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Catalytic Performance of Symmetrical and Unsymmetrical Sulfur-Containing Pincer Complexes: Synthesis and Tandem Catalytic Activity of the First PCS-Pincer Palladium Complex

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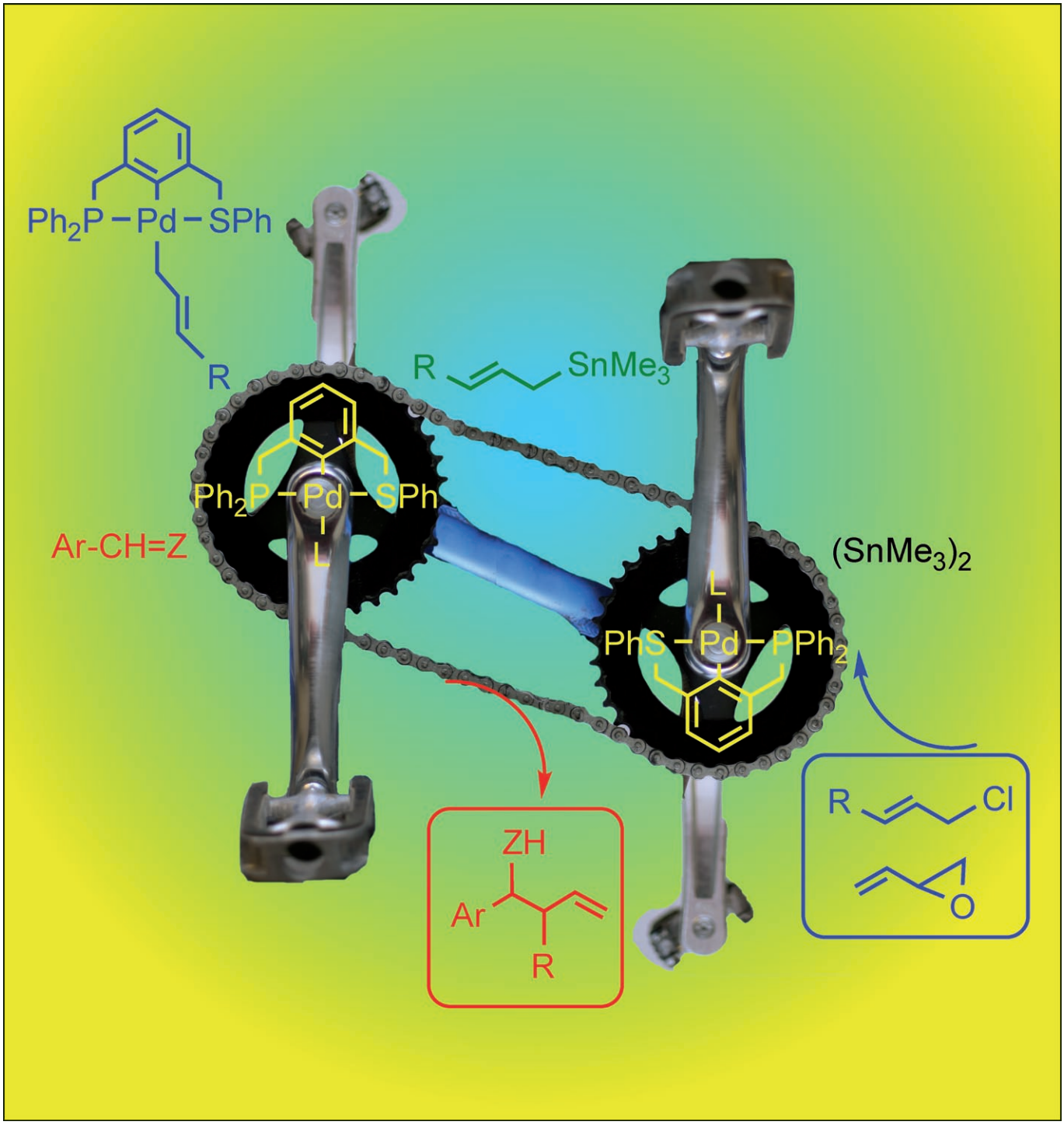

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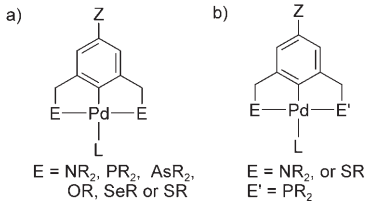
Abstract: The synthesis and catalytic applications of a new aryl-based unsymmetrical PCS-pincer complex are reported. Preparation of the robust air- and moisture-stable PCS-pincer palladium complex **5**[X] started from the symmetrical α,α′-dibromo-*meta*-xylene and involved the selective substitution of one bromide by $PPh_2(BH_3)$, followed by substitution of the second bromide by SPh and subsequent introduction of the palladium. The new PCS complexes (**5**[X]) were employed as catalysts in two important organic transformations. Firstly, complex **5**[Cl] displays high catalytic activity in aldol reactions but enters the catalytic cycle as a precatalyst. Secondly, complex **5**-$[BF_4]$ displays tandem catalytic activity in the coupling of allyl chlorides with aldehydes and imines in the presence of hexamethylditin. In these tandem catalytic reactions the first process is the conversion of allyl chlorides into trimethylallyltin (and trimethyltin chloride) with Sn_2Me_6, which is followed by catalytic allylation of aldehyde and sulfonimine substrates. In addition, we present a new catalytic process for the one-pot allylation of 4-nitrobenzaldehyde with vinyloxirane. The catalytic performance of the novel PCS-pincer palladium complex was compared to those of its symmetrical PCP- and SCS-pincer complex analogues. It was concluded that the unsymmetrical PCS complex advantageously unifies the attractive catalytic features of the corresponding symmetrical pincer complexes including both (π-) electron-withdrawing (such as phosphorus) or (σ-) electron-donating (such as sulfur and nitrogen) heteroatoms. Thus, in the aldol reaction the PCS-pincer palladium complex **5**[X] provides a high turnover frequency, while in the tandem process both reactions are catalysed with sufficiently high activity.

Keywords: aldol reaction · allylation · electrophilic addition · palladium · pincer complexes

Introduction

Aryl-based monoanionic, ECE-pincer ligands—$[C_6H_3(CH_2E)_2\text{-}2,6]^-$, where E = NR_2, PR_2, AsR_2, OR, SR or SeR (Scheme 1a)—are a versatile class of organic species, thanks to their unique properties in binding a metal ion through a strong M–C σ-bond and in forming two metallacycles, representing M–E coordination, with this bond in common.[1] The properties of the metal centre in an ECE-pincer complex can be controlled both by the nature of the E-donor and by the various substituents R on the E-group, as well as by the nature of the *para*-substituent on the aryl ring of the pincer itself.[2] A variety of ECE-pincer metal complexes display interesting activities as catalysts in various synthetically important organic reactions including C–C and C–X bond-formation reactions.[2,3] The fact that the aryl-based ECE-pincer metal complexes can be easily *para*-functionalized (Z in Scheme 1) has allowed exploration of their use as immobilized catalysts on various soluble and insoluble supports, including silica,[4] polymers,[5] functionalized dendrimers,[6] porphyrins,[7] Buckminsterfullerenes,[8] peptides[9] and enzymes.[10] Because aryl-based pincer complexes are highly stable species that are easy to immobilize, these complexes can be applied as the core units of robust and sustainable catalysts. Design of such economically and environmentally benign reusable catalytic systems represents one of the greatest challenges in modern organic synthesis.



Scheme 1. General formula for aryl-based a) symmetrical and b) unsymmetrical pincer complexes.

ECE-pincer palladium complex catalysis[4,11–14] has recently been focused on two particularly important application areas: aldol reactions[4e,12] and transformations involving allylmetal compounds.[13] Symmetrical aryl ECE-pincer metal catalysts (Scheme 1a) have been applied exclusively in these catalytic transformations, because of the stability, modularity and relatively simple availability of these species. It was found[11–14] that the electronic properties of the heteroatoms in the side arms have a particularly powerful influence on the selectivities and reactivities of the pincer palladium catalysts in the above reactions. However, previous studies on aldol reactions have also indicated that there are considerable mechanistic differences between complexes, depending on the σ-donor/π-acceptor properties of the heteroatoms.[11,12i–j,14] In various cases, this leads to catalysts with different selectivities and activities. Allylations of aldehydes and imines, for example, are readily catalysed by PCP-pincer palladium complexes, whereas complexes with σ-donating

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heteroatoms (NCN and SeCSe) have displayed lower (if any) catalytic activity.[13a–d] Interestingly, formation of allylmetal species proceeds smoothly with NCN, SCS and SeCSe complexes, but PCP complexes display very low activity.[13d,f–k]

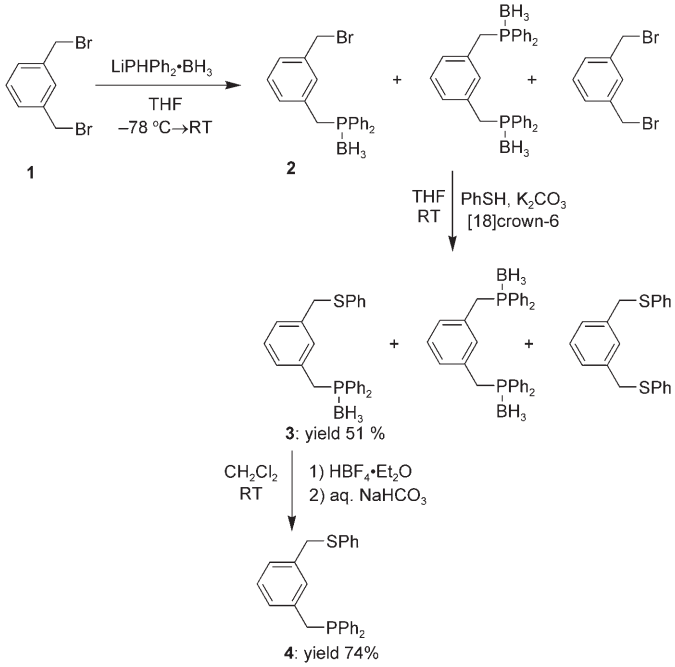
These observations prompted us to synthesise and explore the catalytic activities of a novel class of pincer palladium catalysts using combinations of σ-donor/π-acceptor effects in the pincer ligands. A possible way to accomplish this goal is to use the unsymmetrical ECE′-pincer complexes shown in Scheme 1b.

The first unsymmetrical PCN-pincer palladium complexes were reported by Dupont, Monteiro and co-workers[3b,15a]. These complexes, generated by chloropalladation of heterosubstituted alkynes, proved to be highly reactive catalyst precursors in coupling of arylboronic acids with aryl chlorides. Aryl-based unsymmetrical (PCN) pincer metal (i.e., rhodium) complexes have also been reported by Milstein and co-workers,[15b–d] and during the preparation of this paper an excellent method for the synthesis of PCN-pincer palladium complexes was reported by Song and co-workers.[15e]

In order to study the composite effects of electron-withdrawing and -donating side arms in palladium-catalysed aldol reactions[12] and transformations involving allylmetal compounds,[13] we have designed a new aryl-based pincer complex catalyst. Considering the synthetic aspects of obtaining such a complex (see below), we chose phosphorus as π-acceptor heteroatom and sulfur as the σ-donor one to make up a PCS-pincer complex (Scheme 1b, E = SPh, E′ = PPh_2). We employed the corresponding palladium complex as catalyst in the aldol condensation of methyl isocyanoacetate with benzaldehyde, as well as in tandem catalytic transformations of allyl chloride or vinyloxirane substrates with aldehyde and sulfonimine reagents. The major focus of this study is on the mechanistic aspects of having two electronically different donor atoms (phosphorus and sulfur) present in the pincer ligand. Moreover, it was also of interest to see whether the PCS-pincer palladium complex would combine the different activities and selectivities of PCP- and SCS-pincer palladium complexes in the corresponding C–Sn and C–C coupling reactions discussed and could thus lead to a catalytic tandem reaction. This latter aspect is particularly interesting because previous attempts to perform tandem catalytic reactions with a single, symmetrical ECE-pincer complex failed, and synthetically useful procedures could only be performed by the simultaneous use of two different (NCN and PCP) complexes.[13d] In the reference reactions, we employed symmetrical SCS- (Scheme 1a, E = S) and in some cases PCP-catalysts under the same reaction conditions as the PCS-pincer palladium catalyst. As the performance of the SCS-complexes in many related catalytic transformations have not yet been explored, we have also been able to present some new interesting applications with this system.

Results and Discussion

Synthesis of the unsymmetrical PC(H)S-pincer pro-ligand: The synthesis of symmetrical pincer arene ligands typically starts from α,α′-dibromo-*meta*-xylene (**1**, Scheme 2) by nucleophilic displacement of the benzylic bromines. By application of excesses of NR_2-, PR_2-, SR- or other nucleophiles the corresponding symmetrical ECE-pincer ligand can be obtained in usually excellent yields.[1–3] As the two bromines in **1** are symmetrically equivalent, synthesis of unsymmetrical ECE′-pincer ligands requires selective and sequential nucleophilic substitution of the benzylic leaving groups, which is obviously a more challenging task.



Scheme 2. Synthesis of the PCHS–pincer arene **4**.

Pro-ligand **4** was prepared in three steps from commercially available α,α′-dibromo-*meta*-xylene (**1**, Scheme 2). Treatment of **1** with one equivalent of Li-$PPh_2(BH_3)$ (prepared in situ) yielded a mixture containing monophosphine **2** (63%) and diphosphine $[C_6H_4\{CH_2P(BH_3)Ph_2\}_2$-1,3] (12%), together with unreacted **1** (25%). This mixture of compounds was used without further purification. Full conversion of the benzylic bromides into thioethers was achieved by treatment of the mixture with an excess of thiophenol in the presence of K_2CO_3. Separation of the resulting borane-protected PC(H)S pro-ligand **3** from the symmetrical SCHS- and PCHP-pincer arenes was carried out by column chromatography. Subsequent deprotection of the diphenylphosphino-BH_3 moiety in **3** with $HBF_4{\cdot}OEt_2$, followed by a basic workup, gave the PC(H)S-pincer arene **4** as an air- and moisture-sensitive white solid. In the ^1H NMR spectrum of **4**, recorded in $CDCl_3$, the benzylic protons are found as a singlet at 4.02 ppm (SCH_2) and as a singlet at

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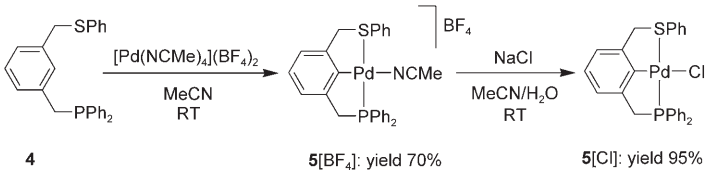
3.39 ppm (PCH_2). The $^{31}P\{^1H\}$ NMR spectrum shows a singlet at −7.23 ppm (PPh_2), whereas the ^{13}C NMR spectrum of **4** (in $CDCl_3$) shows a doublet at 35.99 ppm ($^1J_{C,P}$ = 15.9 Hz) for the benzylic PCH_2 carbon.

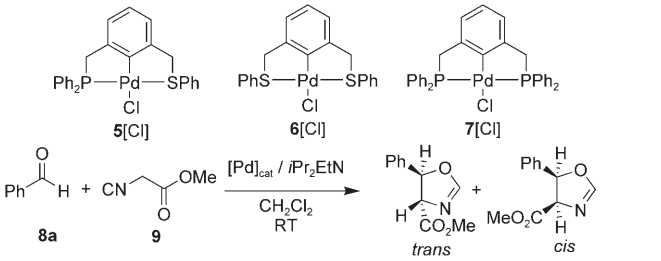
Synthesis of neutral and cationic PCS-pincer Pd^{II} complexes: The cationic PCS–Pd^{II} complex **5**[BF_4] was prepared by electrophilic C–H activation upon treatment of **4** with $[Pd(NCMe)_4](BF_4)_2$[16] (Scheme 3). Complex **5**[BF_4] was



Scheme 3. Synthesis of ionic **5**[BF_4] and neutral **5**[Cl] PCS–Pd^{II} complexes.

readily converted into the neutral **5**[Cl] by treatment with excess NaCl in an acetonitrile/water mixture (Scheme 3). Both complexes were isolated as air-stable, yellow solids, which can be stored without change for months in air at ambient temperature. The ^1H and ^{31}P NMR data for **5**[BF_4] and **5**[Cl] are similar and consistent with binding of the PCS-pincer ligand in a terdentate fashion. The downfield shift of the single resonance for the benzylic SCH_2-protons in the ^1H NMR spectrum of **5**[BF_4], relative to that in the free arene **4**, confirms coordination of the S-donor atom to the palladium centre. This resonance is broadened as a result of fluxional behaviour attributed to various processes such as reversible Pd–S bond breaking and formation, and pyramidal inversion at the sulfur atom. These processes lead to isomers in which the phenyl group coordinated to the S-centre occupies either an axial or equatorial position.[17] The presence of an apparent molecular symmetry plane (the palladium coordination plane) is reflected in the enantiotopicity of the benzylic PCH_2 protons. These appear as a doublet in the ^1H NMR spectrum, due to coupling with the phosphorus centre. The ^{31}P NMR spectrum shows only one resonance at 49.7 ppm for **5**[BF_4], which is shifted with respect to the [Pd(PCP)(NCMe)]$(BF_4)_2$[18] and [PdCl(PCP)][18] complexes.

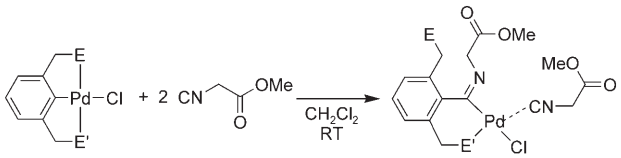
Catalytic performance of 5[Cl] as pre-catalyst in an aldol condensation: The catalytic activities of the new PCS-pincer complex and those of the known SCS- and PCP-pincer complexes **5**[Cl], **6**[Cl][14] and **7**[Cl][18] were compared as Lewis acid pre-catalysts in the aldol condensation reaction between methyl isocyanoacetate (**9**) and benzaldehyde (**8a**, Scheme 4). The data reported in Scheme 4 show that PCS complex **5**[Cl] is the fastest catalyst (entry 1), with a *trans*/*cis* ratio of the product comparable to that obtained when the reaction is carried out with SCS-pincer palladium complex **6**[Cl] (entry 2). In contrast with these results, the PCP-catalyst is the slowest, also giving a different *cis*/*trans* ratio of the products. Previous studies[4e,12j] have shown that **7**[Cl]



entry	[Pd]$_{cat}$	10a	10b	TOF
1	5[Cl]	57%	43%	75
2	6[Cl]	59%	41%	46
3	7[Cl]	82%	18%	17

Scheme 4. Aldol condensation reaction between benzaldehyde (**8a**) and methyl isocyanoacetate (**9**). Turnover frequency (TOF) is given as mol of product per mol of catalyst in the first hour.

as such is indeed the catalyst for this reaction, whereas the SCS-pincer palladium complex **6**[Cl] is in fact a pre-catalyst.[4e] Thus, complex **6**[Cl][4e] and the PCS-complex **5**[Cl]—but not **7**[Cl]—are converted by the methyl isocyanoacetate substrate **9** into the corresponding 1:1 isocyanide insertion products **11a** and **11b** (Scheme 5).



5[Cl]: E = SPh, E' = PPh_2
6[Cl]: E = SPh, E' = SPh
9
11a: E = SPh, E' = PPh_2
11b: E = SPh, E' = SPh

Scheme 5. Insertion of methyl isocyanoacetate into the Pd–C bond of the neutral [PdCl(PCS)] complex **5**[Cl] (this study) and **6**[Cl] (see ref. [4e]).

Insertion of an isocyanide into the M–C bond of a cyclometallated compound has been extensively studied[4e,11,12i–j] and has also been documented for ECE-pincer palladium-d^8 complexes (NCN[12i–j] and SCS[4e,14]). The fact that PCP-pincer complex **7**[Cl] appears to be stable towards insertion[12j] has been ascribed to the stronger P–Pd coordination of the two *ortho*-(diphenylphosphino)methyl substituents relative to the Pd–N and Pd–S bonding in the corresponding NCN- and SCS-pincer palladium(II) complexes. Recently we have shown[4e,12i–j] that a likely reaction mechanism for this insertion reaction involves coordination of the isocyanide as a ligand *cis* to the aryl C atom in the symmetrical ECE-pincer palladium complex (E = NMe_2 or SPh), which may only occur through prior decoordination of one or both of the *ortho*-ligands. These findings prompted us also to study the reactivity of PCS complex **5**[Cl] towards alkyl isocyanide **9** in CH_2Cl_2. It was found that PCS complex **5**[Cl] readily reacted with isocyanide **9** to afford a quantitative yield of complex **11a** (Scheme 5), incorporating two isocyanoacetate molecules. One of the isocyanoacetates has insert-

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ed into the Pd–C bond, whereas the second one is η^1-*C*-coordinated to the palladium centre.

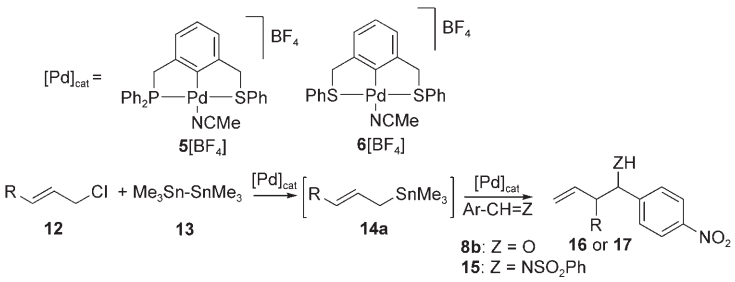
Complex **11a** was characterised by elemental analysis and by IR and NMR spectroscopy. The ^{1}H NMR spectrum of a solution of **11a** in CD_2Cl_2 showed patterns pointing to the presence of both inserted and coordinated methyl isocyanoacetate. The singlet methylene hydrogen signal at 3.52 ppm is indicative of a non-coordinated CH_2SPh group, whereas the doublet ($^2J_{H,P}=10.8$ Hz) of the methylene hydrogen at 4.25 ppm for the CH_2PPh_2 group in the ^{1}H NMR spectrum, as well as the downfield singlet resonance at 47.8 ppm (cf. −7.2 ppm for the free PCHS-pincer arene **4**) in the ^{31}P{^{1}H} NMR spectrum, are consistent with a coordinated CH_2PPh_2 group. Further confirmation of the formation of a 1:1 insertion complex was provided by solution IR spectra, which showed absorptions for a *C*-coordinated isocyanide [$\tilde{\nu}$(C≡N)] at 2230 cm^{-1} (vs. 2166 cm^{-1} for free **10**) and for the imidoyl moiety [$\tilde{\nu}$(C=N) at 1627 cm^{-1}.

The rapid insertion of **9** into the Pd–C bond of complex **5**[Cl] contrasts with the stability of **7**[Cl] towards this reagent and has been ascribed to the more labile coordination of the Pd–S bond in **6**[Cl] relative to that of the Pd–P one. As a consequence, in **11a** it is the S-donor ligand that is the non-coordinated one.

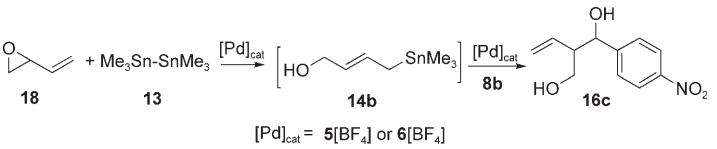
With regard to the mechanistic details of the aldol reaction catalysed by **5**[Cl] it seems likely that prior Pd–S bond cleavage occurs with η^1-coordination of the incoming methyl isocyanoacetate (**9**). This is followed by insertion of the isocyanide into the Pd–C bond, which is followed by η^1-coordination of the second molecule of **9** to give **11a** (cf. reaction in Scheme 5). Subsequently, it is the η^1-coordinated isocyanoacetate (**9**) molecule that then undergoes the aldol reaction. Consequently, the resulting isocyanoacetate (**9**) insertion compounds (**11a–b**) are the active catalysts in the aldol reaction in the cases of PCS (**5**[Cl]) and SCS (**6**[Cl]) which in fact are true pre-catalysts. In contrast, the PCP-pincer complex **7**[Cl] follows a different reaction coordinate involving halide displacement and η^1-*C* coordination of a methyl isocyanoacetate (**9**).[12j]

The catalytic results obtained with complexes **5**[Cl], **6**[Cl] and **7**[Cl] in this aldol condensation show how changes in the nature of the pincer ligand donor arms can affect the reactivity of the corresponding metal complexes. In this specific case, changing the arms from symmetrical sulfur heteroatoms (**6**[Cl]) to symmetrical phosphorus heteroatoms (**7**[Cl]) alters the direct interaction/reaction of these complexes with **9**, and as a result alters the mechanism of the catalysed reaction, resulting in different activities (TOFs and product selectivities).

SCS- and the PCS-pincer complexes as catalysts for tandem catalysis: Recent reports showed[13d,f–i] that NCN- and SeCSe-pincer palladium complexes (Scheme 1a, E=N, Se) are excellent catalysts for preparation of allylmetal species, such as allylstannanes (Scheme 6, **12** → **14a**) and allylboronates, whereas the PCP-pincer palladium complexes (Scheme 1a, E=P) are less efficient catalysts in these processes. On the contrary, allylation of aldehydes and imines (Scheme 6, **14a** → **16**/**17**) can be performed with much more efficiency with PCP-catalysts than with the corresponding NCN- or SeCSe-catalysts.[13d] Accordingly, we anticipated that with PCS-pincer palladium catalyst **5**[BF_4] it should be possible to perform both catalytic processes in a tandem sequence. Indeed, a tandem catalytic coupling of allyl chlorides (**12a** and **12b**) and vinyloxirane (**18**) with aldehyde **8b** or sulfonimine **15** reagents could be achieved with hexamethylditin (**13**) in the presence of catalytic amounts (5 mol%) of **5**[BF_4] (Schemes 6, 7, Table 1). These reactions resulted



Scheme 6. Tandem catalytic approach for stannylation of allyl chlorides followed by allylation of aldehyde and imine substrates **8b** and **15**. The catalyst employed in this process, [Pd]$_{cat}$, is either complex **5**[BF_4] or complex **6**[BF_4].



Scheme 7. Tandem catalytic allylation of **8b** with vinyloxirane (**18**) in the presence of **5**[BF_4] or **6**[BF_4] as catalyst.

in formation of homoallyl alcohols (**16a–c**) and homoallyl amines (**17a–b**) via intermediate formation of allylstannanes (**14a**). These processes could be performed under mild conditions (40°C) as genuine one-pot reactions in a single operational step. Accordingly, all reagents (**12**, **13**, **8b**/**15** and ionic catalyst **5**[BF_4]) were mixed together at the beginning of the reaction, and after the allotted reaction time (16 h) the products (**16** or **17**) were isolated. The reactions with allyl chloride (**12a**) proceeded cleanly and with relatively high isolated yields of 63–78% (entries 1 and 3). When a substituted allyl chloride (such as cinnamyl chloride, **12b**) was used, the yields dropped slightly (59–60%), but they still remained respectable, considering that the product is formed in a tandem catalytic process (entries 5 and 7).

The diastereoselectivity of the reaction is poor in the case of allylation of 4-nitrobenzaldehyde (**8b**, entry 5), but it is rather promising for allylation of sulfonimine **15** (entry 7). The major diastereomer obtained is the *anti* form in the case of allylation of **8b** and the *syn* form in that of allylation of **15**. Previously, we have studied[13b,l] the roles of steric and electronic interactions in determining the stereoselectivity in

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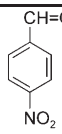
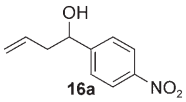
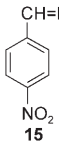
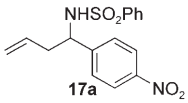
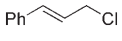
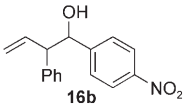
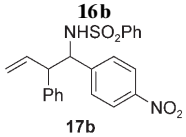
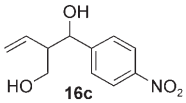
Table 1. Tandem catalytic reactions in the presence of symmetrical (**6**[BF_4]) and unsymmetrical (**5**[BF_4]) pincer complexes as catalysts.

Entry	Allyl reagent	Electrophile	Cat.	[°C]/[h][b]	Product	Yield [%][c]	dr[d]
1	 **12a**	 **8b**	**5**[BF_4]	40/16	 **16a**	63	–
2	**12a**	**8b**	**6**[BF_4]	40/16	**16a**	80	–
3	**12a**	 **15**	**5**[BF_4]	40/16	 **17a**	78	–
4	**12a**	**8b**	**6**[BF_4]	40/16	**17a**	73	–
5	 **12b**	**8b**	**5**[BF_4]	40/16	 **16b**	59	3:1
6	**12b**	**8b**	**6**[BF_4]	40/16	**16b**	74	9:1
7	**12b**	**15**	**5**[BF_4]	40/16	 **17b**	60	1:5
8	**12b**	**15**	**6**[BF_4]	40/16	**17b**	48	1:4
9[e]	 **18**	**8b**	**5**[BF_4]	20/16	 **16c**	46	5:3
10[e]	**18**	**8b**	**6**[BF_4]	20/16	**16c**	57	3:1

[a] In a typical reaction 5 mol% catalyst was employed in THF solvent. [b] Reaction conditions: reaction temperature/time. [c] Isolated yield. [d] Diastereomeric ratio: *anti*/*syn*. [e] LiOAc (10 mol%) and water (2 equiv) were also added to the reaction mixture.

pincer-complex-catalysed allylation reactions. These studies have clearly shown that the allylation of aldehydes (such as **8b**) proceeds with *anti* selectivity, while the opposite regioselectivity (*syn* selectivity) occurs for the corresponding process with imine substrates (such as **15**). These previous observations[13b,l] are in perfect agreement with the stereoselectivity observed in the presented processes catalysed by **5**-[BF_4] and **6**[BF_4] (Table 1).

As reported previously[3f,13d] symmetrical PCP-pincer palladium complexes do not catalyse the formation of the intermediate allylstannanes (Scheme 6, **12** → **14**), and so these complexes alone cannot be employed as catalysts for coupling of allyl chlorides and aldehydes in the presence of hexamethylstannane (**13**). Therefore, reactions with PCP complex **7** as reference catalyst were not performed in this study. On the other hand we also studied the catalytic performance of SCS-pincer complex **6**[BF_4]. To our delight, this complex showed a high catalytic activity, comparable to that of the PCS-pincer complex **5**[BF_4] (entries 2, 4, 6 and 8). The high activity of SCS complex **6**[BF_4] in the tandem catalytic reactions is surprising, because symmetrical ECE-pincer complexes with σ-donor heteroatoms (e.g., NCN) usually perform poorly[13a–b,l] in the allylation step (Scheme 6, **14** → **16**/**17**). The isolated yields obtained with the SCS-pincer complex **6**[BF_4] are particularly high for allylation of aldehyde **8b**, while the stereoselectivity obtained with **12b** as allyl substrate is even higher than with the PCS-pincer complex **5**[BF_4] (entry 6). However, in the allylation reaction of sulfonimine **15** the PCS-pincer complex **5**-[BF_4] clearly outperforms **6**-[BF_4]. The homoallyl amines **17a** and **17b** (entries 3–4 and 7–8) are formed in higher yields with PCS catalyst **5**[BF_4] (78 and 60%) than with the SCS catalyst **6**[BF_4] (73 and 48%). In particular, when the tandem reaction of **12b** and **15** was catalysed with SCS catalyst **6**[BF_4] (entry 8), a substantial amount of cinnamylstannane (**14a**, R = Ph) was present in the crude reaction mixture. This finding indicates that the allylation process (Scheme 6, **14** → **16**) of the imine by cinnamyl stannane proceeds very slowly in the presence of **6**[BF_4] as catalyst.

We have also succeeded in performing (Scheme 7) a tandem catalytic coupling reaction of vinyloxirane (**18**) with **8b** (entries 9 and 10). This reaction proceeds under reaction conditions similar to those used for the allylation with allyl chlorides, except that catalytic amounts of LiOAc and water were added to the reaction mixture. Without this addition of LiOAc and water, vinyloxirane (**18**) is decomposed by the catalysts, probably through opening of the epoxy functionality. The coupling reaction of aldehyde **8b** with vinyloxirane (**18**) leads to formation of an unprotected homoallyl diol (**16c**), which is a useful synthetic intermediate. As far as we know, this reaction represents the first example of a palladium-catalysed coupling of a vinyloxirane with an aldehyde to afford homoallyl alcohol **16c**.

Mechanistic considerations of the tandem coupling reaction: On the basis of the above results and our previous mechanistic and modelling studies,[13b,k,l] it is possible to propose a plausible catalytic cycle for the presented tandem C–Sn and C–C processes (Scheme 8). The first catalytic process is the formation of the allylstannane intermediate **14** from allyl chloride **12** (or vinyloxirane (**18**)) and hexamethylstannane (**13**). This catalytic reaction is initiated by transmetallation of catalyst **5**[L] with **12** to afford complex **5**[$SnMe_3$] and trimetyltin chloride. Formation of trimethyltin-palladium pincer complexes under similar reaction conditions has been

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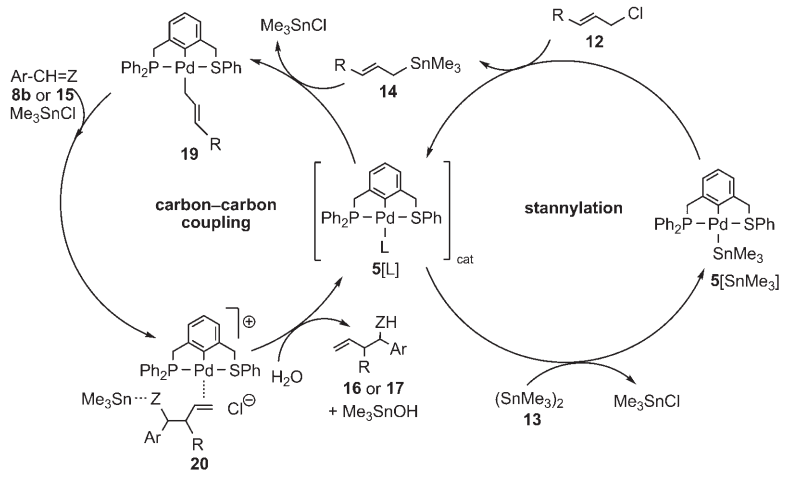

Scheme 8. Proposed catalytic cycle of the auto-tandem reaction. The employed pincer complex **5**[L] catalyses both the stannylation and the allylation processes.

observed for NCN-pincer palladium complexes.[13k] Complex **5**[$SnMe_3$] undergoes a nucleophilic substitution reaction with allyl chloride, furnishing allylstannane **14** and regenerating PCS-pincer palladium chloride **5**[L=Cl].

The regenerated catalyst **5**[L] is able to undergo transmetallation with allylstannane **14** to give η^1-allylpalladium complex **19**. Similar transmetallation reactions were previously reported for PCP-pincer complexes and allylstannanes.[13b] In those studies it was concluded[13a–b] that complexes with heteroatoms exhibiting π-accepting properties in the *ortho*-substituents (such as symmetrical PCP-pincer complexes) undergo more facile transmetallation than the corresponding analogues with strongly σ-electron donating *ortho*-ligands ligands (such as NCN). Considering this, the presence of at least one phosphorus atom in **5**[BF_4] probably allows an efficient transmetallation. On the other hand, the relatively low catalytic activity of **6**[BF_4] in the allylation step (entry 8) may be due to a slow transmetallation of the stannane intermediate **14** to the palladium atom, which is attached to an electron-rich SCS-pincer ligand. According to our mechanistic and modelling studies[13b,l] these η^1-allylpalladium complexes readily react with aldehyde or imine electrophiles (**8b** or **15**). Thus, electrophilic substitution by complex **19** gives **20**, which subsequently undergoes decomplexation to provide the homoallyl alcohol or homoallyl amine products (**16** or **17**) and to regenerate catalyst **5**[L] once again. In this way complex **5**[L] performs as an auto-tandem catalyst controlling two bond formation processes: the stannylation (Sn–C bond formation) of the allyl chloride and the electrophilic substitution (C–C bond formation) of the allylstannane intermediate. Our studies show that the stannylation process (**12** → **14**) in the presence of the PCS catalyst **5**[BF_4] is much faster than the catalytic allylation (**14** → **16/17**). It was found that in the presence of **5**[BF_4] under the applied reaction conditions (entry 1), but in the absence of an electrophile (e.g., **8b**), allyl chloride (**12a**) was converted into allylstannane (**14a**) in 30 min, while the full reaction time required for coupling of **12a** with **8b** is 16 h. This indicates that the catalytic generation of the allylstannane (**14**) is complete before significant progress in the allylation reaction has taken place.

Conclusion

Aryl-based unsymmetrical PCS-pincer palladium complexes **5**-[BF_4] and **5**[Cl] could be prepared in relatively simple four- and five-step synthesis sequences, respectively. These PCS-pincer complexes, as well as the SCS-pincer complex **6**[Cl], proved to be efficient catalysts in the aldol reaction between benzaldehyde and methyl isocyanoacetate, but are obviously pre-catalysts because the methyl isocyanoacetate reactant converts the pincer catalyst into a ketimine-palladium catalyst. In the aldol condensation reaction (Scheme 4) the PCS complex gave higher turnover numbers than its PCP and SCS counterparts. The combination of a sulfur and a phosphorus heteroatom in the side arms, such as in complex **5**-[BF_4], results in a synergetic effect. This effect involves two major components: a weak coordination of the sulfur atom allowing insertion of **9**, as well as a strong coordination of the phosphorus atom, which increases the rate of the catalytic process.

In the tandem catalytic coupling of allyl chlorides or vinyloxirane with aldehyde or sulfonimine substrates, both **5**-[BF_4] and **6**[BF_4] are the true catalytic species. Comparative studies using symmetrical PCP- and SCS-pincer palladium complexes show that a strong synergistic effect is also operative in these catalytic reactions. In the tandem catalytic stannylation and allylation of allyl chlorides (Scheme 6, Table 1) the PCS complex performs much better than the PCP analogue.[13d] Although the SCS complex has a surprisingly high catalytic activity, the PCS complex is more efficient in allylation of sulfonimines. In these processes, the PCS catalyst unifies the attractive catalytic features of the symmetrical analogues: firstly, a high catalytic activity in the stannylation reaction (Scheme 6, **12** → **14**), in which symmetrical complexes with electron-donating heteroatoms and a weaker coordination interaction to the palladium centre (e.g., NCN or SCS) perform well, and secondly, the more efficiently catalysed allylation of the electrophile (Scheme 6, **14** → **16**/**17**) by less electron-rich pincer complexes in which the heteroatom has a stronger interaction with palladium (i.e., as in PCP).

The above study on PCS-complexes has at least three important implications for reactions catalysed by ECE′-pincer palladium complexes. 1) It has been demonstrated that electronic fine-tuning and desymmetrization of pincer-complexes allows development of catalytic auto-tandem proto-

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cols, in which a *single* complex is able to catalyse *several* catalytic events with different mechanisms. 2) New types of PCS-based chiral catalysis can be designed for asymmetric allylation[13e,m] of sulfonimines with allyl chlorides. These reactions are suitable for synthesis of homoallyl amines (such as **17a–b**), which are important motifs in bioactive natural products and pharmaceuticals.[19] 3) Unsymmetrical aryl-based PCS-pincer palladium complexes are particularly suitable catalytic platforms as recyclable, robust catalysts, as these complexes have considerable thermal and kinetic stability and can easily be connected to both soluble and insoluble supports of various length scales, making these (tandem) catalysts suitable for separation by (nano)filtration and re-use.[4–9]

Experimental Section

General: All reactions were performed under dry oxygen-free nitrogen with use of Schlenk techniques. THF and Et_2O were dried over Na/benzophenone. MeCN and CH_2Cl_2 were dried over CaH_2, and all solvents were freshly distilled under nitrogen prior to use. CD_2Cl_2 was purchased from Cambridge Isotopes, dried over CaH_2, distilled prior to use and stored in a Schlenk flask over 4 Å molecular sieves under nitrogen. All standards reagents were purchased from Acros Organics and Aldrich Chemical Co., Inc, and were used as received. Imine **15**[20] and the complexes $[Pd(MeCN)_4][BF_4]_2$,[16] $[Pd\{C_6H_3(CH_2SPh_2)_2\text{-}2,6\}(MeCN)](BF_4)$ (**6**-$[BF_4]$)[5b] and $[PdCl\{C_6H_3(CH_2PPh_2)_2\text{-}2,6\}]$ (**7**[Cl])[18] were synthesized by literature procedures. ^1H NMR (^1H (300.1/400.0 MHz), ^{13}C NMR (75.5/100.6 MHz) and $^{31}P\{^1H\}$ NMR (121.5 MHz)) spectra were recorded on a Varian INOVA 300 MHz spectrometer and a Bruker 400 MHz spectrometer. Chemical shift values are reported in ppm (δ) relative to $(CH_3)_4Si$ (^1H and ^{13}C NMR) and a capillary containing 85% H_3PO_4 in D_2O, ($^{31}P\{^1H\}$ NMR). FT-IR spectra were recorded on a Mattson Instruments Galaxy Series FTIR 5000. Gas chromatographic analyses were performed with a Perkin–Elmer Autosystem XL GC with use of a 30 m, PE-17 capillary column with an FID detector. High-resolution electron spray ionization (ESI) mass spectra were recorded with a Micromass LC-TOF mass and a Bruker MicrOTOF spectrometer. Elemental analyses were performed by H. Kolbe Microanalysis Laboratories, Mülheim, Germany. For column chromatography, Merck silica gel 60 (230–400 mesh) was used.

$[C_6H_4(CH_2Br)\text{-}1\text{-}(CH_2P(BH_3)Ph_2)\text{-}3]$ (2): *n*BuLi (4.5 mL, 7.1 mmol) was added at −78 °C to $HPPh_2{\cdot}BH_3$ (1.29 g, 7.1 mmol) in dry THF (40 mL). The temperature was allowed to rise to room temperature and stirring was continued for 15 h. Next, a solution of **1** (1.87 g, 7.1 mmol) in dry THF (20 mL) was added at −78 °C. The mixture was allowed to warm to room temperature and stirred for 20 h. All volatiles were then removed in vacuo, and the obtained residue was dissolved in CH_2Cl_2. The organic layer was washed with water and brine and dried over $MgSO_4$. After filtration and evaporation of CH_2Cl_2 a white, sticky solid was obtained. Analysis by ^1H NMR in $CDCl_3$ showed the presence of the desired product **2** (63%), $[C_6H_4\{CH_2P(BH_3)Ph_2\}_2\text{–}1,3]$ (12%) and unreacted **1** (25%). Compound **2** was used in the next reaction without further purification. Because of its toxicity, elemental and ESI analyses were not carried out. **CAUTION**: *Substituted benzyl bromides can be powerful lachrymators and should be used with adequate ventilation and precaution against skin contact or ingestion.*

$[C_6H_4(CH_2P(BH_3)Ph_2)\text{-}1\text{-}(CH_2SPh)\text{-}3]$ (3): K_2CO_3 (2.0 g, 15 mmol), 18-crown-6 (0.4 g, 15 mmol) and PhSH (2.2 g, 20 mmol) were added to a THF (40 mL) solution of ligand **2**. The resultant mixture was stirred at room temperature for 15 h. After filtration and evaporation of the solvent, the residue, a colourless oil, was purified by silica gel chromatography with Et_2O/hexane 1:9, to afford **3** as a white solid. The other products of the reaction were characterized by ^1H, ^{13}C and $^{31}P\{^1H\}$ NMR spectroscopy as the pincer ligands $[C_6H_4\{CH_2SPh\}_2\text{-}1,3]$ and $[C_6H_4\{CH_2P(BH_3)Ph_2\}_2\text{-}1,3]$. The solvent was removed in vacuo to give **3** as a white solid in 51% overall yield from **1** in two steps. Yield: 1.49 g, 51%; ^1H NMR ($CDCl_3$, 25 °C): $\delta = 1.2$ (brs, 3H; BH_3), 3.61 (d, $^2J_{H,P} = 12.0$ Hz, 2H; $ArCH_2P$), 3.98 (s, 2H; $ArCH_2S$), 6.8–7.7 ppm (m, 19H; ArH); ^{13}C NMR ($CDCl_3$, 25 °C): $\delta = 33.95$ (d, $^1J_{C,P} = 31.8$ Hz; $ArCH_2PBH_3$), 38.64 (s; $ArCH_2S$), 126.23, 127.42 (d, $J_{C,P} = 3$ Hz), 128.16 (d, $J_{C,P} = 2.4$ Hz), 128.64, 128.77, 128.84, 129.16 (d, $J_{C,P} = 4.9$ Hz), 129.57, 130.87 (d, $J_{C,P} = 4.3$ Hz), 131.32 (d, $J_{C,P} = 2.5$ Hz), 132.21 (d, $J_{C,P} = 4.3$ Hz), 132.64 (d, $J_{C,P} = 9$ Hz), 136.39, 137.25 ppm (d, $J_{C,P} = 2.5$ Hz; ArC); ^{31}P NMR ($CDCl_3$, 25 °C): $\delta = 19.35$ ppm (brs); elemental analysis calcd (%) for $C_{26}H_{26}BPS$ (412.33): C 75.73, H 6.36, P 7.51, S 7.78; found: C 75.66, H 6.35, P 7.64, S 7.73.

$[C_6H_3(CH_2PPh_2)\text{-}2\text{-}(CH_2SPh)\text{-}6]$ (4): $HBF_4{\cdot}Et_2O$ (0.9 mL, 5.9 mmol) was added at 0 °C under nitrogen to a stirred solution of **3** (0.5 g, 1.2 mmol) in CH_2Cl_2. The mixture was then allowed to warm to room temperature, and the stirring was continued for another 18 h. A saturated aqueous $NaHCO_3$ solution was added dropwise at 0 °C, resulting in considerable gas evolution. When the addition was complete, the mixture was stirred at room temperature for another 30 min. The organic layer was collected and dried over $MgSO_4$. After evaporation of all the volatiles, **4** was obtained as an air- and moisture-sensitive, white, sticky solid (0.35 g, 74%). ^1H NMR ($CDCl_3$, 25 °C): $\delta = 3.39$ (s, 2H; $ArCH_2P$), 4.02 (s, 2H; $ArCH_2S$), 6.8–7.8 ppm (m, 19H; ArH); ^{13}C NMR ($CDCl_3$, 25 °C): $\delta = 35.99$ (d, $^1J_{C,P} = 15.9$ Hz; $ArCH_2P$), 39.0 (s; $ArCH_2S$), 126.23, 127.42 (d, $J_{C,P} = 3$ Hz), 128.16 (d, $J_{C,P} = 2.4$ Hz), 128.64, 128.77, 128.84, 129.16 (d, $J_{C,P} = 4.9$ Hz), 129.57, 130.87 (d, $J_{C,P} = 4.3$ Hz), 131.32 (d, $J_{C,P} = 2.5$ Hz), 132.21 (d, $J_{C,P} = 4.3$ Hz), 132.64 (d, $J_{C,P} = 9$ Hz), 136.39, 137.25 ppm (d, $J_{C,P} = 2.5$ Hz; ArC_{ipso}); ^{31}P NMR ($CDCl_3$, 25 °C): $\delta = -7.23$ ppm; elemental analysis calcd (%) for $C_{26}H_{23}PS$ (398.5): C 78.36, H 5.82; found: C 78.26, H 5.71.

$[Pd(NCMe)\{C_6H_3(CH_2PPh_2)\text{-}2\text{-}(CH_2SPh)\text{-}6\}](BF_4)$ (5[BF_4]): A solution of **4** (0.35 g, 0.8 mmol) in dry MeCN (25 mL) was added to a solution of $[Pd(MeCN)_4](BF_4)_2$ (0.39 g, 0.8 mmol) in dry MeCN (25 mL). The resulting yellow solution was stirred for one hour at room temperature. The solvent was removed in vacuo until a small amount remained in the flask. Dry Et_2O was added, causing the precipitation of **5**[BF_4] as a light yellow powder that was collected by centrifugation, washed with Et_2O and dried in vacuo (0.55 g, 70%). ^1H NMR (CD_3CN, 25 °C): $\delta = 4.15$ (d, $^2J_{H,P} = 12.3$ Hz, 2H; $ArCH_2P$), 4.65 (s, 2H; $ArCH_2S$), 7.06 (d, $^3J_{H,H} = 3.9$ Hz, 2H; ArH), 7.13 (t, $^3J_{H,H} = 4.7$ Hz, 1H; ArH), 7.46–7.64 (m, 9H; ArH), 7.72–7.84 ppm (m, 6H; ArH); ^{13}C NMR (CD_3CN, 25 °C): $\delta = 42.37$ (d, $^1J_{C,P} = 36.6$ Hz; $ArCH_2P$), 48.70 (s; $ArCH_2S$), 124.39, 125.32 (d, $^2J_{C,P} = 25$ Hz), 127.89, 130.31, 130.46, 131.01, 131.10, 132.34 (d, $J_{C,P} = 1.8$ Hz), 133.14 (d, $J_{C,P} = 3.02$ Hz), 133.73, 133.88, 148.02 (d, $^3J_{C,P} = 17.06$ Hz), 151.81, 156.75 ppm (d, $J_{C,P} = 2.49$ Hz; ArC_{ipso}); ^{31}P NMR (CD_3CN, 25 °C): $\delta = 49.7$ ppm (s); IR (ATR): $\tilde{\nu} = 3058$, 2976, 2935, 2317, 2287, 1579, 1484, 1437, 1049, 1023, 743, 689 cm^{-1}; MS (ES) (70 eV): *m*/*z* (%): 544.19 (100) $[M-BF_4]^+$, 503.16 (70) $[M-MeCN-BF_4]^+$; elemental analysis calcd (%) for $C_{28}H_{25}BF_4NPPdS$ (631.77): C 53.23, H 3.99, N 2.22; found: C 53.09, H 4.06, N 2.14.

$[PdCl\{C_6H_3(CH_2PPh_2)\text{-}2\text{-}(CH_2SPh)\text{-}6\}]$ (5[Cl]): An excess of NaCl (0.24 g, 4.1 mmol) in H_2O (5 mL) was added in one portion to a solution of **5**[BF_4] (0.2 g, 0.28 mmol) in MeCN (5 mL). The resulting suspension was stirred at room temperature for 3 h. The solvent was removed in vacuo, and the obtained yellow residue was dissolved in CH_2Cl_2 (5 mL). Subsequently, the organic layer was washed with H_2O (2×15 mL) and dried in vacuo, yielding **5**[Cl] as a yellow powder, which was washed with Et_2O and dried in vacuo (0.14 g, 95%). ^1H NMR ($CDCl_3$, 25 °C): $\delta = 3.99$ (d, $^2J_{H,P} = 12.2$ Hz, 2H; $ArCH_2P$), 4.48 (s, 2H; $ArCH_2S$), 6.99 (d, $^3J_{H,H} = 4.2$ Hz, 2H; ArH), 7.09 (t, $^3J_{H,H} = 4.8$, 3.6 Hz, 1H; ArH), 7.24–7.46 (m, 9H; ArH), 7.74–7.92 ppm (m, 6H; ArH); ^{13}C NMR ($CDCl_3$, 25 °C): $\delta = 43.94$ (d, $^1J_{C,P} = 36.07$ Hz; $ArCH_2P$), 49.01 (s; $ArCH_2S$), 122.52, 123.30 (d, $J_{C,P} = 24.38$ Hz), 125.56, 128.80, 128.94, 129.01, 129.48, 131.04, 131.07, 132.85, 133.0, 147.02 (d, $J_{C,P} = 18.34$ Hz), 150.32, 160.67 ppm (ArC_{ipso}); ^{31}P NMR ($CDCl_3$, 25 °C): $\delta = 45.02$ ppm (s); IR (ATR): $\tilde{\nu} = 3051$, 2972, 2864, 1579, 1482, 1435, 1103, 1055, 1025, 740, 688 cm^{-1}; MS (ES) (70 eV): *m*/*z* (%): 503.2 (100) $[M-Cl]^+$; elemental analysis calcd (%) for

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$C_{26}H_{22}ClPPdS$ (539.36): C 57.90, H 4.11, P 5.74, S 5.94; found: C 57.83, H 4.19, P 5.84, S 5.86.

Methyl isocyanoacetate insertion complex (11a): Compound **9** (36 μL, 0.4 mmol) was added to a solution of **5**[Cl] (0.1 g, 0.18 mmol) in CH_2Cl_2 (5 mL). The resulting solution was stirred at room temperature for 20 minutes. Subsequently, the solvent was evaporated until a small amount remained. Addition of pentane (10 mL) caused the precipitation of **11a** as a yellow solid, which was collected by centrifugation and dried under vacuo (0.07 g, 50%). ^{1}H NMR (CD_2Cl_2, 25°C): δ=3.52 (s, 2H; SCH_2), 3.78 (brs, 6H; OMe), 4.1 (brs, 2H; $C(O)CH_2$), 4.25 (d, $^2J_{H,P}$=10.8 Hz, 2H; PCH_2), 4.85 (s, 2H; $C(O)CH_2$), 6.89 (1H; ArH), 7.05–7.24 (m, 3H; ArH), 7.3–7.6 (m, 10H; ArH), 7.7–7.94 (m, 3H; ArH), 8.0–8.1 ppm (m, 1H; ArH); ^{13}C NMR (CD_2Cl_2, 25°C): δ=30.8 (s; $ArCH_2S$), 44.0 (d, $^1J_{C,P}$=36 Hz; $ArCH_2P$), 46.0 (s; $C(O)CH_2$), 49.5 (s; OCH_3), 51.0 (s; CCH_3), 62.0 (s; $C(O)CH_2$), 122.8, 123.0, 125.0, 125.8, 126.5, 127.5, 127.8, 129.2, 129.7, 131.1, 131.5, 131.9, 133.1, 138.2, 150.5, 163.0, 171.0, 186.0 ppm; ^{31}P NMR (CD_2Cl_2, 25°C): δ=47.76 ppm; IR (CH_2Cl_2 solution): $\tilde{\nu}$=3053, 2953, 2230, 1750, 1627, 1582, 1482, 1436, 1219, 1179, 1102, 1055, 1025, 999, 742, 690 cm^{-1}; elemental analysis calcd (%) for $C_{34}H_{32}ClN_2O_4PPdS$ (737.54): C 55.37, H 4.37, N 3.80; found: C 55.26, H 4.44, N 3.69.

Standard protocol for the aldol condensation reaction: In a typical experiment, the catalyst **5**[Cl] (0.016 mmol, 1 mol% [Pd]) was added to a solution of methyl isocyanoacetate (**9**, 1.6 mmol), benzaldehyde (1.6 mmol) and pentadecane (internal standard, 0.4 mmol) in distilled CH_2Cl_2 (5 mL). *i*Pr_2EtN (Hunig's base, 0.16 mmol, 10 mol%) was added to this mixture at room temperature at the time noted as 0 h. Samples of the reaction mixtures were taken with an airtight syringe at regular intervals. The degrees of conversion relative to benzaldehyde were monitored over time by GC analysis.

Standard protocol for the tandem coupling reactions (Table 1): In a typical experiment, the catalyst **5**[BF_4] (0.008 mmol, 5 mol% [Pd]) was added to a solution of the allylic substrate **12** (0.192 mmol) and aldehyde **8b** or sulfonimine **15** (0.16 mmol) in distilled THF (0.7 mL). In the allylation of sulfonimine, molecular sieves (0.025 g) were also added. Hexamethylditin (**13**, 0.192 mmol) was added to this mixture by airtight syringe under inert atmosphere. This reaction mixture was stirred for the allotted temperatures and times listed in Table 1 and was then quenched with water and extracted with diethyl ether. After drying and evaporation of the ether phase, the products were purified by silica gel column chromatography. The ratios of diastereomers were determined from the crude ^{1}H NMR spectra.

1-(4-Nitrophenyl)but-3-en-1-ol (16a): This compound was prepared by the standard protocol for the tandem coupling reactions with **12a** and **8b**. The NMR data obtained for **16a** are identical with the literature[21] values. ^{1}H NMR ($CDCl_3$, 25°C): δ=2.21 (d, $^3J_{H,H}$=3.3 Hz, 1H), 2.41–2.50 (m, 1H), 2.53–2.61 (m, 1H), 4.87 (m, 1H), 5.16–5.23 (m, 2H), 5.79 (dddd, $^3J_{H,H}$=6.5, 7.8, 10.4, 16.9 Hz, 1H), 7.54 (d, $^3J_{H,H}$=8.8 Hz, 2H), 8.21 ppm (d, $^3J_{H,H}$=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 25°C): δ=43.92, 72.13, 119.72, 123.65, 126.55, 133.17, 147.30, 151.03 ppm; HRMS (ESI): *m*/*z*: calcd for $[C_{10}H_{11}NO_3+Na]^+$: 216.0631; found: 216.0632.

1-(4-Nitrophenyl)-2-phenylbut-3-en-1-ol (16b): This compound was prepared by the standard protocol for the tandem coupling reactions with **12b** and **8b**. The diastereoselectivity was assigned on the basis of ^{1}H NMR data given in the literature[22] for **16b**. ^{1}H NMR for *anti*-**16b** ($CDCl_3$, 25°C): δ=2.51 (d, $^3J_{H,H}$=2.3 Hz, 1H), 3.48 (brt, $^3J_{H,H}$=8.5 Hz, 1H), 4.93 (dd, $^3J_{H,H}$=2.3, 7.8 Hz, 1H), 5.27 (d, $^3J_{H,H}$=17.0 Hz, 1H), 5.32 (d, $^3J_{H,H}$=10.1 Hz, 1H), 6.23 (ddd, $^3J_{H,H}$=9.1, 10.1, 17.0 Hz, 1H), 7.04 (m, 2H), 7.18–7.25 (m, 3H), 7.28 (d, $^3J_{H,H}$=8.8 Hz, 2H), 8.05 ppm (d, $^3J_{H,H}$=8.8 Hz, 2H); ^{1}H NMR for *syn*-**16b** ($CDCl_3$, 25°C): δ=2.12 (d, $^3J_{H,H}$=3.2 Hz, 1H), 3.59 (brt, $^3J_{H,H}$=8.0 Hz, 1H), 4.91 (m, 1H), 5.05 (m, 2H), 5.94 (ddd, $^3J_{H,H}$=8.2, 10.3, 17.0 Hz, 1H), 7.17–7.45 (m, 7H), 8.16 ppm (d, $^3J_{H,H}$=8.8 Hz, 2H); ^{13}C NMR for both diastereomers ($CDCl_3$, 25°C): δ= 58.70, 59.51, 76.37, 118.20, 119.48, 123.05, 123.21, 127.16, 127.44, 127.50, 127.80, 128.12, 128.64, 128.70, 128.93, 136.62, 136.79, 139.48, 147.16, 149.12 ppm; HRMS (ESI): *m*/*z*: calcd for $[C_{16}H_{15}NO_3+Na]^+$: 292.0944; found: 292.0942.

1-(4-Nitrophenyl)-2-vinylpropane-1,3-diol (16c): For the preparation of **16c**, the standard protocol was slightly modified. The catalyst **5**[BF_4] (0.008 mmol, 5 mol% [Pd]) was dissolved in THF, followed by addition of LiOAc·2H_2O (0.016 mmol, 10 mol%) and water (0.32 mmol, 2 equiv). The mixture was stirred for 10 minutes at room temperature, followed by addition of the vinyloxirane (**18**) (0.192 mmol), aldehyde **8b** (0.16 mmol) and **15** (0.192 mmol). The workup procedure was the same as described in the standard protocol. The diastereoselectivity was assigned on the basis of ^{1}H NMR data given in the literature[23] for an analogous stereodefined compound. ^{1}H NMR for *anti*-**16c** ($CDCl_3$, 25°C): δ=1.89 (br, 1H), 2.58 (m, 1H), 3.02 (br, 1H), 3.79 (d, $^3J_{H,H}$=5.5 Hz, 2H), 5.05 (d, $^3J_{H,H}$=17.3 Hz, 1H), 5.09 (d, $^3J_{H,H}$=4.4 Hz, 1H), 5.21 (d, $^3J_{H,H}$=10.4 Hz, 1H), 5.80 (ddd, $^3J_{H,H}$=8.7, 10.4, 17.3 Hz, 1H), 7.51 (d, $^3J_{H,H}$=8.8 Hz, 2H), 8.19 ppm (d, $^3J_{H,H}$=8.8 Hz, 2H); ^{1}H NMR for *syn*-**16c** ($CDCl_3$, 25°C): δ=1.89 (br, 1H), 2.58 (m, 1H), 3.02 (br, 1H), 3.85 (d, $^3J_{H,H}$= 5.6 Hz, 2H), 4.93 (d, $^3J_{H,H}$=7.5 Hz, 1H), 5.02 (d, $^3J_{H,H}$=17.3 Hz, 1H), 5.09 (d, $^3J_{H,H}$=10.4 Hz, 1H), 5.60 (ddd, $^3J_{H,H}$=8.6, 10.4, 17.3 Hz, 1H), 7.50 (d, $^3J_{H,H}$=8.8 Hz, 2H), 8.19 ppm (d, $^3J_{H,H}$=8.8 Hz, 2H); ^{13}C NMR for both diastereomers ($CDCl_3$, 25°C): δ=52.19, 52.74, 64.19, 64.79, 74.08, 119.11, 120.08, 123.38, 123.47, 127.09, 127.51, 133.38, 134.35, 147.21, 149.85, 149.98 ppm; HRMS (ESI): *m*/*z*: calcd for $[C_{11}H_{13}NO_4+Na]^+$: 246.0737; found: 246.0739.

***N*-[1-(4-Nitrophenyl)but-3-enyl]benzenesulfonamide (17a)**: This compound was prepared by the standard protocol for the tandem coupling reactions with **12a** and **15**. ^{1}H NMR ($CDCl_3$, 25°C): δ=2.43 (dd, $^3J_{H,H}$=7.0, 7.0 Hz, 2H), 4.50 (dt, $^3J_{H,H}$=6.5, 6.5 Hz, 1H), 5.04–5.14 (m, 3H), 5.45 (ddt, $^3J_{H,H}$=7.2, 10.2, 17.3 Hz, 1H), 7.29 (d, $^3J_{H,H}$=8.7 Hz, 2H), 7.36–7.41 (m, 2H), 7.48–7.53 (m, 1H), 7.68 (d, $^3J_{H,H}$=8.7 Hz, 2H), 8.04 ppm (d, $^3J_{H,H}$=8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 25°C): δ=41.60, 56.39, 120.60, 123.59, 127.07, 127.51, 128.93, 131.78, 132.83, 139.89, 147.20, 147.76 ppm; HRMS (ESI): *m*/*z*: calcd for $[C_{16}H_{16}N_2SO_4+Na]^+$: 355.0723; found: 355.0724.

***N*-[1-(4-Nitrophenyl)-2-phenylbut-3-enyl]benzenesulfonamide (17b)**: This compound was prepared by the standard protocol for the tandem coupling reactions with **16b** and **18**. The diastereoselectivity was assigned on the basis of ^{1}H NMR data given in the literature[22] for an analogous stereodefined compound. Only the major isomer was isolated and characterized: ^{1}H NMR for *syn*-**17b** ($CDCl_3$, 25°C): δ=3.50 (brt, $^3J_{H,H}$=8.4 Hz, 1H), 4.60 (dd, $^3J_{H,H}$=4.9, 8.2 Hz, 1H), 4.85 (d, $^3J_{H,H}$=4.9 Hz, 1H), 4.87 (d, $^3J_{H,H}$=17.0 Hz, 1H), 5.02 (d, $^3J_{H,H}$=10.2 Hz, 1H), 5.71 (ddd, $^3J_{H,H}$= 8.7, 10.2, 17.0 Hz, 1H), 6.92–6.96 (m, 2H), 7.15 (d, $^3J_{H,H}$=8.8 Hz, 2H), 7.24–7.35 (m, 5H), 7.48–7.51 (m, 3H), 7.99 ppm (d, $^3J_{H,H}$=8.8 Hz, 2H); ^{13}C NMR for *syn*-**17b** ($CDCl_3$, 25°C): δ=56.39, 61.04, 119.27, 123.10, 127.08, 127.96, 128.03, 128.74, 128.84, 129.27, 132.72, 135.25, 137.88, 139.40, 146.14, 147.25 ppm; HRMS (ESI): *m*/*z*: calcd for $[C_{22}H_{20}N_2SO_4+Na]^+$: 431.1036; found: 431.1030.

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