Mastalir, Karl Kirchner, Wolfgang Linert, Miki Hasegawa

BOSS14, Louvain-la-Neuve, Belgium, 13.07-18.07.2014

Solid supported pincer metal complexes as functional monolayers and surface immobilized catalysts

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Publications Part II

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A practical synthesis of substituted 2,6-diaminopyridines via microwave-assisted copper-catalyzed amination of halopyridines

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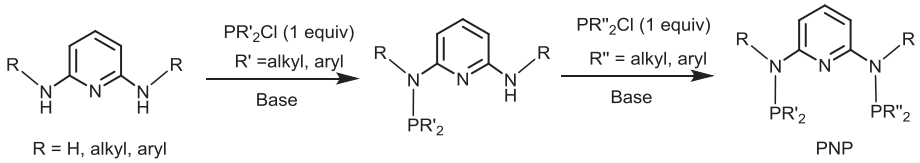
ABSTRACT

A microwave assisted copper-catalyzed amination protocol is reported utilizing a series of 2,6-dihalo- and 2-amino-6-halo pyridine precursors. Using this procedure, selective substitution of one or two halogens by aryl or alkylamines was achieved within 2–6 h with temperatures between 80 and 225 °C affording 2,6-diaminopyridines in good to excellent isolated yields. The reaction allows easy variation between educts and different *N*-substitutions. The target compounds are valuable precursors for the synthesis of bis-phosphorylated 2,6-diaminopyridines which are used as PNP pincer ligands in transition metal complexes.

1. Introduction

The 2,6-diaminopyridine molecule is a useful scaffold for the design of tridentate ligands in coordination and organometallic chemistry, agrochemicals, dyes, and pharmacologically potent building blocks.[1–6] The most frequently applied methods are nucleophilic substitutions often catalyzed by copper, copper salts or proline[7–9] and Buchwald–Hartwig aminations.[10–14] Recently, Kempe et al. developed an Ir-catalyzed protocol for both symmetrically and non-symmetrically *N*,*N*′-dialkylated 2,6-diamino pyridines from 2,6-diaminopyridine and alcohols.[15] All methods basically yield the 2,6-diaminopyridines and it depends on the specific target which one performs better.

In recent years we have been focusing on the chemistry of transition metal complexes bearing PNP pincer ligands based on the 2,6-diaminopyridine scaffold.[16] In these PNP ligands the central pyridine ring contains -NRPR′$_2$ (R′=H, alkyl, R=alkyl, aryl) substituents in the two ortho positions. This methodology was first developed for the synthesis of *N*,*N*′-bis(diphenylphosphino)-2,6-diaminopyridine (PNP-Ph).[17] In these ligands the aromatic pyridine ring and the phosphine moieties are connected via NH, *N*-alkyl, or *N*-aryl linkers (Scheme 1). Accordingly, the development of a simple general method for the selective formation of N,N′-disubstituted 2,6-diamino pyridines is of great importance for the design of new PNP ligands. It has to be noted that most substituted 2,6-diaminopyridines are commercially not available.



Scheme 1.

Here we describe a simple microwave assisted copper catalyzed amination protocol utilizing various 2,6-dihalo- and 2-amino-6-halo pyridine precursors **I**–**VII** as shown in Scheme 2. This simple

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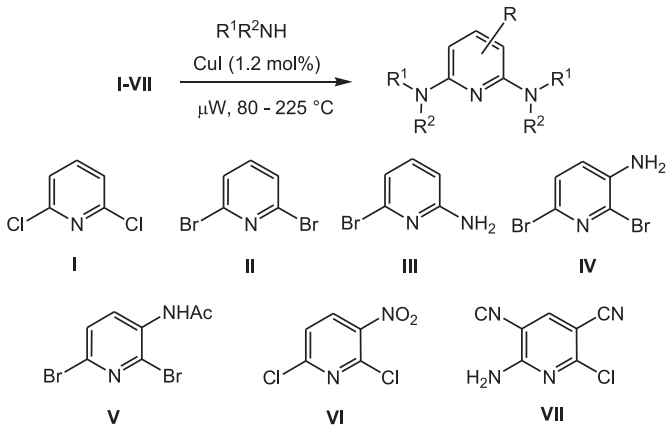


Scheme 2.

procedure permits the selective substitution of one or two halogens by primary and secondary aryl and alkylamines in a relatively short time to afford a series of 2-amino- and/or 2,6-diaminopyridines in high isolated yields. This methodology constitutes a practical alternative to other methods.

2. Results and discussion

Treatment of compounds **I**–**VII** (4.2 mmol) with various primary and secondary amines in the presence of catalytic amounts of CuI (1.2 mol %) and traces of water (100 μL) afforded selectively mono or disubstituted aminopyridines depending on the reaction conditions (Table 1). The addition of small amounts of water was necessary in order to achieve the required temperature under microwave conditions. None of these reactions required any additional organic solvents.

In general, the reactions of amines with 2,6-dichoropyridine (**I**) led to the exclusive formation of mono substituted products **1**–**3** in good to excellent isolated yields. It has to be noted, that even at higher temperatures the formation of disubstituted products was not observed. In the case of piperazine, both amine sites reacted with **I** and no mono substituted piperazine derivative was formed (entry 3). With 2,6-dibromopyridine (**II**), on the other hand, depending on the reaction temperature both mono and the desired disubstituted products were obtained in high yields (entries 4, 5, 7–19) and showed a good substrate scope. Alkyl, aryl and benzylamines reacted readily to form compounds **4**–**15**. The use of chiral amines *R*- and *S*-1-phenylethane amine, allowed the preparation of chiral 2,6-diaminpyridnes (entries 11 and 12). By lowering the temperature also mono substituted aminopyridines could be obtained. This has been exemplarily shown for isopropylamine. Compound **6** could be obtained selectively (entry 6) which is an interesting building block for mixed diaminopyridines. In the case of anilines (entries 14 and 15) the reaction required a small amount of $Pd(PPh_3)_4$ as co-catalyst (0.2 mol %) and the yields were rather low. In this particular case, other established methods achieve much high yields.[18–20] Surprisingly, under the standard reaction conditions allyl amine and *N*,*N*-methylbenzylamine reacted only to yield the mono substituted compounds **16** and **17**. With benzylamine no identifiable products could be isolated. At higher reaction temperatures decomposition to intractable materials took place. The formation of compounds **18** and **19** demonstrates that also with secondary amines and **II** directly 2,6-diaminopyridines can be obtained. Precursors **III** and **17** were utilized as entries into mixed 2,6-diaminopyridines (entries 20–24). Finally we tested mono and dichloro and bromopyridines bearing both activating and deactivating groups (**IV**–**VII**) as synthetic entry into mixed 2,6-diaminopyridines (entries 25–30). Deactivating groups from **VI** and **VII** led to faster and better conversion under milder conditions. Moreover, the amination in the case of chlorides was faster and proceeded at much lower temperatures as compared to the bromide precursors (entries 27–30). Also the amination of **VI** and **VII** with aqueous ammonia to yield **27** and **28** worked very well with 93 and 97% isolated yields (entries 27 and 28). Compounds **25**–**30** are particularly interesting since the functional groups may allow cleavage or conversion into other functionalities. It has to be mentioned that all functionalized systems were less air sensitive than the diamines lacking additional substituents in the pyridine ring.

3. Conclusion

A microwave assisted copper-catalyzed amination protocol is reported utilizing a series of 2,6-dihalo- and 2-amino-6-halo pyridine precursors. With the exception of NH_3, methyl- and ethylamine, where aqueous solutions were used, the reaction is basically solvent free and only traces of water were added to achieve the required temperatures under microwave conditions. This protocol generally afforded the corresponding products in good yields with easy purification steps. Using this procedure, selective substitution of one or two halogens by aryl- or alkylamines was achieved within 2–6 h at temperatures between 80 and 225 °C affording 2,6-diaminopyridines in good to excellent isolated yields. The target compounds are valuable precursors for the synthesis of bis-phosphorylated 2,6-diaminopyridines which are used as PNP pincer ligands in transition metal complexes.

4. Experimental section

4.1. General notes

Unless otherwise noted, chemicals were purchased from commercial suppliers and were used without further purification. Precursors **III**, **IV**, **V** and **VII** where synthesized according to the literature.[21–23] Microwave reactions were performed on a CEM Explorer PLS microwave unit. Column chromatography was performed on silica gel 60 from Merck. For thin layer chromatography (TLC) aluminum backed silica gel was used. Melting points were determined using a Kofler-type Leica Galen III micro hot stage microscope and are uncorrected. All samples were analyzed by LC-IT-TOF-MS in the positive ion detection mode with the recording of MS and MS/MS spectra. Room temperature ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on Bruker DXP 200 and AVANCE-250 spectrometers and were referenced internally to residual protio-solvent, and solvent resonances, respectively, and are reported relative to tetramethylsilane (δ=0 ppm).

4.2. Typical experimental procedure for the synthesis of *N*-alkyl and *N*-aryl 2,6-diamino pyridines

Compounds **I**–**VII** (4.22 mmol), catalytic amounts of CuI (10 mg, 0.052 mmol) and water (100 μL) were treated with 6 equiv of the respective amine and sealed in a 5 mL microwave vial. $Pd(PPh_3)_4$ (10 mg, 0.008 mmol) was added in the case of anilines. After the reaction was completed (see Table 1), 2 equiv of solid K_2CO_3 were added. The resulting product was obtained after filtration and washing with water as an analytically pure crystalline solid. Otherwise all volatiles were then evaporated and purified by flash column chromatography (**A**) or bulb-to-bulb distillation (**B**). In the case of methylamine and ethylamine the corresponding aqueous solution was used without extra water addition.

Table 1
Synthesis of *N*-substituted and *N,N′* disubstituted amino pyridines

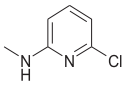
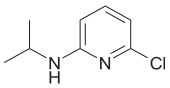
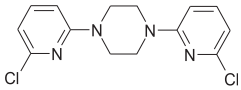
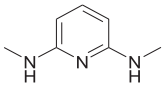
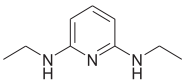
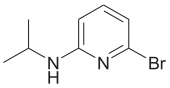
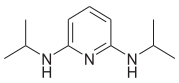
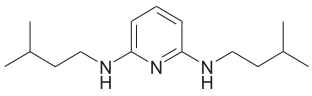
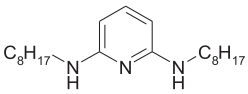
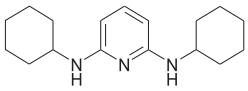
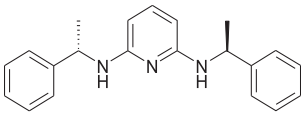
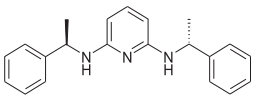
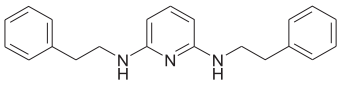
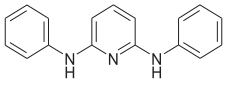
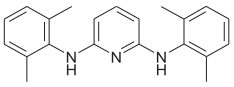
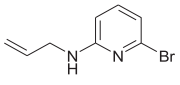
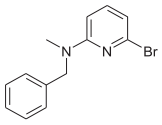
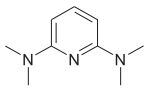
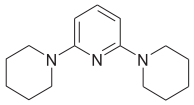
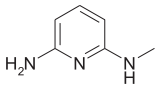
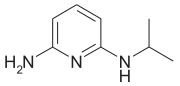
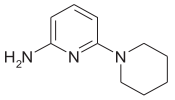
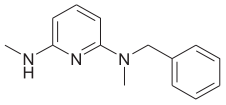
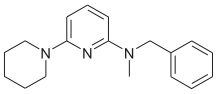
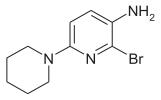
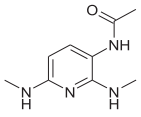
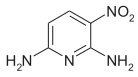
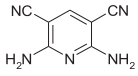
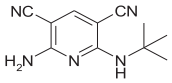
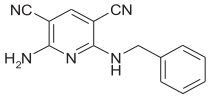
Entry	Reactant	Product	*t* [h]	*T* [°C]	Yield [%]
1	**I**		2	180	94
2	**I**		4	180	82
3	**I**		4	180	78
4	**II**		2	180	93
5	**II**		2	180	90
6	**II**		3	150	83
7	**II**		5	180	63
8	**II**		4	200	75
9	**II**		4	200	73
10	**II**		5	200	61
11	**II**		4	210	85
12	**II**		4	210	84
13	**II**		3	210	88
14	**II**		6	225	43
15	**II**		6	225	19
16	**II**		3	160	82

Table 1 (*continued*)

Entry	Reactant	Product	*t* [h]	*T* [°C]	Yield [%]
17	**II**		30	140	92
18	**II**		4	180	78
19	**II**		4	190	78
20	**III**		5	160	83
21	**III**		8	150	62
22	**III**		5	150	95
23	**17**		5	160	83
24	**17**		5	150	96
25	**IV**		4	160	78
26	**V**		4	165	75
27	**VI**		3	135	93
28	**VII**		1.5	130	97
29	**VII**		1	80	69
30	**VII**		1	80	72

*4.2.1. (6-Chloropyridine-2-yl)-methyl-amine (**1**).* Prepared according to general procedure **A** with 3 equiv of methylamine. Product was obtained as white crystals. Mp: 59–60 °C. ^{1}H NMR (DMSO-d_6) δ: 7.36 (dd, J=8.3 Hz, J=7.3 Hz, 1H, Py), 6.88 (bq, 1H, NH), 6.48 (d, J=7.3, 1H, Py), 6.38 (d, J=8.3 Hz, 1H, Py), 2.72 (d, 3H, CH_3). ^{13}C{^{1}H} NMR (DMSO-d_6) δ: 159.6 (Py), 148.5 (q, Py), 139.3 (Py), 109.6 (Py), 105.9 (Py), 27.7 (CH_3). HRMS (ESI): $[M+H]^+$, found 143.0374. $C_6H_7N_2Cl$ requires 143.0371.

*4.2.2. (6-Chloropyridine-2-yl)-isopropyl-amine (**2**).* Prepared accor ding to general procedure **A** with 3 equiv of isopropylamine. Product was obtained as yellow oil. ^{1}H NMR (DMSO-d_6) δ: 7.36 (t,

J=7.8 Hz, 1H, Py), 6.70 (br, 1H, NH), 6.38 (d, *J*=7.2 Hz, 1H, Py), 6.33 (d, *J*=8.0 Hz, 1H, Py), 3.9 (sept, 1H, CH), 1.10 (d, *J*=6.5 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 159.6 (q, Py), 148.5 (q, Py), 139.3 (Py), 109.6 (Py), 105.9 (Py), 27.8 (CH_3). HRMS (ESI): $[M+H]^+$, found 171.0680. $C_8H_{11}N_2Cl$ requires 171.0684.

*4.2.3. 1,4-Bis-(6-chloropyridine-2-yl)-piperazine (**3**).* Prepared according to general procedure. The product precipitated as colorless crystals from the reaction mixture. Mp: 139–140 °C. ^1H NMR (DMSO-d_6) δ: 7.6 (t, *J*=7.8 Hz, 2H, Py), 6.8 (d, *J*=8.5 Hz, 2H, Py), 6.68 (d, *J*=7.3 Hz, 2H, Py), 3.60 (s, 8H, CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.6 (Py), 148.1 (q, Py), 140.6 (Py), 111.6 (Py), 105.4 (Py), 43.8 (CH_2). HRMS (ESI): $[M+H]^+$, found 309.0680. $C_{14}H_{14}N_4Cl_2$ requires 309.0668.[24]

*4.2.4. N,N′-Dimethyl-2,6-diaminopyridine (**4**).* Prepared according to general procedure **B**. Product was obtained as beige crystals. Mp: 60–63 °C. ^1H NMR (DMSO-d_6) δ: 7.02 (t, *J*=7.9 Hz, 1H, Py), 5.78 (br, *J*=3.4 Hz, 2H, NH), 5.52 (d, *J*=7.9 Hz, 2H, Py), 2.64 (d, *J*=4.9 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 159.1 (Py), 138.1 (Py), 93.8 (Py), 28.5 (CH_3). HRMS (ESI): $[M+H]^+$, found 138.1036. $C_7H_{11}N_3$ requires138.1026.[18]

*4.2.5. N,N′-Diethyl-2,6-diaminopyridine (**5**).* Prepared according to general procedure **B**. Product was obtained as yellow oil. ^1H NMR (DMSO-d_6) δ: 6.97 (t, *J*=8.0 Hz, 1H, Py), 5.73 (t, *J*=4.8 Hz, 2H, NH), 5.51 (d, *J*=7.7 Hz, 2H, Py), 3.12 (m, 4H, CH_2), 1.06 (t, *J*=7.1 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.5 (Py), 138.0 (Py), 94.2 (Py), 35.9 (CH_2), 15.4 (CH_3). HRMS (ESI): $[M+H]^+$, found 166.1351. $C_9H_{15}N_3$ requires 166.1339.[25]

*4.2.6. (6-Bromopyridin-2-yl)-isopropyl-amine (**6**).* Prepared according to general procedure **A** with 3 equiv of methylamine. Product was obtained as yellow oil. ^1H NMR (DMSO-d_6) δ: 7.22 (t, *J*=7.8 Hz, 1H, Py), 6.6 (s, 1H, NH), 6.6 (d, *J*=7.3 Hz, 1H, Py), 6.4 (d, *J*=8.0 Hz, 1H, Py), 3.9 (m, 1H, CH), 1.12 (d, *J*=6.5 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.4 (Py), 139.5 (Py), 139.0 (Py), 139.2 (Py), 113.3 (Py), 106.7 (Py), 41.8 (CH), 22.3 (CH_3). HRMS (ESI): $[M+H]^+$, found 215.0187. $C_8H_{11}N_3Br$ requires 215.0178.[26]

*4.2.7. N,N′-Diisopropyl-2,6-diaminopyridine (**7**).* Prepared according to general procedure **B**. Product was obtained as yellow oil. ^1H NMR ($CDCl_3$) δ: 7.19 (t, *J*=8.0 Hz 1H, Py), 5.64 (d, *J*=7.9 Hz, 2H, Py), 4.09 (s, br, 2H, NH), 3.73 (m, 2H, CH), 1.16 (d, *J*=6.5 Hz, 12H, CH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 157.6 (Py), 138.9 (Py), 94.4 (Py), 43.0 (CH), 23.1 (CH_3). HRMS (ESI): $[M+H]^+$, found 194.1650. $C_{11}H_{19}N_3$ requires 194.1652.

*4.2.8. N,N′-Bis-(3-methylbutyl)-2,6-diaminopyridine (**8**).* Prepared according to general procedure **A**. Product was obtained as yellow oil. ^1H NMR (DMSO-d_6) δ: 6.97 (t, *J*=7.8 Hz, 1H, Py), 5.77 (t, *J*=5.5 Hz, 2H, NH), 5.56 (d, *J*=7.9 Hz, 2H, Py), 3.16 (q, 4H, CH_2), 1.63 (m, 2H, CH), 1.38 (q, 4H, CH_2), 0.87 (d, *J*=6.6 Hz, 12H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.1 (Py), 137.3 (Py), 93.7 (Py), 38.9 (CH_2), 38.5 (CH_2), 25.4 (CH), 22.5 (CH_3). HRMS (ESI): $[M+H]^+$, found 250.2278. $C_{15}H_{27}N_3$ requires 250.2278.

*4.2.9. N,N′-Dioctyl-2,6-diaminopyridine (**9**).* Prepared according to general procedure **A**. Product was obtained as yellow oil. ^1H NMR (DMSO-d_6) δ: 6.95 (t, *J*=7.9 Hz, 1H, Py), 5.80 (t, *J*=5.2 Hz, 2H, NH), 5.52 (d, *J*=7.7 Hz, 2H, Py), 3.12 (q, 4H, CH_2), 1.45 (quint, 4H, CH_2), 1.24 (m, 20H, CH_2), 0.85 (t, *J*=6.3 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.1 (Py), 137.3 (Py), 93.7 (Py), 40.8 (CH_2), 31.3 (CH_2), 29.4 (CH), 28.9 (CH), 28.8 (CH), 26.7 (CH), 22.1 (CH), 13.9 (CH_3). HRMS (ESI): $[M+H]^+$, found 334.3221. $C_{21}H_{39}N_3$ requires 334.3217.

*4.2.10. N,N′-Dicyclohexyl-2,6-diaminopyridine (**10**).* Prepared according to general procedure **A**. Product was obtained as yellow oil. ^1H NMR ($CDCl_3$) δ: 7.20 (t, *J*=8.1 Hz, 1H, Py), 5.66 (d, *J*=8.0 Hz, 2H, Py), 4.16 (d, *J*=8.2 Hz, 2H, NH), 3.42 (quint, 2H, CH), 2.05 (m, 4H, CH_2), 1.76 (m, 6H, CH_2), 1.24 (m, 10H, CH_2). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 157.7 (Py), 139.1 (ArH), 94.3 (Py), 50.4 (CH), 33.6 (CH_2), 26.0 (CH_2), 25.1 (CH_2). HRMS (ESI): $[M+H]^+$, found 274.2274. $C_{17}H_{27}N_3$ requires 274.2278.

*4.2.11. N,N′-Bis-(S-1-phenylethyl)-2,6-diaminopyridine (**11**).* Prepared according to general procedure **A** with 4.2 equiv of amine. Product was obtained as colorless oil. ^1H NMR (DMSO-d_6) δ: 7.38–7.12 (m, 10H, Ph), 6.92 (t, *J*=7.3 Hz, 1H, Py), 6.33 (d, *J*=7.9 Hz, 2H, NH), 5.56 (d, *J*=7.9 Hz, 2H, Ph), 4.87 (quint, 2H, CH), 1.27 (d, *J*=6.8 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 157.0 (Py), 146.9 (Ph), 137.3 (Py), 128.0 (Ph), 126.0 (Ph), 126.0 (Ph), 94.8 (Py), 49.6 (CH), 23.6 (CH_3). HRMS (ESI): $[M+H]^+$, found 318.1956. $C_{21}H_{23}N_3$ requires 318.1965.

*4.2.12. N,N′-Bis-((R)-1-phenylethyl)-2,6-diaminopyridine (**12**).* Prepared according to general procedure **A** with 4.2 equiv of amine. Product was obtained as colorless oil. ^1H NMR (DMSO-d_6) δ: 7.38–7.13 (m, 10H, Ph), 6.91 (t, *J*=7.3 Hz, 1H, Py), 6.33 (d, *J*=7.9 Hz, 2H, NH), 5.57 (d, *J*=7.9 Hz, 2H, Py), 4.83 (m, 2H, CH), 1.27 (d, *J*=6.8 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 157.0 (Py), 146.9 (q, Ph), 137.3 (Py), 128.0 (Ph), 126.0 (Ph), 126.0 (Ph), 94.8 (Py), 49.6 (CH), 23.6 (CH_3). HRMS (ESI): $[M+H]^+$, found 318.1956. $C_{21}H_{23}N_3$ requires 318.1965.

*4.2.13. N,N′-Diphenethylpyridine-2,6-diamine (**13**).* Prepared according to general procedure **A** with 4.2 equiv of amine. Product was obtained as white solid. Mp: 90–91 °C. ^1H NMR (DMSO-d_6) δ: 7.22 (m, 10H, ArH), 7.03 (t, *J*=8.0 Hz, 1H, ArH), 6.06 (t, *J*=5.0 Hz, 2H, NH), 5.62 (d, *J*=7.8 Hz, 2H, ArH), 3.38 (q, 4H, CH_2), 2.82 (t, *J*=7.3 Hz, 4H, CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 157.9 (Py), 140.1 (Ph), 137.6 (Py), 128.6 (Ph), 128.2 (Ph), 125.8 (Ph), 94.3 (Py), 42.8 (CH_2), 35.7 (CH_2). HRMS (ESI): $[M+H]^+$, found 318.1957. $C_{21}H_{23}N_3$ requires 318.1965.

*4.2.14. N,N′-Diphenyl-pyridine-2,6-diamine (**14**).* Prepared according to general procedure **A** with $Pd(PPh_3)_4$ (10 mg). Product was obtained as fawn crystals. Mp: 102–103 °C. ^1H NMR (DMSO-d_6) δ: 8.78 (s, 2H, NH), 7.59 (d, 4H, Ph), 7.36 (t, *J*=8.2 Hz, 1H, Py), 7.22 (m, 4H, Ph), 6.87 (t, 2H, Ph), 6.22 (d, 2H, Py). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 154.4 (Py), 141.7 (Ph), 138.4 (Py), 128.4 (Ph), 120.2 (Ph), 118.6 (Ph), 99.7 (Py). HRMS (ESI): $[M+H]^+$, found 262.1327. $C_{17}H_{15}N_3$ requires 262.1339.[19,20]

*4.2.15. N,N′-Bis-(2,6-dimethylphenyl)-pyridine-2,6-diamine (**15**).* Prepared according to general procedure **A** with $Pd(PPh_3)_4$ (10 mg). Product was obtained as fawn crystals. Mp: 183–185 °C. ^1H NMR (DMSO-d_6) δ: 7.44 (s, 2H, NH), 7.08–7.03 (m, 7H, Ph, Py), 5.35 (d, *J*=7.9 Hz, 2H, Py), 2.15 (s, 12H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 157.0 (Py), 138.5 (Py), 137.9 (Ph), 136.0 (Ph), 127.9 (Ph), 125.4 (Ph), 94.3 (Py), 18.3 (CH_3). HRMS (ESI): $[M+H]^+$, found 318.1955. $C_{21}H_{23}N_3$ requires 318.1965.[20]

*4.2.16. Allyl-(6-bromopyridine-2-yl)-amine (**16**).* Prepared according to general procedure **A**. Product was obtained as beige crystals. Mp: <30 °C. ^1H NMR (DMSO-d_6) δ: 7.27 (t, *J*=7.45 Hz, 1H, Py), 7.10 (t, br, 1H, NH), 6.62 (d, *J*=7.2 Hz, 1H, Py), 6.42 (d, *J*=7.8 Hz, 1H, Py), 5.97–5.78 (m, 1H, C*H*=CH_2), 5.23–5.03 (m, 2H, CH=C*H*$_2$), 3.85–3.79 (m, 2H, CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.9 (Py), 139.4 (Py), 139.4 (Py), 135.4 (*C*H=CH_2), 115.2 (CH=*C*H_2), 43.0 (CH_2). HRMS (ESI): $[M+H]^+$, found 213.0012. $C_8H_9N_2Br$ requires 213.0022.[27]

*4.2.17. Benzyl-(6-bromopyridine-2-yl)-methyl-amine (**17**).* Prepared according to general procedure with 2.2 equiv of amine. Product was obtained as beige crystals. Mp: 62.5–63.5 °C. ^1H NMR (DMSO-

d_6) δ: 7.27 (m, 6H, ArH), 6.74 (d, J=7.4 Hz, 1H, ArH), 6.61 (d, J=8.5 Hz, 1H, ArH), 4.71 (s, 2H, CH_2), 3.00 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.4 (Py), 140.1 (Py), 139.2 (Py), 138.1 (Ph), 128.5 (Ph), 127.0 (Ph), 126.9 (Ph), 114.2 (Py), 104.5 (Py), 52.6 (CH_2), 36.0 (CH_2). HRMS (ESI): $[M+H]^+$, found 277.0330. $C_{13}H_{13}N_2Br$ requires 277.0335.[28]

*4.2.18. N,N,N′,N′-Tetramethylpyridine-2,6-diamine (**18**).* Prepared according to general procedure **B**. Product was obtained as colorless crystals. Mp: 32–33 °C. ^1H NMR (DMSO-d_6) δ: 7.23 (t, J=8.0 Hz, 1H, Py), 5.83 (d, J=8.2 Hz, 2H, Py), 2.94 (s, 12H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 157.9 (Py), 138.4 (Py), 92.9 (Py), 37.3 (CH_3). HRMS (ESI): $[M+H]^+$, found 138.1035. $C_7H_{11}N_3$ requires 138.1026.[29]

*4.2.19. 2,6-Di-piperidine-1-yl-pyridine (**19**).* Prepared according to general procedure **A**. Product was obtained as colorless oil. ^1H NMR (DMSO-d_6) δ: 7.22 (t, J=8.2 Hz, 1H, Py), 5.95 (d, J=8.2 Hz, 2H, Py), 3.40 (s, 8H, CH_2), 1.52 (s, 12H; CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 157.8 (Py), 138.7 (Py), 94.7 (Py), 45.5 (CH_2), 25.0 (CH_2), 24.4 (CH_2). HRMS (ESI): $[M+H]^+$, found 246.1958. $C_{15}H_{23}N_3$ requires 246.1965.[30]

*4.2.20. N-Methyl-2,6-diaminopyridine (**20**).* Prepared according to general procedure **A**. Product was obtained as colorless crystals. Mp: 92–93 °C. ^1H NMR (DMSO-d_6) δ: 7.02 (t, J=7.7 Hz, 1H, Py), 5.79 (pd, 1H), 5.57 (t, J=8.4 2H), 5.33 (s, 2H), 2.65 (d, J=4.8 Hz, 3H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.9 (Py), 158.6 (Py), 137.9 (Py), 94.6 (Py), 93.8 (Py), 28.1 (CH_3). HRMS (ESI): $[M+H]^+$, found 124.0875. $C_6H_9N_3$ requires 124.0869.

*4.2.21. N-Isopropylpyridine-2,6-diamine (**21**).* Prepared according to general procedure **A**. Product was obtained as yellow oil. ^1H NMR (DMSO-d_6) δ: 6.98 (t, J=7.7 Hz, 1H, Py), 5.58–5.54 (m, 3H, Py, NH), 5.27 (s, 2H, NH_2), 3.83 (m, 1H, CH), 1.07 (d, J=6.3 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.6 (Py), 157.6 (Py), 137.8 (Py), 94.9 (Py), 94.3 (Py), 41.3 (CH), 22.8 (CH_3). HRMS (ESI): $[M+H]^+$, found 152.1183. $C_8H_{13}N_3$ requires 152.1182.

*4.2.22. N-(Piperidin-1-yl)-pyridine-2,6-diamine (**22**).* Prepared according to general procedure **A**. Product was obtained as colorless oil. ^1H NMR (DMSO-d_6) δ: 7.11 (t, J=7.9 Hz, 1H, Py), 5.84 (d, J=8.2 Hz, 1H, Py), 5.70 (d, J=7.9 Hz, 1H, Py), 5.42 (s, 2H, NH_2), 3.39–3.34 (m, 4H, CH_2), 1.51 (s, 6H, CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.4 (Py), 158.2 (Py), 138.4 (Py), 96.0 (Py), 93.9 (Py), 45.4 (CH_2), 25.0 (CH_2), 24.4 (CH_2). HRMS (ESI): $[M+H]^+$, found 178.1338. $C_{10}H_{15}N_3$ requires 178.1339.

*4.2.23. N-Benzyl-N,N′-dimethyl-pyridine-2,6-diamine (**23**).* Prepared according to general procedure **A**. Product was obtained as yellow oil. ^1H NMR (DMSO-d_6) δ: 7.28–7.10 (m, 6H, Ph, Py), 5.99 (q, 1H, NH), 5.70 (t, J=7.4 Hz, 2H, Py), 4.73 (s, 2H, CH_2), 2.91 (s, 3H, CH_3), 2.69 (d, J=4.9 Hz, 3H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.3 (Py), 157.5 (Py), 139.7 (Ph), 138.1 (Py), 128.2 (Ph), 127.1 (Ph), 126.5 (Ph), 94.5 (Py), 92.0 (Py), 51.9 (CH_2), 35.6 (CH_3), 27.9 (CH_3). HRMS (ESI): $[M+H]^+$, found 228.1485. $C_{14}H_{17}N_3$ requires 228.1495.

*4.2.24. Benzyl-methyl-(6-piperidine-1-yl-pyridin-2-yl)-amine (**24**).* Prepared according to general procedure **A**. Product was obtained as yellow oil. ^1H NMR (DMSO-d_6) δ: 7.31–7.18 (m, 6H, Ph, Py), 5.97 (d, J=7.3 Hz, 2H, Py), 5.83 (d, J=7.3 Hz, 2H, Py), 4.70 (s, 2H, CH_2), 3.42–3.39 (m, 4H, CH_2), 2.93 (s, 3H, CH_3), 1.50 (s, 6H, CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.3 (Py), 157.5 (Py), 139.7 (Ph), 138.1 (Py), 128.2 (Ph), 127.1 (Ph), 126.5 (Ph), 94.5 (Py), 92.0 (Py), 51.9 (CH_2), 35.6 (CH_3), 27.9 (CH_3). HRMS (ESI): $[M+H]^+$, found 282.1954. $C_{18}H_{23}N_3$ requires 282.1965.

*4.2.25. 2-Bromo-N′6′-(piperidine-1-yl)-pyridine-3,6-diamine (**25**).* Prepared according to general procedure **A**. Product was obtained as colorless oil. ^1H NMR (DMSO-d_6) δ: 5.84 (d, J=8.2 Hz, 1H, Py), 5.70 (d, J=7.9 Hz, 1H, Py), 5.42 (s, 2H, NH_2), 3.39–3.34 (m, 4H, CH_2), 1.51 (s, 6H, CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 158.4 (Py), 158.2 (Py), 138.43 (Py), 96.0 (Py), 93.9 (Py), 45.4 (CH_2), 25.0 (CH_2), 24.4 (CH_2). HRMS (ESI): $[M-H]^+$, found 254.0285. $C_{10}H_{14}BrN_3$ requires 254.0287.

*4.2.26. N-(2,6-Bis-methylaminopyridine-3-yl)-acetamide (**26**).* Prepared according to general procedure **A**. Product was obtained as pink solid. ^1H NMR (DMSO-d_6) δ: 7.52 (d, J=8.2 Hz, 1H, Py), 6.41 (br, 1H, NH), 6.28 (d, J=8.2 Hz, 1H, Py), 3.58 (s, 3H, CH_3), 2.80 (s, 3H, CH_3), 2.42 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 156.2, 147.4, 127.1, 125.1, 103.3, 82.1, 28.2, 27.6, 13.5. HRMS (ESI): $[M+H]^+$, found fragment without—H_2O 177.1133. $C_9H_{14}N_4O$ requires 194.1168.

*4.2.27. 3-Nitropyridine-2,6-diamine (**27**).* Prepared according to general procedure with an addition of DMF (2 mL). The product was diluted with water, filtrated and recrystallized and obtained as yellow solid. Mp: 227–228 °C. ^1H NMR (DMSO-d_6) δ: 7.97 (d, 1H, J=9.2 Hz, Py), 7.64 (s, br, 2H, NH_2), 7.25 (s, 2H, NH_2), 5.92 (d, J=9.2 Hz). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 162.5 (Py), 155.9 (Py), 135.3 (Py), 117.7 (Py) 101.6 (Py). HRMS (ESI): $[M+H]^+$, found 155.0562. $C_5H_6N_4O_2$ requires 155.0564.[31]

*4.2.28. 2,6-Diaminopyridine-3,5-dicarbonitrile (**28**).* Prepared according to general procedure with 3 equiv of concentrated NH_3 and *i*PrOH (7 mL). The product was filtrated and washed with *i*PrOH and Et_2O and obtained an off-white solid. Mp: >265 °C. ^1H NMR (DMSO-d_6) δ: 8.01 (s, 1H, Py), 7.19 (s, 4H, NH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 160.7 (q, Py), 148.1 (Py), 116.8 (Py), 78.7 (CH_3). HRMS (ESI): $[M+H]^+$, found 160.0619. $C_7H_5N_5$ requires 160.0618.[30]

*4.2.29. 2-Amino-6-tert-butylamino-pyridine-3,5-dicarbonitrile (**29**).* Prepared according to general procedure with 3 equiv of amine and *i*PrOH (7 mL). The product was filtrated and washed with *i*PrOH and Et_2O and obtained an off-white solid. Mp: 154–155 °C. ^1H NMR (DMSO-d_6) δ: 8.02 (s, 2H, NH_2), 7.31 (s, 1H, NH), 5.98 (s, 1H, Py), 1.37 (s, 6H, CH_3), 1.21 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 160.5 (Py), 158.9 (Py), 148.1 (Py), 117.4 (2CN), 80.9 (Py), 78.1 (Py), 52.9 ($C(CH_3)_3$), 29.0 (CH_3), 27.6 (CH_3). HRMS (ESI): $[M+Na]^+$, found 238.1064. $C_{11}H_{13}N_5$ requires 238.1063.

*4.2.30. 2-Amino-6-benzylaminopyridine-3,5-dicarbonitrile (**30**).* Prepared according to general procedure with 3 equiv of concentrated NH_3 and *i*PrOH (7 mL). The product was filtrated and washed with *i*PrOH and Et_2O and obtained as an off-white solid. Mp: 260.5–262 °C. ^1H NMR (DMSO-d_6) δ: 8.00 (s, 2H, NH_2), 7.24 (m, 7H, NH, ArH), 4.50 (d, 2H, CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ: 161.1 (Ar), 159.1 (Ar), 148.1 (Py), 139.9 (Ph), 128.6 (Ph), 128.1 (Ph), 127.2 (Ph), 117.3 (CN), 117.2 (CN), 79.8 (Py), 78.6 (Py), 44.0 (CH_2). HRMS (ESI): $[M+H]^+$, found 250.1081. $C_{14}H_{11}N_5$ requires 250.1087.

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Supplementary data

^1H and $^{13}C\{^1H\}$ NMR spectra of compounds **1**–**30**. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.08.042.

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2,6-Diamination of substituted pyridines via heterogeneous Chichibabin reaction

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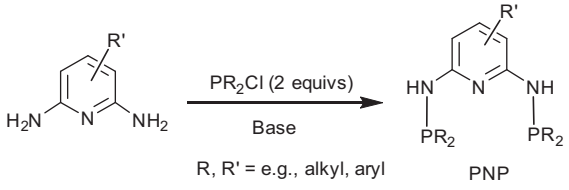
ABSTRACT

A series of ring substituted pyridines were selected for the sodium amide initiated heterogeneous Chichibabin amination to obtain 2,6-diaminopyridine derivatives which are important synthons for the preparation of PNP pincer ligands. The substrates were treated with an excess of sodium amide in neat mineral oil as solvent under an argon atmosphere. The reaction required temperatures of up to 215 °C under vigorous stirring with an overall reaction time of 3–5 h. In the case of methyl, *tert*-butyl, phenyl, pyridinyl, and hydroxyl substituted pyridines the desired products were obtained in good to excellent yields (63–96%). Thus, the Chichibabin reaction provides an inexpensive and economic alternative to methodologies starting from halopyridines or pyridine *N*-oxides provided that the substituents are inert under the harsh reaction conditions.

Introduction

Ring-substituted 2,6-diaminopyridines are an important class of heterocycles which are useful building blocks for macrocycles, polymers, agrochemicals, dyes, and pharmacologically potent molecules.[1–6] Furthermore 2,6-diaminopyridines are valuable scaffolds for the design of tridentate ligands in coordination and organometallic chemistry. We are particularly interested in using ring-substituted 2,6-diaminopyridines as building blocks for new tridentate PNP ligands, so called pincer ligands, which are typically obtained according to Scheme 1.[7]

Since 2,6-diaminopyridine is the only commercially available and convenient precursor, we sought a new efficient general synthetic route to obtain ring substituted 2,6-diaminopyridines. For this purpose, we selected the sodium amide initiated amination of pyridine, known as the Chichibabin reaction.[8] A DFT calculated mechanism of the Chichibabin reaction was recently reported.[9] This method is very useful for the preparation of 2-aminopyridine and parent 2,6-diaminopyridine by the reaction of pyridine with sodium amide under heterogeneous conditions, but was hardly applied to ring-substituted pyridines. A rare example of a 2,6-diamination under Chichibabin conditions was reported recently by Kempe and co-workers who prepared 4-methylpyridine-2,6-diamine from 4-methylpyridine albeit in only 22% yield.[10] It has to be emphasized that the Chichibabin reaction provides an inexpensive and economic alternative to methodologies starting from halo pyridines via nucleophilic substitutions catalyzed by copper, copper salts or proline,[11–14] and Buchwald–Hartwig aminations,[15–19] or pyridine N-oxides.[20] Moreover, this reaction allows the synthesis of unsymmetrically alkylated diaminopyridines which are otherwise difficult to prepare (2,6-diamino-4-methylpyridin).[21]



Scheme 1. Synthesis of PNP pincer ligands based on the 2,6-diaminopyridine scaffold.

Results and discussion

A series of substituted pyridines were treated with an excess (3–6-equiv) of sodium amide in mineral oil (white oil, liquid paraffin) as solvent under an argon atmosphere. It has to be noted that Bojarska-Dahlig reported the use of Vaseline as solvent,[22] while Banerjee recently significantly improved and optimized the

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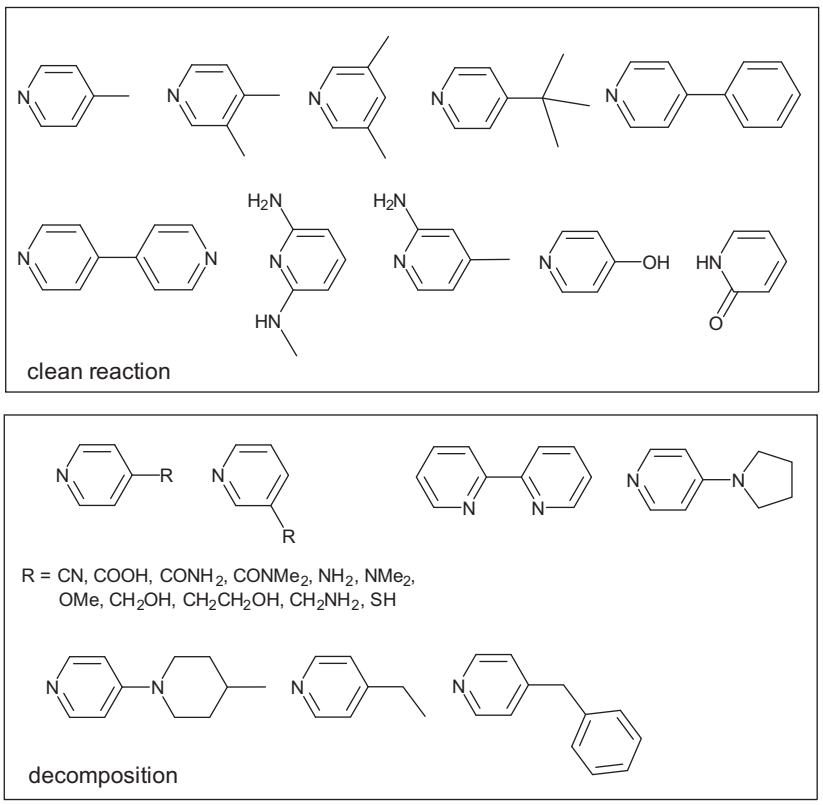
heterogeneous Chichibabin reaction by using mineral oil as reaction medium.[23] Running the reactions in neat *N*,*N*-dimethylaniline improved the solubility of the reactants and increased the reaction rates, but due the toxicity of this solvent as well as its high polarity, workup to obtain pure products turned out to be difficult and was thus not further used. Additives (10%) such as *n*-dodecylamine, and *n*-tributylamine showed no appreciable effects as reaction rates and yields are concerned. Moreover, it is important to mention that with the solvents *N*,*N*-dimethylaniline, decalin, or tetralin the required high temperatures are not obtained resulting in lower yields. [24] Accordingly, neat mineral oil was used as reaction medium throughout where reaction temperatures of 215 °C were easily reached. An overview of all substrates tested is given in Scheme 2. However, only in the case of methyl, *tert*-butyl, phenyl, pyridinyl, and hydroxyl substituted pyridines the desired products were obtained (Table 1). The reaction mixture was typically heated stepwise from 120 up to 215 °C under vigorous stirring with an overall reaction time of 3–5 h. Higher temperatures and/or longer reaction times did not result in higher yields rather than partial decomposition of the products. A color change from orange to brown to black was observed in all reactions. The evolution of hydrogen gas indicated the beginning of the reaction at about 120 °C due to the formation of 2-aminopyridines. At about 180 °C the second amination step was initiated which, after 3 h additional heating at 215 °C, led to formation of the 2,6-diaminopyridines (**1**–**9**) and 6-aminopyridine-2(1*H*)-one (**10**) (Table 1). It has to be noted that **1** was also obtained with 4-methylpyridine-2-amine (Table 1, entry 2). All these compounds were obtained in good to excellent isolated yields. 4-Hydroxy-pyridine-2,6-diamine (**9**) was first isolated from the reaction mixture as its nitrate salt **8** (Table 1, entry 9) which is sparingly water soluble. Isolation of free **9** was carried out by treating the nitrate salt with potassium hydroxide and was obtained in 96% isolated yield. Arienzo[25] and Fullam [26] described an alternative procedure to obtain **9** via a Hofmann or Curtius rearrangement using chelidamic acid as precursor. Bojarska-Dahlig and Banerjee also used the Chichibabin reaction for the synthesis of **9** utilizing a slightly different procedure.[22,23] Compound **10** was prepared recently via deamination of 2,6-diaminopyridine in concentrated hydrochloric acid with 83% isolated yield.[27] This emphasizes the advantage of the Chichibabin reaction reported here in comparison with alternative procedures for the synthesis of **9** and **10**.

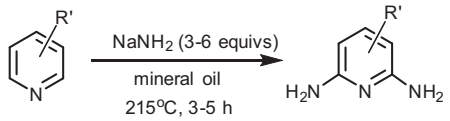
For the Chichibabin reaction, the optimal p*K*a range of pyridines is believed to be in the range of 5–8 and it was postulated that outside this range no reaction takes place. However, also 2-hydroxypyridine/2-pyridinone and 4-hydroxypyridine/4-pyridinone with p*K*a values of 11.7/1.3 and 11.1/3.1, respectively, reacted readily with sodium amide to yield **8** and **10** (Table 1, entries 9 and 10). All compounds were fully characterized by their melting points, HRMS, ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy (see Supporting information).

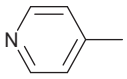
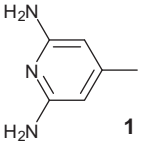
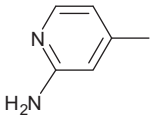
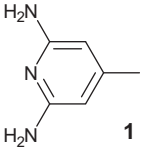
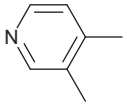
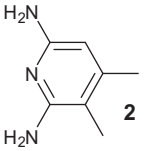
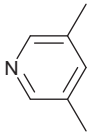
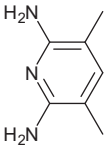
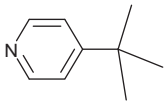
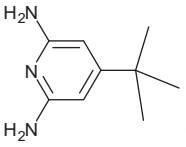
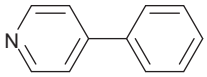
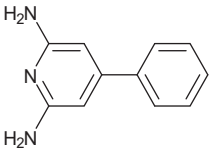
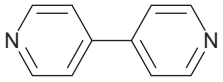
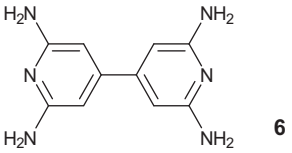
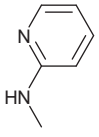
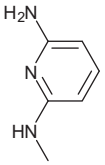
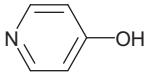
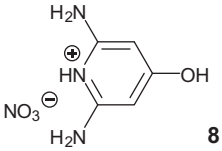
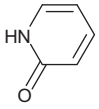
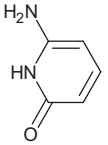
Finally, under the standard reaction conditions all other substrates used (Scheme 2) did not afford the desired 2,6-diaminopyridines. For instance, pyridines featuring –COOH, $–CONH_2$ and $–CON(CH_3)_2$ substituents in the 3- and 4-position were decarboxylated yielding parent 2,6-diaminopyridine. For comparison, McGill and co-workers reported the conversion of nicotinic acid to 6-amino-nicotinic acid at lower temperature (122–145 °C) and 360 psi albeit in low yields (26%).[28] Likewise, all other 3- and -4-substituted pyridines did not react at all or underwent elimination and polymerization reactions yielding intractable material which could not be characterized. Moreover, while pyridines with methyl and *tert*-butyl substituents (Table 1, entries 1–5) reacted cleanly to afford 2,6-diaminopyridines, 4-ethylpyridine and 4-benzylpyridine formed 4-vinylpyridine and intractable polymeric materials, respectively. Accordingly, for these types of 2,6-diaminopyridines different methodologies have to be used.[29]



Scheme 2. Overview of ring-substituted pyridines tested in the heterogeneous Chichibabin reaction.

Table 1
Synthesis of 2,6-diaminopyridines and 6-aminopyridine-2(1*H*)-one



Entry	Reactant	Product	Yield (%)
1		 **1**	66
2		 **1**	76
3		 **2**	84
4		 **3**	83
5		 **4**	85
6		 **5**	83
7		 **6**	73
8		 **7**	63
9		 **8**	77
10		 **10**	83

Conclusion

A series of substituted pyridines were selected for the sodium amide initiated heterogeneous Chihibabin amination to obtain 2,6-diaminopyridine derivatives. The substrates were treated with an excess of sodium amide in neat mineral oil as solvent under an argon atmosphere. The reaction required temperatures of up to 215 °C under vigorous stirring with an overall reaction time of 3–5 h. In the case of methyl, *tert*-butyl, phenyl, pyridinyl, and hydroxyl substituted pyridines the desired products were obtained in good to excellent yields. All other 3- and -4-substituted pyridines featuring, for instance COOH, $-CONH_2$ and $-CON(CH_3)_2$, $-NH_2$, $-NMe_2$, –SH, benzyl, and ethyl substituents, underwent uncontrolled elimination and polymerization reactions to yield intractable materials. The Chichibabin reaction provides an inexpensive and atom economic alternative to methodologies starting from halopyridines or pyridine *N*-oxides provided that the substituents are inert under the harsh reaction conditions.

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Supplementary data

Supplementary data (detailed experimental procedures and NMR data for all compounds) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.12.013.

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A Convenient Solvothermal Synthesis of Group 6 PNP Pincer Tricarbonyl Complexes

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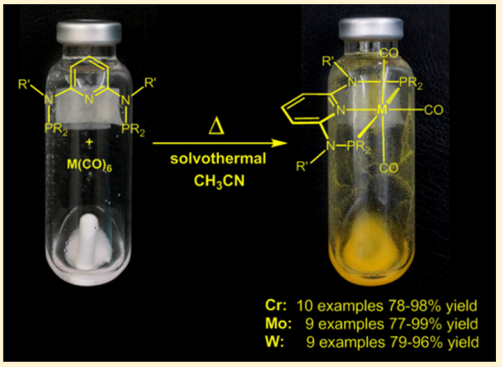
Supporting Information

ABSTRACT: The solvothermal synthesis of a series of zerovalent Cr, Mo, and W complexes of the type $[M(PNP)(CO)_3]$ featuring PNP pincer ligands based on 2,6-diaminopyridine is described. We demonstrate that the solvothermal synthesis technique presented provides a powerful, simple, and practical synthetic method resulting in high isolated yields in a short time. In particular, Cr and W complexes are not readily accessible via conventional methods. Moreover, this study allows a direct comparison of steric and electronic properties of group 6 metal PNP pincer tricarbonyl complexes.

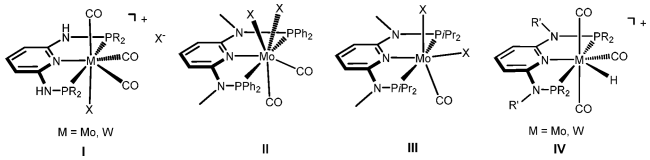


INTRODUCTION

Among the many ligand systems that can be found in the chemical literature, pincer ligands play an important role and their complexes have attracted tremendous interest due to their high stability, activity, and variability.[1] These tridentate ligands are often planar scaffolds consisting of an anionic or neutral central aromatic backbone tethered to two, mostly bulky, phosphine donors by different spacers. In this family of ligands steric, electronic, and also stereochemical parameters can be manipulated by modifications of the substituents at the donor sites and/or the spacers. Accordingly, many applications of mostly precious transition-metal pincer complexes in the fields of catalysis, molecular recognition, and supramolecular chemistry were discovered, turning this area into an intensively investigated subject in organometallic chemistry.

Surprisingly, as far as group 6 pincer complexes are concerned, only a few examples have been reported in the literature.[2−11] For the first time, Haupt and co-workers prepared PNP pincer complexes of the type $[M(PNP\text{-}Ph)(CO)_3]$ (M = Cr, Mo, W; PNP-Ph = *N*,*N*′-bis(diphenylphosphino)-*N*,*N*′-2,6-diaminopyridine), albeit in low yields (19, 34, and 22%).[2] We are focusing on the chemistry of molybdenum and tungsten complexes containing PNP pincer ligands based on the 2,6-diaminopyridine scaffold, where the pyridine ring and the phosphine moieties are connected via NH, *N*-alkyl, or N-aryl linkers.[4] These studies resulted in the preparation of halocarbonyl and hydridocarbonyl complexes of the types $[M(PNP)(CO)_3X]X$ (M = Mo, W; X = I, Br, Cl) (**I**), $[Mo(PNP)(CO)_2X_2]$ (X = I, Br, Cl, F) (**II**), $[Mo(PNP)(CO)X_2]$ (X = I, Br, Cl) (**III**), and $[M(PNP)(CO)_3H]^+$ (M = Mo, W) (**IV**), as illustrated in Scheme 1.[5−7] Analogous Cr complexes have, as yet, not been described. The synthesis of

Scheme 1. Halo Carbonyl and Hydrido Carbonyl Mo(II) and W(II) PNP Pincer Complexes as a Function of the PR_2 Moieties and the NR′ Spacers



a series of hydrido carbonyl and halo carbonyl tungsten pincer complexes featuring a related PNP pincer-type ligand based on silazane, viz. $HN(SiMe_2CH_2PPh_2)_2$, were described by Templeton and co-workers.[8] Gambarotta et al. could show that the Cr(II) and Cr(III) PNP complexes $[Cr(PNP\text{-}Ph)Cl_2]$ and $[Cr(PNP\text{-}Ph)Cl_2]$ (PNP-Ph = 2,6-bis(diphenylphosphinomethyl)pyridine) are active catalysts for the oligomerization of ethylene.[9] Recently, Schrock and co-workers showed[10] that the molybdenum PCP pincer complex based on the 1,3-bis(phosphinito)benzene scaffold is capable of cleaving molecular dinitrogen to give a Mo(IV) PCP nitride complex. Another impressive reaction of group 6 PNP pincer complexes was discovered by the group of Nishibayashi.[11] They found that dinuclear molybdenum and tungsten dinitrogen complexes bearing bulky PNP pincer ligands (PNP = 2,6-bis(dialkylphosphinomethyl)pyridines) are effective catalysts for the formation of ammonia from molecular dinitrogen. These few examples provide already a fortaste of the potential

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of group 6 pincer complexes with respect to stoichiometric and catalytic reactions involving, for instance, small molecules.

Accordingly, in order to further develop the chemistry of group 6 pincer systems, the availability of efficient synthetic protocols is essential. The most common synthetic entries into group 6 carbonyl complexes are the substitutionally inert hexacarbonyl complexes $M(CO)_6$, which are treated directly with a ligand under refluxing conditions in CH_3CN as a coordinating solvent stabilizing the labile $[M(CO)_3(CH_3CN)_3]$ intermediate. This reaction requires typically several hours for Cr and Mo but several days for W, with generally rather low yields in the case of Cr and W. Under conventional reaction conditions the use of $M(CO)_6$ complexes is also hampered by sublimation and deposition of the metal hexacarbonyl on the reflux condenser. The synthesis of transition-metal carbonyl complexes is sometimes significantly improved if the reactions are performed under microwave conditions.[12−15] In some cases, special Teflon-lined vessels rather than simple glass vials were required.

In this paper, we report on the synthesis of the zerovalent Cr, Mo, and W complexes $[M(PNP)(CO)_3]$ featuring PNP pincer ligands based on the 2,6-diaminopyridine scaffold via a simple and fast solvothermal approach with no need for microwave equipment.[16] All reactions are performed in standard aluminum-capped, microwave glass vials which allow the generation of higher pressures and superheating of the solvent. This results in significantly decreased reaction times and highly increased product yields in a clean fashion over methodologies reported using traditional procedures. Moreover, this study allows comparisons among a complete series of Cr, Mo, and W PNP tricarbonyl complexes as far as electronic and steric properties are concerned.

RESULTS AND DISCUSSION

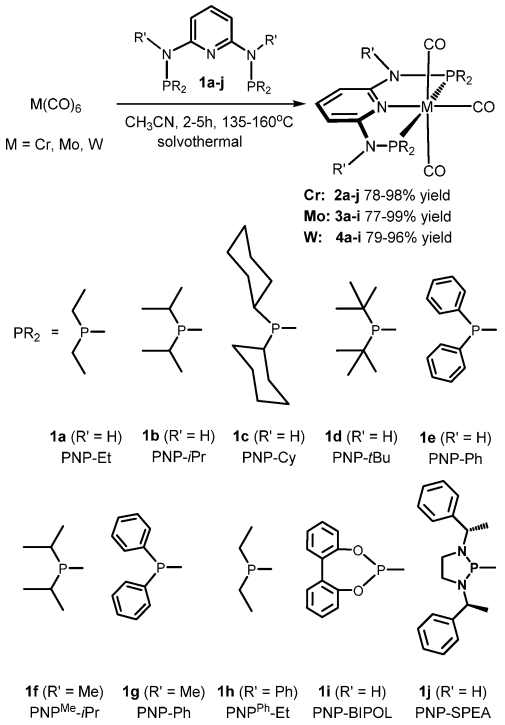
A suspension of hexacarbonyl complexes $M(CO)_6$ and PNP ligands **1a−j** in CH_3CN were placed in a sealed microwave glass tube and stirred for 2−5 h at 135−160 °C. After workup, the analytically pure products **2−4** were obtained in 78−99% isolated yields (Scheme 2). Several years ago Haupt and co-workers reported the synthesis of $[M(PNP\text{-}Ph)(CO_3)]$ (M = Cr, Mo, W) (**2e−4e**).[2]

We reported recently a comparatively time consuming three-step synthesis of W(0) complexes $[W(PNP)(CO)_3]$ via the dinuclear complex $[W(CO)_4(\mu\text{-}Br)Br]_2$, prepared in situ from $W(CO)_6$ and stoichiometric amounts of Br_2. Treatment of $[W(CO)_4(\mu\text{-}Br)Br]_2$ with the PNP ligands **1b,d,e** afforded the tungsten(II) intermediates $[W(PNP)(CO)_3Br]Br$, which subsequently were reduced with sodium amalgam to yield the W(0) complexes **4b**, **1d**, and **4e** in 56, 46, and 68% overall yields, respectively (Scheme 3).[9]

All complexes were fully characterized by a combination of ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectroscopy, IR spectroscopy, and elemental analysis. Characteristic features comprise, in the $^{13}C\{^1H\}$ NMR spectrum, two low-field triplet resonances (1:2 ratio) in the range of 240−196 ppm assignable to the carbonyl carbon atoms *trans* and *cis* to the pyridine nitrogen, respectively. The $^{31}P\{^1H\}$ NMR spectra exhibit singlet resonances with $^1J_{WP}$ coupling constants of 315−494 Hz in the case of tungsten complexes (Table 1).

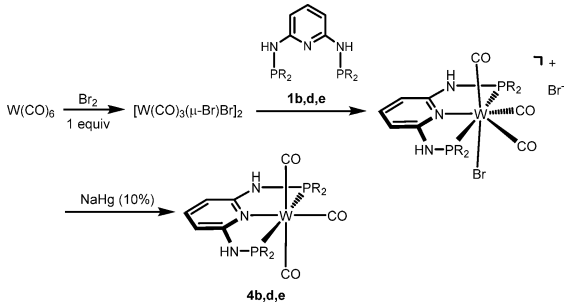
The tungsten−phosphorus coupling was observed as a doublet satellite due to ^{183}W (14% abundance with $I = 1/2$) superimposed over the dominant singlet. Both the carbonyl resonances (δ_{co}) and the phosphorus resonances (δ_P) exhibit a

Scheme 2. Synthesis of $[M(PNP)(CO)_3]$ (M = Cr, Mo, W) Complexes under Solvothermal Conditions in CH_3CN[a]



[a]Labeling of complexes refers to letters of ligands depicted here.

Scheme 3. Three-Step Synthesis of W(0) Complexes via $[W(CO)_4(\mu\text{-}Br)Br]_2$ and $[W(PNP)(CO)_3Br]Br$ Intermediates



significant upfield shift on going from Cr to Mo to W (Table 1). The IR spectra show, in most cases, the typical three strong to medium absorption bands of a *mer* CO arrangement in the range of 1985−1756 cm^{-1} assignable to one weaker symmetric and two strong asymmetric ν_{CO} stretching modes. The ν_{CO} frequencies, in particular the symmetric CO stretch, is indicative of increasing electron donor strengths of the PNP ligands and follow roughly the order PNP-BIPOL < PNP-Ph < PNP^{Me}-Ph < PNP-Cy < PNP-*i*Pr ≈ PNP^{Me}-*i*Pr < PNP-Et < PNP-*t*Bu (Table 2).

In addition to spectroscopic characterization, the solid-state structures of **2a,b,d** were determined by single-crystal X-ray diffraction. Structural views are depicted in Figures 1 and 2 with selected bond distances given in the captions (the structure of **2b** is provided in the Supporting Information).

The coordination geometry around the chromium center, as in the case of analogous Mo and W complexes,[2,6,7] corresponds to a distorted octahedron. In particular, the carbonyl−metal−

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Table 1. Selected $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ NMR Data of $[M(PNP)(CO)_3]$ (M = Cr, Mo, W) Complexes

	metal					
	Cr		Mo		W	
ligand	δ_{CO}, ppm	δ_P, ppm	δ_{CO}, ppm	δ_P, ppm	δ_{CO}, ppm	δ_P, ppm
1a	235.7	130.0	230.3	111.3	222.0	94.0
	223.8		213.8		208.2	
1b	236.2	146.7	231.4	143.6	221.1	128.5
	225.6		216.9		210.6	
1c	236.1	149.7	231.1	122.6	222.3	106.5
	225.8		216.4		211.3	
1d	238.7	164.4	233.1	161.9	224.7	147.2
	233.0		224.0		219.4	
1e	234.6	125.7	228.4	116.2	206.0	100.2
	220.6		211.2		196.6	
1f	235.2	171.5	230.8	159.0	222.5	144.0
	226.0		217.9		211.6	
1g	223.4	152.1	227.8	131.0	221.1	114.7
	220.8		211.9		207.4	
1h	234.8	147.8	229.9	129.5	221.7	112.7
	222.8		214.3		208.4	
1i	230.2	230.0	224.7	204.8	215.5	188.2
	217.9		208.4		201.4	
1j	236.2	193.5				
	223.9					

carbonyl angles of the CO ligands *trans* to one another deviate significantly from 180°. They vary with the bulkiness of the PR_2 moiety and decrease from 166.68(4)° in $[Cr(PNP\text{-}Et)(CO)_3]$ (**2a**) to 164.04(1)° in $[Cr(PNP\text{-}iPr)(CO)_3]$ (**2b**) to 155.22(5)° in $[Cr(PNP\text{-}tBu)(CO)_3]$ (**2d**). The same trend is found in the analogous Mo and W complexes: 171.1(8)° in $[Mo(PNP\text{-}Ph)(CO)_3]$ (**3d**), 166.03(5)° in $[Mo(PNP\text{-}iPr)(CO)_3]$ (**3b**), 162.93(7)° in $[Mo(PNP^{Me}\text{-}iPr)(CO)_3]$ (**3f**), 156.53(4)° in $[Mo(PNP\text{-}tBu)(CO)_3]$ (**3d**), 165.7(2)° in $[W(PNP\text{-}iPr)(CO)_3]$ (**4b**), and 156.46(9)° in $[W(PNP\text{-}tBu)(CO)_3]$ (**4d**). Accordingly, the bulkiness of the PNP ligands follows roughly the order (PNP-Ph ≈ PNP-Et < PNP-iPr_2 < PNP^{Me}-iPr < PNP-tBu).

In summary, we demonstrated that the solvothermal synthesis technique provides a powerful, simple, and practical synthetic method to afford group 6 PNP pincer carbonyl complexes of the type $[M(PNP)(CO)_3]$ (M = Cr, Mo, W) in high isolated yields in a short time. It has to be emphasized that in particular the short reaction times allow the use of thermally more sensitive ligands. As far as Cr and W complexes are concerned, these complexes are not readily accessible with conventional methods. Moreover, this study also allows a direct comparison of steric and electronic properties of group 6 metal PNP pincer complexes.

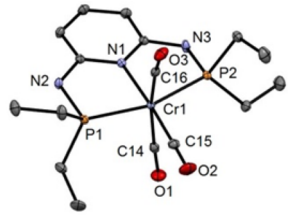

Figure 1. Structural view of $[Cr(PNP\text{-}Et)(CO)_3]$ (**2a**) showing 50% thermal ellipsoids (H atoms omitted for clarity). Selected bond lengths (Å) and bond angles (deg): Cr1−P1 2.2678(3), Cr1−P2 2.2724(3), Cr1−C14 1.8704(9), Cr1−C15 1.8295(10), Cr1−C16 1.18551(9), Cr1−N1 2.139(1); P1−Cr1−P2 160.03(1), C14−Cr1−C16 166.68(4).

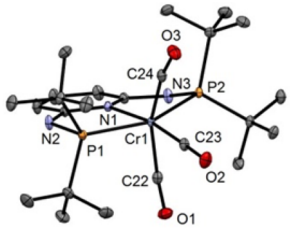

Figure 2. Structural view of $[Cr(PNP\text{-}tBu)(CO)_3]\cdot CH_3CN$ (**2d**·CH_3CN) showing 50% thermal ellipsoids (H atoms and CH_3CN omitted for clarity). Selected bond lengths (Å) and bond angles (deg): Cr1−P1 2.3627(4), Cr1−P2 2.3706(4), Cr1−22 1.864(1), Cr1−C23 1.793(1), Cr1−C24 1.867(1), Cr1−N1 2.187(1); P1−Cr1−P2 154.76(1), C22−Cr1−C24 155.22(5).

EXPERIMENTAL SECTION

General Considerations. All manipulations were performed under an inert atmosphere of argon by using Schlenk techniques or in an MBraun inert-gas glovebox. The solvents were purified according to standard procedures.[17] The deuterated solvents were purchased from Aldrich and dried over 4 Å molecular sieves. The ligands PNP-Et (**1a**),[18] PNP-iPr (**1b**),[4] PNP-Cy (**1c**),[19] PNP-tBu (**1d**),[4] PNP-Ph (**1e**),[2] PNP^{Me}-iPr (**1f**),[7] PNP^{Me}-Ph (**1g**),[5] PNP^{Ph}-Et (**1h**),[19] and PNP-BIPOL[4] (**1i**) were prepared according to the literature. The synthesis of PNP-SPEA (**1j**) is described in the Supporting Information. ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded on Bruker AVANCE-250 and AVANCE-400 spectrometers. ^1H and $^{13}C\{^1H\}$ NMR spectra were referenced internally to residual protio solvent and solvent resonances, respectively, and are reported relative to tetramethylsilane (δ 0 ppm). $^{31}P\{^1H\}$ NMR spectra were referenced

Table 2. Carbonyl Stretching Frequencies (ν_{CO}, cm^{-1}) of $[M(PNP)(CO)_3]$ (M = Cr, Mo, W) Complexes

	ligand									
metal	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**	**1j**
Cr	1905	1923	1913	1908	1973	1926	1954	1945	1972	1936
	1821	1785	1807	1792	1840	1795	1842	1807	1860	1827
	1763		1793	1756	1807	1774	1819			1811
Mo	1929	1936	1941	1922	1964	1936	1956	1949	1985	
	1840	1809	1828	1808	1858	1810	1911	1815	1876	
	1780	1790	1790	1771	1765	1795	1850			
W	1921	1929	1933	1914	1955	1928	1954	1934	1979	
	1834	1805	1807	1799	1847	1890	1839	1804	1858	
	1768	1784	1790	1759	1759	1797	1801			

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externally to H_3PO_4 (85%) (δ 0 ppm). Aluminum-capped 20 mL microwave vials from Biotage or VWR were used as reaction vessels.

General Procedure for the Synthesis of [M(PNP)(CO)$_3$] (M = Cr, Mo, W). A suspension of the metal hexacarbonyl (0.60 mmol) and 1.1 equiv of the respective PNP ligand (0.63 mmol) in acetonitrile (3 mL) were placed in a 20 mL sealed glass tube and stirred for 2 h at 135 °C (unless otherwise noted; see the Supporting Information), whereupon a clear solution was obtained. The reaction mixture was cooled to room temperature without stirring. In most cases the product was obtained as a crystalline material and was decanted and washed with *n*-hexane. In all other cases the solvent was removed under reduced pressure. The remaining solid was washed with *n*-hexane and dried under vacuum. Complexes **2a**−**j**, **3a**−**i**, and **4a**−**i** were obtained in 77−99% isolated yields.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.5b00940.

Experimental procedures, characterization data of all complexes, and crystallographic details of **2a**, **2b**·CH_3CN, and **2d**·CH_3CN (PDF)

Crystallographic data for **2a**, **2b**·CH_3CN, and **2d**·CH_3CN (CIF)

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Notes

The authors declare no competing financial interest.

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Title: A Convenient Solvothermal Synthesis of Group 6 PNP Pincer Tricarbonyl Complexes

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Synthesis, characterization and reactivity of vanadium, chromium, and manganese PNP pincer complexes

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ABSTRACT

The synthesis of a series of vanadium, chromium, and manganese PNP complexes of the types [M(PNP)Cl_3] (M = V, Cr) and [M(PNP)Cl_2] (M = Cr, Mn) is reported. Vanadium and manganese PNP pincer complexes are described for the first time. All complexes are characterized by their magnetic moments, elemental analysis, and ESI MS. In addition, some compounds are characterized by X-ray crystallography. In a preliminary study, these complexes catalyze the oxidative homo-coupling of aryl Grignard reagents in the presence of MeI as oxidizing agents to give symmetrical biaryls, but are inactive in Kumada cross-coupling reactions. The reactivity of V(III), Cr(III), Cr(II) and Mn(II) is compared with related Fe(II) and Co(II) complexes of the types [Fe(PNP-*i*Pr)Cl_2], and [Co(PNP-*i*Pr)Cl_2]. In all cases, good to excellent isolated yields are obtained. However, since the respective metal chlorides in the absence of PNP ligands exhibited comparable reactivities, the new PNP complexes offer no real advantage for this type of coupling reactions.

1. Introduction

Among the many ligand systems that can be found in the chemical literature pincer ligands play an important role and their complexes have attracted tremendous interest due to their high stability, activity and variability [1]. These tridentate ligands are often planar scaffolds consisting of neutral central pyridine backbone tethered to two, mostly bulky, two-electron donor groups by different spacers. In this family of ligands steric, electronic, and also stereochemical parameters can be manipulated by modifications of the substituents at the donor sites and/or the spacers. Accordingly, many applications of mostly precious second and third row transition metal pincer complexes in the fields of catalysis, molecular recognition and supramolecular chemistry were discovered turning this area into an intensively investigated subject in organometallic chemistry. As non-precious first-row transition metals are concerned, the chemistry of neutral pyridine-based iron [2–7] and cobalt [8,9] PNP complexes experienced an impressive upswing in recent years. Reports on chromium [10], nickel [11,12], and copper [13] PNP pincer complexes are still rare, while vanadium, manganese, and titanium PNP pincer complexes appear to be unknown as yet.

We are currently focusing on the chemistry of non-precious metal complexes containing PNP pincer ligands based on the 2,6-diaminopyridine scaffold, where the pyridine ring and the phosphine moieties are connected via NH, N-alkyl, or N-aryl linkers (Scheme 1) [14].

Herein we report on the synthesis, characterization and reactivity of a series of new vanadium, chromium, and manganese PNP complexes of the types [M(PNP)Cl_3] (M = V, Cr) and [M(PNP)Cl_2] (M = Cr, Mn). In a preliminary study, these complexes were found to catalyze the homo-coupling of PhMgBr in the presence of MeI or atmospheric oxygen as oxidizing agents, but were inactive for cross coupling reactions.

2. Results and discussion

Treatment of [$MCl_3(THF)_3$] (M = V, Cr) with the PNP ligands **1a**–**g** in THF affords the six-coordinate 14e and 15e complexes [V(PNP)Cl_3] (**2a**–**e**,**2g**) and [Cr(PNP)Cl_3] (**3a**–**f**) in high isolated yields (93–99%), respectively (Scheme 2). Likewise, the reaction of anhydrous MCl_2 (M = Cr, Mn) with 1 equiv of the PNP ligands **1a**–**g** in THF at room temperature afforded the five-coordinate 14e and 15e complexes [Cr(PNP)Cl_2] (**4a**–**f**) and [Mn(PNP)Cl_2] (**5a**–**e**,**5g**) in 92–98% isolated yields (Scheme 3). All complexes display large paramagnetic shifted and very broad ^{1}H NMR signals and thus were not

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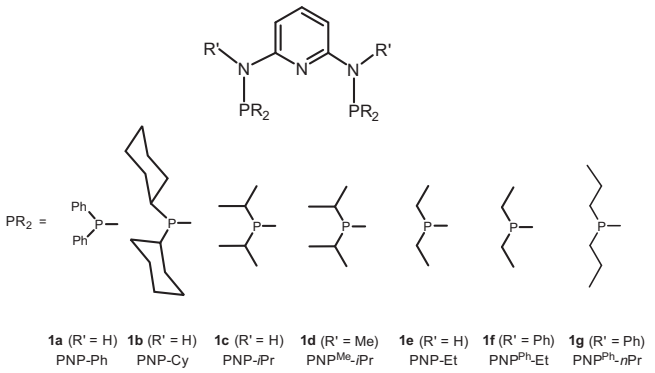
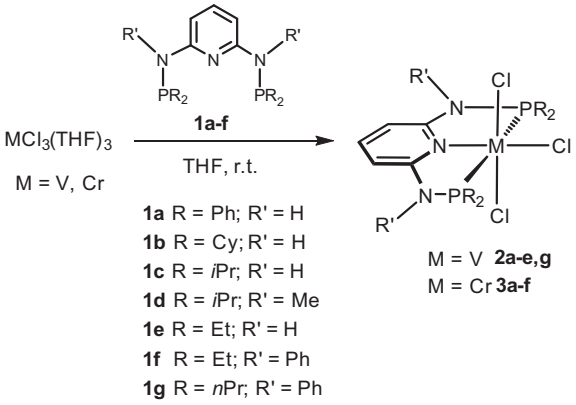


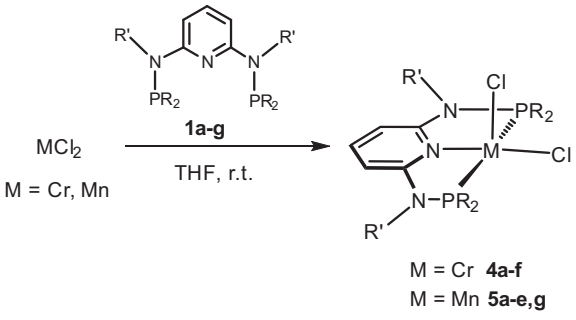
Scheme 1. PNP ligands used in this work (labeling of complexes refers to letters of ligands depicted here).



Scheme 2. Synthesis of V(III) and Cr(III) complexes [V(PNP)Cl_3] (**2**) and [Cr(PNP)Cl_3] (**3**).

very informative. $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ NMR could not be detected at all. Complexes **2–5** exhibit solution magnetic moments μ_{eff} of 2.7–2.9 μ_B, 3.9 μ_B, 4.9–5.0 μ_B, and 5.9–6.0 μ_B (Evans method, in CH_3OH) [15], in agreement with d^2, d^3, high spin d^4, and high spin d^5 electron configurations, respectively.

In order to unequivocally establish the ligand arrangement around the metal centers, the solid state structure of complexes [V(PNP-Ph)Cl_3] (**2a**), [V(PNP^{Ph}-*n*Pr)Cl_3] (**2g**), [Cr(PNP-*i*Pr)Cl_3] (**3d**), [Cr(PNP^{Me}-*i*Pr)Cl_2] (**4d**), and [Mn(PNP-*i*Pr)Cl_2] (**5c**) was determined by X-ray diffraction. Representations of these molecules are shown in Figs. 1–5 with selected metrical parameters given in Table 1. The structures of **2a**, **2g** and **3d** show a distorted-octahedral trivalent vanadium and chromium center surrounded by three meridionally placed donor atoms of the PNP ligand. The three chlorine atoms



Scheme 3. Synthesis of Cr(II) and Mn(II) complexes [Cr(PNP)Cl_2] (**4**) and [Mn(PNP)Cl_2] (**5**).

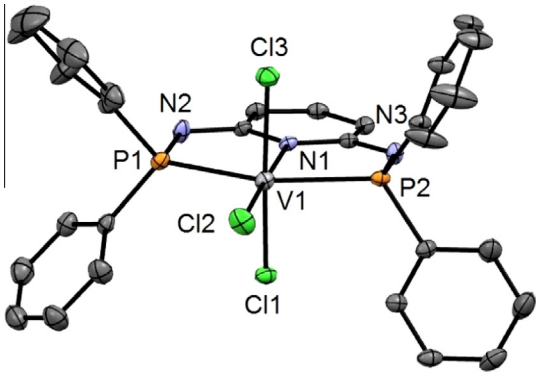


Fig. 1. Structural view of [V(PNP-Ph)Cl_3]·3.5$(CH_3)_2CO$ (**2a**·3.5$(CH_3)_2CO$) showing 50% displacement ellipsoids (H atoms and solvent molecules omitted for clarity).

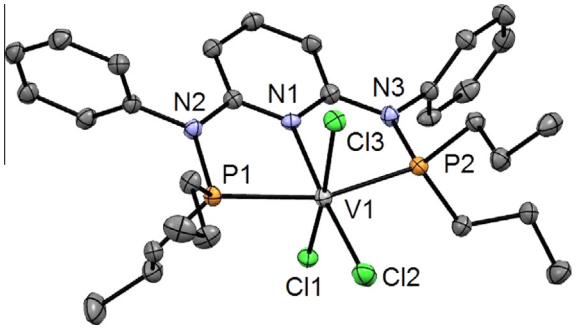


Fig. 2. Structural view of [V(PNP^{Ph}-nPr)Cl_3] (**2g**) showing 50% displacement ellipsoids (H atoms omitted for clarity).

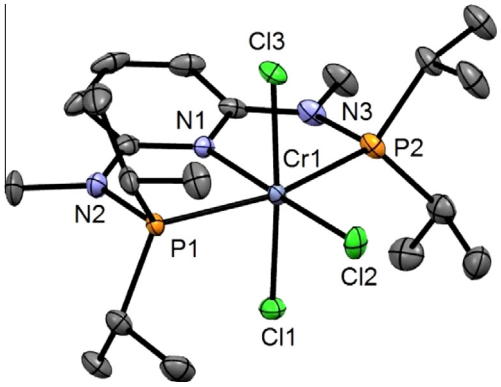


Fig. 3. Structural view of [Cr(PNP^{Me}-*i*Pr)Cl_3] (**3d**) showing 50% displacement ellipsoids (H atoms and a second independent complex are omitted for clarity).

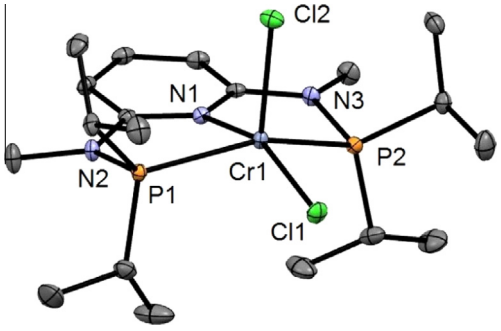


Fig. 4. Structural view of [Cr(PNP^{Me}-*i*Pr)Cl_2]·0.5CH_2Cl_2 (**4d**·0.5CH_2Cl_2) showing 50% displacement ellipsoids (H atoms and solvent molecules omitted for clarity).

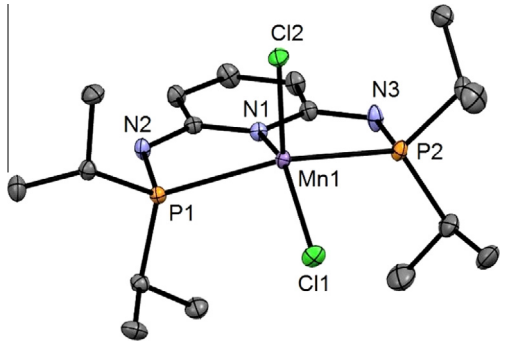


Fig. 5. Structural view of [Mn(PNP-*i*Pr)Cl_2]·THF (**5c**·THF) showing 50% displacement ellipsoids (H atoms and solvent molecules omitted for clarity).

occupy the three remaining positions. In all complexes the Cl1–metal–Cl3 angles deviate from linearity being 165.92(2)°, 168.13 (3)°, and 172.30(3)°, respectively, and are contracted towards the pyridine ring. The same pattern is observed for the P1–metal–P2 angles which are 156.25(2)°, 158.38(3)°, and 162.41(3)°, respectively. The coordination geometry of the metal center in **4d** and **5c** is distorted square pyramidal with the chromium and manganese atoms lying 0.463(1) and 0.416(1) Å out of the pyridine plane. For comparison, in [Fe(PNP-*i*Pr)Cl_2] [14b] and [Fe(PNP^{Me}-*i*Pr)Cl_2] [14k] these values are 0.288(1) and 0.708(1) Å. The Cr–Cl1 (basal) bond length is significantly shorter (2.3381(5) Å) than the distance to the apical chlorine (Cr–Cl2 2.4684(5) Å). This order is reversed in **5c**, where the Mn–Cl1 (basal) bond length is slightly longer (2.3940(5) Å) than the Mn-Cl2 distance being 2.3658(5) Å as well as for [Fe(PNP^{Me}-*i*Pr)Cl_2] (2.347(1) versus 2.301(1) Å) and [Fe(PNP-*i*Pr)Cl_2] (2.3708(7) versus 2.3040(6) Å) (Table 1). Thus, the metal–Cl2 (apical) bond distance is most sensitive to the nature of the metal decreasing in the order Cr(II) > Mn(II) > Fe(II) > Co(II).

Since ESI-MS enables not only the detection and the study of reaction substrates and products but also short-lived reaction intermediates and decomposition products as they are present in solution, representative PNP complexes were investigated by means of this technique. Methanol solutions of [V(PNP^{Me}-*i*Pr)Cl_3] (**2d**), [Cr(PNP-*i*Pr)Cl_3] (**3c**), [Cr(PNP^{Me}-*i*Pr)Cl_2] (**4d**), [Mn(PNP-*i*Pr)Cl_2] (**5c**), and, for comparison, [Fe(PNP-*i*Pr)Cl_2] and [Co(PNP-*i*Pr)Cl_2] in the presence of NaCl were subjected to ESI-MS analysis in the positive ion mode. The full scan ESI-MS spectra are depicted in Fig. 6 (spectra **A** – **F**).

In the case of the V(III) complex **2d**, the most abundant signal at *m*/*z* 443.1 corresponds to an oxidized mono chloro V(IV) species bearing an oxo ligand [M(V^{4+})+O-2Cl]$^+$ emphasizing the sensitivity of this complex towards oxygen (spectrum **A**). It has to be noted that, even though solutions are prepared under an argon atmosphere, traces of oxygen in the mass spectrometer are unavoidable. For the Cr(III) complex **3c** the sodiated complex [M(Cr^{3+})+Na]$^+$ and also [M(Cr^{3+})−Cl]$^+$), where one chloride ligand is lost, were found as the main fragment ions in the full mass spectrum at *m*/*z* 521.1 and 463.1, respectively, (spectrum **B**).

In the divalent M(II) series, the various fragments are shown in Scheme 4. The Cr(II) complex **4d** undergoes oxidation to form Cr (III) complexes (spectrum **C**). Signals of the formal NaCl adduct [M(Cr^{3+})+NaCl]$^+$ and [M(Cr^{3+})]$^+$ are detected at *m*/*z* 549.1 and 491.1, respectively. In the case of Mn(II), the fully intact but sodiated complex [M(Mn^{2+})+Na]$^+$ was observed at *m*/*z* 489.1 (spectrum **D**). Both Fe(II) and Co(II) complexes [Fe(PNP-*i*Pr)Cl_2] and [Co(PNP-*i*Pr)Cl_2] lose one chloride ligand giving rise to the cationic fragments [M(Fe^{2+})−Cl]$^+$ and [M(Co^{2+})−Cl]$^+$ at *m*/*z* 432.1 and 435.1 (spectra **E**, **F**). In addition, the iron complex forms a methanol adduct [M(Fe^{2+})+CH_3OH−Cl]$^+$ (*m*/*z* 464.1) revealing the high affinity of CH_3OH towards Fe(II) complexes. Similar observations were made recently with Fe(II) PNP pincer complexes based on *R*,*R*-TADDOL in combination with bulky *i*Pr and *t*Bu substituents [14i].

Having a series of well-defined V(III), Cr(III), Cr(II), and Mn(II) PNP complexes in hands, we decided to investigate their catalytic activity in the Kumada cross-coupling of PhMgBr and aryl halides. Unfortunately, no cross coupling took place and only homo-coupling product (biphenyl) was obtained. Thus, complexes **2a–c**, **3c**, **4a–d**, and **5c** as well as [Fe(PNP-*i*Pr)Cl_2], and [Co(PNP-*i*Pr)Cl_2] were reacted with PhMgBr in the presence of MeI in THF as solvent at room temperature. For comparison, also the chloride salts of V (III), Cr(III), Cr(II), Mn(II), Fe(II) and Co(II) in the absence of PNP ligands were tested as catalysts. This reaction constitutes an easy and efficient method to obtain symmetrical biaryl compounds. In recent years, several non-precious metal complexes were found to catalyze this reaction including manganese [16,17] and iron complexes [17,18]. As oxidants typically 1,2-dichloroethane or atmospheric oxygen are used. As shown in Table 2, excellent isolated yields (62–93%) of biphenyl were obtained by using 0.1 mol % of catalyst with very short reaction times (15 min with MeI and 45 min in the presence of dry air). Yields up to 93% were achieved with Cr(II) PNP complexes and MeI. It has to be noted that all reactions with MeI proceed with gas evolution presumably due to the formation of ethane. The reactions with the chloride salts were less efficient in the case of V(III), Cr(III), and Mn(II), but only slightly worse with Cr(II), Fe(II), and Co(II) chlorides. Accordingly, the new PNP complexes offer no real advantage for homo coupling reactions.

[Cr(PNP-*i*Pr)Cl_2] (**4c**) was also tested as catalyst for the oxidative homo-coupling of several aryl magnesium bromides and PhMgCl with MeI as oxidant. The results of this study are presented in Table 3. With **4c** and aryl magnesium bromides excellent yields of symmetrical biaryls were obtained (entries 1 and 3–6, 62–91%). Also with PhMgCl biphenyl was formed in high yields but required a slightly longer reaction time (entry 2).

Table 1
Selected bond distances and angles (U+00C5, °) of the square pyramidal high-spin Cr(II), Mn(II), Fe(II), and Co(II) complexes [Cr(PNP^{Me}-*i*Pr)Cl_2] (**4d**), [Mn(PNP-*i*Pr)Cl_2] (**5c**), [Fe(PNP-*i*Pr)Cl_2] [14b], [Fe(PNP^{Me}-*i*Pr)Cl_2] [14k], and [Co(PNP-Ph)Cl_2] [2c].

	4d	5c	Fe(PNP-*i*Pr)Cl_2	Fe(PNP^{Me}-*i*Pr)Cl_2	Co(PNP-Ph)Cl_2
M–Cl1 (basal)	2.3381(5)	2.3940(5)	2.3708(7)	2.347(1)	2.247(2)
M–Cl2 (apical)	2.4684(5)	2.3658(5)	2.3040(6)	2.301(1)	2.279(2)
M–N1	2.1270(9)	2.356(5)	2.250(2)	2.290(3)	2.097(5)
M–P1	2.4257(5)	2.5931(5)	2.4631(7)	2.464(1)	2.550(2)
M–P2	2.4301(5)	2.5794(5)	2.4844(7)	2.443(1)	2.542(2)
Cl1–M–Cl2	101.10(1)	113.19(2)	107.60(3)	106.71(4)	117.68(8)
P1–M–P2	148.31(2)	142.16(1)	146.56(3)	140.89(4)	155.36(6)
N1–M–Cl2	157.10(3)	139.71(1)	144.13(6)	145.45(8)	130.4(2)

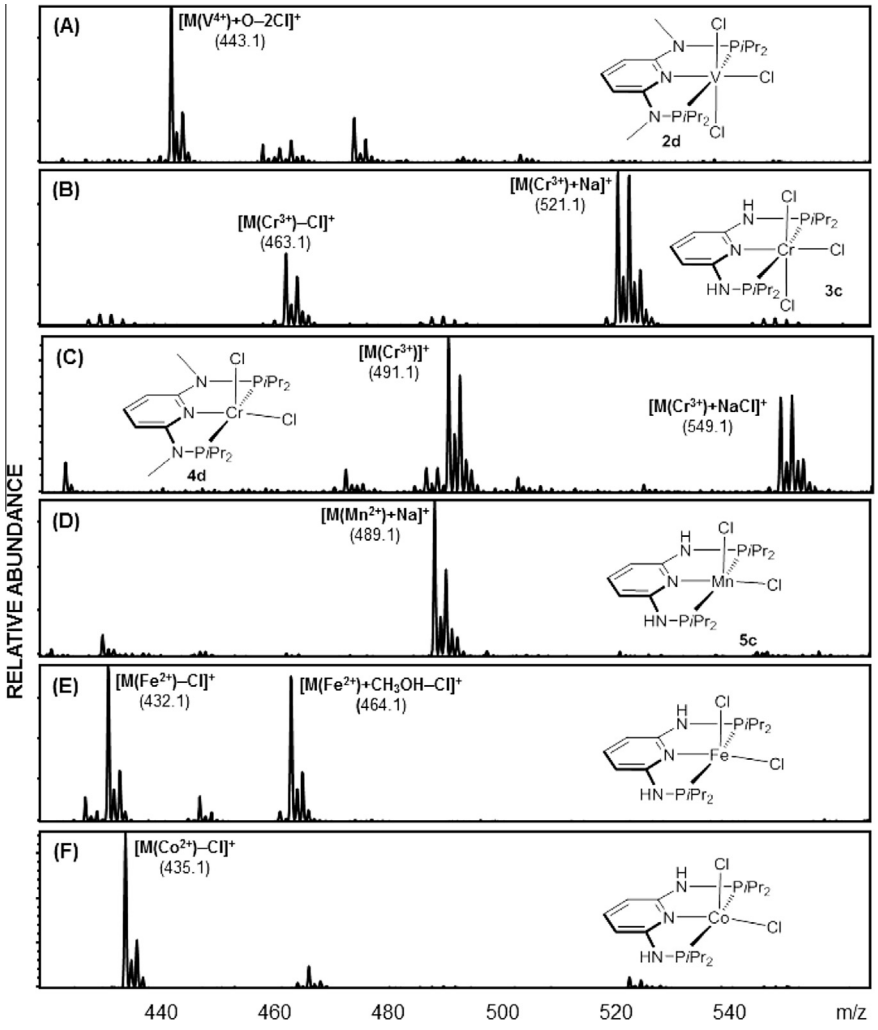


Fig. 6. Positive-ion ESI full scan mass spectra of complexes **2d**, **3c**, **4d**, **5c**, [Fe(PNP-*i*Pr)Cl_2], and [Co(PNP-*i*Pr)Cl_2]. All mass calculations and mass assignments are based on the most abundant metal isotope (^{51}V, ^{52}Cr, ^{55}Mn, ^{56}Fe, ^{59}Co-isotopes) and the Cl isotope of lowest mass (^{35}Cl).

3. Conclusion

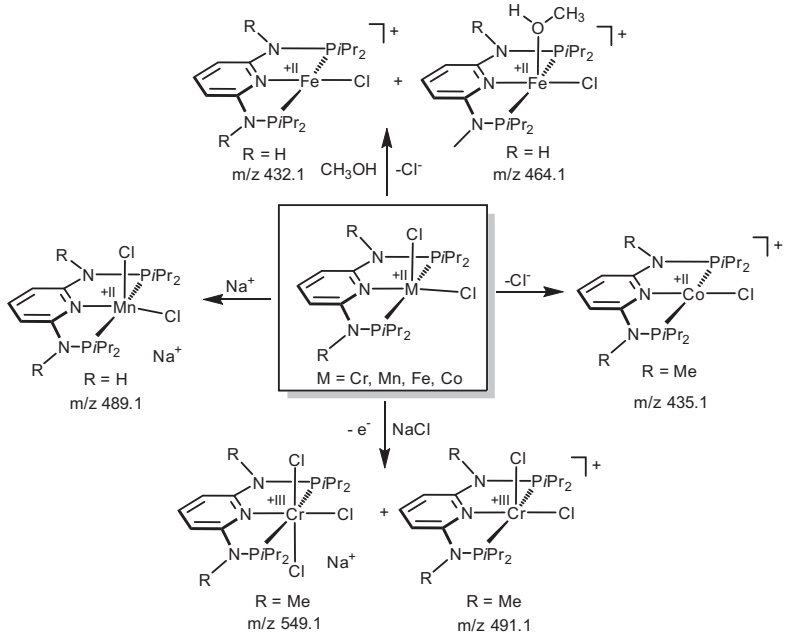
In sum, we describe here the synthesis of a series of vanadium, chromium, and manganese PNP complexes of the types [M(PNP)Cl_3] (M = V, Cr) and [M(PNP)Cl_2] (M = Cr, Mn). Vanadium and manganese PNP pincer complexes were as yet not reported. All complexes are characterized by their magnetic moments, elemental analysis and ESI MS. In addition, some compounds were characterized by X-ray crystallography. In a preliminary study, these complexes catalyze the oxidative homo-coupling of aryl Grignard reagents in the presence of MeI as oxidizing agents to give symmetrical biaryls, but are inactive in Kumada cross-coupling reactions. The reactivity of V(III), Cr(III), Cr(II) and Mn(II) is compared with related Fe(II) and Co(II) complexes of the types [Fe(PNP-*i*Pr)Cl_2], and [Co(PNP-*i*Pr)Cl_2]. In all cases, good to excellent isolated yields are obtained. However, since the respective metal chlorides in the absence of PNP ligands exhibited comparable reactivities, the new PNP complexes offer no real advantage for this type of coupling reactions.

4. Experimental

4.1. General

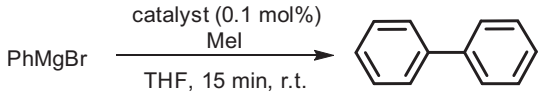
All manipulations were performed under an inert atmosphere of argon by using Schlenk techniques or in an MBraun inert-gas glovebox. The solvents were purified according to standard procedures [19]. The deuterated solvents were purchased from Aldrich and dried over 4 Å molecular sieves. The ligands N,N′-bis(diphenylphosphino)-2,6-diaminopyridine (PNP-Ph) (**1a**) [10a] N,N′-bis(dicyclohexyl)-2,6-diaminopyridine (PNP-Cy) (**1b**) [14k] N,N′-bis(diisopropylphosphino)-2,6-diaminopyridine (PNP-*i*Pr) (**1c**) [14a], N,N′-bis(diisopropylphosphino)-N,N′-dimethyl-2,6-diaminopyridine (PNP^{Me}-*i*Pr) (**1d**) [20], N,N′-bis(diethylphosphino)-2,6-diaminopyridine (PNP-Et) (**1e**), N,N′-bis(ethylphosphino)-N,N′-diphenyl-2,6-diaminopyridine (PNP^{Ph}-Et) (**1f**), and N,N′-bis(*n*-propylphosphino)-N,N′-diphenyl-2,6-diaminopyridine (PNP^{Ph}-*n*Pr) (**1g**) [14h] and complexes [Fe(PNP-*i*Pr)Cl_2] [14b], and [Co(PNP-*i*Pr)Cl_2] [8d] were prepared according to the literature. ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra were recorded on Bruker AVANCE-250, AVANCE-300 DPX, and AVANCE-400 spectrometers. ^{1}H and ^{13}C{^{1}H} NMR spectra were referenced internally to residual protio-solvent, and solvent resonances, respectively, and are reported relative to tetramethylsilane (δ = 0 ppm). ^{31}P{^{1}H} NMR spectra were referenced externally to H_3PO_4 (85%) (δ = 0 ppm). Room-temperature solution (CH_3OH) magnetic moments were determined by ^{1}H NMR spectroscopy using the method of Evans [15].

All mass spectrometric measurements were performed on an Esquire 3000^{plus} 3D-quadrupole ion trap mass spectrometer (Bruker Daltonics, Bremen, Germany) in positive-ion mode by means of electrospray ionization (ESI). Mass calibration was done with a



Scheme 4. Fragmentation pathways of M(II) complexes [M(PNP^{R}-*i*Pr)Cl$_2$] (M = Cr, Mn, Fe, Co; R = H or Me) in CH_3OH in the presence of NaCl as established by ESI MS experiments.

Table 2
Catalyst screening in the homo-coupling of PhMgBr with MeI[a] as oxidizing agents.



Oxidation state	Catalyst	Additive	*t* (min)	Yield[b] (%)
V(III)	V(PNP-Ph)Cl$_3$ (**2a**)	MeI	15	81
V(III)	V(PNP-*i*Pr)Cl$_3$ (**2c**)	MeI	15	85
V(III)	V(PNP^{Me}-*i*Pr)Cl$_3$ (**2d**)	MeI	15	85
V(III)	VCl$_3$	MeI	15	59
Cr(III)	Cr(PNP-*i*Pr)Cl$_3$ (**3c**)	MeI	15	82
Cr(III)	CrCl$_3$	MeI	15	33
Cr(II), h. s.[c]	Cr(PNP-Ph)Cl$_2$ (**4a**)	MeI	15	89
Cr(II), h. s.	Cr(PNP-Cy)Cl$_2$ (**4b**)	MeI	15	92
Cr(II), h. s.	Cr(PNP-*i*Pr)Cl$_2$ (**4c**)	MeI	15	91
Cr(II), h. s.	Cr(PNP^{Me}-*i*Pr)Cl$_2$ (**4d**)	MeI	15	93
Cr(II), h. s.	CrCl$_2$	MeI	15	73
Mn(II), h. s.	Mn(PNP-*i*Pr)Cl$_2$ (**5c**)	MeI	15	81
Mn(II), h. s.	MnCl$_2$	MeI	15	38
Fe(II), h. s.	Fe(PNP-*i*Pr)Cl$_2$	MeI	15	73
Fe(II), h. s.	FeCl$_2$	MeI	15	69
Co(II), h. s.	Co(PNP-*i*Pr)Cl$_2$	MeI	15	88
Co(II), h. s.	CoCl$_2$	MeI	15	71

[a] The reactions were carried out using PhMgBr (10.5 mmol), MeI (10.0 mmol), and catalyst (0.01 mmol) in THF (8.5 mL).
[b] Isolated yields after column chromatography.
[c] h. s. = high spin.

commercial mixture of perfluorinated trialkyl-triazines (ES Tuning Mix, Agilent Technologies, Santa Clara, CA, USA). All analytes were dissolved in methanol "hypergrade for LC–MS Lichrosolv" quality (Merck, Darmstadt, Germany) to form a concentration of roughly 1 mg/mL and doped with sodium chloride to suppress dissociation of chloride ligands from the metal complexes and/or to promote the corresponding $[M+Na]^+$ or $[M+NaCl]^+$ (formally added by oxidation of the central metal cation by a one electron oxidation step) ion formation. Direct infusion experiments were carried out using a Cole Parmer model 74900 syringe pump (Cole Parmer Instruments, Vernon Hills, IL, USA) at a flow rate of 2 μL/min. Full scan and MS/MS (low energy CID)-scans were measured in the range *m*/*z* 100–1100 with the target mass set to *m*/*z* 1000. Further experimental conditions include: drying gas temperature: 150 °C; capillary voltage: −4 kV; skimmer voltage: 40 V; octapole and lens voltages: according to the target mass set. All mass calculations are based on the most abundant metal isotopes (^{50}V, ^{52}Cr, ^{55}Mn, ^{56}Fe, ^{59}Co-isotopes) and the Cl isotope of lowest mass (^{35}Cl). Mass spectra were averaged during data acquisition time of 1–2 min and one analytical scan consisted of five successive micro scans resulting in 50 and 100 analytical scans, respectively, for the final full scan mass spectrum.

4.2. Synthesis

4.2.1. [$CrCl_3(THF)_3$]

Anhydrous $CrCl_3$ (20 g, 126.3 mmol) and Zn powder (200 mg, 3.05 mmol) were mixed in a glass frit and extracted with dry THF (400 mL) in a Soxhlet extractor under inert conditions for 48 h. The extracted suspension was reduced to 100 mL, the purple powder was collected by filtration and dried under reduced pressure. Yield: 33.5 g (89%) [21].

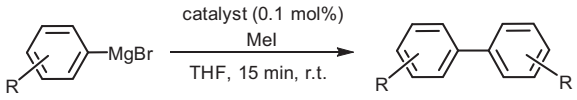
4.2.2. [V(PNP-Ph)Cl_3] (***2a***)

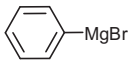
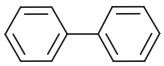
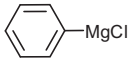
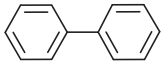
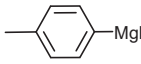
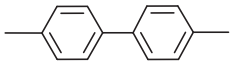
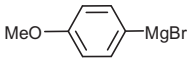
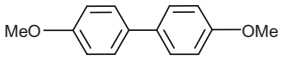
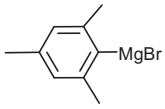
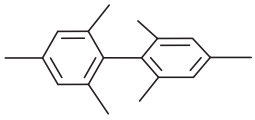
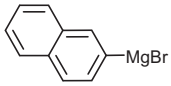
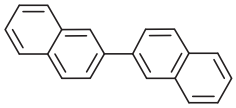
A suspension of PNP-Ph (**1a**) (477 mg, 1.0 mmol) and $VCl_3(THF)_3$ (374 mg, 1.0 mmol) in THF (15 mL) was stirred for 3 h. The suspension was then reduced to 4 mL and *n*-hexane (15 mL) was added for precipitation. The solid was collected on a glass frit as a brown powder, washed with *n*-hexane, and dried under reduced pressure. Yield: 628 mg (99%). *Anal.* Calc. for $C_{29}H_{25}Cl_3N_3P_2V$ (634.78): C, 54.87; H, 3.97; N, 6.62. Found: C, 54.95; H, 4.06; N, 6.54%. μ_{eff} = 2.7 μ_B.

4.2.3. [V(PNP-Cy)Cl_3] (***2b***)

This complex was prepared analogously to **2a** using PNP-Cy (**1b**) (502 mg, 1.0 mmol) and $VCl_3(THF)_3$ (374 mg, 1.0 mmol) as

Table 3
Homo-coupling of aryl magnesium halides with MeI as oxidizing agents utilizing [Cr(PNP-*i*Pr)Cl_2] (**4c**) as catalysts.[a]



Entry	Catalyst	RMgX	Product	Additive	*t* (min)	Yield[b] (%)
1	Cr(PNP-*i*Pr)Cl_2			MeI	15	91
2				MeI	30	79
3				MeI	15	91
4				MeI	15	65
5				MeI	15	62
6				MeI	15	83

[a] The reactions were carried out using ArMgX (10.5 mmol), MeI (10.0 mmol), and catalyst (0.01 mmol) in THF (8.5 mL).
[b] Isolated yields after column chromatography.

starting materials. Yield: 633 mg (96%). *Anal.* Calc. for $C_{29}H_{49}Cl_3N_3P_2V$ (658.97): C, 52.86; H, 7.49; N, 6.38. Found: 52.92; H, 7.55; N, 6.31%. μ_{eff} = 2.7 μ_B.

*4.2.4. [V(PNP-iPr)Cl_3] (**2c**)*

This complex was prepared analogously to **2a** using PNP-*i*Pr (**1c**) (341 mg, 1.0 mmol) and $VCl_3(THF)_3$ (374 mg, 1.0 mmol) as starting materials. Yield: 450 mg (95%). *Anal.* Calc. for $C_{17}H_{33}Cl_3N_3P_2V$ (498.71): C, 40.94; H, 6.67; N, 8.43. Found: C, 41.10; H, 6.68; N, 8.52%. μ_{eff} = 2.7 μ_B.

*4.2.5. [V(PNP^{Me}-iPr)Cl_3] (**2d**)*

This complex was prepared analogously to **2a** using PNP^{Me}-*i*Pr (**1d**) (370 mg, 1.0 mmol) and $VCl_3(THF)_3$ (374 mg, 1.0 mmol) as starting materials. Yield: 511 mg (97%). Anal. Calc. for $C_{19}H_{37}Cl_3N_3P_2V$ (526.77): C, 43.32; H, 7.08; N, 7.98. Found: C, 43.34; H, 7.09; N, 7.97. μ_{eff} = 2.7 μ_B.

*4.2.6. [V(PNP-Et)Cl_3] (**2e**)*

This complex was prepared analogously to **2a** using PNP-Et (**1e**) (285 mg, 1.0 mmol) and $VCl_3(THF)_3$ (374 mg, 1.0 mmol) as starting materials. Yield: 438 mg (99%). *Anal.* Calc. for $C_{13}H_{25}Cl_3N_3P_2V$ (442.61): C, 35.28; H, 5.69; N, 9.49. Found: C, 35.31; H, 5.68; N, 9.51%. μ_{eff} = 2.8 μ_B.

*4.2.7. [V(PNP^{Ph}-Pr)Cl_3] (**2g**)*

This complex was prepared analogously to **2a** using PNP^{Ph}-*n*Pr (**1g**) (494 mg, 1.0 mmol) and $VCl_3(THF)_3$ (374 mg, 1.0 mmol) as starting materials. Yield: 631 mg (97%). *Anal.* Calc. for $C_{29}H_{41}Cl_3N_3P_2V$ (650.90): C, 53.51; H, 6.35; N, 6.46. Found: 53.48; H, 6.32; N, 6.49%. μ_{eff} = 2.8 μ_B.

*4.2.8. [Cr(PNP-Ph)Cl_3] (**3a**)*

A solution of PNP-Ph (**1a**) (477 mg, 1.0 mmol) and $CrCl_3(THF)_3$ (374 mg, 1.0 mmol) in THF (10 mL) was stirred for 16 h at 50 °C. The purple solution was then reduced to 2 mL and *n*-hexane (10 mL) was added for precipitation. The purple powder was collected on a glass frit, washed with *n*-hexane, dried under vacuum. Yield: 616 mg (97%). *Anal.* Calc. for $C_{29}H_{25}Cl_3CrN_3P_2$ (635,83): C, 54.76; H, 3.95; N, 6.60. Found: C, 54.65; H, 3.89; N, 6.70%. μ_{eff} = 3.9μ_B.

*4.2.9. [Cr(PNP-Cy)Cl_3] (**3b**)*

This complex was prepared analogously to **3a** using PNP-Cy (**1b**) (501 mg, 1.0 mmol) and $CrCl_3(THF)_3$ (374 mg, 1.0 mmol). Yield: 620 mg (94%). *Anal.* Calc. for $C_{29}H_{49}Cl_3CrN_3P_2$ (660.03): C, 52.77; H, 7.48; N, 6.36. Found: C, 52.83; H, 7.65; N, 6.21%. μ_{eff} = 3.9 μ_B.

*4.2.10. [Cr(PNP-iPr)Cl_3] (**3c**)*

This complex was prepared analogously to **3a** using PNP-*i*Pr (**1c**) (341 mg, 1.0 mmol) and $CrCl_3(THF)_3$ (374 mg, 1.0 mmol). Yield: 464 mg (93%). *Anal.* Calc. for $C_{17}H_{33}Cl_3CrN_3P_2$ (499.77): C, 40.85; H, 6.65; N, 8.41. Found: C, 40.85; H, 6.65; N, 8.41%. μ_{eff} = 3.9 μ_B.

*4.2.11. [Cr(PNP^{Me}-iPr)Cl_3] (**3d**)*

This complex was prepared analogously to **3a** using PNP-*i*Pr (**1d**) (369 mg, 1.0 mmol) and $CrCl_3(THF)_3$ (374 mg, 1.0 mmol) as starting materials. Yield: 506 mg (96%). *Anal.* Calc. for $C_{19}H_{37}Cl_3CrN_3P_2$ (527.82): C, 43.23; H, 7.07; N, 7.95. Found: C, 43.15; H, 7.15; N, 8.00%. μ_{eff} = 3.9 μ_B.

*4.2.12. [Cr(PNP^{Ph}-Et)Cl$_3$] (**3f**)*

This complex was prepared analogously to **3a** using PNP^{Ph}-Et (**1f**) (437 mg, 1.0 mmol) and $CrCl_3(THF)_3$ (374 mg, 1.0 mmol) as starting materials. Yield: 567 mg (93%). *Anal.* Calc. for $C_{25}H_{33}Cl_2CrN_3P_2$ (595.84): C, 50.37; H, 5.57; N, 7.04. Found: C, 50.15; H, 5.45; N, 7.11%. μ_{eff} = 3.9 μ_B.

*4.2.13. [Cr(PNP-Ph)Cl$_2$] (**4a**)*

A solution of PNP-Ph (**1a**) (477 mg, 1.0 mmol) and $CrCl_2$ (122 mg, 1.0 mmol) in THF (10 ml) was stirred for 16 h. The green solution was reduced to 2 mL and *n*–hexane (10 mL) was added for precipitation. The dark green powder was collected on a glass frit, and dried under reduced pressure. Yield: 557 mg (95%). *Anal.* Calc. for $C_{29}H_{25}Cl_2CrN_3P_2$ (600.38): C, 58.01; H, 4.19; N, 7.00. Found: C, 58.15; H, 4.15; N, 6.91%. μ_{eff} = 5.0 μ_B.

*4.2.14. [Cr(PNP-Cy)Cl$_2$] (**4b**)*

This complex was prepared analogously to **4a** using PNP-Cy (**1b**) (501 mg, 1.0 mmol) and $CrCl_2$ (122 mg, 1.0 mmol) as starting materials. Yield: 607 mg (97%). *Anal.* Calc. for $C_{29}H_{49}Cl_2CrN_3P_2$ (624.58): C, 55.77; H, 7.90; N, 6.72. Found: C, 55.85; H, 7.65; N, 6.82%. μ_{eff} = 5.0 μ_B.

*4.2.15. [Cr(PNP-iPr)Cl$_2$] (**4c**)*

This complex was prepared analogously to **4a** using PNP-*i*Pr (**1c**) (341 mg, 1.0 mmol) and $CrCl_2$ (122 mg, 1.0 mmol) as starting materials. Yield: 441 mg (95%). *Anal.* Calc. for $C_{17}H_{33}Cl_2CrN_3P_2$ (464.32): C, 43.91; H, 7.14; N, 9.04. Found: C, 43.99; H, 7.25; N, 9.11%. μ_{eff} = 5.0 μ_B.

*4.2.16. [Cr(PNP^{Me}-iPr)Cl$_2$] (**4d**)*

This complex was prepared analogously to **4a** using PNP^{Me}-*i*Pr (**1d**) (369 mg, 1.0 mmol) and $CrCl_2$ (122 mg, 1.0 mmol) as starting materials. Yield: 472 mg (96%). *Anal.* Calc. for $C_{19}H_{37}Cl_2CrN_3P_2$ (492.37): C, 46.34; H, 7.56; N, 8.52. Found: C, 46.25; H, 7.61; N, 8.62%. μ_{eff} = 5.0 μ_B.

*4.2.17. [Cr(PNP^{Ph}-Et)Cl$_2$] (**4f**)*

This complex was prepared analogously to **4a** using PNP^{Ph}-Et (**1f**) (437 mg, 1.0 mmol) and $CrCl_2$ (122 mg, 1.0 mmol) as starting materials. Yield: 515 mg (92%). *Anal.* Calc. for $C_{25}H_{33}Cl_2CrN_3P_2$ (560.40): C, 53.57; H, 5.94; N, 7.49. Found: C, 53.65; H, 5.85; N, 7.44%. μ_{eff} = 5.0 μ_B.

*4.2.18. [Mn(PNP-Ph)Cl$_2$] (**5a**)*

PNP-Ph (**1a**) (477 mg, 1.0 mmol) and anhydrous $MnCl_2$ (126 mg, 1.0 mmol) were suspended in THF (10 mL) and stirred for 16 h. The suspension was reduced to 4 mL and *n*-hexane (20 mL) was added for precipitation. The off-white powder was collected by filtration and dried under reduced pressure. Yield: 579 mg (96%). *Anal.* Calc. for $C_{29}H_{25}Cl_2MnN_3P_2$ (603.32): C, 57.73; H, 4.18; N, 6.96. Found: C, 57.71; H, 4.17; N, 6.94%. μ_{eff} = 6.0 μ_B.

*4.2.19. [Mn(PNP-Cy)Cl$_2$] (**5b**)*

This complex was prepared analogously to **5a** using PNP-Cy (**1b**) (501 mg, 1.0 mmol) and anhydrous $MnCl_2$ (126 mg, 1.0 mmol) as starting materials. Yield: 596 mg (95%). *Anal.* Calc. for $C_{29}H_{49}Cl_2MnN_3P_2$ (627.51): C, 55.51; H, 7.87; N, 6.70. Found: C, 55.56; H, 7.84; N, 6.74%. μ_{eff} = 5.9 μ_B.

*4.2.20. [Mn(PNP-iPr)Cl$_2$] (**5c**)*

This complex was prepared analogously to **5a** using PNP-*i*Pr (**1c**) (341 mg, 1.0 mmol) and anhydrous $MnCl_2$ (126 mg, 1.0 mmol) as starting materials. Yield: 450 mg (96%). *Anal.* Calc. for $C_{17}H_{33}Cl_2MnN_3P_2$ (467.26): C, 43.70; H, 7.12; N, 8.99. Found: C, 43.82; H, 7.15; N, 9.05%. μ_{eff} = 6.1 μ_B.

*4.2.21. [Mn(PNP^{Me}-iPr)Cl$_2$] (**5d**)*

This complex was prepared analogously to **5a** using PNP^{Me}-*i*Pr (**1d**) (369 mg, 1.0 mmol) and anhydrous $MnCl_2$ (126 mg, 1.0 mmol) as starting materials. Yield: 466 mg (94%). *Anal.* Calc. for $C_{19}H_{37}Cl_2MnN_3P_2$ (495.31): C, 46.07; H, 7.53; N, 8.48. Found: C, 46.16; H, 7.59; N, 8.41%. μ_{eff} = 6.0 μ_B.

*4.2.22. [Mn(PNP-Et)Cl$_2$] (**5f**)*

This complex was prepared analogously to **5a** using PNP-Et (**1f**) (285 mg, 1.0 mmol) and anhydrous $MnCl_2$ (126 mg, 1.0 mmol) as starting materials. Yield: 402 mg (98%). *Anal.* Calc. for $C_{13}H_{25}Cl_2MnN_3P_2$ (411.15): C, 37.98; H, 6.13; N, 10.22. Found: C, 37.89; H, 6.23; N, 10.30%. μ_{eff} = 6.1 μ_B.

*4.2.23. [Mn(PNP^{Ph}-Pr)Cl$_2$] (**5g**)*

This complex was prepared analogously to **5a** using PNP^{Ph}-*n*Pr (**1g**) (494 mg, 1.0 mmol) and anhydrous $MnCl_2$ (126 mg, 1.0 mmol) as starting materials. Yield: 588 mg (95%). *Anal.* Calc. for $C_{29}H_{41}Cl_2MnN_3P_2$ (619.45): C, 56.23; H, 6.67; N, 6.78. Found: C, 56.18; H, 6.55; N, 6.86%. μ_{eff} = 6.0 μ_B.

4.3. General procedure for the oxidative homocoupling of ArMgBr with MeI

A 3.0 M solution of ArMgBr in Et_2O (3.5 mL, 10.5 mmol) was mixed with 1 mL of a 10 mM stock solution of the catalyst (0.01 mmol) in THF under stirring. A 5 M solution of MeI (2 mL, 10.0 mmol) was added and the mixture was allowed to react for 15 min and was then quenched with *i*PrOH (0.5 mL). The product was purified by silica column chromatography.

4.4. Crystal structure determination

X-ray diffraction data of **2a**·3.5$(CH_3)_2CO$, **2g**, **3d**, **4d**·0.5CH_2Cl_2, and **5c**·THF were collected at T = 100 K in a dry stream of nitrogen on a Bruker KAPPA APEX II diffractometer system with graphite monochromatized Mo Kα radiation (λ = 0.71073 Å) and fine sliced φ- and ω-scans. Data were reduced to intensity values with SAINT and an absorption correction was applied with the multi-scan approach implemented in SADABS [22]. The structures of **2a**·3.5$(CH_3)_2CO$, **3d**, **4d**·0.5CH_2Cl_2, and **5c**·THF were solved by charge-flipping implemented in SUPERFLIP [23] and refined using JANA2006 [24] against F. The structure of **2g** was solved with direct methods implemented in SHELXS and refined using SHELXL [25] against F^2. Non-hydrogen atoms were refined with anisotropic displacement parameters. The H atoms connected to C atoms were placed in calculated positions and thereafter refined as riding on the parent atoms. The H atoms of the amine groups were located in difference Fourier maps. The N–H distances were restrained to 0.870(1) Å in **2a**. In **5c** the H atoms attached to N were freely refined. Molecular graphics were generated with the program MERCURY [26].

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Appendix A. Supplementary material

CCDC 1434128–1434132 contains the supplementary crystallographic data for compounds **2a**·3.5$(CH_3)_2CO$, **2g**, **3d**, **4d**·0.5CH_2Cl_2, and **5c**·THF. These data can be obtained free of charge from The

Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ica.2016.02.064.

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Air-Stable Triazine-Based Ni(II) PNP Pincer Complexes As Catalysts for the Suzuki–Miyaura Cross-Coupling

Matthias Mastalir,[†] Berthold Stöger,[‡] Ernst Pittenauer,[‡] Günter Allmaier,[‡] and Karl Kirchner*[,†]

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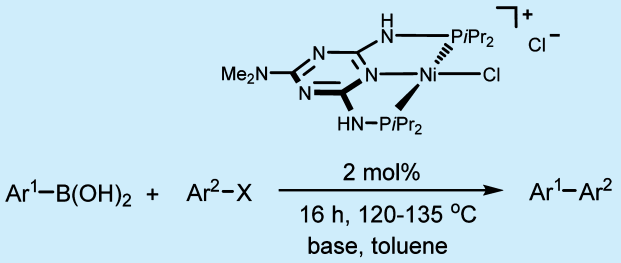
Supporting Information

ABSTRACT: Air-stable, thermally robust, and well-defined cationic Ni(II) PNP pincer complexes based on the 2,4-diaminotriazine scaffold are described. These complexes are active catalysts for the Suzuki–Miyaura cross-coupling of a wide range of aryl, heteroaryl (including benzoxazole, thiazole, pyridine, pyrimidine, thiazole), primary and secondary alkyl halides, and pseudohalides with different organoboronate reagents giving excellent to good isolated yields. Neutral deprotonated complexes seem to play a key role in the catalytic process.



Since its discovery in 1979,[1] the Suzuki–Miyaura (SM) cross-coupling involving the coupling of an organoboron reagent and organic halides or pseudohalides has become one of the most important and prevalent methods for the construction of carbon–carbon bonds.[2−4] An advantage over other cross-coupling reactions is the wide accessibility of organoboronate reagents, which reveal a broad functional group tolerance, are markedly stable, and are generally environmentally benign. Accordingly, applications of SM couplings comprise a wide array of synthetic targets, ranging from manufacturing of materials and pharmaceuticals to the synthesis of building blocks and natural products.[2−4] Although palladium catalysts still dominate the field, the use of nickel catalysts has become increasingly important.[5−7] Nickel is more abundant, less toxic, and inexpensive as compared to palladium and thus preferable in terms of sustainability and economic viability. Moreover, nickel has a pronounced ability to cleave not only C-halide[8,9] but also C–O and C–N bonds such as in aryl ethers,[10]

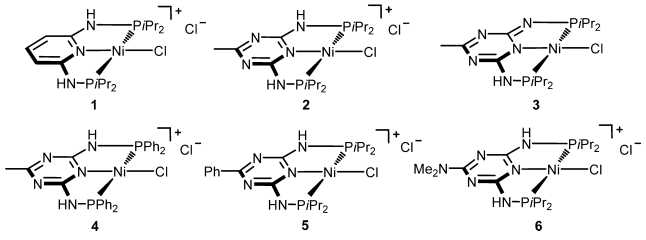


Figure 1. Ni(II) PNP pincer complexes **1**–**6**.

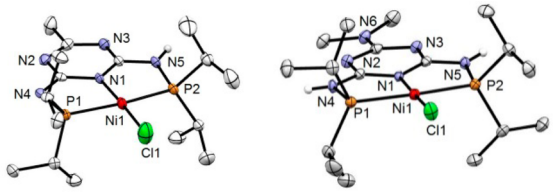
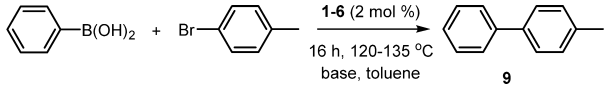


Figure 2. Structural views of $[Ni(Triaz^{Me}\text{-}i\text{Pr}^*)Cl]\cdot C_4H_8O_2$ (**3**·$C_4H_8O_2$) (left) and $[Ni(Triaz^{NMe2}\text{-}i\text{Pr})Cl]Cl$ (**6**) (right) showing 50% thermal ellipsoids (most H atoms omitted for clarity). Selected bond lengths (Å) and angles (deg): **3**: Ni1–Cl1 2.177(2), Ni1–P1 2.203(2), Ni1–P2 2.178(2), Ni1–N1 1.885(3), P1–Ni1–P2 167.4(1), Cl1–Ni1–N1 177.4(1). **6**: Ni1–Cl1 2.1491(8), Ni1–P1 2.1729(8), Ni1–P2 2.1670(8), Ni1–N1 1.868(2), Cl1–Ni1–N1 175.97(6), P1–Ni1–P2 170.31(3).

Table 1. Efficiency of Nickel Precatalysts 1–6 in Suzuki–Miyaura Cross-Couplings



entry	precatalyst	base	yield[a] [%]
1	**1**	*t*-BuOK	12
2	**2**	*t*-BuOK	80
3	**2**	K_3PO_4	69
4	**3**	*t*-BuOK	81
5	**3**	K_3PO_4	72
6	**4**	*t*-BuOK	71
7	**4**	K_3PO_4	60
8	**5**	*t*-BuOK	78
9	**5**	K_3PO_4	52
10	**6**	*t*-BuOK	93
11	**6**	K_3PO_4	85

[a]Isolated yields after purification with silica column chromatography.

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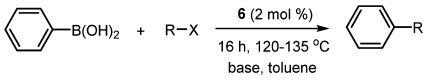
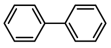
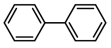
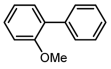
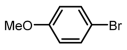
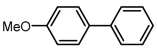
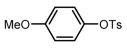
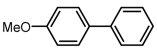
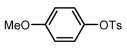
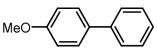
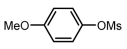
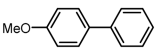
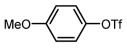
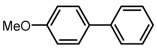
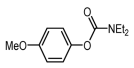
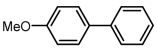
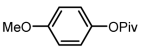
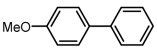
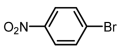
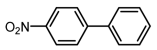
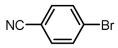
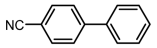
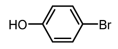
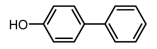
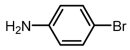
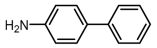
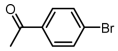
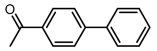
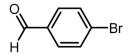
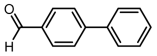
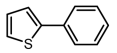
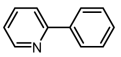
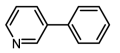
Table 2. Nickel Catalyzed Suzuki–Miyaura Cross-Coupling of Phenylboronic Acid with Aromatic Halides and Pseudohalides



entry	R-X	base	product	yield[a] [%]
1		*t*-BuOK	 **10**	92
2[b]		*t*-BuOK	 **10**	70
3		*t*-BuOK	 **11**	89
4		*t*-BuOK	 **12**	92
5		*t*-BuOK	 **12**	87
6		K_3PO_4	 **12**	81
7		K_3PO_4	 **12**	75
8		*t*-BuOK	 **12**	92
9		K_3PO_4	 **12**	84
10		K_3PO_4	 **12**	51
11		K_3PO_4	 **13**	80
12		K_3PO_4	 **14**	78
13		*t*-BuOK	 **15**	67
14		*t*-BuOK	 **16**	61
15		*t*-BuOK	 **17**	75
16		K_3PO_4	 **18**	44
17		*t*-BuOK	 **19**	73
18		*t*-BuOK	 **20**	72
19		*t*-BuOK	 **21**	85
20		*t*-BuOK	**22**	82
21		*t*-BuOK	**23**	77
22		*t*-BuOK	**24**	83

[a]Isolated yields after purification with silica column chromatography. [b]At 135 °C for 24 h.

acetates,[11] pivalates, carbamates, sulfonates, sulfamates,[12] esters,[13] or amides[14] which renders these electrophiles to attractive coupling partners. With respect to the oxidation state of the Ni complexes for SM reactions both Ni(0) and Ni(II) compounds are utilized,[15] with the latter not being air and moisture sensitive and thermally stable; these are thus synthetically more easily accessible.

Here, we report air-stable and well-defined Ni(II) PNP pincer complexes based on the triazine scaffold as catalysts for the SM cross-coupling of several sp^2 and sp^3 halides and pseudohalides with different organoboronate reagents. This type of ligands was recently successfully applied by Kempe and co-workers[16] for the synthesis of stable cobalt complexes which turned out to be active catalysts for the hydrogenation of C=O bonds and the alkylation of aromatic amines by alcohols. It has to be noted that pincer complexes have been rarely used for nickel catalyzed SM reactions.[17]

We prepared the air-stable cationic Ni(II) complexes **1**, **2**, **4**–**6** by treatment of $NiCl_2{\cdot}6H_2O$ with the respective PNP ligands in 94–96% isolated yields (Figure 1).[18] The deprotonated complex **3** was obtained by reacting **2** with 1 equiv of *t*-BuOK toluene in 62% isolated yield. This complex was prepared since deprotonated species appear to play a key role in Kempe's cobalt catalyzed reactions.[16] The solid state structures of **3** and **6** were determined by single-crystal X-ray diffraction. Structural views are depicted in Figure 2 with selected bond distances given in the caption.

The reaction of 4-bromotoluene and phenyl boronic acid in toluene at 120–135 °C for 16 h was investigated to identify the most efficient catalyst for the SM coupling in the presence of the bases *t*-BuOK and K_3PO_4 (Table 1). All complexes are poorly soluble in toluene at room temperature, but readily dissolve at elevated temperatures in the presence of a base. Complexes **2**, **3**, and **6** turned out to the best catalyst with 80%, 81%, and 93% isolated yields in the presence of *t*-BuOK (Table 1, entries 2, 4, and 10), while the pyridine-based complex **1** was the least active one. The yields with K_3PO_4 as a base are generally slightly lower under the same reaction conditions. Interestingly, the deprotonated complex **3** compared to complex **2** showed similar reactivity, suggesting that a deprotonated complex may play a key role in the catalytic process.[16] In contrast to all other complexes, this species is air and moisture sensitive.

In the following, precatalyst **6** is used for this study in combination with the bases *t*-BuOK and K_3PO_4. To explore the scope of this catalyst we evaluated first the coupling of various

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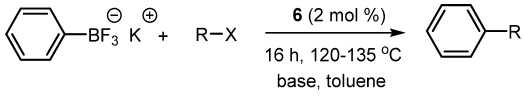
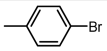
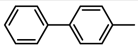
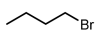
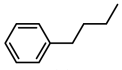
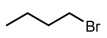
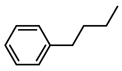
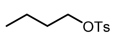
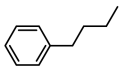
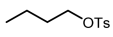
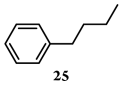
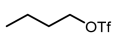
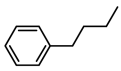
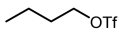
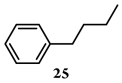
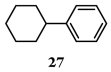
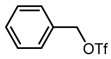
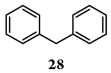
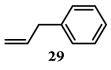
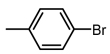
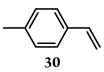
Table 3. Nickel Catalyzed Suzuki–Miyaura Cross-Coupling of Aromatic and Aliphatic Bromides, Tosylates, and Triflates with Potassium Phenyltrifluoroborate

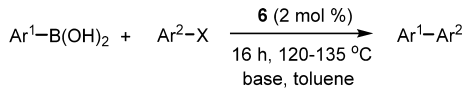


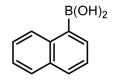
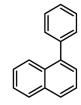
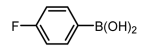
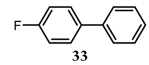
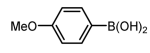
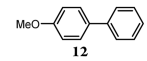
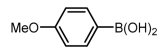
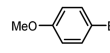
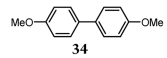
entry	R-X	base	product	yield[a] [%]
1		*t*-BuOK	 **9**	98
2		*t*-BuOK	 **25**	63
3		K_3PO_4	 **25**	45
4		*t*-BuOK	 **25**	76
5		K_3PO_4	 **25**	71
6		*t*-BuOK	 **25**	87
7		K_3PO_4	 **25**	90
8		K_3PO_4	 **26**	34
9		K_3PO_4	 **27**	39
10		K_3PO_4	 **28**	63
11		K_3PO_4	 **29**	42
12[b]		*t*-BuOK	 **30**	93
13[b]		*t*-BuOK	 **31**	84

[a]Isolated yields after purification with silica column chromatography. [b]With potassium vinyltrifluoroborate (0.15 mmol).

aryl and heteroaryl halides and "pseudo halides" (triflates, tosylates, mesylates, pivalates, and carbamates) with phenyl boronic acid. The results of the couplings catalyzed by complex **6** are summarized in Table 2. In general, good to excellent isolated yields were observed for most substrates containing electron-donating groups (OH, OMe, NH_2) or electron-withdrawing groups (CN, NO_2, acyl, formyl) thus not following any obvious trend. Also heteroaryl halides (based on benzoxazole, thiazole, pyridine, pyrimidine, thiophene, thiazole) afforded good yields. This is particularly interesting in the case of pyridines and pyrimidines due their coordinating properties (Table 2, entries 18–20). Chlorobenzene (Table 2, entry 2) and 4-bromobenzaldehyde (Table 2, entry 16) were also suitable substrates, although the isolated yield was moderate in the case of the latter (44%). This may be attributed to side reactions of the substrate with a base under these reaction conditions.

Table 4. Nickel Catalyzed Suzuki–Miyaura Cross-Coupling of Boronic Acids and Esters with Aryl Bromides



entry	Ar^1-B(OH)$_2$	Ar^2-Br	product	yield[a] [%]
1			 **32**	87
2			 **33**	94
3			 **12**	86
4			 **34**	88
5[b]			**9**	97
6			**19**	81
7			**35**	85

[a]Isolated yields after purification with silica column chromatography. [b]With phenylboronic acid pinacol ester (0.15 mmol).

Moreover, we tested the reactivity of some nonactivated primary and secondary aliphatic bromides and "pseudo halides" for the cross-coupling with phenyltrifluoroborates and vinyltrifluoroborate (Table 3). This reaction proceeds in good isolated yields (63–98%).

In particular, the vinylation of 4-bromo toluene and 4-bromo pyridine afforded high yields of 4-methylstyrene and 4-vinylpyridine (Table 3, entries 12 and 13). Only with butyl bromide (with K_3PO_4 as base), isopropyl and cyclohexyl triflates (Table 3, entries 2, 8 and 9), and vinyl triflate (Table 3, entry 11) lower yields were observed. The lower yields may be due to elimination reactions of the alkyl chain under basic conditions at elevated temperature.

Finally, we also varied the organoboronate reagent and investigated the coupling of several aryl and heteroarylboronic acids and one arylboronic acid ester with aryl bromides. The results of this study are shown in Table 4 revealing in all cases good to excellent isolated yields.

In conclusion, air-stable, thermally robust, and well-defined cationic Ni(II) PNP pincer complexes based on the 2,4-diaminotriazine scaffold are synthesized. The cationic Ni(II) complexes are readily deprotoanted to give neutral complexes. This has been shown on one example which has been isolated and even structurally characterized. With these easy to handle Ni(II) complexes, we have developed a protocol for the

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arylation, alkylation, and vinylation of a wide range of aryl, heteroaryl, alkyl halides, and pseudohalides with different organoboronate reagents using the Suzuki−Miyaura coupling. In most cases, high yields of isolated products are obtained. Deprotonated neutral Ni(II) complexes seem to be key intermediates in the catalytic reaction. In one case, it has been exemplarily shown that such a species is indeed an active catalyst.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01398.

Crystallographic data **3** and **6** (CCDC entries 1472541 (**3**) and 1472542 (**6**)) (CIF)

Complete crystallographic data, synthetic procedures, ^{1}H, $^{13}C\{^{1}H\}$, and $^{31}P\{^{1}H\}$ NMR spectra of all complexes and organic products (PDF)

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Notes

The authors declare no competing financial interest.

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