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Palladium Catalyzed Asymmetric Hydrophosphination of *α,β*- and *α,β,γ,δ*-unsaturated Malonate Esters – Efficient Control of Reactivity, Stereo- and Regio-Selectivity

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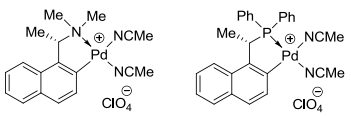
Both PC-cyclometalated and PCP-pincer type palladium catalysts have recently been found to be robust and efficacious catalysts for the asymmetric P-H addition reaction involving activated olefins. Our studies on the asymmetric P-H addition of diphenylphosphine to malonate ester and *α,β,γ,δ*-alkylidenemalonate ester revealed for the first time, that catalyst choice can have a dramatic impact in terms of reactivity as well as regio- and stereo-control for this asymmetric hydrofunctionalization reaction. Besides showing significantly contrasting reactivity and stereoselectivity in the hydrophosphination reaction involving malonate ester, in the case of *α,β,γ,δ*-alkylidenemalonate ester, a novel regiodivergent method was developed with the 1,4-adduct being obtained exclusively with the PC-catalyst while the pincer catalyst produced only the 1,6-adduct.

Introduction

Chiral phosphines are probably one of the most important auxiliaries for asymmetric catalysis.[1] They are powerful metal sequesters and form stable complexes with platinum-group metal ions, particularly in their electron rich lower oxidation states. These soft ligands not only stabilize the metal ions during the catalytic cycle but also control the stereochemical outcome of the transformation reactions. Interestingly, due to this same profound affinity, excess phosphines are often considered as *catalyst poisons* in a palladium catalyzed process as all the available catalytic sites would be occupied by these phosphine ligands. Therefore, it is rather rare that an enantiomerically pure *tertiary* phosphine could be generated efficiently *via* a metal catalyzed asymmetric synthesis method which is arguably the most practical and economical approach to generate these chiral molecules.[2]

Since 2010, however, it has been reported that chiral palladium(II) complexes are able to efficiently catalyze the asymmetric addition of P-H bonds to certain activated unsaturated organic substrates to form new P-C bonds (more commonly known as the hydrophosphination reaction).[3] The catalysts reported so far for this relatively new protocol can be classified into two general categories: (1) NCN-,[4] PCN-,[5] and PCP-[6]pincer type complexes and (2) NC- and PC-cyclometalated complexes, such as (*S*)-**1** and (*S*)-**2**.[7]



(*S*)-**1** (*S*)-**2**

Figure 1. Cyclometalated complexes employed in asymmetric hydrophosphination.

From a purely mechanistic viewpoint, it is quite evident that these two types of catalysts operate via different catalytic pathways during the course of the hydrophosphination reaction. It is generally believed that the pincer catalysts operate by activating the P-H bonds *via* an initial P→Pd coordination, followed by the inter-molecular P-C bond formation while the CP-cyclopalladated catalysts allow both the phosphine nucleophile and the reacting substrate to coordinate *simultaneously* to the catalyst center in the transition state thus allowing an intra-molecular P-C bond formation mechanism to be adopted.[7a] Although this divergence in mechanistic pathway may not always have significant impact on stereochemistry, especially for *α,β*-unsaturated substrates, from a regioselectivity standpoint, different hydrophosphination products may be obtained when the pincer and the cyclopalladated-catalysts are applied to substrates that contain more than one chemically reactive positions such as *α,β,γ,δ*-unsaturated substrates. Therefore, whilst the pincer catalyst should generate the corresponding 1,6-addition product, the formation of the same adduct by the cyclopalladated catalyst *via* an inter-molecular mechanism would involve an unfavorable 8-membered intermediate since both reacting species needs to be coordinated simultaneously on the palladium center during the course of the catalytic cycle.

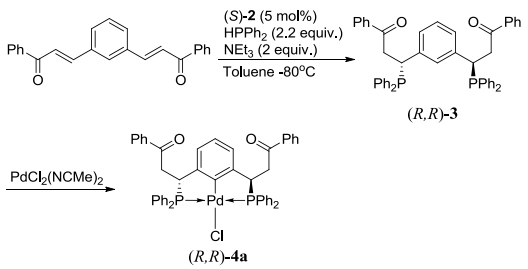
Alternatively, the cyclometalated catalyst can operate *via* an intra-molecular mechanism that involves a sterically favourable 6-membered intermediate to produce the alternative 1,4-addition product.

We herein examined the asymmetric addition of the P-H bond to *α,β*-malonate ester and the conjugated *α,β,γ,δ*-diunsaturated olefin, diethyl 2-cinnamylidenemalonate, by using a series of rationally chosen chiral catalysts belonging to both classes. It needs to be reiterated that the asymmetric hydrophosphination of *α,β,γ,δ*-unsaturated substrates poses the twin challenges of controlling both regio- and stereo-selectivity due to the presence of three electrophilic sites. Unlike in the case of asymmetric C-C bond formation protocols, this particular aspect of regiocontrol has not hitherto been analyzed systematically for the asymmetric P-C bond formation protocol. What is also significantly missing from literature is a regiodivergent method which allows selective access to either 1,4- or 1,6-adducts in high yields and enantioselectivity *via* a conjugate addition on the same substrate.

Results and Discussion

The N→Pd bond in the cationic complex (*S*)-**1** offers a stable *trans* N-Pd-P orientation during the course of the hydrophosphination reaction. This electronic feature, however, results in a slow product elimination process. Furthermore the prochiral NMe groups do not project the catalyst chirality efficiently on to the neighboring catalytic active sites on the square planar Pd center. These stereoelectronic deficiencies do not exist in complex (*S*)-**2**. Indeed we have recently determined that (*S*)-**2** is generally a much better hydrophosphination catalyst than (*S*)-**1**.[7b-c] Thus the PC-catalyst (*S*)-**2** was employed for the current investigation.

There are several pincer complexes that have been reported to be catalytically active for asymmetric P-H addition reaction.[6] However, they are not readily available commercially. For convenience and economic reasons, we have recently developed a synthetic methodology for synthesis of PCP-pincer complexes that involve the catalytic hydrophosphination of specially designed substrates utilizing, incidentally, catalyst (*S*)-**2**. Accordingly, we have reported the high yield synthesis of the optically pure diphosphine (*R,R*)-**3** (*de* = 99%, *ee* >99%) and its palladium complex (*R,R*)-**4a** (Scheme 1).[7c] Unfortunately, a preliminary study revealed that this neutral chloro complex is catalytically inactive for the hydrophosphination protocol. However this can be easily rectified by replacing the Cl with a better leaving moiety. Therefore, we modified (*R,R*)-**4a** into derivatives (*R,R*)-**4b-d** (Table 1). The molecular structure of new iodo complex (*R,R*)-**4d** was confirmed crystallographically (Figure 2). All the four pincer complexes were evaluated in the targeted hydrophosphination reaction alongside the PC-palladacycle, (*S*)-**2**.



Scheme 1. Synthesis of PCP Pd Pincer (*R,R*)-**4a**.

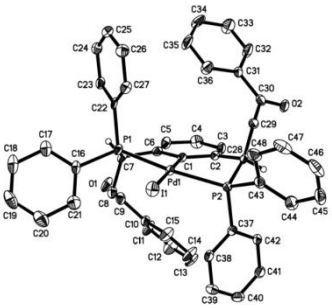


Figure 2. Molecular Structure of (*R,R*)-**4d**. All hydrogen atoms except H(C7) and H(C28) were omitted for clarity.

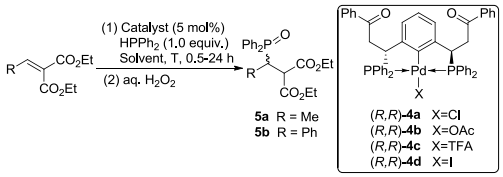


Table 1. Screening of Reaction Conditions.

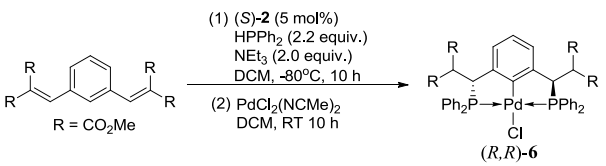
Entry[a]	Cat. [b]	Solvent	Base	T [°C]	Yield[c] [%]	ee[d] [%]
1	**4b**	MeCN	-	RT	93	3
2	**4b**	Acetone	-	RT	84	6
3	**4b**	DCM	-	RT	88	5
4	**4b**	DCM	-	-80	93	9
5	(*S*)-**2**	DCM	NEt_3	-80	93	67
6	**4b**	Toluene	-	RT	89	16
7	**4b**	Toluene	-	-80	93	44
8	(*S*)-**2**	Toluene	NEt_3	-80	81	7
9	**4a**	Toluene	-	RT	2	ND[e]
10	**4c**	Toluene	-	RT	0	-
11	**4a**	Toluene	NEt_3	RT	50	1
12	**4c**	Toluene	NEt_3	RT	71	5
13	**4d**	Toluene	-	RT	13	5
14	**4b**	Toluene	-	RT	78	1
15	(*S*)-**2**	Toluene	NEt_3	-80	70	27
16	**4b**	DCM	-	RT	76	3
17	**4b**	DCM	-	0	52	18
18	(*S*)-**2**	DCM	NEt_3	-80	81	94

[a] For entries 1-13, R = Me and for entries 14-18, R = Ph. [b] The absolute configurations of the pincer catalyst is (*R,R*). [c] Isolated yields. [d] Determined by chiral HPLC. [e] Not determined.

While the cyclometalated complex (*S*)-**2** has been used previously as the catalyst in several P-H addition reactions, the catalytic performance of the four new pincer derivatives (*R,R*)-**4a-d** is hitherto unknown especially in the context of the conjugate addition of diphenylphosphine to an ester. The only previous report in literature by Duan et. al employing an *α,β,γ,δ*-unsaturated ethyl substituted carboxylic ester and using a PCP-Pd pincer catalyst resulted in zero yields.[6b] Therefore, prior to the investigation of the more challenging *α,β,γ,δ*-diunsaturated substrate, we studied the general catalytic properties of the selected palladium(II) complexes using simpler alkylidenemalonate ester wherein regioselectivity concerns do not exist. With these chemically well-defined substrates, the same 1,4-addition products are expected from all the selected complexes, if they are catalytically active. The results are summarized in Table 1.

Overall, it is clear that the cyclometalated complex (*S*)-**2** is a significantly more efficient catalyst than even the best performing (*R,R*)-**4** variant *viz* (*R,R*)-**4b** for the asymmetric hydrophosphination of alkylidenemalonate esters. The addition of an external base (NEt_3) is necessary with catalyst (*S*)-**2**, but not with (*R,R*)-**4b** due to the presence of an internal base (AcO^-). The presence of a base is necessitated by its role in generating the reactive phosphido species from the Ph_2PH moiety during the course of the catalytic cycle (*vide infra*).

To further compare the efficiency of these two catalysts to diunsaturated substrates, we applied them to the hydrophosphination reaction of tetramethyl 2,2'-(1,3-phenylene-bis(methanylylidene))dimalonate using dichloromethane as the solvent (Scheme 2). When the cyclometalated catalyst (*S*)-**2** was used at -80 °C in this reaction, the $^{31}P\{^1H\}$ NMR spectroscopy revealed that the reaction is completed in less than 10 hours. It further needs to be noted that the resulting enantio-enriched diphosphine ligand can yield the pincer complex (*R,R*)-**6** by the direct treatment with $PdCl_2(NCMe)_2$, in 85% isolated yield with 99% optical purity. The single crystal molecular structure of (*R,R*)-**6** is shown in Figure 3. On the other hand, when the pincer (*R,R*)-**4b** was used, the hydrophosphination reaction proceeded significantly slowly. At room temperature, monitoring by $^{31}P\{^1H\}$ NMR spectroscopy revealed that the reaction was completed in 2 days. Furthermore, the diphosphine was obtained in very low optical purity (<10%). Attempts to improve on the enantio- and diastereo-selectivities by lowering the reaction temperature were not successful and no reaction could be observed when the catalysis was conducted below 0 °C. The above model studies clearly revealed that the cyclometalated complex (*S*)-**2** is a better catalyst at low temperatures and the pincer complex (*R,R*)-**4b** shows the optimum activity at room temperature but with concomitant poor enantioselectivity.



Scheme 2. Synthesis of Pincer (*R,R*)-**6.**

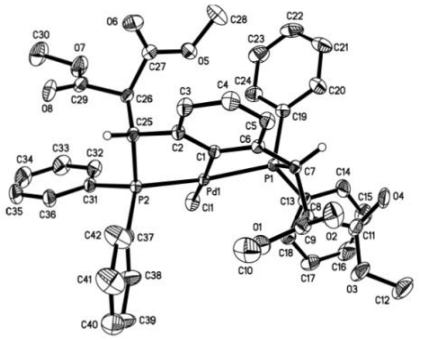


Figure 3. Molecular Structure of (*R,R*)-**6**. All hydrogen atoms except H(C7) and H(C25) were omitted for clarity.

Indeed, similar reactivity trends were observed when the two catalysts were applied to the more challenging *α,β,γ,δ*-diunsaturated substrate *viz*., diethyl 2-cinnamylidenemalonate, as seen in Table 2. However, the two catalysts also showed dramatic regioselectivity preference for this reaction. When the cyclometalated catalyst (*S*)-**2** was used in dichloromethane at -80 °C, the ^1H NMR spectroscopy of the crude reaction mixture confirmed that the 1,4-addition product **7a** was obtained exclusively with >99% *ee* (entry 7). On the other hand, when the same reaction was conducted at room temperature, a small amount (3%) of the 1,6-addition product **7b** was generated, alongside the major product **7a** (entry 6). The reaction became progressively less regioselective when (*S*)-**2** was used at higher temperatures. It needs to be highlighted that this is the only instance in literature wherein a 1,4-regioselectivity was observed in the conjugate addition of diphenylphosphine to an ester in high yields and enantioselectivity of >99%. Only two previous instances have been reported in literature by Duan *et. al* and they involved an *α,β,γ,δ*-unsaturated ketone (93% ee) and its N-pyrrole derivative (96% ee).[6b]

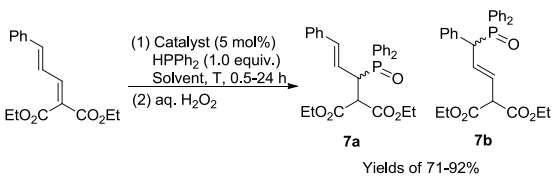


Table 2. Screening of Reaction Conditions.

Entry[a]	Solvent	Base	T [°C]	**7a**:**7b**[b] Ratio	ee[c] [%]
1	DCM	-	RT	0:100	38
2	DCM	-	-80	6:94	60
3	MTBE	-	RT	2:98	22
4	Toluene	-	RT	3:97	29
5	Toluene	-	-80	5:95	70
6	DCM	NEt_3	RT	97:3	55(S)
7	DCM	NEt_3	-80	100:0	>99(S)[d]
8	DCM	NEt_3	50	62:38	24(35)[e]

9[f]	DCM	NEt_3	50	100:0	-
10[f]	DCM	NaOAc	50	100:0	-

[a] Catalyst (*R*,*R*)-**4b** was used in entries 1-5 and (*S*)-**2** in entries 6-8 respectively. No catalyst was used for entries 9 and 10. [b] Ratio of **7a**:**7b** was determined by integration of their respective proton signals at 6.41 and 5.73 ppm. [c] *ee* of major product was determined by chiral HPLC. [d] Absolute configuration was determined by X-ray analysis of the product. [e] *ee* in parentheses belongs to the minor product. [f] <5% conversion was calculated based on $^{31}P\{^{1}H\}$ NMR after 96 h. Only the 1,4-adduct **7a** was observed.

When the pincer catalyst (*R*,*R*)-**4b** was employed at room temperature (entry 1), the reaction yielded the 1,6-addition product **7b** as the sole product in 79% isolated yield with 38% *ee*. The ^{1}H NMR spectroscopy of the oxidized crude reaction mixture confirmed that no 1,4-addition product was generated under this reaction condition. Notably, the same P-H addition reaction to diethyl-2-cinnamylidenemalonate reported earlier[6b] afforded the 1,6-adduct **7b** in 68% yield, 43% *ee* and with a lower regioselectivity of 9:1. When the reaction was conducted at -80 °C, the pincer catalyst generated **7b** as the major product with 60% *ee* (entry 2). Interestingly, a small quantity of the 1,4-addition product **7a** was also obtained from this low temperature process. The aforementioned results therefore revealed the subtle interplay of reactivity and regioselectivity considerations associated with the different catalyst designs for this protocol. It needs to be noted at this juncture that the reason why the previous attempt by Duan *et. al* to execute a asymmetric hydrophosphination reaction on the *α*,*β*,*γ*,*δ*-unsaturated ethyl substituted carboxylic ester failed[6b] (0% yield) can be attributed solely to insufficient activation of the C=C bonds and not to either catalyst design or conditions employed.

For direct characterization of the addition products, they were converted to their corresponding oxides. The molecular structure and the absolute stereochemistry of (*S*)-**7a** was established by X-ray crystallography (Figure 4). Due to the low enantioselectivity associated with the 1,6-addition reaction, adduct **7b** crystallized as a racemic mixture (Figure 5). It should be noted that, in the absence of a catalyst, the reaction between diphenylphosphine and the *α*,*β*,γ,*δ*-diunsaturated substrate (entries 9 and 10) was extremely slow even at elevated temperatures, affording only <5% of the hydrophosphination product after 96 hours as determined by $^{31}P\{^{1}H\}$ NMR spectroscopy.

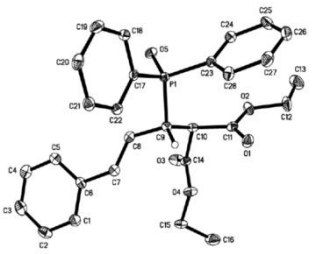


Figure 4. Molecular structure of (*S*)-**7a**. All hydrogen atoms except H(C9) were omitted for clarity.

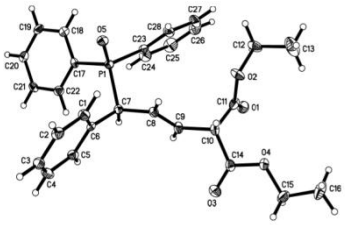


Figure 5. Molecular structure of (±)-**7b**.

In theory, the PC-cyclometalated complex (*S*)-**2** catalyzed hydrophosphination reaction of the *α*,*β*,γ,*δ*-diunsaturated olefin may adopt either an inter- or intra-molecular reaction mechanism. Due to both steric and electronic factors, an inter-molecular mechanism would favor the formation of the 1,6-addition product. However, the exclusive formation of the 1,4-product (Table 2, entry 7) at low temperature indicated that the cyclometalated catalyst prefers to form a reaction intermediate in which both the Ph_2P-H and the substrate are coordinated to palladium simultaneously during the course of the P-C bond formation (see SI). Due to the nature of this intra-molecular pathway, the cyclometalated catalyst offers both high stereoselectivity and reactivity, even at low temperatures. This reaction mechanism is indeed consistent with the hydrophosphination reactions for other olefins that are catalyzed by (*S*)-**2**.[7b-e] In line with the experimental observations, the formation of the 1,6-addition product *via* this intra-molecular mechanism is sterically unfavorable as it requires the formation of a large eight-membered intermediate on the cyclometalated catalyst. On the other hand, the formation of the minor 1,6-addition product observed at elevated temperatures (Table 2, entries 6-8) can be attributed to the increasing competition between the intra- and inter-molecular pathways under harsher reaction conditions.

In contrast to the cyclometalated catalyst, it is necessary for the hydrophosphination reactions that are catalyzed by the pincer complex (*R*,*R*)-**4b** to adopt an inter-molecular mechanism, as the catalyst offers only one easily accessible catalytic site. Technically, the complex may either activate the olefin substrates or the P-H bond of the phosphine moiety.

In order to gain a better understanding of this aspect we conducted a series of closely monitored NMR experiments. The $^{31}P\{^{1}H\}$ NMR ($CDCl_3$) studies showed that the original singlet signal of complex (*R*,*R*)-**4b** at δ 44.4 remained unchanged when a large excess of the olefin substrate was added into the NMR sample. On the other hand, in a separate NMR sample, 2 broad peaks at δ -10.2 and 49.9 corresponding to the -PPh_2 moiety (from H-PPh_2) and the PCP phosphines from [Pd(PCP)(PPh_2)] appeared after stochiometric amount of Ph_2P-H was introduced and stirred at room temperature for 1 h. Indeed, spontaneous changes of the catalyst signal was also observed when other phosphines, such as Ph_2P-Cl, were added to the NMR samples containing the pincer complex. These NMR experiments suggested that pincer complex activates the P-H bond, thus allowing for the deprotonation by the free acetate anion that has

been displaced from the pincer catalyst (see SI). Following the inter-molecular P-C bond formation, a proton transfer from AcOH generates the 1,6-adduct **7b**. This inter-molecular mechanism only allows for the 1,6-addition reaction to proceed. The inter-molecular 1,4-addition reaction involving the pincer catalyst would be sterically highly unfavorable, as illustrated in Figure 6.

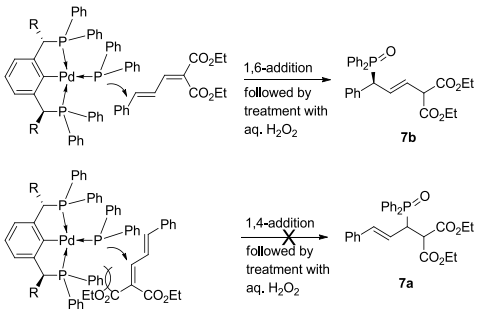
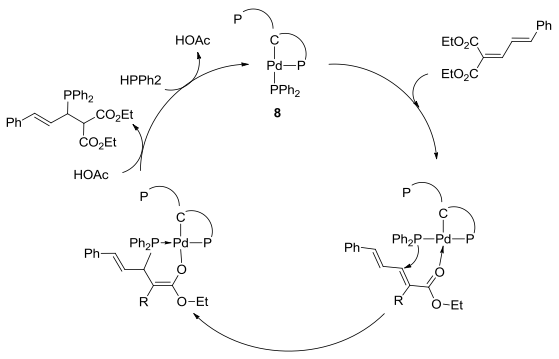


Figure 6. Steric Effects Associated with the Pincer Catalyst.

It is interesting to note that a small amount of the 1,4-adduct **7a** was generated, only when the pincer catalyzed reaction was conducted at the low temperature (Table 2, entry 2). As discussed earlier, the formation of this minor product cannot be explained by the above inter-molecular mechanism, especially at the low temperature. From the organometallic chemistry standpoint, the two P→Pd bonds in the *trans* P-Pd-P moiety are electronically unfavorable and kinetically labile, as the two soft donors are competing for the electrons from the same d-orbitals.[8] It is possible that one of the *trans* P→Pd bonds in the pincer complex undergoes ligand dissociation in solution. A variable low temperature $^{31}P\{^{1}H\}$ NMR studies of the pincer catalyst in dichloromethane was conducted and we believe that the broadening of the signal indicates the kinetic lability of the P→Pd bonds (see SI). The resulting kinetic bidentate species **8** resembles the structure of the PC-cyclometalated catalyst and is stabilized at low temperature. This species is able to catalyze the intra-molecular 1,4-addition reaction at low temperature, in a manner similar to catalyst (*S*)-**2** (Scheme 3). Alternatively, a sterically unfavorable five-coordinate intermediate involving the coordination of the carbonyl moiety of the substrate to the axial position of the square planar catalyst (*R*,*R*)-**4b** at lower temperature might also be plausible.



Scheme 3. Proposed Alternative Catalytic Pathway of the Pincer Catalyst at Low Temperature.

Conclusions

We have conclusively demonstrated that the judicious choice of the ligand motif associated with the Pd catalyst offers significant control over reactivity as well as stereo-selectivity in the addition of PPh_2- to mono- and di-unsaturated malonate esters. For the addition involving conjugated *α,β,γ,δ*-unsaturated malonate ester, a regiodivergent method was revealed for the first time in asymmetric hydrophosphination protocol that allows 1,4-addition adduct to be obtained exclusively with the PC-catalyst while the pincer catalyst produced only the 1,6-adduct. This catalyst-product specificity concept is critical for the development of future catalysts for targeted isomeric molecules and is hitherto not understood for this P-C bond formation protocol. The understanding of the difference in regio- and stereo-control afforded by the two classes of catalyst along with reactivity aspects will bear heavily on the design of catalysts for future development of asymmetric hydrophosphination reactions. These findings are also relevant in view of the fact that we have recently extended the application of this catalyst to the asymmetric P-O bond formation.[9]

Experimental

All reactions were carried out under a positive pressure of nitrogen using standard Schlenk technique. NMR spectra were recorded on Bruker AV 300, AV 400 and AV 500 spectrometers. Chemical shifts were reported in ppm and referenced to an internal $SiMe_4$ standard (0 ppm) for ^{1}H NMR, chloroform-d (77.23 ppm) for ^{13}C NMR, and an external 85% H_3PO_4 for $^{31}P\{^{1}H\}$ NMR. DCM, toluene, THF, acetone, acetonitrile and MTBE were purchased from their respective companies and used as supplied. Solvents were degassed prior to use when necessary. A Low Temp Pairstirrer PSL-1800 was used for controlling low temperature reactions. Column chromatography was carried out with Silica gel 60 (Merck). Melting points were measured using SRS Optimelt Automated Point System SRS MPA100. Optical rotation were measured with JASCO P-1030 Polarimeter in the specified solvent in a 0.1 dm cell at 22.0°C. The palladacycle (*S*)-**2**[7c] was prepared according to literature methods. All other reactants and reagents were used as supplied.

General Procedure for Catalytic Hydrophosphination. The catalyst (25 umol, 5 mol %) was added to a solution of diphenylphosphine (0.5 mmol, 1.0 equiv) in the stated solvent (0.5 mL) and brought to the desired temperature. The substrate (0.5 mmol, 1.0 equiv) and where necessary, NEt_3 (0.5 mmol, 1.0 equiv) in the same solvent (0.5 mL) was consecutively added and stirred at the stated temperature. Completion of the reaction was determined by the disappearance of the phosphorous signal attributed to diphenylphosphine (-40 ppm) in the $^{31}P\{^{1}H\}$ NMR spectrum. Upon completion of the reaction, aq. H_2O_2 (0.1 mL, 31% v/v) was added to form the respective product. The volatiles were removed under reduced pressure and the crude product was directly loaded onto silica gel column (ethyl acetate:*n*-hexane = 2:1) to afford the pure product.

Synthesis of PCP Pd Pincer (*R*,*R*)-6. To a solution of Ph_2PH (227 mg, 1.22 mmol, 2.1 equiv) in DCM (10 mL) was added catalyst (*S*)-**2** (21.8 mg, 0.061 mmol, 5 mol %) and stirred for 10 minutes before cooling to -80°C. Tetramethyl 2,2'-(1,3-phenylene-bis(methanylylidene))dimalonate (209 mg, 0.578 mmol, 1.0 equiv) was added followed by the addition of NEt_3 (162 uL, 1.16 mmol, 2.0 equiv) in DCM (1 mL) dropwise. The solution was stirred at -80°C and the completion of the reaction was monitored by $^{31}P\{^1H\}$ NMR. Upon completion, the solution was allowed to room temperature. Volatiles were removed under reduced pressure to afford crude diphosphine. $PdCl_2(CH_3CN)_2$ (151 mg, 0.578 mmol, 1.0 equiv) was added to a solution of diphosphine ligand in DCM (10 mL) and stirred overnight at room temperature. The solvent was removed and the crude (*R*,*R*)-**6** was purified *via* silica gel column chromatography (eluted with DCM) to afford white solid of (*R*,*R*)-**6**. (85% yield). $[\alpha]_D$ = -559 (*c* 0.1, DCM). Mp: 244-246°C (dec). $^{31}P\{^1H\}$ NMR δ_P ($CDCl_3$, 162 MHz), 47.9; δ_H ($CDCl_3$, 400 MHz), 7.98-7.94 (m, 4H, Ar), 7.84-7.80 (m, 4H, Ar), 7.45-7.37 (m, 12H, Ar), 7.07 (d, 2H, ^3J = 7.60 Hz, Ar), 6.92 (t, 1H, ^3J = 7.50 Hz, Ar), 4.82-4.78 (m, 2H, PC*H*CH), 3.84 (dd, 2H, ^3J = 16.4 Hz, 7.45 Hz, PCHC*H*); δ_C ($CDCl_3$, 100 MHz), 167.3 (d, 4C, $^3J_{PC}$ = 10.6 Hz, *C*O_2Me), 147.0-125.6 (30C, Ar), 56.3 (2C, PCH*C*H), 52.4 (2C, *C*O_2Me), 51.7 (2C, *C*O_2Me), 51.1 (2C, P*C*HCH). HRMS (+ESI) m/z: $(M - Cl)^+$ calcd for $C_{42}H_{39}O_8P_2Pd$, 839.1155; found, 839.1174. Anal. Calcd for $C_{42}H_{39}ClO_8P_2Pd$: C, 57.61; H, 4.49. Found: C, 57.74; H, 4.61%.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental and spectral data, crystallographic refinement data, HPLC spectra. See DOI: 10.1039/b000000x/

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10 CCDC 1019491 ((*R*,*R*)-**4d**), 991033 ((*R*,*R*)-**6**), 991034 ((*S*)-**7a**) and 991035 (**7b**) contains the supplementary crystallographic data.

Table of Contents

A judicious choice of palladium catalysts and conditions afforded the hydrophosphination product in >99% regioselectivity (1,4- *vs* 1,6-addition).