Bispalladacycle Catalyzed Nucleophilic Enantioselective Allylation of Aldehydes by Allylstannanes

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Enantiopure homoallylic secondary alcohols are very important synthetic building blocks due to the versatility of the hydroxyl and olefin moieties. A key strategy to prepare them is by nucleophilic allylation of aldehydes. A large number of catalyst concepts emerged that allow for high enantioselectivity. Still, in many target-oriented syntheses of complex structures stoichiometric methods are preferred over catalytic ones. The need for high catalyst loadings and long reaction times, plus unsatisfying reproducibility and substrate scopes are reasons for that. In the present study we report the first palladium catalysts capable of controlling asymmetric nucleophilic allylations of aldehydes with allyltbutyltin.TONs up to 620 were achieved, which is significantly higher than for any other reported catalyst. The method is also tolerating electronically and sterically unfavorable substrates. We show that a transmetallation occurs, favoring an η1-allyl coordination mode with the bispalladacycles. In contrast, for the corresponding monopalladacycle an unproductive η3 coordination is dominant.

Introduction

The enantioselective generation of a C–C bond by nucleophilic allylation of carbonyl derivatives is an important strategy to synthesize scemical homoallylic alcohols which are building blocks of high added value owing to the rich chemistry of olefin and alcohol moieties.[1] A large number of useful methods has been reported employing various types of nucleophilic allylation reagents.[1] For Lewis acid catalysis, organometallic allyl reagents based on silicon and tin proved to be effective.[1] With the more reactive tin reagents next to the frequently used hard Lewis acid catalysts like those based on titanium,[2] also soft Lewis acid catalysts featuring a silver(I)[3] and palladium(II)[4] metal center have been described. In this context, highly enantioselective methods could for instance be developed for imine substrates using chiral Pd(II) catalysts.[5] In addition, related non-enantioselective Pd-catalyzed allylations of aldehydes were studied in detail by Szabó et al., including thorough spectroscopic and computational investigations.[6] They showed that these reactions most likely proceed via a transmetallation pathway featuring a nucleophilic η1-allyl palladium intermediate, which reacts with an aldehyde via a Zimmerman-Traxler-type transition state (Scheme 1, top).[6]

Previous work:

Enantioselective aryl addition to imines:

This work:

Enantioselective allyl addition to aldehydes:

Szabó et al. emphasized the beneficial use of (a) a tridentate ligand to enforce an η1-allyl coordination mode and avoid reductive coupling with the allyl and (b) an electron rich ligand to ensure sufficient allyl nucleophilicity.[6b]

In spite of these fundamental studies, enantioselective asymmetric variants for the allylation of aldehydes with stannanes and silanes were so far elusive using Pd(II)
catalysts. In general, despite the considerable progress for catalytic enantioselective Lewis acid catalyzed allylations with the previously reported catalyst types, the need for a high catalyst loadings and long reaction times, plus unsatisfying reproducibility and substrate scopes are issues that await to be further addressed, because in many cases stoichiometric methods are still preferred over catalytic ones in the synthesis of complex homoallylic structures.

Recently, our group reported that ferrocene based imidazoline palladacycles\[9,10\] are proficient catalysts for 1,2-addition reactions of arylboronates to imines, which allowed for nearly perfect enantioface differentiation for a large number of examples (Scheme 1, middle).\[9\] With the applied electron rich soft Lewis acid catalyst, reductive coupling between an aryl moiety and the ferrocenyl ligand was found to be suppressed.

We are interested in exploring the general reactivity of this and related catalyst systems\[9–11\] using other useful electrophiles and nucleophile (organometallic) reagents. Since the use of aldehydes was previously not successful in highly enantioselective Pd catalyzed nucleophilic allylations with allylstannanes or -silanes, we were curious if our palladacycle catalysts could manage this substrate type.

The binding affinity of aldehydes to a soft Pd(II) center is considered low and should hamper the search for a highly active, enantioselective catalyst. If successful though, a Pd catalyst might open up further possibilities in the conversion of substrates with sensitive functionalities or in coping with unresolved synthetic problems. Soft palladacycles might offer the advantage of tolerating a number of functional groups as a result of their lower oxophilicity compared to hard Lewis acid catalysts.

Here we report that ferrocene bisimidazoline bispalladacycle complexes\[9,10\] are proficient catalysts for the nucleophilic allylation of aldehydes with allyltin reagents. The procedure allows for high enantioselectivity in the depicted 1,2-addition to a broad range of aldehydes including electronically challenging ones.

Results and Discussion

For our initial studies the addition of allylttributyltin 2 to p-chlorobenzaldehyde 1a was selected (Table 1). Different metalloocene based palladacycles from our portfolio were surveyed. They were activated prior to use by chloride exchange with AgOTs.\[9–11\] For each chloride ligand of the precatalysts one equiv. of silver salt was used. Already with [FIP–Cl]\[2\] based on sterically demanding 1’,2’,3’,4’,5’-pentaphenylferrocene the product in moderate yields and in (nearly) racemic form (entries 4 & 5). A similar activity was found for the heterobimetallic [FBIP–Cl]\[2\], precatalyst\[10g\] (entry 6). Formally exchanging one palladium(II) for a platinum(II) center resulted in moderate yield and enantioselectivity. In addition we examined the ruthenocene based bispalladacycle\[9\] [RuBIP–Cl]\[2\], which demonstrated a similar activity as [FBIP–Cl]\[2\] but acted less enantioselectively (entry 7).

In contrast, the catalysts [PPFIP–Cl]\[2\] and [PPFOP–Cl]\[2\] based on sterically demanding 1’,2’,3’,4’,5’-pentaphenylferrocene delivered the product in moderate yields and in (nearly) racemic form (entries 4 & 5). A similar activity was found for the heterobimetallic [FBIPP–Cl]\[2\], precatalyst\[10g\] (entry 6). Formally exchanging one palladium(II) for a platinum(II) center resulted in moderate yield and enantioselectivity. In addition we examined the ruthenocene based bispalladacycle\[9\] [RuBIP–Cl]\[2\], which demonstrated a similar activity as [FBIP–Cl]\[2\] but acted less enantioselectively (entry 7).

Based on these results, [FBIP–Cl]\[2\] was chosen to probe the effect of the anionic ligands Y− installed by silver salts during catalyst activation.\[10d\] We also tested the precatalyst as such, without activation, hosting the tightly binding chloride ligands (entry 8). This complex was also capable of forming 3a in high yield, but enantioselectivity was only moderate. On the other side, the effect of the weakly coordinating triflate and the non-coordinating hexafluorophosphate was studied. The former allowed for moderate enantioselectivity and with the latter almost racemic product was formed (entries 9 & 10).

In addition, silver carboxylates were screened. While the less electron-rich trifluoroacetate (entry 11) resulted in poor enantioselectivity, with acetate (entry 12 & 13) the best screening results were accomplished. With the standard precatalyst loading of 0.5 mol%, the product was formed in nearly

| Table 1. Development and optimization of the asymmetric nucleophilic allylation of aldehydes. |
| --- |
| X mol% [Pd–Cl]2 | Y | Z | Yield [%] | ee [%] |
| 1 | [FIP–Cl]2 | 5 | 10 | OTs | 87 | 85 |
| 2 | [FBIP–Cl]2 | 2.5 | 10 | OTs | 94 | 97 |
| 3 | [FIP–Cl]2 | 0.5 | 2 | OTs | 93 | 94 |
| 4 | [PPFIP–Cl]2 | 0.5 | 2 | OTs | 49 | 7 |
| 5 | [PPFOP–Cl]2 | 0.5 | 2 | OTs | 59 | 0 |
| 6 | [FBIPP–Cl]2 | 0.5 | 2 | OTs | 51 | 49 |
| 7 | [RuBIP–Cl]2 | 0.5 | 2 | OTs | 94 | 73 |
| 8 | [FIP–Cl]2 | 2.5 | 10 | OTf | 93 | 72 |
| 9 | [FBIP–Cl]2 | 2.5 | 10 | OTf | 54 | 5 |
| 10 | [FBIP–Cl]2 | 2.5 | 10 | PF6 | 87 | 7 |
| 11 | [FBIP–Cl]2 | 0.5 | 2 | TFA | 70 | 16 |
| 12 | [FIP–Cl]2 | 0.5 | 2 | OAc | 97 | 95 |
| 13 | [FBIP–Cl]2 | 0.05 | 2 | OAc | 62 | 89 |

\[a\] Yield determined by 1H-NMR. \[b\] Enantiomeric excess determined by GC. OTs: p-tolylsulfonate; TFA: trifluoroacetate; OAc: acetate; OTf: triflate.
quantitative yield and with an ee of 95%. With a loading of just 0.05 mol%, an ee of 89% and a TON of 1240 (based on the dimeric precatalyst, 620 per ferrocene unit) was attained. AgOAc was thus selected as activation reagent for the further studies.[12]

The nature of the FBIP-OAc catalyst was investigated spectroscopically. H- and 13C-NMR spectra show a single C, symmetric species. Elucidation of the structure by X-ray single crystal analysis shows a monomeric complex in which both Pd(II) centers are bridged by two symmetric acetate ligands (Figure 1).[13]

As a result of this double bridging the Pd(II) centers get in close contact to each other with a Pd···Pd interspace of 2.8486(4) Å. An interatomic Pd–Pd distance of ≥ 3.26 Å would be expected based on the van der Waals radii if there is no bonding character between both Pd centers.[14] We have previously shown by DFT calculations of similar structurally characterized FBIP complexes that weak d–d interactions can support short Pd···Pd distances in such systems.[15]

The optimized conditions were then applied to different aldehyde types (Table 2). Like the electron poor model substrate 1a (entry 1), other aromatic substrates equipped with σ-acceptor substituents provided attractive results (entries 2–9). Ortho-, meta- and para-substitution as well as disubstitution patterns were all well tolerated. Very similar results were obtained for substrates bearing π-acceptor substituents at the various positions (entries 10–13). Using the ortho-nitro substituted aldehyde, the minor enantiomer was not detectable (entry 12).

Remarkably, also particularly electron rich substrates possessing π-donor substituents at all positions of the aromatic ring were well accommodated (entries 20–26). In the case of methoxy substituents, 1.0 to 2.0 mol% of FBIP–OAc was used to form the product in high yields (88–90%) and with high enantioselectivity (94–96% ee, entries 20–23). With a dimethylamino moiety as very strong π-donor, a loading of 5.0 mol% FBIP–OAc was employed to ensure useful yields (61–78%) and good to excellent enantioselectivity (79–99% ee, entries 24–26). To our knowledge, the successful use of ortho-amino benzaldehyde substrates has not been reported before.[16]

Likewise, the use of electron-rich heteroaromatic aldehydes was studied. With 1 mol% of FBIP–OAc the allyl 2-furan, 2-thienyl and N-Ts-2-pyryl methyl and N-Ts-2-pyryl carbinols were formed in good yields

Table 2. Investigation of the aldehyde scope.

| θ | R        | X (mol%) | yield [%][a] | ee [%][b] |
|---|----------|----------|--------------|-----------|
| 1 | 4-Cl-C6H4 | a        | 1.0          | 92        | 96        |
| 2 | 3-Cl-C6H4  | b        | 1.0          | 86        | 91        |
| 3 | 2-Cl-C6H4  | c        | 1.0          | 73        | 87        |
| 4 | 3,5-Cl2-C6H3 | d       | 1.0          | 97        | 90        |
| 5 | 4-Br-C6H4  | e        | 1.0          | 94        | 91        |
| 6 | 2-Br-C6H4  | f        | 1.0          | 80        | 88        |
| 7 | 3-OMe-C6H4 | g        | 1.0          | 89        | 95        |
| 8 | 3,5-(MeO)2-C6H3 | h   | 1.0          | 88        | 92        |
| 9 | 4-F-C6H4   | i        | 1.0          | 89        | 95        |
| 10| 4-O-N-C6H4 | j       | 1.0          | 93        | 89        |
| 11| 3-O-N-C6H4 | k       | 1.0          | 99        | 91        |
| 12| 2-O-N-C6H4 | l       | 1.0          | 70        | > 99      |
| 13| 4-NC-C6H4  | m        | 1.0          | 81        | 90        |
| 14| Ph        | n        | 1.0          | 86        | 93        |
| 15| 4-Me-C6H4  | o        | 1.0          | 69        | 91        |
| 16| 3-Me-C6H4  | p        | 1.0          | 77        | 96        |
| 17| 2-Me-C6H4  | q        | 1.0          | 83        | 96        |
| 18| 3-MeOCH2-C6H4 | r  | 1.0          | 71        | 91        |
| 19| 2-MeOCH2-C6H4 | s  | 1.0          | 78        | 96        |
| 20| 4-MeO-C6H4 | t        | 2.0          | 89        | 94        |
| 21| 2-MeO-C6H4 | u        | 2.0          | 88        | 96        |
| 22| 2,3-(MeO)2-C6H3 | v | 1.0          | 90        | 96        |
| 23| 3-Me-4-MeO-C6H4 | w | 1.0          | 90        | 95        |
| 24| 4-Me-N-C6H4 | x | 5.0          | 61        | 79        |
| 25| 3-Me-N-C6H4 | y | 5.0          | 78        | 99        |
| 26| 2-Me-N-C6H4 | z | 5.0          | 70        | 95        |
| 27| 2-furyl    | za       | 1.0          | 80        | 95        |
| 28| 2-thienyl  | zb       | 1.0          | 75        | 98        |
| 29| N-Ts-2-pyryl | zc  | 1.0          | 74        | 93        |
| 30| 2-naphthyl | zd       | 1.0          | 87        | 99        |
| 31| 9-anthracenyl | ze  | 1.0          | 78        | 93        |
| 32| 2-vinyl-C6H4 | zf  | 1.0          | 88        | 95        |
| 33| 2-(TMS-Cl)=C6H4 | zg | 2.0          | 91        | 93        |
| 34| (E)-PhCH=CH | zh      | 1.0          | 77        | 91        |
| 35| 1-Cyclohexenyl | zl | 5.0          | 61        | 82        |
| 36| Ph=C≡C     | zm       | 1.0          | 76        | 84        |
| 37| N-OCH3     | zn       | 1.0          | 75        | 80        |
| 38| Ph-(CH2)3  | zl       | 1.0          | 67        | 88        |
| 39| n-heptyl   | zm       | 5.0          | 77        | 86        |
| 40| n-propyl   | zn       | 5.0          | 68        | 96        |

[a] Yield of product 3 isolated by chromatography. [b] Enantiomeric excess determined by GC or HPLC. [c] Based on the optical rotation, the (R)-configured product was formed in excess (see Supporting Information). [d] Determined by 1H-NMR. Ts: tosyl.

Figure 1. X-ray single crystal structure analysis of FBIP–OAc (color code: C (gray); N (blue); O (red); S (yellow); Fe (orange); Pd (magenta). Thermal ellipsoids are drawn at a 50% probability level. Hydrogen atoms and acetone (2 molecule per unit cell) are omitted for clarity.
and with high enantioselectivity (entries 27–29). To our surprise, it was found that product 3zc featuring the N-Ts-2-pyrorroyl moiety seems to have a different absolute configuration than that depicted in the general formula of 3 in Table 2 as judged from optical rotation data (see Supporting Information).

Furthermore, aromatic aldehydes with extended conjugation were used. Next to 2-naphthyl and 9-anthracenyl residues, also 2-vinyl- and 2-alkynyl-phenyl residues allowed for attractive yields and enantioselectivities employing 1.0–2.0 mol% of catalyst (entries 30–33).

Besides, enals (entries 34 & 35) and ynals (entry 36) can be utilized. In the case of the trisubstituted 1-cyclohexenyl system 5.0 mol% FBIP were used to accomplish a useful yield (entry 35).

Importantly, the catalyst system is not only applicable to conjugated aldehydes, but also to aliphatic ones possessing enolizable alkyl chains. With benzzyloxyacetaldehyde and phenethylcarbaldehyde 1.0 mol% catalyst provided useful yields and good enantioselectivity (entries 37 & 38). With π-octanal and n-butanal (entries 39 & 40) 5.0 mol% were used and 86% and 96% ee were attained, respectively.

These 40 examples demonstrate a broad applicability of the palladacycle catalyst, which is readily prepared in 5 steps from ferrocene featuring a direct diastereoselective biscyclopalladation as key step.[10] The most noteworthy results are arguably those with ortho-substituted aldehydes and strong π-donors. FBIP–OAc demonstrated its capability of effectively and efficiently activating these difficult substrates, building products 3 in good yields and with high enantioselectivity. For instance, there are only few examples of useful catalysts for the highly enantioselective synthesis of 3u in literature.[17–19] With a TON of 44 and 96% ee, FBIP–OAc is comparable with the so far best catalyst for this reaction type, a Rh(III)–N,C,N pincer complex (TON 16, 93% ee).[17–19]

To demonstrate the utility of the new method we also applied it to a larger scale. 0.5 g of 1a were thus treated under the standard conditions of Table 2/entry 1 with the allyl tin reagent and gave 0.628 g of 3a (97% yield).

As a general literature trend, Lewis acid catalyzed metalloylations usually proceed with lower effectiveness and enantioselectivity compared to the transfer of the parent allyl group and thus represent a challenge.[20,21] Treating aldehydes 1 with metallytin reagent 4 as outlined in Table 3, catalyst activation by AgOTs was found to allow for high enantioselectivity (Table 3, entry 2).

Under these conditions, further substrates containing electron-withdrawing substituents at the ortho, meta or para position of the aryl moiety were applied, providing useful yields and selectivities (entries 4–7). The best enantioselectivity was attained for the para-nitro substituted benzaldehyde (entry 7). In contrast, the best yield was obtained for the parent benzaldehyde (entry 8). With π-donors, the results were less useful (e.g. 4-methoxybenzaldehyde: 37%, 63% ee, not shown).

In addition, we also briefly looked into the use of γ-substituted allyl tin reagents. There are numerous examples for Lewis acid catalyzed reactions in literature showing a stereoconvergent reaction outcome with allylstannanes and -silanes. Both (E)- and (Z)-configured allyl moieties often resulted in a syn-configured homoallylic alcohol product which was explained by open transition states.[22]

In our investigation, for crotylation of model substrate 1a, a 6:1 mixture of (Z)- and (E)-crotyl reagent was used. Unfortunately, FBIP–OAc showed no significant activity. Instead precatalyst activation by AgOTs allowed for a useful product yield (Scheme 2).

However, in toluene at 60 °C the homoallylic alcohol was formed as nearly 1:1 syn/anti mixture. The anti-isomer was formed with an ee of 53%, whereas an 18% ee was determined for the syn-isomer. In MeCN at room temperature, both isomers were formed with around 60% ee, but still as 1:1 mixture. While these results are synthetically not attractive, these experiments provide the mechanistic information that the γ-C-atom is transferred to the carbonyl moiety.

By mass spectrometry (ESI, positive) of a sample of the reaction mixture, an FBIP complex carrying two allyl ligands was detected with m/z = 1228.098 (calculated: 1228.103) and the expected characteristic isotopic pattern (See Supporting Information).

1H-NMR experiments in both THF-d8 and benzene-d6 were performed to elucidate if a transmetallation takes place between the allylin reagent and the bipalladacycles activated by AgOTs and AgOAc. In each case, the catalysts were treated with 1.0 equiv. of allyl tributyltin per Pd atom at room temperature. Shortly after the addition, the initial catalyst species and the tin reagent were not detectable anymore. Signals that

| Table 3. Asymmetric nucleophilic metallylation of aldehydes. |
|---|
| | 1 | 4 | 5 |
| # | R | Y | 1/5 yield [%] | ee [%] |
| 1 | 4-Cl-C6H4 | OAc | a | 70 | 51 |
| 2 | 4-Cl-C6H4 | OTs | a | 45 | 92 |
| 3 | 4-Cl-C6H4 | O2CCF3 | a | 59 | 87 |
| 4 | 3-Cl-C6H4 | OTs | b | 64 | 88 |
| 5 | 2-Cl-C6H4 | OTs | c | 73 | 78 |
| 6 | 4-Br-C6H4 | OTs | e | 68 | 92 |
| 7a | 4-Br-C6H4 | OTs | j | 79 | 95 |
| 8 | Ph | OTs | n | 84 | 81 |
| 7b | Ph | OTs | | |

[a] Yield of product isolated by chromatography. [b] Enantiomeric excess determined by GC. Ts: tosyl.
might belong to the protons at the \( \gamma \)-position of an \( \eta^1 \) bound allyl moiety rapidly appeared in \(^1\)H-NMR spectra. In benzene-\( d_6 \), they are located at 4.12 and 3.88 ppm, comparable to the work of Szabó.\(^{[6a]} \) In addition there is a broad signal at 6.06 ppm (\( \beta \)-position). \(^{[6b]} \) Bu_3Sn-OAc was detected in benzene-\( d_6 \) as the only Sn-species after 1 h by \(^{119}\)Sn-NMR at 93.15 ppm (reagent: \(-18.61 \) ppm).\(^{[22]} \) In control experiments, FBIP-OAc was also treated with either allyl magnesiumbromide or allyl trifluoroborate in THF-\( d_8 \). In both cases, the same species was found as with the allyl tin reagent, thus confirming that transmetallation of the allyl fragment took place.

Based on the literature, only an \( \eta^1 \) allyl ligand is expected to have a proper nucleophilic character.\(^{[6]} \) Usually, \( \eta^1 \) allyl Pd(II) complexes are more stable though and only certain ligand structures can enforce the preferential formation of \( \eta^1 \) allyl species.\(^{[23]} \) By comparison of FIP (between 2.9 and 3.5 ppm four new signals visible for the major species in \(^1\)H-NMR in benzene-\( d_6 \)) and FBIP, the bimetallic nature of the FBIP system arguably favors the \( \eta^1 \) over \( \eta^2 \) allyl binding.

Substrate coordination was studied by IR spectroscopy. Defined aldehyde amounts were gradually added to the activated catalyst dissolved in dry, degassed CH\(_2\)Cl\(_2\). IR spectra were recorded, from which the spectrum of the catalysts was subtracted. The characteristic carbonyl signal of the \( \eta^1 \)-allyl Pd(II) derivative \( 1z \) appeared at a wavenumber of 1711 cm\(^{-1} \) for the non-coordinated substrate (Figure 2, top, black curve).

Addition of 0.1 equiv. of \( 1z \) to FBIP-OAc resulted in a decrease of the wavenumber by 26 cm\(^{-1} \) to 1695 cm\(^{-1} \) (orange curve), like expected for a coordination of the carbonyl group.\(^{[26]} \) There was still a shoulder at 1711 cm\(^{-1} \) which got more prominent with addition of more aldehyde. Next to coordinated aldehyde, also free aldehyde was thus present.

Characteristic is also the C–N valence vibration at 1219 cm\(^{-1} \) for the free substrate.\(^{[27]} \) In the presence of FBIP-OAc, another band appears at 1148 cm\(^{-1} \) (Figure 2, bottom). The decreased wavenumber indicates a weakening of the C–N bond and might be explained by additional coordination of the amino group. Between both bands there is a broad area of increased signal intensity which might indicate the presence of different coordination modes or conformations. Qualitatively similar results were also obtained with \( \text{ortho} \)-methoxy benzaldehyde \( 1u \) (see Supporting Information).

For the corresponding meta-substituted aldehydes \( 1y \) and \( 1g \), coordination seems less defined. For \( 1g \) the shift of the carbonyl band from 1710 cm\(^{-1} \) to lower wavelengths leads to a complex broad absorption band between 1620 and 1670 cm\(^{-1} \) (Figure 3). Compared to \( 1u \), the band is much more diffuse. Moreover, a shift to lower wavenumbers was observed for the C–O valence vibration. Similar results were obtained for \( 1y \) (see Supporting Information).

These different results might be interpreted by different coordination behavior. A bidentate coordination might occur for both the \( \text{ortho} \)- and \( \text{meta} \)-substituted aldehydes based on the characteristic signal shifts. For the former substrates this might be a chelate formation. In the latter case chelate formation is unlikely for geometric reasons, but a bridging bimetallic coordination is conceivable for the \( \text{meta} \)-substitution pattern. Since the ferrocene core is quite flexible around the Cp–Fe axis, the system could be dynamic thus explaining the undefined bands after coordination. Control experiments were also performed with the different aldehyde types using [FIP-OAc]_\( 2 \). In this case no shifts of the aldehydes’ IR signals were found. This indicates that aldehyde coordination to the monopalladacycles is less efficient than with the bispalladacycles. As shown above, in the latter case the Pd center is not coordinatively blocked by an \( \eta^1 \) allyl ligand. Nevertheless, also

**Figure 2.** Details of the IR-spectra of free aldehyde \( 1z \) (black curve) and for \( 1z \) in the presence of FBIP–OAc in CH\(_2\)Cl\(_2\), in the latter case with gradual increase of the aldehyde amount. Signals of catalyst were subtracted. Top: shift of the C–O signal to lower wavenumbers in the presence of catalyst. Bottom: shift of the signal of the C–N valence vibration to lower wave-numbers in the presence of catalyst.

**Figure 3.** Detail of the IR-spectra of free aldehyde \( 1g \) (black curve) and for \( 1g \) in the presence of FBIP–OAc in CH\(_2\)Cl\(_2\), in the latter case with gradual increase of the aldehyde amount. Signals of catalyst were subtracted. Diffuse shift of the C–O signal to lower wavenumbers in the presence of catalyst.
for FBIP–OAc the binding affinity of the aldehydes is still too low to detect the catalyst/aldehyde adduct by 1H-NMR.

[FIP–OAc] and FBIP–OAc were also examined in terms of a possible non-linear effect. Catalytic experiments were thus performed with catalyst batches of different enantiomeric purity. For the dimeric monopalladacycle a small negative non-linear effect was found (see Supporting Information). In contrast, for the monomeric bispalladacycle FBIP–OAc, a linear correlation was found indicating that only one catalyst molecule is probably involved in the turnover limiting step and that the catalyst stays monomeric during the course of the reaction.

The reaction progress kinetic was analyzed making use of 1H-NMR spectroscopy for monitoring (details are given in the supporting information). The robustness of the catalyst during the model reaction using 1a and 2 and a possible inhibition by product 3a was investigated. Table 4 summarizes the initial concentrations for the different experiments. In each case the catalyst concentration was 0.0044 mol/L.

Figure 4 depicts the reaction profiles of these three experiments showing the decay of aldehyde 1a. K1 (blue curve) is used as the standard experiment. In K2 (red curves) the starting concentration of 1a equals the concentration at 50% conversion in K1. By time adjustment it gets clear that K2 proceeded significantly faster than K1. Possible reasons might be catalyst decomposition during the first 50% of conversion in K1 and/or product inhibition, because K2 started with no product present, which might inhibit the reaction. In experiment K3 (green curves) 50 mol% of product 3a was thus added using conditions that are otherwise identical to K2. By the added product the reaction got significantly slower.

After time shift the green curve is only slightly below the blue curve thus indicating that a product inhibition is likely. Moreover, this comparison suggests that there might be some catalyst decomposition taking place which is in agreement with the observation of the formation of some Pd black during the reaction.

The empirical rate law was determined from the initial reaction rates using the differential method, because catalyst decomposition should not play a significant role yet due to the low conversions. Monitoring was performed again by 1H-NMR spectroscopy using 1,2-diphenylethane as standard. Eq. (1) shows a first order kinetic dependence for catalyst FBIP–OAc and orders of 0.6 for the aldehyde and 0.8 for the allyltin reagent:

\[
  r = k_{\text{obs}} [\text{FBIP–OAc}]^{0.99} [1\text{a}]^{0.57} [2]^{0.75}
\]  

Figure 5. Feasible bimetallic mode of action.

Table 4. Initial concentrations for the reaction progress kinetic analysis experiments.

| Experiment          | [1a] (mol/L) | [2] (mol/L) | [3a] (mol/L) |
|---------------------|--------------|-------------|--------------|
| K1 (standard)       | 0.44         | 0.53        | –            |
| K2 (same excess)    | 0.22         | 0.31        | –            |
| K3 (product addition)| 0.22         | 0.31        | 0.22         |

Figure 4. Reaction profiles showing 1a according to Table 4.
nucleophilic allyl attack by a Lewis acidic Pd(II) center in Pd sinker complexes was demonstrated before by the theoretical studies of Le Floch et al.\(^6\) Our previous work showed that neutral substrates possess a distinct preference to coordinate trans to the catalyst’s N-ligand atom.\(^{10,11}\) We assume that the carbonyl moiety is almost in plane with the Pd(II) coordination sphere to minimize repulsive interactions with the other catalyst half. In contrast, anionic ligands usually bind trans to the C donor atom.\(^{10,11}\) Nucleophilic attack of an η\(^1\) bound allyl ligand in that position at the second Pd center would then occur at the aldehyde’s Si face.

Conclusion

In conclusion, we have reported that FBIP–OAc is the first example of a Pd catalyst capable of catalyzing the asymmetric nucleophilic allylation of aldehydes with allyltributyltin. Compared to literature known non-Pd catalysts, the catalytic activity of FBIP–OAc is superior. While in literature maximum TONs are typically <20, with FBIP–OAc a TON of up to 620 was achieved. The method could be applied to a broad range of different aldehydes, usually providing the desired products in high yields and with high enantioselectivities. Particularly remarkable is the efficiency with aromatic aldehydes carrying π-donors. For instance, this is the first case where an amino group in ortho position was well tolerated on an aldehyde substrate. Attractive results were also achieved with the challenging metalaryl transfer. Spectroscopic studies suggest that a transmetallation of the allyl residue to Pd takes place, favoring an η\(^2\)-coordination with the bimetallic catalyst and a probably unproductive η\(^1\)-coordination for the monometallic catalyst. Only for the bimetallic catalyst system we detected aldehyde coordination by IR spectroscopy. The η\(^1\)-binding mode might impede the efficient substrate coordination in the monometallic system.

Experimental Section

Reagents were purchased from commercial suppliers and used without further purification unless otherwise stated in the Supporting Information. Prior to use, liquid aldehydes were purified by distillation under inter gas atmosphere, solid aldehydes were purified by dry silica and dry CH\(_2\)Cl\(_2\) distillation under inter gas atmosphere, solid aldehydes were recorded on a Bruker Avance spectrometer at 25 °C using the corresponding Lamor frequencies of the investigated nuclei at 300 or 400 MHz (\(^{1}H\)), 100 MHz (\(^{13}C\)) and 375 MHz (\(^{2}Cl\)). The enantiomeric excess of alcohols was measured by analytical GC or HPLC on chiral stationary phase. ESI-mass spectra were measured on a MicroTOFQ.

Further experimental procedures and data are given in the Supporting Information.

Acknowledgements

This work was financially supported by the Deutsche Forschungsgemeinschaft (DFG, PE 818/4-2). We thank the analytical service of the Institute of Organic Chemistry at the University of Stuttgart for their support. Open Access funding enabled and organized by Projekt DEAL.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: 1,2-addition · asymmetric catalysis · bimetallic catalysis · ferrocene · palladium

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Manuscript received: January 21, 2022
Revised manuscript received: February 10, 2022
Accepted manuscript online: February 14, 2022
Version of record online: March 2, 2022