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Highly Enantioselective Ferrocenyl Palladacycle-Acetate Catalysed Arylation of Aldimines and Ketimines with Arylboroxines

Carmen Schrapel,[a] Wolfgang Frey,[a] Delphine Garnier,[a] and René Peters*[a]

Abstract: Benzylic *N*-substituted stereocenters constitute a frequent structural motif in drugs. Their highly enantioselective generation is hence of technical importance. An attractive strategy is the arylation of imines with organoboron reagents. Chiral Rh complexes have reached a high level of productivity for this reaction type. In this article we describe that an electron rich Pd^{II} catalyst also performs well in the arylation of aldimines, comparable to the best Rh catalysts. The ferrocenyl palladacycle-acetate catalyst allows for a broad substrate scope and very high enantioselectivities. Commonly observed side reactions like aryl-aryl homocouplings and imine hydrolysis could be blocked. Mechanistic studies implicate that (a) the acetate ligand is crucial for transmetallation, (b) the active catalyst is most likely a palladacycle-OAc monomer, (c) the rate limiting step is probably the product release. By added KOAc the arylation could also be applied to ketimines.

Introduction

Chiral enantiomerically pure amines often display a high biological activity and are thus employed in a number of active pharmaceutical ingredients (APIs) and agrochemicals.[1,2] An important subclass form chiral benzylic amines containing a *N*-substituted stereocenter,[3] because this structural motif can be found in a number of drugs or drug candidates (Figure 1). Prominent examples include *Cetirizine*[4] for the treatment of hayfever, *Sertraline*[5] and *Tianeptine*[6] for the treatment of depression, *Rasagiline*[7] (treatment of Parkinson's disease), *Rivastigmine*[8] (treatment of Alzheimer's disease) or (+)-BW373U86[9] (a non-peptidic δ-opioid agonist). Due to the importance of chiral benzylic amines in medicine, efficient methods suitable for their preparation on technical scale are indispensable. For that reason a number of new synthetic methods have been developed in the last few years, which might provide advantages with regard to practicality, sustainability, cost-efficiency, enantioselectivity, scope, catalytic activity, catalyst robustness, etc.[10]

In this context the arylation of aldimines has been intensively studied using various catalyst types and aryl transfer reagents.[10] The latter include, e.g., aryl zinc,[11] titanium[12] a tin[13] reagents.

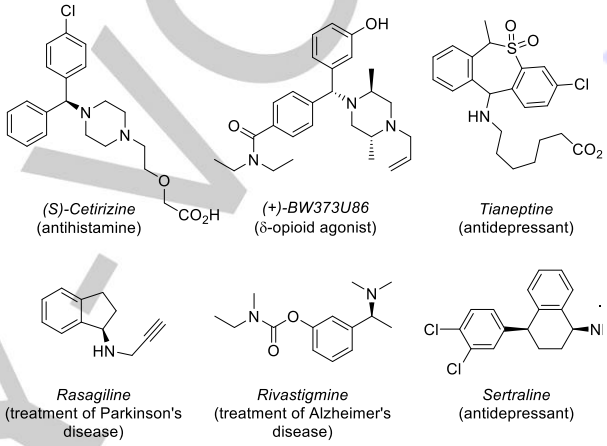

Figure 1. Examples for pharmacologically important chiral benzylic am containing a *N*-substituted stereocenter.

Most frequently studied have arguably been arylboronic a derivatives.[3,10] The latter are synthetically particularly attrac due to their high robustness, their high compatibility with m functional groups and low toxicity.[10] In addition, t preparation is operationally simple and they are o commercially available at relatively low prices.[10] Rhodi complexes are today well established as versatile catalysts the asymmetric arylation of imines with arylboronic a derivatives.[10,14,15] Moreover, several palladium(II)-catal have recently been described as an attractive alternative the arylation of aldimines.[16-18]

Aryl-Pd species have been considered to be less nucleop than aryl-Rh species,[19] possibly rendering the addition to C=N bond more difficult.[20] In contrast to the Rh^{I}-catal reactions, the Pd^{II}-catalysed additions to aldimines are o accompanied by a significant competing imine hydroly Molecular sieve was often necessary to minimise hydrolysis.[16] Another problem using Pd^{II} catalysts is the formation of bisaryl homocoupling side products (Ar-Ar).[16] The latter are most likely generated by formation of *off-cycle* bisaryl-Pd^{II} intermediates, which are prone to undergo a reductive elimination to deliver the bisaryl product and at the same time a catalyst at a non-productive Pd^{0} oxidation state. Both the imine hydrolysis and the formation of the bisaryl-Pd^{II} intermediate were probably facilitated by the fact that neutral bidentate chiral ligands were employed thus resulting in a

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relatively high Lewis acidity of the catalytically active Pd^{II} center.[16]

To address these issues we envisioned a monoanionic *C*,*N*-ligand[21] to be beneficial. In particular the generation of an undesired bisaryl-Pd^{II} intermediate seemed to be much less favourable in that case, because a monoanionic Pd-center would be formed. Additionally, to attain enantioselectivities comparable to the best Rh-catalysts we studied planar chiral palladacycles in order to facilitate a differentiation of the enantiotopic imine faces at defined binding sites in the catalyst. They were expected to be defined, because the position of different ligand types in *C*,*N*-palladacycles is usually controlled by their charges. Neutral ligands (substrates) usually prefer the position *trans* to the *N*-donor, whereas anionic ligands bind *trans* to the *C*-donor.[21]

In this article we describe that a readily accessible ferrocene imidazoline palladacycle (abbreviated as **FIP**), which was originally used by our group for allylic imidate rearrangements,[22a,b] behaves as a highly enantioselective catalyst for the arylation of imines[23] with arylboroxines.[24] By that a large number of benzylic amines were obtained in almost enantiomerically pure form with an efficiency that is comparable to the best Rh catalysts. An important factor for this performance is the use of acetate as anionic ligand.

Results and Discussion

Optimisation of the Arylation of Aldimines

The addition of commercial Ph-$B(OH)_2$ (**2A**) to *N*-tosylimine **1a** was studied as a model reaction (Table 1). The resulting product **4aA** has previously been demonstrated to be a precursor for *Cetirizine*.[14a] Two classes of metallocene derived imidazoline metallacycles have recently been identified by our research group to be efficient for various catalytic asymmetric reactions: (*i*) metallocene bisimidazoline bismetallacycles[25] and (*ii*) ferrocenyl monoimidazoline monopalladacycles.[22] The ferrocen-2,2'-diyl bisimidazoline bispalladacycle precatalyst **[FBIP-Cl]$_2$** (3.0 mol%) – activated by AgOTf (12 mol%) to remove the four chloride bridges in order to facilitate a coordination of the substrates[25] – provided the addition product in only moderate yield when the reaction was performed at room temperature in THF in the presence of activated 4Å molecular sieves (MS). KF was utilised as stoichiometric base to enable the transmetallation of the boronic acid's aryl residue to the Pd(II) center.[26] On the other hand, **4aA** was delivered in almost enantiomerically pure form (Table 1, entry 1) and hydrolysis was not detected under these conditions.

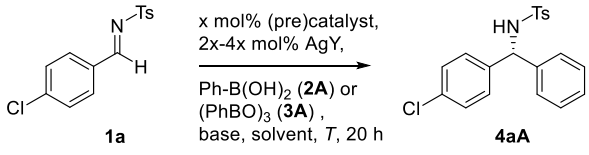
Also with monopalladacycle **[FIP-Cl]$_2$** (6 mol% to use the same Pd loading as with the bispalladacycle) – again activated by AgOTf (12 mol%)[22a,d] – **4aA** was formed in almost enantiopure form under otherwise unchanged conditions, but with an improved yield (entry 2). The product yield was further improved when the reaction was run in toluene as solvent (entry 3). However, with a synthetically more useful catalyst loading (1 mol% precatalyst), hydrolysis could not be completely suppressed anymore (entry 4).

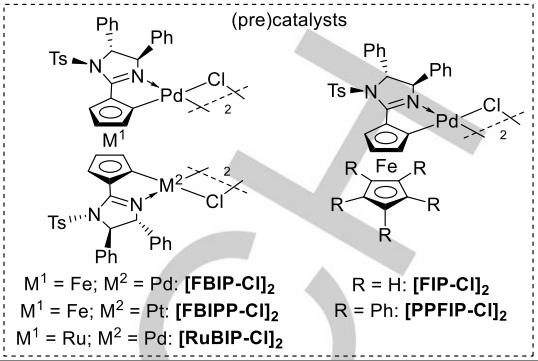
To our surprise the direct use of the chloride-bridged **[FIP-Cl]$_2$** as catalyst (1 mol%), without an activation by a silver salt, could initially solve this problem. The arylation product was formed in a nearly quantitative yield and in almost enantiomerically pure form (entry 5). Also with just 0.5 mol% of **[FIP-Cl]$_2$** excellent data were obtained (entry 6).[27] Nevertheless, the reactivity strongly depended on the boronic acid batch which was used. NMR analysis of various batches of **2A** freshly bought from different commercial suppliers showed that they usually contain large quantities of the corresponding boroxine. In one case, a commercial batch labelled as boronic acid **2A** was nearly pure boroxine **3A**. This batch resulted in no product formation applying the conditions of entry 5. As a general rule product yields decreased with an increasing percentage of the boroxine.[28] Our trials to synthesise boronic acids of sufficient quality failed, because an anhydrous material was essential in order to avoid the im hydrolysis. During removal of residual water the formatior varying amounts of boroxine was always found.

In order to avoid the described reproducibility problems a because anhydrous boronic acid **2A** of reproducibly h quality was not accessible, we considered the developmen a method which makes use of arylboroxine reagents to more attractive. The observation that phenylboroxine displ a much lower reactivity indicated that the transmetallation s initiated by KF was slower than with phenylboronic acid. were speculating that addition of an alcohol additive mi solve this problem, as the reaction of boroxines and alcoh should create B-OH units in-situ, which might facilitate transmetallation step via a 'boronate-pathway'.[26] In presence of two equivalents of MeOH the reactivity was inde partly regained, yet at the expense of increased levels of im hydrolysis and a reduced enantioselectivity (entry 7).

Alternatively, the transmetallation step might be facilita by an anionic ligand with an adequate Lewis-basicity fo simultaneous coordination to the boroxine reagent, related the 'oxo-palladium-pathway' in Suzuki-Miyaura couplings.[2 Acetate was found to be a suitable anionic ligand, with wh the transmetallation is apparently accelerated. During course of these studies, Fairlamb *et al.* described investigation of a stoichiometric transmetallation using a F OAc species, which confirmed this hypothesis.[30] So reactivity towards nearly enantiomerically pure **4aA** v already found at room temperature in the presence stoichiometric NaOAc (entry 8). This reactivity disappea again in the absence of NaOAc as additive at ro temperature (entry 9), whereas at a reaction temperature 70 °C **4aA** was formed in a quantitative yield (entry 1 Different silver salts for chloride removal were tl investigated in the catalyst activation. These experime confirmed that the choice of the anionic ligand is central fo satisfactory reactivity. Less Lewis-basic anions than acet like triflate and 2,4,6-triisopropylbenzensulfonate resulted in or trace amounts of product (entries 11 & 12). W trifluoroacetate a yield of 24% of enantiomerically pure **4aA** was determined (entry 13). These results support the crucial role of the acetate ligand in the transmetallation event.

Table 1. Development of the model reaction.





#	Precatalyst (x mol%)	Y (2 or 4x mol%)	**2A** or **3A** (equiv.)	Base (equiv.)	Solvent	additive	*T* [°C]	imine hydrolysis [%][a]	Yield **4aA** [%][a]	4 [%
1	[FBIP-Cl]$_2$ (3)	OTf (4x)	**'2A'** (2)[c]	KF (1.0)	THF	4Å MS	20	<1	35	>
2	[FIP-Cl]$_2$ (6)	OTf (2x)	**'2A'** (2)[c]	KF (1.0)	THF	4Å MS	20	<1	51	>
3	[FIP-Cl]$_2$ (6)	OTf (2x)	**'2A'** (2)[c]	KF (1.0)	toluene	4Å MS	20	3	92	>
4	[FIP-Cl]$_2$ (1)	OTf (2x)	**'2A'** (2)[c]	KF (1.0)	toluene	4Å MS	20	13	74	>
5	[FIP-Cl]$_2$ (1)	-	**2(3)A** (2)	KF (1.0)	toluene	4Å MS	20	<1-7	<1-99	>
6	[FIP-Cl]$_2$ (0.5)	-	**'2A'** (2)[c]	KF (1.0)	toluene	4Å MS	20	2	98	>
7	[FIP-Cl]$_2$ (1)	-	**3A** (0.8)	KF (1.0)	toluene	MeOH[d]	20	8	75	
8	[FIP-Cl]$_2$ (1)	OAc (2x)	**3A** (1)	NaOAc (1.0)	toluene	-	20	<1	25	>
9	[FIP-Cl]$_2$ (1)	OAc (2x)	**3A** (1)	-	toluene	-	20	<1	2	r
10	[FIP-Cl]$_2$ (1)	OAc (2x)	**3A** (1)	-	toluene	-	70	<1	99	>
11	[FIP-Cl]$_2$ (1)	OTf (2x)	**3A** (1)	-	toluene	-	70	11	<1	r
12	[FIP-Cl]$_2$ (1)	O_3S-2,4,6-*i*Pr$_3$C$_6$H$_2$ (2x)	**3A** (1)	-	toluene	-	70	2	6	r
13	[FIP-Cl]$_2$ (1)	O_2CCF_3 (2x)	**3A** (1)	-	toluene	-	70	<1	24	>
14	[FIP-Cl]$_2$ (1)	OAc (2x)	**3A** (1)	-	$F_3CC_6H_5$	-	70	<1	95	>
15	[FIP-Cl]$_2$ (1)	OAc (2x)	**3A** (1)	-	ClC_6H_5	-	70	<1	98	>
16	[FIP-Cl]$_2$ (1)	OAc (2x)	**3A** (1)	-	1,2-$Cl_2C_6H_4$	-	70	<1	76	>
17	[FIP-Cl]$_2$ (0.5)	OAc (2x)	**3A** (1)	-	ClC_6H_5	-	70	<1	82	>
18	**[FIP-Cl]$_2$ (1)**	**OAc (2x)**	**3A (1)**	**-**	**ClC_6H_5**	**-**	**65**	**<1**	**99**	**>**
19	[FBIP-Cl]$_2$ (0.5)	OAc (4x)	**3A** (1)	-	ClC_6H_5	-	65	<1	35	>
20	[FBIPP-Cl]$_2$ (0.5)	OAc (4x)	**3A** (1)	-	ClC_6H_5	-	65	1	3	n.d.
21	[RuBIP-Cl]$_2$ (0.5)	OAc (4x)	**3A** (1)	-	ClC_6H_5	-	65	<1	38	n.d.
22	[PPFIP-Cl]$_2$ (1)	OAc (2x)	**3A** (1)	-	ClC_6H_5	-	65	<1	1	n.d.
23	[FIP(Tf)-Cl]$_2$ (1)	OAc (2x)	**3A** (1)	-	ClC_6H_5	-	65	<1	47	>99

[a] Determined by ^{1}H-NMR of the crude product using mesitylene as internal standard. [b] Determined by HPLC. [c] Commercial batch of 2a with a ratio boronic acid/boroxine = 1.3:1, ≙ 0.68 Äquiv. $PhB(OH)_2$). [d] 2 equiv. were used.

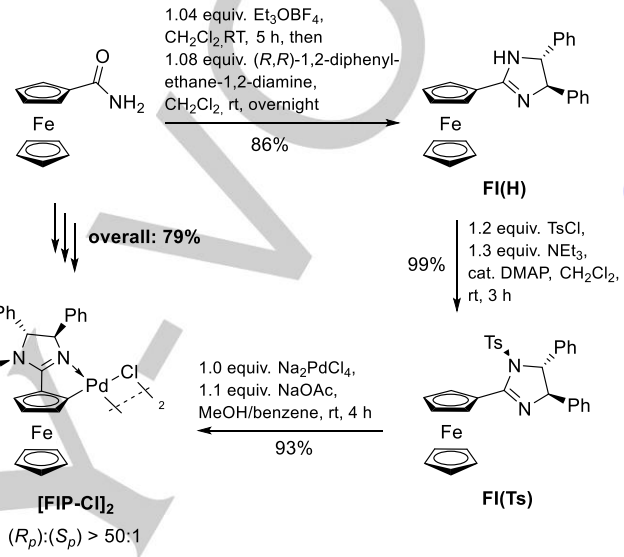
Because imine **1a** and also product **4aA** possess a poor solubility in toluene, a precipitation of both compounds was observed at the phase transitions solution/gas phase/glass wall. Because the reactions were performed in a parallel synthesiser (*Heidolph Synthesis 1*) which was constantly shaking during the course of the reaction, a careful adjustment of the shaking frequency was required (200-250 rpm) in order to avoid that precipitated starting material at the vial's wall would not react anymore as it had not contact with the solution anymore. To increase the reproducibility/yields, a screening of different solvents was performed. In ethereal solvents (1,4-dioxane, THF, diglyme) product formation was in general inferior (not shown) compared to the use of toluene. In addition, several halogenated aromatic solvents were tested. (α,α,α)-Trifluorotoluene and chlorobenzene allowed for efficient arylation reactions (entries 14 & 15). In these solvents the formation of much less Pd-black was observed indicating that there is less catalyst decomposition. In particular chlorobenzene is a good choice as the solubility was largely improved, whereas 1,2-dichlorobenzene led to inferior results (entry 16). In chlorobenzene the precatalyst amount could also be reduced to 0.5 mol% still providing a good yield after 20 h at 70 °C (entry 17). A temperature screening showed that the best data is obtained at 65 °C (entry 18).

The optimised conditions were also applied using different bismetallacycles and a pentaphenylferrocene based monopalladacycle. None of them performed with a similar proficiency (entries 19-23). For the bismetallacycles a catalyst loading of 0.5 mol% was used to have the same Pd loading as with the monopalladacycle **[FIP-Cl]$_2$**. With the mixed platina-/palladacycle **[FBIPP-Cl]$_2$**[31] only trace amounts of product were formed (entry 20), whereas the bispalladacycles **[FBIP-Cl]$_2$**[25] and **[RuBIP-Cl]$_2$**[32] provided moderate product yields (entries 19 & 21). With the sterically demanding pentaphenylferrocene based monopalladacycle **[PPFIP-Cl]$_2$**[22] almost no product was detected (entry 22). The *N*-triflyl protected ferrocenyl monopalladacycle **[FIP(Tf)-Cl]$_2$**[22a] gave the desired product in moderate yield (entry 23).

Improved Synthesis and X-Ray Crystal Structure Analysis of [FIP-Cl]$_2$

For the synthesis of the best precatalyst identified in this study – **[FIP-Cl]$_2$** – our original procedure[22a] was slightly modified resulting in an improved overall yield and a diastereomerically pure catalyst (Scheme 1). Ferrocene carboxamide[33] was converted into the imidazoline **FI(H)** by activation with Meerwein's salt and subsequent treatment with enantiomerically pure (1*R*,2*R*)-1,2-diphenylethane-1,2-diamine. **FI(H)** was characterised in the solid state by X-ray crystal structure analysis (Figure 2).[34] The torsion angle between the C=N bond and the substituted Cp ligand is relatively small in the solid state, meaning that the basicity of the imidazoline unit is probably increased by resonance with the electron-rich ferrocene core. The less basic ligand **FI(Ts)** was obtained after *N*-tosylation in an overall yield of 85% starting from ferrocene carboxamide.

In contrast to our previous studies, the direct cyclopalladation could be achieved with full diastereoselectivity regarding the introduced element of planar chirality. In the previous studies (*dr* = 18:1) the cyclopalladation was accomplished with Na_2PdCl_4 / NaOAc in MeOH at room temperature.[22a] This older version proceeded very rapidly as visible from the nearly instantaneous product precipitation. In the modified procedure a MeOH/benzene mixture was used, in which the product has a significantly higher solubility. This might favour the diastereoselective formation of the thermodynamically more stable diastereomer (93% yield).



Scheme 1. Improved synthesis of the precatalyst **[FIP-Cl]$_2$**.

Figure 2. Representation of the X-ray crystal structure analysis of the imidazoline **FI(H)**. Only one of four molecules per unit cell, which slightly differ in their conformations, is shown. Colour code: C (gray); N (blue); H (white); Fe (orange).[34]

On the dimeric stage the *dr* determination by NMR is in principal rendered difficult by the existence of geometrical isomers around the Pd-Cl square-planes, which can in general result in up to 6 different species (S_p/S_p-*cis*, S_p/S_p-*trans*, S_p/R_p-*cis*, S_p/R_p-*trans*, R_p/R_p-*cis*, R_p/R_p-*trans*). In our case only two of these isomers

were visible in a ratio of 2:1 indicating that S_p-configured palladacycles were nearly exclusively formed.

To confirm the complete diastereoselectivity with regard to the element of planar chirality, **[FIP-Cl]$_2$** was also transformed into an isomerically pure monomeric complex with PPh_3 or PMe_3 (quantitative yields) according to a literature procedure.[22a]

For the S_p/S_p-*trans*-configured dimer crystals suitable for X-ray structure analysis could be obtained (Figure 3).[35] Both Pd-centers show the expected slightly distorted square-planar coordination geometry in a nearly C_2-symmetric solid state molecular structure. Two Pd centers and the two bridging chloride ligands form a puckered four-membered ring. The dihedral angle in the Cl-Pd-Cl-Pd entity is around 25°. As a result of the deviation from planarity, which is found for most halide bridged ferrocenyl monopalladacycles,[36] both ferrocene units are placed on the concave face of the four-membered ring. The axes of both ferrocene moieties are thus tilted by ca. 60° relative to each other. Both the Pd-C and Pd-N distances are very similar to the bismetallacycle **[FBIP-Cl]$_2$**.[25a] By the puckering of the $(PdCl)_2$-ring the Pd···Pd separation is about 4% shorter than in the almost flat $(PdCl)_2$-rings in **[FBIP-Cl]$_2$**.

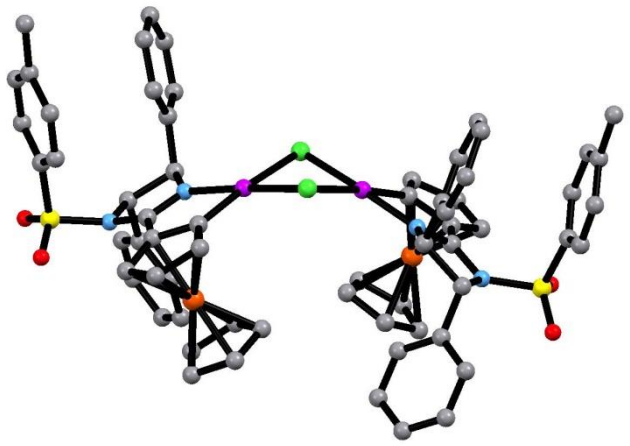


Figure 3. Representation of the X-ray crystal structure analysis of the precatalyst **[FIP-Cl]$_2$** possessing a *trans* geometry around the Pd-Cl-square-planes. Solvent molecules and hydrogen atoms are omitted for clarity. Colour code: C (gray); N (blue); O (red); S (yellow); Cl (green); Fe (orange); Pd (magenta). H atoms and solvent molecules are omitted for clarity. [35]

Substrate Scope of the Arylation of Aldimines

The scope of the optimised reaction conditions was then examined using different aldimines and boroxines (Table 2). All reactions were conducted in chlorobenzene at 65 °C for 20 h applying a precatalyst loading of 1 mol% if not mentioned otherwise. They were performed at a shaking frequency of 250 rpm. In the large majority of examples nearly enantiomerically pure products were formed with good to excellent yields. A number of different boroxines **3A-I** were investigated for the reaction with imine **1a**. Methoxy substituents at the boroxine were well tolerated in the *para* (π-donor), *meta* (σ-acceptor) and *ortho* (π-donor) positions (entries 2-4). In particular the high productivity in the presence of the *ortho*-substituent on the boroxine is noteworthy (entry 4), because this type of substrate is in general very challenging.[10] A similar result as with phenylboroxine **3A** (entry 1) was also achieved with *para*-biphenylboroxine (**3E**, entry 5). Also less nucleophilic boroxines **3F-H** carrying two chlorine or fluorine σ-acceptor atoms (entries 6 & 7) or an ester as π-acceptor moiety (entry 8) still provided useful yields of nearly enantiopure products. The heteroaromatic extended π-system of a 4-dibenzofuranyl moiety was also well accommodated (entry 9). Not accepted were bromo atoms on the boroxine, neither were they on the imine (not shown).

Ortho-, *meta*- and *para*-substituents were also well tolerated on the aromatic imine component **1**. Next to the model imine **1a** with a chloro substituent at the 4-position, chloro atoms at the 3- and 2-positions also allowed for high yields of nearly enantiopure products (imines **1b** and **1c**, entries 10-12 and 13-15, respectively). In addition, reactivity differences caused by electronic effects by substituents on R^1 were found to be rather small. A σ-acceptor substituent on the aromatic residue was thus not necessary as shown for R^1 = Ph (entries 16-19), but also a σ-donor (entry 20), π-donor (entries 21 & 22), π-acceptor (entries 23-25) and a polycyclic aromatic hydrocarbon (entries 26-28) were well accommodated.

A more special behaviour was found for imine **1i** carrying a 2-thiophenyl residue R^1. Whereas with phenylboroxine (**3A**) as reaction partner a similarly high enantioselectivity was attained (entry 29) as in all other cases described above, with the 4-methoxylphenylboroxine (**3B**) and the *para*-biphenylboroxine (**3E**) only moderate enantioselectivity was noticed (entries 30 & 31).

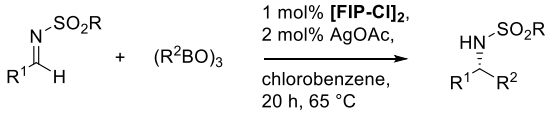
Noteworthy is also the fact that aliphatic imines **1j-l** can be employed. With α-branched alkyl residues slightly harsher reaction conditions were required, but the products were still formed in high yields and almost enantiopure form (entries 32&33). A particular challenge is the use of α-unbranched alkyl residues due to the expected imine/enamine tautomerism. The latter did not disturb the enantioselectivity, but side-reactions and a product instability during isolation led to a moderate product yield (entry 34).

From a practical point of view it is important that the arylation reactions are also applicable to aldimines with *N*-sulfonyl residues other than tosyl. For example, nearly enantiopure products were formed with substrates carrying *para*-nosyl[37] and dimethylaminosulfonyl groups[38] (entries 35 & 36). Both of these groups are established as versatile *N*-protective groups which can be readily removed under relatively mild reaction conditions.

Due to the broad scope regarding the possible imine and boroxine components, it is also possible to synthesise both possible product enantiomers in almost enantiopure form, using the same catalyst batch in an enantiodivergent manner by simply exchanging the substitution patterns of imine and boroxine. This is showcased by entries 16 and 21 (products **4dB** and **4fA**), entries 18 and 26 (products **4dJ** and **4hA**) and entries 19 and 29 (products **4dK** and **4iA**)

The absolute configurations of products **4aA** and **4dB** were unambiguously determined by X-ray crystal structure analysis confirming the attack at the *Re*-face of the imine.[39]

Table 2. Application of the optimised reaction conditions to various substrates.



1 **3** **4**

#	**4**	R^1	R^2	SO_2R	Yield [%][a]	*ee* [%][b]
1	**4aA**	4-ClC_6H_4	Ph	*p*Ts	99	>99
2	**4aB**	4-ClC_6H_4	4-$MeOC_6H_4$	*p*Ts	84	>99
3	**4aC**	4-ClC_6H_4	3-$MeOC_6H_4$	*p*Ts	95	>99
4	**4aD**	4-ClC_6H_4	2-$MeOC_6H_4$	*p*Ts	96	>99
5	**4aE**	4-ClC_6H_4	4-PhC_6H_4	*p*Ts	98	>99
6	**4aF**	4-ClC_6H_4	3,4-$Cl_2C_6H_3$	*p*Ts	50	99
7	**4aG**	4-ClC_6H_4	3,4-$F_2C_6H_3$	*p*Ts	70[c,d]	>99
8	**4aH**	4-ClC_6H_4	4-$MeO_2CC_6H_4$	*p*Ts	50[d]	>99
9	**4aI**	4-ClC_6H_4	4-dibenzofuranyl	*p*Ts	75[c]	98
10	**4bA**	3-ClC_6H_4	Ph	*p*Ts	86	99
11	**4bB**	3-ClC_6H_4	4-$MeOC_6H_4$	*p*Ts	99	>99
12	**4bE**	3-ClC_6H_4	4-PhC_6H_4	*p*Ts	82	99
13	**4cA**	2-ClC_6H_4	Ph	*p*Ts	91	>99
14	**4cB**	2-ClC_6H_4	4-$MeOC_6H_4$	*p*Ts	85	96
15	**4cE**	2-ClC_6H_4	4-PhC_6H_4	*p*Ts	85	99
16	**4dB**	Ph	4-$MeOC_6H_4$	*p*Ts	98	99
17	**4dE**	Ph	4-PhC_6H_4	*p*Ts	99	>99
18	**4dJ**	Ph	2-naphthyl	*p*Ts	86[c,d]	>99
19	**4dK**	Ph	thiophen-2-yl	*p*Ts	99	90
20	**4eA**	4-MeC_6H_4	Ph	*p*Ts	96	>99
21	**4fA**	4-$MeOC_6H_4$	Ph	*p*Ts	86	>99
22	**4fE**	4-$MeOC_6H_4$	4-PhC_6H_4	*p*Ts	82	95
23	**4gA**	4-$O_2NC_6H_4$	Ph	*p*Ts	63	99
24	**4gB**	4-$O_2NC_6H_4$	4-$MeOC_6H_4$	*p*Ts	78	>99
25	**4gE**	4-$O_2NC_6H_4$	4-PhC_6H_4	*p*Ts	85	>99
26	**4hA**	2-naphthyl	Ph	*p*Ts	91	>99
27	**4hB**	2-naphthyl	4-$MeOC_6H_4$	*p*Ts	88	99
28	**4hE**	2-naphthyl	4-PhC_6H_4	*p*Ts	66	99
29	**4iA**	thiophen-2-yl	Ph	*p*Ts	55[c,d]	98
30	**4iB**	thiophen-2-yl	4-$MeOC_6H_4$	*p*Ts	96	81
31	**4iE**	thiophen-2-yl	4-PhC_6H_4	*p*Ts	57	77
32	**4jA**	*cyclo*-Hex	Ph	*p*Ts	95[c,d]	>99
33	**4kA**	*i*-Pr	Ph	*p*Ts	92[c,d]	>99
34	**4lA**	$Ph(CH_2)_2$	Ph	*p*Ts	32[d,e]	99
35	**4aA'**	4-ClC_6H_4	Ph	*p*Ns	91[d]	>99
36	**4aA''**	4-ClC_6H_4	Ph	DAS	58[d]	99

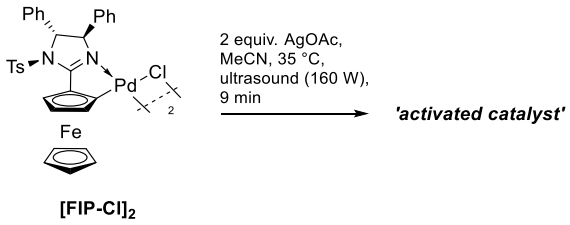
[a] Yield of isolated product. [b] Determined by HPLC. [c] Reaction temperature: 80 °C. [d] 2 mol% of **[FIP-Cl]$_2$**. [e] Determined by ^{1}H-NMR using an internal standard. (*p*Ts = 4-$MeC_6H_4SO_2$, *p*Ns = 4-$O_2NC_6H_4SO_2$, DAS = N,N-dimethylaminosulfonyl).

Mechanistic Studies and Considerations

a) The Activated Catalyst

As mentioned above, the precatalyst **[FIP-Cl]$_2$** is a chloride bridged dimer and the best activity was achieved by catalyst activation with silver acetate. Unfortunately, all attempts towards direct cyclopalladation of the ligand **FI(Ts)** with $Pd(OAc)_2$ failed. In previous studies, the activation of our chloride bridged palladacycle catalysts usually led to monomeric catalysts, when the activation was performed in the presence of acetonitrile, because the latter adopts the position *trans* to the imidazoline N-donor.[22,25] In the present study, **[FIP-Cl]$_2$** was initially stirred for 4.5 h with AgOAc (2.0 equiv.) in acetonitrile at room temperature Later a more time-efficient activation procedure was used in which the precatalyst/silver salt mixture was sonicated (160 W) for few minutes. Inspection of the ^{1}H-NMR spectra of the activated catalyst batches revealed that they consisted of at least two different species. The relative ratio of these two species depended on how the activation was performed and had an influence on the catalytic activity. For comparison, different catalyst batches were investigated in the model arylation reaction of **1a** and **3A** in chlorobenzene at 65 °C for 20 h using a precatalyst loading of 0.5 mol%.

Under some catalyst activation conditions, a uniform catalyst species could also be obtained. This was for instance the case, when the activation was done in dry toluene in the absence of MeCN (with and without sonication). However, this uniform species, which could be assigned to the acetate bridged dimeric structure **[FIP-OAc]$_2$** as described below, showed a relatively low catalytic activity (34% yield). In contrast, when using the standard protocol in MeCN, the second species – a monomer (see below) – appeared and showed significantly broader signals in the ^{1}H-NMR spectra than the dimer.[40] Various catalyst activation experiments at different temperatures (20 – 70 °C) confirmed that catalyst batches with a higher amount of the second species provided better catalytic activities. A relatively high amount of it could be obtained by ultrasound activation at 35 °C (9 min, 160 W, Scheme 2). Under these conditions a ratio dimeric/monomeric species = 1:1.6 was determined and a yield of 73% was obtained (quantitative yield with 1 mol% precatalyst). This activation procedure allowed for high reproducibility under the standard conditions and was used for the experiments described in Table 2.



Scheme 2. Activation procedure of the precatalyst **[FIP-Cl]$_2$**.

Analysis of both the catalyst mixture and pure **[FIP-OAc]$_2$** by ESI-MS did not detect the corresponding molecular ions, but two major fragments. In these fragments the acetate ligands were not bound anymore to the Pd-centers. One of the fragments is the palladacycle which carries an additional acetonitrile ligand. It thus seemed likely that the second monomeric catalyst species that was detected above in the initial ^{1}H-NMR studies, might be the monomeric **FIP-OAc/MeCN** complex (Figure 4). In addition, an ammonia adduct was found, which is formed under the conditions of the ESI-MS experiments.

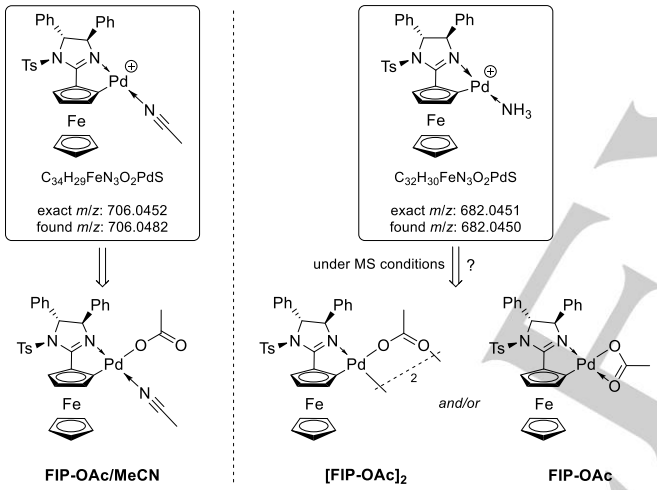


Figure 4. Results and interpretation of ESI-MS experiments.

The presence of acetate in the activated catalyst could be confirmed by negative mode ESI-MS experiments (found: *m*/*z* = 59.01). In addition, HSQC-TOCSY NMR experiments of the acetate bridged dimer showed cross-peaks for a ^{13}C-NMR signal at 23.0 ppm (CH_3), a ^{1}H-NMR signal at 0.88 ppm (CH_3) and a ^{13}C-NMR signal at 177.5 ppm (C=O).

However, when the catalyst activation was repeated in CH_2Cl_2 in the absence of any MeCN, the same two catalyst species as described above (dimer and monomer) were surprisingly found in the ^{1}H-NMR. It thus can be excluded that the second species, which apparently leads to a better catalytic activity, is an acetonitrile complex. On the other hand, using the above described standard activation protocol performed in MeCN, the acetonitrile complex must also be present, as it was detected by ESI-MS, but it was not clearly visible in the standard ^{1}H-NMR.

We hypothesised that the active second species might be the monomeric complex **FIP-OAc** depicted in Figure 4. Catalyst activation by sonication using higher temperatures might favour the monomer entropically. Broader ^{1}H-NMR signals as compared to the dimer **[FIP-OAc]$_2$** might be due to dynamic effects in which the acetate might behave as either monodentate or bidentate ligand (coordination numbers 3 and 4 at Pd, respectively, see Figure 6). For that reason, ^{1}H-NMR spectra of the same catalyst batch were recorded at temperatures between –8 and +50 °C (500 MHz). The spectra at +40 and +50 °C led to significantly sharper signals of the monomeric species. In contrast, at 0 °C and below two different signals sets were resolved for this species, displaying e.g. different signals for the Cp-spectator ligand at 4.47 and 4.36 ppm. Moreover, at the low temperature an additional minor catalyst species became visible by a broad resonance at 3.84 ppm, which was usually too broad to be detected in the temperature range of 20-50 °C. Addition of acetonitrile to this sample led to an increase of the signal's intensity. 2D-NMR experiments showed that this {CH} moiety is a spin system on its own. Therefore, it can be assigned to another C_5H_5 spectator ligand. Our data suggest that this signal belongs to the hidden monomeric acetonitrile complex **FIP-OAc/MeCN**. This species is probably not the active catalyst, because MeCN was found to inhibit the catalytic reaction, but probably in rapid equilibrium with **FIP-OAc**.

The presence of more than two catalyst species is also supported by ^{13}C-NMR, because three distinct C(2)-imidazoline signals at 172.1, 171.7 (**[FIP-OAc]$_2$**) and 171.5 ppm have been resolved at room temperature. In addition three acetate resonances were found at 177.8, 177.5 and 176.8 ppm.

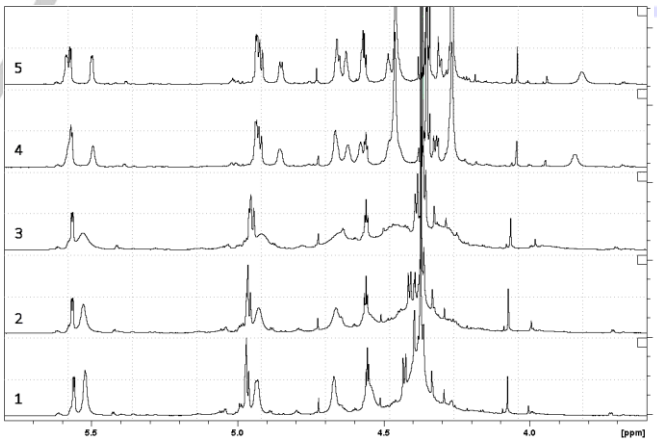
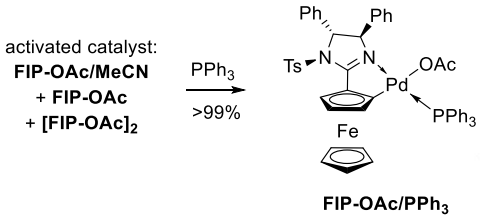


Figure 5. Varying temperature NMR experiments (500 MHz) activated according to Scheme 2: 323 K (1), 313 K (2), 303 K (3), 273 K (4), 265 K (5).

In a recent study Richards *et al.* investigated the nature of related ferrocenylphosphine palladacycles bearing acetate ligands by IR spectroscopy.[41] A key conclusion was that these complexes form the expected dimeric acetate bridged structure in the solid state (IR-ATR, reported ν(CO) signals at 1571 and

1405 cm^{-1}), but in solution they exist as monomeric species bearing bidentate acetate ligands (IR in $CHCl_3$ solution, reported ν(CO) signals at 1486 and 1448 cm^{-1}).[42,43] In our case we found for the uniform **[FIP-OAc]$_2$** species in the solid state ν(CO) signals at 1553 and 1451 cm^{-1} (IR-ATR).[44] Nearly identical data were obtained for the mixture of dimeric **[FIP-OAc]$_2$**, monomeric **FIP-OAc** and **FIP-OAc/MeCN** in the solid state after removal of all solvent by carefully drying in high-vacuum (IR-ATR: ν(CO) signals at 1552 and 1452 cm^{-1}). In contrast, the IR spectrum of a solution in chlorobenzene showed, along these two ν(CO) bands at 1555 and 1458 cm^{-1}, two additional bands at 1596 and 1476 cm^{-1}. The latter are both negligible for the solution of the uniform **[FIP-OAc]$_2$** species in chlorobenzene. These data support the presence of the monomeric species with bidentate and monodentate acetate ligands next to the dimeric species in solution for the active catalyst.[45]

To confirm that all present catalyst species possess after the activation exclusively acetate as an anionic ligand, the mixture was also treated with PPh_3. By that monomeric **FIP-OAc/PPh$_3$** was obtained as the only product in a quantitative yield. A hypothetical hydroxide containing species responsible for the transmetallation of the arylboroxine is thus unlikely under anhydrous conditions. ν(OH) signals were also not visible in the recorded IR spectra. In contrast, the IR spectra of **FIP-OAc/PPh$_3$** in chlorobenzene solution shows an intensive ν(C=O) signal at 1603 cm^{-1} confirming that the peak mentioned above at 1596 cm^{-1} for the most active catalyst mixture belongs to the monomeric species with a monodentate acetate ligand.



Scheme 3. Control experiment to confirm that all species of the activated catalyst carry an acetate ligand.

The aggregation behaviour of the various catalyst species in solution was further investigated by pulsed gradient spin echo (PGSE) NMR experiments in $CDCl_3$.[46] Using the Stokes-Einstein equation and the DiffAtOnce software package,[47] the self-diffusion constant $D = 5.964 \cdot 10^{-10}$ m^2 s^{-1} grants access to the hydrodynamic radius (r_H = 6.35 Å) and the hydrodynamic volume (V_H = 1070.2 Å) of **[FIP-OAc]$_2$**. By contrast, the monomeric, phosphine-containing complex **FIP-Cl/PMe$_3$** measured under the same conditions possesses a much higher self-diffusion constant $D = 7.458 \cdot 10^{-10}$ m^2 s^{-1}, accounting for a smaller hydrodynamic radius (r_H = 5.07 Å) and a considerably smaller hydrodynamic volume (V_H = 547.2 Å) compared to **[FIP-OAc]$_2$**. It is noteworthy that in both cases the self-diffusion coefficients and hydrodynamic radius / volume values obtained from the doublet signal of the methyl of the PMe_3 ligand (δ(^{1}H) = 1.74 ppm, **FIP-Cl/PMe$_3$**) show no deviation compared to those obtained from the ferrocenyl ligand. This is indicative that the faster-than-NMR-time-scale association-dissociation process ([(C∩N)Pd(Cl)(PMe_3)] ⇄ [[(C∩N)Pd(Cl)] + PMe_3 does not occur in solution (or at least is negligible). Such a rapid chemical equilibrium would modify the apparent volume of the corresponding phosphine-containing species, and thus prevent comparison. Based on these data, it seems reasonable to assume that the **[FIP-OAc]$_2$** species is indeed a dimer.

Since the active catalyst apparently consists of monomeric and dimeric complexes, the catalytic model reaction of **1a** and **3B** was also investigated for a possible non-linear effect under the standard conditions of Table 2, entry 1.[48] The *ee* values of the precatalyst batches used were adjusted in 10% steps by mixing the corresponding **[FIP-Cl]$_2$** enantiomers with either (S_p)- or (R_p)-configuration. All 11 catalyst samples investigated provided the product in quantitative yields. In addition, an almost perfectly linear correlation between the product *ee* values and the catalyst *ee* values was found (for details see the Supporting Information). This might indicate that homo- and heterochiral **[FIP-OAc]$_2$** dimers possess a similar stability/reactivity under the reaction conditions with regard to the transformation to the catalytically probably relevant monomeric **FIP-OAc**.

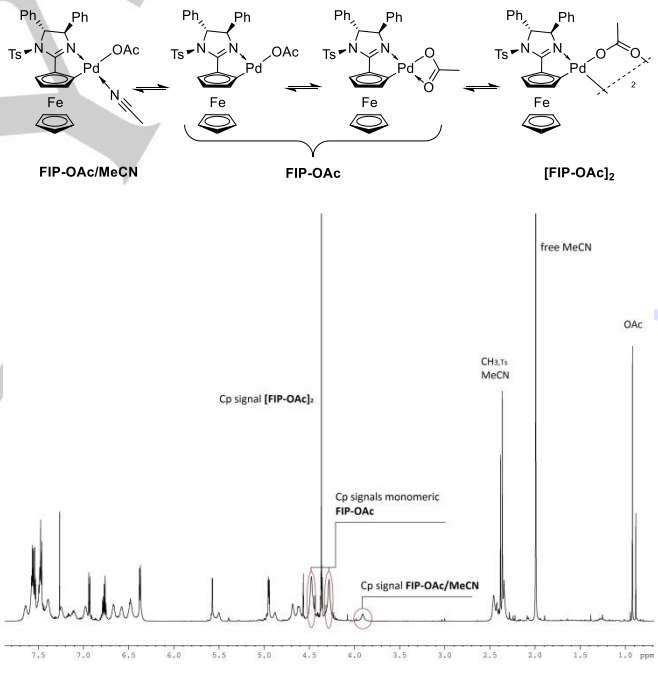
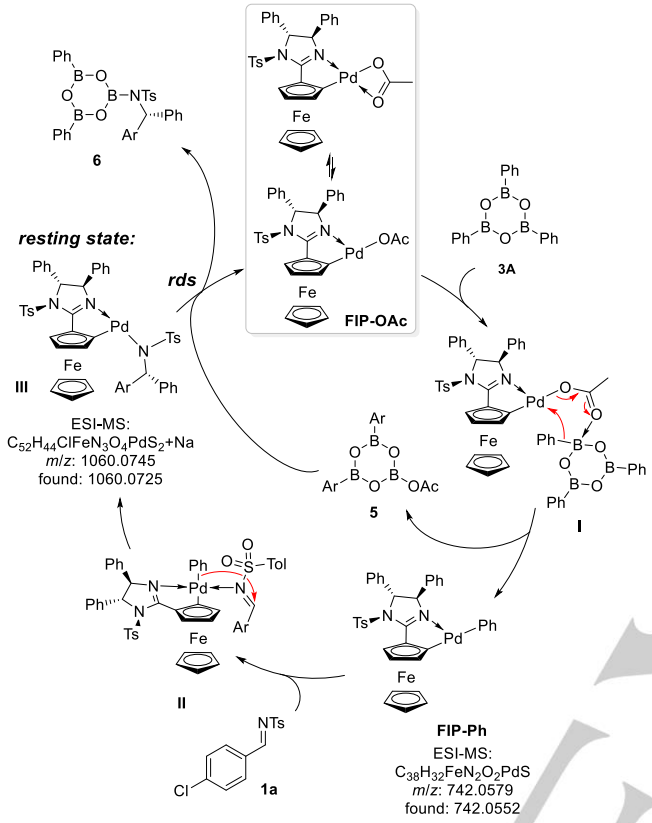


Figure 6. Composition of the activated catalyst and characteristic ^{1}H-NMR signals.

b) The Catalytic Cycle

A mechanistic proposal for a possible catalytic cycle is shown in Scheme 4. As MeCN has an inhibiting influence and the amount of monomeric **FIP-OAc** has a significant impact on the catalytic activity, we suggest that this is the catalytically active species. This compound is supposed to undergo a transmetallation reaction with the boroxine related to the so-called 'oxo-pathway' in Suzuki-Miyaura reactions.[26] The Lewis-basic acetate is

expected in this 'acetate-pathway' to coordinate by its available carbonyl group to a Lewis acidic boron center thus increasing the nucleophilicity of the aromatic residue to be transferred to the Pd-center.



Scheme 4. Proposal of a simplified catalytic cycle including evidence by ESI-MS data.

The success of the transmetallation of an aryl residue of a boroxine to the activated catalyst bearing an acetate ligand in the absence of an exogenous base could be demonstrated by ESI-HRMS experiments. In these experiments a solution of the activated catalyst (2 mol%) and boroxine **3A** was stirred for 60 min in chlorobenzene at 65 °C and was then analysed mass-spectrometrically. The prevailing Pd-containing species that was detected was the Pd-Ph adduct **FIP-Ph** (found *m/z*: 742.0552; calculated: 742.0579). The transmetallation suggests the simultaneous formation of a B-OAc containing compound like **5** (the other Ar groups in **5** might later also be replaced).

Coordination of the imine is expected to occur preferentially *trans* to the imidazoline N-donor based on the typical coordination behaviour of *C,N*-palladacycles.[21,22b] The observed almost exclusive *Re*-face attack at the imine could be explained by a stereochemical model in which the imine's sulfonyl group in **II** points away from the ferrocenyl core in order to reduce repulsive interactions. Product release might be achieved by reaction of the catalyst/product-adduct **III** with the B-OAc species **5**. Thus the catalyst **FIP-OAc** would be regenerated.

Our spectroscopic data point to the product release as the rate limiting step of this reaction. ESI-MS investigation of the reaction mixture under standard reaction conditions and a reaction time of 1 h identified the mass of the catalyst resting state intermediate, which would fit to both **II** or **III** (found *m/z*: 1060.0725; calculated: 1060.0745). Differentiation between both species was possible by ^{1}H-NMR spectroscopy, which showed the absence of the imino N=CH proton, whereas a new broad signal is present at ca. 6.0 ppm which can be assigned to the N-CH proton in intermediate **III** after the 1,2-addition has taken place. After the reaction time of 20 h, nearly all catalyst has been transformed into the product catalyst adduct (determined by the use of an internal standard; next to the Cp signal also the expected 5 characteristic catalyst protons of the substituted Cp ring and the imidazoline core can be clearly resolved at chemical shifts between 4 and 5.5 ppm), whereas after 1 h approximately 50% of catalyst is present in this state as judged from the C_5H_5 signals (for details see the Supporting Information). Additionally, this data indicates that finally the dimeric **[FIP-OAc]$_2$** is also transformed into the catalytically active form, but much slower than the monomer explaining the differences in catalytic activity, in particular using low loadings.

On the other hand this mechanistic picture suggests that the transmetallation which was initially the bottleneck using boroxines (see Table 1) is now an efficient elemental step in the catalytic cycle.

The Arylation of Ketimines

The method development presented above was done with aldimine substrates and hence for the generation of *N*-substituted tertiary stereocenters. However, we were also interested, if **FIP-OAc** is an efficient catalyst for ketimine substrates to form *N*-substituted quaternary stereocenters as well.

In 2010, Hayashi *et al.* reported a Rh-catalysed highly enantioselective arylation of *N*-sulfonylketimines with Ar_4BNa.[49] The reactions proceeded efficiently for arylmethyl ketimines as well as indanone- and tetralone-derived imines, usually in the presence of 5 mol% of Rh. Shortly thereafter, they reported a modified version with improved atom-economy using potassium organotrifluoroborates, for which also a high efficiency was demonstrated using 5 mol% Rh.[50] Triaryl-substituted stereogenic centers could finally be created with high enantioselectivity using boroxine reagents.[51]

The first Pd catalysed enantioselective arylation of ketimines using an organoboron reagent was reported by Zhang *et al.* in 2013.[52] They utilised cyclic ketimines and arylboronic acids, which very efficiently reacted in the presence of an *in-situ* formed Pd^{II} catalyst (5 mol%) bearing a neutral chiral pyridine/oxazoline bidentate ligand. An initial issue of catalyst decomposition by formation of Pd-black was addressed by performing the reaction in the presence of O_2. Moreover, by portionwise addition of the boronic acid (10x) to minimise the formation of Pd-black the catalyst loading could be reduced to 1 mol% still allowing for a high yield and enantioselectivity.

Soon after, Hayashi *et al*. reported a highly enantioselective addition of arylboronic acids to less reactive six-membered

cyclic *N*-sulfonyl ketimines which provided synthetically versatile sulfamidate products.[53,54] A neutral phosphinooxazoline ligand was employed and usually 5-10 mol% of catalyst were used.

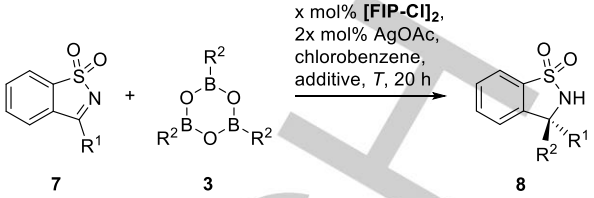
From a mechanistic standpoint there should be a couple of differences in the reactions of either aldimines or ketimines. For instance, in aldimines and cyclic ketimines the non-bonding orbital at the Lewis-basic imino N atom can be located in a different environment. In the former case it is preferentially located *cis* to the aryl moiety of the imine, whereas in the latter case it adopts the *trans*-position. Moreover, it appears that the challenges using ketimines are somewhat shifted compared to aldimines. Thus the nucleophilic addition step is naturally more difficult as a result of larger steric hindrance in ketimines than in aldimines and a usually lower electrophilicity. On the other side, in case of ketimines it can be expected that the initial catalyst/product adduct being generated in the 1,2-addition elemental step is less prone to undergo a decomposition, since a β-hydride elimination cannot occur, as it is the case with aldimines. In addition, the ketimine substrates are considerably less sensitive towards hydrolysis than aldimines due to their diminished electrophilicity. The use of aldimines and cyclic ketimines in the arylation with organoboron reagents thus creates a different scenario for the reaction development.

We initially chose the alkyl substituted ketimine **7a** as model substrate (Table 3, entry 1, R^1 = *n*Bu). Applying the reaction conditions optimised for aldimines did not furnish any of the desired product, using either 1 or 2 mol% of precatalyst both in the absence and presence of NaOAc (1.0 equiv.) as additive. Traces of product **8aA** were found for a precatalyst amount of 5 mol% in the presence of NaOAc. An improvement of the reactivity was found with KOAc. The product was obtained in a yield of 23% and with an *ee* value of 96% under these conditions (entry 2).

Since we assume that the C-H acidic alkyl chain R^1 caused the low yield, we examined substrate **7b** bearing a Ph group instead in the reaction with boroxine **3B**. In that case the reactivity was considerably higher. Both at 50 and 40 °C the product **8bB** was formed in nearly quantitative yields and with high enantioselectivity (entries 3 & 4). A useful reactivity was even noticed in the absence of the additional exogenous base (entries 5 & 6). Unexpectedly though, this resulted in a switch of the preferentially formed enantiomer. Whereas in the presence of KOAc a *Si*-face attack at imine **7b** was largely dominating,[55] in the absence of KOAc the *Re*-face of **7b** was more reactive. In that latter case the enantioselectivity also strongly depended on the reaction temperature. At reaction temperatures of 40 and 50 °C the product was formed with *ee* values of –51% and –34%, respectively. This enantiodivergency was *not* observed for aldimine substrates.

In the presence of KOAc, different catalyst loadings were investigated at a reaction temperature of 50 °C (in analogy to entry 3). Using 1 mol% of precatalyst, the product could be isolated in a quantitative yield in highly enantioenriched form (*ee* = 95%, entry 7). Also for just 0.5 mol% of precatalyst a good yield and enantioselectivity were determined (entry 8).

Table 3. Asymmetric arylation of cyclic ketimines **7**.



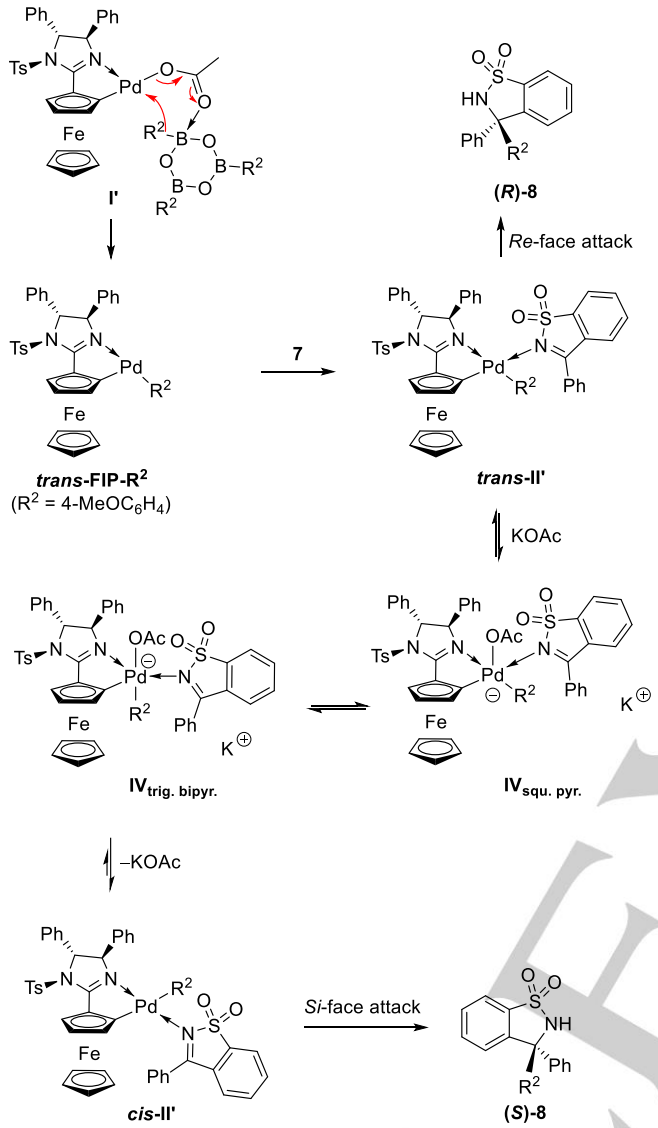
7 **3** **8**

#	**8**	R^1	R^2	x	*T* [°C]	additive (equiv.)	Yield [%][a]	*ee* [%][b]
1	**8aA**	*n*Bu	Ph	5	65	NaOAc (1.0)	6	n.d.
2	**8aA**	*n*Bu	Ph	5	65	KOAc (1.0)	23	96
3	**8bB**	Ph	4-$MeOC_6H_4$	5	50	KOAc (1.0)	99	95
4	**8bB**	Ph	4-$MeOC_6H_4$	5	40	KOAc (1.0)	99	94
5	**8bB**	Ph	4-$MeOC_6H_4$	5	50	-	86	–34
6	**8bB**	Ph	4-$MeOC_6H_4$	5	40	-	51	–51
7	**8bB**	Ph	4-$MeOC_6H_4$	1	50	KOAc (1.0)	>99 [c]	95
8	**8bB**	Ph	4-$MeOC_6H_4$	0.5	50	KOAc (1.0)	80	92
9	**8cB**	3-$MeOC_6H_4$	4-$MeOC_6H_4$	1	50	KOAc (1.0)	75[c]	91
10	**8dB**	4-MeC_6H_4	4-$MeOC_6H_4$	1	50	KOAc (1.0)	98[c]	94
11	**8eA**	CO_2Et	Ph	1	50	KOAc (1.0)	45[c],[d]	82

[a] Determined by ^{1}H-NMR of the crude product using mesitylene as internal standard if not indicated otherwise. [b] Determined by HPLC. A negative sign indicates that the other enantiomer than the one depicted was formed (n.d.= not determined). [c] Yield of isolated product. d) 5 mol% of **[FIP-Cl]$_2$**.

The conditions of entry 7 were then applied to some other substrates. Unfortunately, ketimine **7b** did not undergo an arylation with boroxines carrying electron-withdrawing groups (not shown). In contrast, an electron withdrawing (entry 9), but also an electron donating group (entry 10) on the ketimine residue R^1 was well tolerated. The use of the electron deficient α-iminoester **7e** resulted in a lower enantioselectivity and reactivity than in the other cases (*ee* = 82%, entry 12), maybe for a different coordination behaviour of this substrate or the formed product due to the possibility of chelate formation.[56]

The observation that the arylation of ketimines could not be performed with electron-deficient boroxines indicates that either the transmetallation or the 1,2-addition are the limiting steps in the catalytic cycle. The fact that KOAc massively improves the reactivity also seems to support a scenario, in which the transmetallation is problematic. On the other hand, the transmetallation already worked smoothly using the aldimine substrates even in the absence of KOAc and using electron deficient boroxines. As the same catalyst is used it thus seems unlikely that with ketimines the transmetallation is rate-limiting. We suggest that the 1,2-addition is the most difficult step in this case. To explain the effect of KOAc on both the enantioface differentiation and the reactivity we propose a mechanistic scenario that is depicted in Scheme 5.



Scheme 5. Possible explanation for the observed enantiodivergency in the absence/presence of KOAc.

In this scenario, KOAc is responsible for a smooth isomerisation necessary to obtain high enantioselectivity. We suggest that the acetate triggered transmetallation starting from **FIP-OAc** is a concerted process which initially places the aryl moiety R^2 in *trans*-position to the imidazoline N-donor, whereas the *cis*-position would be available for the ketimine coordination. Like for aldimine substrates, we think that the imine coordination should proceed in a way that the sterically demanding sulfonyl residue points away from the ferrocene core to minimise repulsive interactions. This kinetically preferred coordination mode would result in the (*R*)-configured product by a *Re*-face attack. On the other hand, it is expected that that a switch of the positions of the anionic aryl residue and the neutral ketimine substrate would be thermodynamically preferred in agreement with the commonly observed coordination modes in palladacycles (see above).[21,22b] The Lewis-basic exogenous acetate is proposed to promote this isomerisation via the formation of pentacoordinate intermediate **IV** and acetate dissociation. The switch of the coordination positions would result in a switch of the enantioselectivity. The isomerised complex is probably not only thermodynamically preferred, but also more reactive explaining the improved yields with KOAc. NaOAc is less efficient, as it is less Lewis basic than KOAc due to its lower ionic character.[57] Without exogenous acetate the enantioselectivity is moderate due to a relatively slow isomerisation. Lower temperatures further slow down the isomerisation explaining the considerably higher preference for the unexpected enantiomer in the absence of KOAc.

The question remains why no exogenous acetate is required for high enantioselectivity with aldimines as the isomerisation would also be necessary there. This might be rationalised by a higher Lewis-basicity of the aldimines caused by a better steric accessibility. The imine substrate might thus already play the role reserved for acetate with ketimines.

Conclusions

In conclusion, we have reported a very efficient Pd catalyst for the arylation of aldimines by an organoboron reagent. The performance of this catalyst is on a comparable level with the best Rh catalysts. Compared to cationic Pd^{II} catalysts bearing neutral bidentate ligands the catalyst reported herein is electronically different. It is a more electron-rich palladacycle with an anionic *C*,*N*-ligand. By that the often found tendency to form bisaryl homocoupling products could be successfully eliminated. Using acetate as anionic ligand on the Pd-center is of key importance for two reasons: a) in the presence of acetate there was nearly no more imine hydrolysis observed and b) the acetate apparently promotes the transmetallation from the boroxine to the Pd-center, which was initially the limiting step with boroxine reagents. Synthetically attractive results were obtained for a very broad substrate scope. The element of planar chirality of the ferrocenyl ligand was probably responsible for the remarkably high level of enantioselectivity for most examples. Mechanistic studies suggest that a monomeric ferrocenyl palladacycle acetate complex is the catalytically relevant species and that the product release is rate limiting. The catalyst/product-adduct is thus the resting state in the catalytic cycle. Using ketimine substrates, the presence of KOAc as exogenous base was necessary for an optimal reactivity and enantioselectivity. A surprising enantiodivergency in the absence/presence of this additive might be explained by an isomerisation of the catalytic intermediate ready to undergo the 1,2-addition. With ketimines, the arylation step itself is probably the slowest step, explaining why electron-deficient boroxines were not applicable. This is in contrast to the study with aldimines. Whereas the electron rich nature of the catalyst thus limits the scope with ketimines, it is crucial for the high efficiency with aldimines.

Experimental Section

General Procedure for the Activation of [FIP-Cl]$_2$

Method A: **[FIP-Cl]$_2$** (1 equiv., 11.58 µmol, 16.2 mg) and silver acetate (2 equiv., 23.16 µmol, 3.8 mg) were suspended in acetonitrile (2 mL) under N_2 atmosphere and stirred in the absence of light for 4.5 h at room temperature. The mixture was then filtered through a syringe filter (PTFE) and the solvent was removed under a permanent nitrogen flow. A stock solution was prepared (*c* = 11.58 µmol/2 mL chlorobenzene) and used directly for catalysis.

Method B: **[FIP-Cl]$_2$** (1 equiv., 11.58 µmol, 16.2 mg) and silver acetate (2 equiv., 23.16 µmol, 3.8 mg) were suspended in acetonitrile (2 mL) under N_2 atmosphere and treated with ultra-sound (160 W) for 9 min at 35 °C. The mixture was then filtered through a syringe filter (PTFE) and the solvent was removed under a permanent nitrogen flow. A stock solution was prepared (*c* = 11.58 µmol/2 mL chlorobenzene) and used directly for catalysis.

General Procedure for the Catalytic Asymmetric Arylation of *N*-Sulfonyl-Aldimines with Arylboroxines

To the corresponding *N*-tosylaldimine **1** (1 equiv., 0.058 mmol) and the corresponding boroxine **3** (1 equiv., 0.058 mmol) was added the activated catalyst (prepared from 1 mol% **[FIP-Cl]$_2$**, see above) in chlorobenzene (*c* = 0.29 mol imine/L) under N_2 atmosphere. The mixture was heated to 65 °C in a synthesizer shaking at 250 rpm. After 20 h the reaction mixture was cooled to room temperature and applied to silica gel column chromatography (petrol ether/ethyl acetate (10:1 + 1% NEt_3 to 4:1 + 1% NEt_3)).

General Procedure for the Catalytic Asymmetric Arylation of Cyclic Ketimines with Arylboroxines

To the corresponding *N*-sulfonyl ketimine **7** (1 equiv., 0.058 mmol), the corresponding boroxine **3** (1 equiv., 0.058 mmol) and potassium acetate (1 equiv., 0.058 mmol) was added the activated catalyst (prepared from 1 mol% **[FIP-Cl]$_2$**, see GP1) in chlorobenzene (*c* = 0.29 mol imine/L). The mixture was heated to 50 °C at 250 rpm. After 20 h the reaction mixture was cooled to room temperature, washed with aqueous HCl (1 equiv.) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (petrol ether/ethyl acetate (10:1 to 5:1)).

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Keywords: 1,2-additions • boronic acids • ferrocene • imine • transmetallation

[1] D. Ghislieri, N. J. Turner, *Top. Catal.* **2014**, *57*, 284.

[2] C. A. Busacca, D. R. Fandrick, J. J. Song, C. H. Senanayake, *Adv. Synth. Catal.* **2011**, *353*, 1825.

[3] A. J. Burke, C. S. Marques, *Catalytic Arylation Methods - From the Academic Lab to Industrial Process*, WILEY-VCH GmbH & Co. KGaA, Weinheim, **2015**.

[4] D. A. Pflum, D. Krishnamurthy, Z. Han, S. A. Wald, C. H. Senanayake, *Tetrahedron Lett.* **2002**, *43*, 923.

[5] W. M. Welch, A. R. Kraska, R. Sarges, K. B. Koe, *J. Med. Chem.* **1984**, *27*, 1508.

[6] A. J. Wagstaff, D. Ormrod, C. M. Spencer, *CNS Drugs* **2001**, *15*, 231.

[7] F. Stocchi, C. Fossati, M. Torti, *Expert Opin. Pharmacother.* **2015**, *16*, 2231.

[8] J. Corey-Bloom, R. Anand, J. Veach, *Int. J. Geriatr. Psychopharmacol*. **1998**, *1*, 55.

[9] K.-J. Chang, G. C. Rigdon, J. L. Howard, R. W. McNutt, *J. Pharmacol. Exp. Ther*. **1993**, *267*, 852.

[10] C. S. Marques, A. J. Burke, *ChemCatChem* **2011**, *3*, 635.

[11] a) N. Hermanns, S. Dahmen, C. Bolm, S. Bräse, *Angew. Chem. Int. Ed.* **2002**, *41*, 3692; *Angew. Chem.* **2002**, *114*, 3844; b) M. Shi, W. Zhang, *Tetrahedron: Asymmetry* **2003**, *14*, 3407; c) T. Nishimura, Y. Yasuhara, T. Hayashi, *Org. Lett.* **2006**, *8*, 979.

[12] T. Hayashi, M. Kawai, N. Tokunaga, *Angew. Chem. Int. Ed.* **2004**, *43*, 6125; *Angew. Chem.* **2004**, *116*, 6251.

[13] M. Hayashi, M. Ishigedani, *J. Am. Chem. Soc.* **2000**, *122*, 976.

[14] Selected examples with aldimines: a) N. Kuriyama, T. Soeta, X. Hao, Q. Chen, K. Tomioka, *J. Am. Chem. Soc.* **2004**, *126*, 8128; b) N. Tokunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2004**, *126*, 13584; c) R. B. C. Jagt, P. Y. Toullec, D. Geerdink, J. G. de Vries, B. L. Feringa, A. J. Minnaard, *Angew. Chem. Int. Ed.* **2006**, *45*, 2789; *Angew. Chem.* **2006**, *118*, 2855; d) Z.-Q. Wang, C.-G. Feng, M.-H. Xu, G.-Q. Lin, *J. Am. Chem. Soc.* **2007**, *129*, 5336; e) H. Nakagawa, J. C. Rech, R. W. Sindelar, J. A Ellman, *Org. Lett.* **2007**, *9*, 5155; f) R. Shintani, R. Narui, Y. Tsutsumi, S. Hayashi, T. Hayashi, *Chem. Commun.* **2011**, *47*, 6123; g) T. Korenaga, A. Ko, K. Uotani, Y. Tanaka, T. Sakai, *Angew. Chem. Int. Ed* **2011**, *50*, 10703; *Angew. Chem.* **2011**, *123*, 10891; h) R. H. Crampton, M. Fox, S. Woodward, *Tetrahedron: Asymmetry* **2013**, *24*, 599; i) G.-Z. Zhao, G. Sipos, A. Salvador, A. Ou, P. Gao, B. W. Skelton, R. Dorta, *Adv. Synth. Catal.* **2016**, *358*, 1759; j) T. Yasukawa, T. Kuremoto, H. Miyamura, S. Kobayashi, *Org. Lett.* **2016**, *18*, 2716; k) quinolinium salts: Y. Wang, Y. Liu, D. Zhang, H. Wei, M. Shi, F. Wang, *Angew. Chem. Int. Ed.* **2016**, *55*, 3776.

[15] For an early study of a non-enantioselective reaction, see: M. Ueda, N. Miyaura, *J. Organomet. Chem.* **2000**, *595*, 31.

[16] a) H. Dai, M. Yang, X. Lu, *Adv. Synth. Catal.* **2008**, *350*, 249; b) G.-N. Ma, T. Zhang, M. Shi, *Org. Lett.* **2009**, *11*, 875; c) H. Dai, X. Lu, *Tetrahedron Lett.* **2009**, *50*, 3478; d) Z. Liu, M. Shi, *Tetrahedron* **2010**, *66*, 2619; e) C. S. Marques, A. J. Burke, *Eur. J. Org. Chem.* **2010**, 1639; f) J. Chen, X. Lu, W. Lou, Y. Ye, H. Jiang, W. Zeng, *J. Org. Chem.* **2012**, *77*, 8541; g) X. Gao, B. Wu, Z. Yan, Y.-G. Zhou, *Org. Biomol. Chem.* **2016**, *14*, 55; h) T. Johnson, B. Luo, M. Lautens, *J. Org. Chem.* **2016**, *81*, 4923; i) T. Beisel, A. M. Diehl, G. Manolikakes, *Org. Lett.* **2016**, *18*, 4116.

[17] For non-enantioselective methods, see: a) P. He, Y. Lu, Q.-S. Hu, *Tetrahedron Lett.* **2007**, *48*, 5283; b) F. J. Williams, E. R. Jarvo, *Angew. Chem. Int. Ed.* **2011**, *50*, 4459; *Angew. Chem.* **2011**, *123*, 4551.

[18] There is also one report using a Ru-catalyst: C. S. Marques, A. J. Burke, *Eur. J. Org. Chem.* **2012**, 4232.

[19] a) M. Miura, M. Nomura, *Top. Curr. Chem.* **2002**, *219*, 211; b) D. A. Culkin, J. F. Hartwig, *Acc. Chem. Res.* **2003**, *36*, 234; c) R. Jana, T. P. Pathak, M. S. Sigman, *Chem. Rev.* **2011**, *111*, 1417.

[20] Q. Zhang, J. Chen, M. Liu, H. Wu, J. Cheng, C. Qin, W. Su, J. Ding, *Synlett* **2008**, 935.

[21] a) J. Dupont, M. Pfeffer, *Palladacycles*; Wiley-VCH: Weinheim, Germany, 2008; b) C. J. Richards, in *Chiral Ferrocenes in Asymmetric*

Catalysis, (Eds: L.-X. Dai and X.-L. Hou,), Wiley-VCH, Weinheim, 2010, pp. 337-368; c) H. Nomura, C. J. Richards, *Chem. Asian J.* **2010**, *5*, 1726; d) R. Peters, D. F. Fischer, S. Jautze, *Top. Organomet. Chem.* **2011**, *33*, 139.

[22] Selected studies using ferrocenyl imidazoline monopalladacycles: a) M. E. Weiss, D. F. Fischer, Z.-q. Xin, S. Jautze, W. B. Schweizer, R. Peters, *Angew. Chem. Int. Ed.* **2006**, *45*, 5694; *Angew. Chem.* **2006**, *118*, 5823; b) D. F. Fischer, A. Barakat, Z.-q. Xin, M. E. Weiss, R. Peters, *Chem. Eur. J.* **2009**, *15*, 8722; c) R. Peters, Z.-q. Xin, F. Maier, *Chem. Asian J.* **2010**, *5*, 1770; d) S. H. Eitel, M. Bauer, D. Schweinfurth, N. Deibel, B. Sarkar, H. Kelm, H.-J. Krüger, W. Frey, R. Peters, *J. Am. Chem. Soc.* **2012**, *134*, 4683; e) M. Weber, R. Peters, *J. Org. Chem.* **2012**, *77*, 10846; f) S. H. Eitel, S. Jautze, W. Frey, R. Peters, *Chem. Sci.* **2013**, *4*, 2218; g) J. M. Bauer, W. Frey, R. Peters, *Angew. Chem. Int. Ed.* **2014**, *53*, 7634; *Angew. Chem.* **2014**, *126*, 7764; h) T. Hellmuth, W. Frey, R. Peters, *Angew. Chem. Int. Ed.* **2015**, *54*, 2788; *Angew. Chem.* **2015**, *127*, 2829; selected studies on imidazoline pincer complexes: i) K. Hyodo, S. Nakamura, N. Shibata, *Angew. Chem. Int. Ed.* **2012**, *51*, 10337; j) H. Huang, R. Peters, *Angew. Chem. Int. Ed.* **2009**, *48*, 604; k) M. Ohara, S. Nakamura, N. Shibata, *Adv. Synth. Catal.* **2011**, *353*, 3285; l) K. Hyodo, S. Nakamura, K. Tsuji, T. Ogawa, Y. Funahashi, N. Shibata, *Adv. Synth. Catal.* **2011**, *353*, 3385; m) S. Nakamura, K. Hyodo, M. Nakamura, D. Nakane, H. Masuda, *Chem. Eur. J.* **2013**, *19*, 7304; n) K. Hyodo, M. Kondo, Y. Funahashi, S. Nakamura, *Chem. Eur. J.* **2013**, *19*, 4128; o) M. Kondo, T. Nishi, T. Hatanaka, Y. Funahashi, S. Nakamura, *Angew. Chem. Int. Ed.* **2015**, *54*, 8198; p) M. Kondo, N. Kobayashi, T. Hatanaka, Y. Funahashi, S. Nakamura, *Chem. Eur. J.* **2015**, *21*, 9066; q) M. Kondo, T. Nishi, T. Hatanaka, Y. Funahashi, S. Nakamura, *Angew. Chem. Int. Ed.* **2015**, *54*, 8198; r) M. Kondo, M. Sugimoto, S. Nakamura *Chem. Commun.* **2016**, *52*, 13604.

[23] Selected alternative addition reactions of arylboronic acids (or derivatives) to non-imine electrophiles: a) J. Wong, K. Gan, H. J. Chen, S. A. Pullarkat, *Adv. Synth. Catal.* **2014**, *356*, 3391; b) A. L. Gottumukkala, J. Suljagic, K. Matcha, J. G. de Vries, A. J. Minnaard, *ChemSusChem* **2013**, *6*, 1636; c) A. L. Gottumukkala, K. Matcha, M. Lutz, J. G. de Vries, A. J. Minnaard, *Chem. Eur. J.* **2012**, *18*, 6907; d) Y. Suzuma, S. Hayashi, T. Yamamoto, Y. Oe, T. Ohta, Y. Ito, *Tetrahedron: Asymmetry* **2009**, *20*, 2751; e) Q. Zhang, J. Chen, M. Liu, H. Wu, J. Cheng, C. Qin, W. Su, J. Ding, *Synlett* **2008**, 935; f) T.-K. Zhang, D.-L. Mo, L.-X. Dai, X.-L. Hou, *Org. Lett.* **2008**, *10*, 3689; g) Y.-X. Liao, C.-H. Xing, P. He, Q.-S. Hu, *Org. Lett.* **2008**, *10*, 2509; h) P. He, Y. Lu, C.-G. Dong, Q.-S. Hu, *Org. Lett.* **2007**, *9*, 343; i) T. Yamamoto, T. Ohta, Y. Ito, *Org. Lett.* **2005**, *7*, 4153; j) P. He, Y. Lu, Q.-S. Hu, *Tetrahedron Lett.* **2007**, *48*, 5283; k) Y. Suzuma, T. Yamamoto, T. Ohta, Y. Ito, *Chem. Lett.* **2007**, *36*, 470; l) F. Gini, B. Hessen, A. J. Minnaard, *Org. Lett.* **2005**, *7*, 5309; m) T. Nishikata, Y. Yamamoto, N. Miyaura, *Angew. Chem. Int. Ed.* **2003**, *42*, 2768; *Angew. Chem.* **2003**, *115*, 2874.

[24] Preliminary results were published as a communication: C. Schrapel, R. Peters, *Angew. Chem. Int. Ed.* **2015**, *54*, 10289; *Angew. Chem.* **2015**, *127*, 10428.

[25] Selected studies using ferrocenyl bisimidazoline bispalladacycles: a) S. Jautze, P. Seiler, R. Peters, *Angew. Chem. Int. Ed.* **2007**, *46*, 1260; *Angew. Chem.* **2007**, *119*, 1282; b) S. Jautze, R. Peters, *Angew. Chem. Int. Ed.* **2008**, *47*, 9284; *Angew. Chem.* **2008**, *120*, 9424; c) S. Jautze, S. Diethelm, W. Frey, R. Peters, *Organometallics* **2009**, *28*, 2001; d) M. Weber, S. Jautze, W. Frey, R. Peters, *J. Am. Chem. Soc.* **2010**, *132*, 12222; e) M. Weber, W. Frey, R. Peters, *Adv. Synth. Catal.* **2012**, *354*, 1443; f) M. Weber, S. Jautze, W. Frey, R. Peters, *Chem. Eur. J.* **2012**, *18*, 14792; g) S. H. Eitel, S. Jautze, W. Frey, R. Peters, *Chem. Sci.* **2013**, *4*, 2218; h) M. Weber, W. Frey, R. Peters, *Chem. Eur. J.* **2013**, *19*, 8342; i) M. Weber, J. E. M. N. Klein, B. Miehlich, W. Frey, R. Peters, *Organometallics* **2013,** *32*, 5810; j) M. Weber, W. Frey, R. Peters, *Angew. Chem. Int. Ed.* **2013**, *52*, 13223; *Angew. Chem.* **2013**, *125*, 13465.

[26] Excellent review about the transmetallation mechanism of boronic acids or derivatives in Suzuki-Miyaura-reactions: A. J. J. Lennox, G. C. Lloyd-Jones, *Angew. Chem. Int. Ed.* **2013**, *52*, 7362; *Angew. Chem.* **2013**, 125, 7506.

[27] The use of lower catalyst amounts was also studied. With 0.1 mol% **[FIP-Cl]$_2$** a yield of 93% of nearly enantiopure (>99% *ee*) product **3aA** was obtained, but reproducibility was problematic with such very low loadings.

[28] The different commercial suppliers were not able to overcome this purity problem after we informed them about this issue.

[29] During the course of these studies a transmetallation product has been characterised, which was generated from a Pd-OAc species: A. R. Kapdi, G. Dhangar, J. L. Serrano, J. Pérez, L. Garcia, I. J. S. Fairlamb, *Chem. Commun.* **2014**, *50*, 9859.

[30] A. R. Kapdi, G. Dhangar, J. L. Serrano, J. Pérez, L. Garcia, I. J. S. Fairlamb, *Chem. Commun.* **2014**, *50*, 9859.

[31] M. Weiss, W. Frey, R. Peters, *Organometallics* **2012**, *31*, 6365.

[32] T. Hellmuth, S. Rieckhoff, M. Weiss, K. Dorst, W. Frey, R. Peters, *ACS Catal.* **2014**, *4*, 1850.

[33] For ferrocenecarboxamide the solid state structure was also analysed. CCDC-1463864 contains the supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[34] CCDC-1463866 contains the supplementary crystallographic data for compound **FI(H)**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[35] CCDC-1463867 contains the supplementary crystallographic data for compound **[FIP-Cl]$_2$**. In addition CCDC-1463863 contains the supplementary crystallographic data for the enantiomeric compound *ent*-**[FIP-Cl]$_2$** These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[36] See *e.g*. C. E. Anderson, Y. Donde, C. J. Douglas, L. E. Overman, *J. Org. Chem.* **2005**, *70*, 648 and cited references.

[37] P. G. M. Wuts, T. W. Greene, *Greene's Protective Groups in Organic Synthesis*, Wiley-Interscience; 4th ed., **2006**.

[38] a) R. B. C. Jagt, P. Y. Toullec, D. Geerdink, J. G. deVries, B. L. Feringa, A. J. Minnaard, *Angew. Chem. Int. Ed.* **2006**, *45*, 2789; *Angew. Chem.* **2006**, *118*, 2855; b) J. M. Bauer, W. Frey, R. Peters, *Chem. Eur. J.* **2016**, 22, 5767.

[39] CCDC-1050456 (**4aA**) and CCDC-1050457 (**4dB**) contain supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[40] Catalyst activation with TlOAc (2 equiv.) instead resulted in the same catalyst species with comparable activity. This indicated that Ag(I) ions should not play a significant role in the activated catalyst and that redox processes like formation of Pd(III) or Fe(III) complexes as catalytically active species can be ruled out.

[41] K. Panchal, J. Amin, F. X. Roca, M. Motevalli, P. N. Horton, S. J. Coles, C. J. Richards, *J. Organomet. Chem.* **2015**, *775*, 12.

[42] A dynamic behaviour which was assigned to an interconversion of dimeric and monomeric *C*,*P*-palladacycle complexes bearing weakly coordinating acetate ligands has previously been reported: a) A. J. Cheney, B. L. Shaw, *J. Chem. Soc. Dalton Trans.* **1972**, 860; b) W. A. Herrmann, C. Brossmer, C.-P. Reisinger, T. H. Riermeier, K. Öfele, M. Beller, *Chem. Eur. J.* **1997**, *3*, 1357; c) B. L. Shaw, S. D. Perera, E. A. Staley, *Chem. Commun.* **1998**, 1361.

[43] K. Nakamoto, *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 3rd ed., Wiley-Interscience, New York, **1978**.

[44] For **[FIP-Cl]$_2$** a signal at 1542 cm^{-1} is also detected (IR-ATR), but the signal intensity is much lower than for the ν(CO) signals. This signal

can be assigned to the C=N bond in the imidazoline similar to the free ligand (ref. 22a). The C=N bands in the activated catalyst species are probably hidden by the much more intensive acetate signals.

[45] Unfortunately, all trials to get single crystal of the activated catalyst suitable for X-ray analysis have failed so far, often as a result of a slow catalyst decomposition. As one decomposition product the compound $[Fe_3O(OAc)_7 \cdot H_2O]$ was identified, which consist of $[Fe_3(\mu_3\text{-}O)(\mu\text{-}OAc)_6]^+$ clusters that are linearly connected by acetate ions (see the Supporting Information). CCDC-1463868 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. A related material forming 3D-networks was recently reported: J.-P. Zhao, S.-D. Han, X. Jiang, J. Xu, Z. Chang, X.-H. Bu, *Chem. Commun.* **2015**, *51*, 4627. For the molecular structure of the cluster see also: A. R. Burgoyne, R. Meijboom, A. Muller, B. O. Omondi, *Acta Cryst.* **2011**, *67*, 1092.

[46] The PGSE experiments were run as three sets of 12 PGSE experiments as described in T. Augenstein, F. Dorner, K. Reiter, H. E. Wagner, D. Garnier, W. Klopper, F. Breher, *Chem. Eur. J.* **2016**, *22*, 7935. For details see the supporting information.

[47] DiffAtOnce Molecular Diffusion, available at www.diffatonce.com.

[48] T. Satyanarayana, S. Abraham, H. B. Kagan, *Angew. Chem. Int. Ed.* **2009**, *48*, 456; *Angew. Chem.* **2009**, *121*, 464.

[49] R. Shintani, M. Takeda, T. Tsuji, T. Hayashi, *J. Am. Chem. Soc.* **2010**, *132*, 13168.

[50] R. Shintani, M. Takeda, Y. T. Soh, T. Ito, T. Hayashi, *Org. Lett.* **2011**, *13*, 2977.

[51] a) T. Nishimura, A. Noishiki, G. Chit Tsui, T. Hayashi, *J. Am. Chem. Soc.* **2012**, *134*, 5056; b) see also: T. Nishimura, A. Noishiki, Y. Ebe, T. Hayashi, *Angew. Chem. Int. Ed.* **2013**, *52*, 1777; *Angew. Chem.* **2013**, *125*, 1821.

[52] a) G. Yang, W. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 7540; *Angew. Chem.* **2013**, *125*, 7688; see also: b) Q. He, L. Wu, X. Kou, N. Butt, G. Yang, W. Zhang, *Org. Lett.* **2016**, *18*, 288; c) M. Quan, G. Yang, F. Xie, I. D. Gridnev, W. Zhang, *Org. Chem. Front.* **2015**, *2*, 398.

[53] C. Jiang, Y. Lu, T. Hayashi, *Angew. Chem. Int. Ed.* **2014**, *53*, 9936; *Angew. Chem.* **2014**, *126*, 10094.

[54] Very recently, a Pd-catalyzed enantioselective arylation of trifluoromethylated/perfluoroalkylated 2-quinazolinones could also be achieved: B. Zhou, C. Jiang, V. R. Gandi, Y. Lu, T. Hayashi, *Chem. Eur J.* **2016**, *22*, 13068.

[55] The absolute configurations were assigned by comparison to literature data reported for **8aA** (see ref. 52) and for **8bB** (see ref. 51a).

[56] Very recently, a Pd-catalyzed enantioselective arylation of cyclic α-ketiminophosphonates with arylboronic acids could also be achieved: Z. Yan, B. Wu, X. Gao, Y.-G. Zhou, *Chem. Commun.* **2016**, *52*, 10882.

[57] R. S. Sah, B. Sinha, M. N. Roy, *Fluid Phase Equilib.* **2011**, *307*, 216.

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Entry for the Table of Contents

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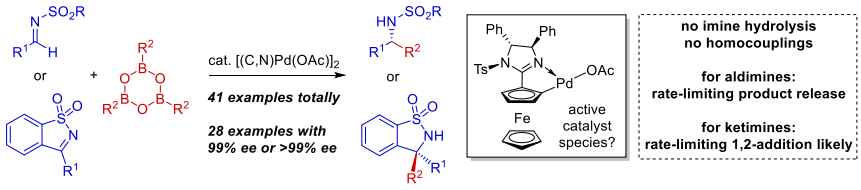

A planar chiral ferrocenyl palladacycle acetate complex catalyzes the 1,2-addition of arylboroxines to *N*-sulfonyl aldimines and cyclic ketimines with high enantioselectivity. Spectroscopic studies suggest that (1) a monomeric species is the active catalyst, (2) the acetate ligand promotes the transmetallation, (3) the product release is rate-limiting for aldimines. With ketimines additional acetate is necessary for high enantioselectivity causing a switch of the preferred enantiomer.

*Carmen Schrapel, Wolfgang Frey, Delphine Garnier, and René Peters**

Page No. – Page No.

Highly Enantioselective Ferrocenyl Palladacycle-Acetate Catalysed Arylation of Aldimines and Ketimines with Arylboroxines