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CHAPTER 2

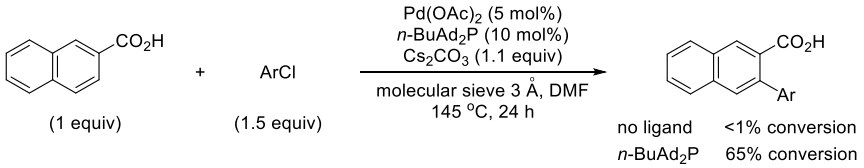
SYNTHESIS OF P,O-LIGANDS AND THEIR PALLADIUM COMPLEXES

Part of this chapter has been published in:
Naksomboon, K.; Valderas, C.; Maciá, B.; Fernández-Ibáñez, M. Á. *Synlett* **2017**, 28, 221–224.

2.1 Introduction

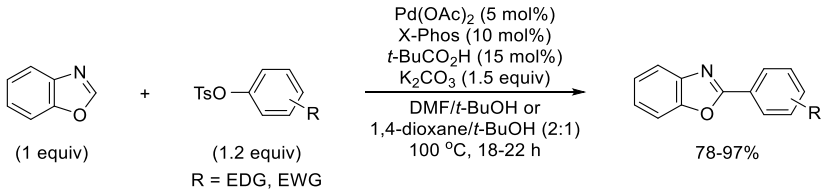
Design of P,O-bidentate ligands

Phosphines are considered a privileged class of ligands for their versatility to effect a wide range of reactions in homogeneous catalysis.[1] This is because of their easily tunable electronic and steric properties. This type of ligands has been successfully applied in palladium-catalyzed C–H functionalization reactions.[2] In particular, the ones that involve the oxidative addition of Pd(0) species into the C–X bond prior the C–H activation step.[3] For example, the Pd-catalyzed *ortho*-arylation of 2-naphthoic acid with aryl chlorides was enhanced dramatically when a phosphine ligand was used (Scheme 2.1).[3g]



Scheme 2.1 Phosphine ligand promoted Pd-catalyzed *ortho*-arylation of 2-naphthoic acid.

As stated in Chapter 1, it is well known that carboxylates can promote the C–H bond cleavage, which is in general the rate-determining step, via hydrogen bonding interaction.[4] Interestingly, several catalytic systems for palladium-catalyzed C–H functionalization reactions are based on the combination of both ligands, phosphine and carboxylic acid.[5] For example, Ackermann and co-workers reported the C–H arylation of benzoxazole using the combination of $Pd(OAc)_2$, X-Phos ligand and pivalic acid (Scheme 2.2).[5e]



Scheme 2.2 C–H Arylation of benzoxazole.

With this information in mind, we hypothesize that the combination of phosphine and carboxylic acid functionalities in a bidentate ligand (P,O-ligands) could be beneficial in promoting palladium-catalyzed C–H functionalization reactions.

Preparation of α-substituted phosphinoacetic acids

P,O-ligands play an important role in the Shell higher olefin process (SHOP).[6] The synthesis of some of these ligands involves either nucleophilic phosphanylation (synthesis of **A**, **B** and **C**, Figure 2.1)[7] or Pd-catalyzed cross coupling reactions of arylhalides with phosphanes (synthesis of **B**, Figure 2.1).[8]

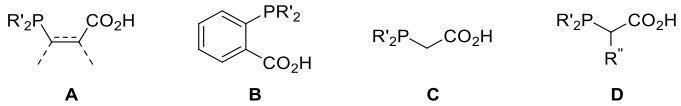
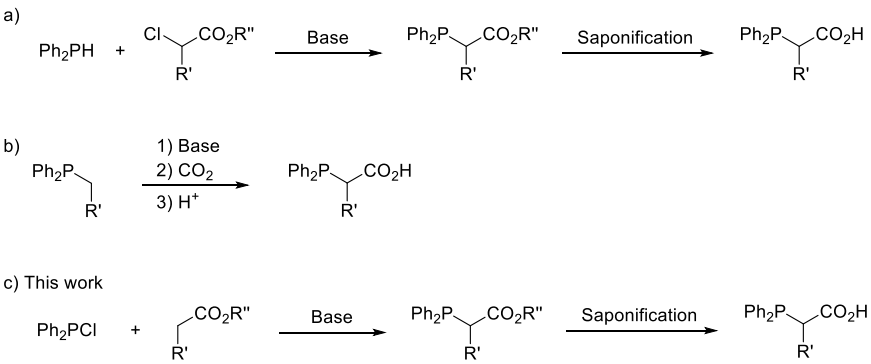


Figure 2.1 Different classes of P,O-ligands.

Few methods for the synthesis of α-substituted phosphinoacetic acids (**D**, Figure 2.1) have been reported to date (Scheme 2.3).[9] However, these methods lack of generality, as a seminal contribution from Shell Research Laboratories concludes: 'it is impossible to prepare a large diversity of functionalized aliphatic phosphinocarboxylic acids by one generally applicable synthetic method'.[9a] The reaction of metal phosphide with halocarboxylic acids or esters (Scheme 2.3, route a) is, at present, the most straightforward route for the synthesis of α-substituted phosphinoacetic acids. Unfortunately, using this strategy, only the 2-methyl diphenylphosphinoacetic acid derivative was obtained in good yield. In addition, halocarboxylic acids are not readily available, which limits the broad applicability of this strategy. The second approach to the synthesis of α-substituted phosphinoacetic acids is the carbonation of metallated alkyldiarylphosphines substrates, which again, are not readily available either (Scheme 2.3, route b). Moreover, this method also lacks generality and only allows the preparation of a few α-substituted phosphinoacetic acids. Therefore, a general and efficient route for the synthesis of α-substituted phosphinoacetic acids **D** is still lacking.



Scheme 2.3 Methods for synthesizing α-substituted phosphinoacetic acids.

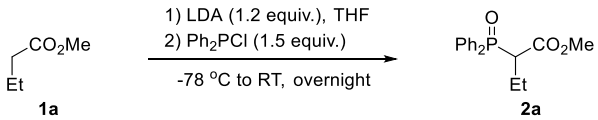
In this chapter, we present a general protocol for the synthesis of bidentate ligands based on both phosphorus and carboxylic acid moieties (α-substituted phosphinoacetic acids; P,O-ligands) using simple esters and diphenylchlorophosphine-borane as starting materials. We observed that these P,O-ligands are highly sensitive towards oxidation but the corresponding sodium salts are more stable. The synthesis of a palladium complex bearing two P,O-ligands is also described.

2.2 Results and discussion

Our proposal towards the synthesis of α-substituted phosphinoacetic acids was based on the phosphonylation of lithium enolates (Scheme 2.3, route c). In this context, it was reported that

the reaction of lithium 2-lithiopropionate with diphenylchlorophosphine does not provide the desired phosphonylated product.[9a] This might be the reason why this simple approach has not been explored to date.

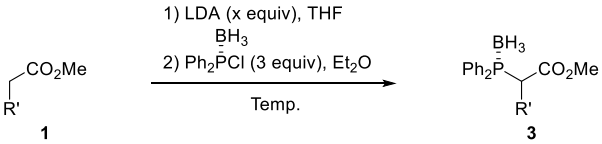
We started the synthesis of α-substituted phosphinocarboxylic acids using methyl butyrate (**1a**) and diphenylchlorophosphine as model substrates (Scheme 2.4). Unfortunately, formation of the ester enolate by adding 1.2 equiv of LDA, followed by 1.5 equiv of diphenylchlorophosphine provided the undesired phosphine oxide compound **2a**.



Scheme 2.4 Reaction of methyl butyrate (**1a**) with diphenylchlorophosphine.

To avoid oxidation of the phosphine, we decided to perform the reaction using diphenylchlorophosphine-borane as a starting material. The slow addition of 3 equiv of the phosphine adduct, which can be easily synthesized *in situ* by reacting Ph_2PCl and BH_3·THF in dry Et_2O for 30 minutes at room temperature,[10] to the enolate of methyl butyrate (**1a**) at -78 °C provided the desired methyl 2-ethyl diphenylphosphinoacetate-borane (**3a**) in 73% isolated yield (Table 2.1, entry 1). The enolate was generated by adding a diluted solution of ester **1a** in THF to LDA at -78 °C. The yield was not improved when the amount of LDA was increased from 1.2 to 2 equiv (entry 2). Under the optimal reaction conditions, the synthesis of different methyl α-substituted diphenylphosphinoacetate-boranes was explored. The reaction of methyl 3-phenylpropionate (**1b**) furnished the corresponding methyl 2-benzyl diphenylphosphinoacetate-borane (**3b**) in 72% isolated yield (entry 3). When the same reaction conditions were applied to the synthesis of methyl 2-phenyl diphenylphosphinoacetate-borane (**3c**), 53% conversion to the desired product **3c** was obtained (entry 4). Increasing the reaction time from 1 h to overnight did not rise the conversion significantly (57%, entry 5). To ensure the formation of the enolate, we decided to add neat methyl 2-phenylacetate (**1c**) directly to LDA (entry 6), which afforded 77% conversion to the desired product. When we increased the amount of LDA to 2 equiv, similar conversion was detected (entry 7). However, we observed that the addition of the phosphine adduct to the enolate anion at -78 °C led to the formation of a frozen solution. This could prohibit the mass transfer and be the reason for the incomplete conversion. Therefore, after generating the enolate at -78 °C, the reaction temperature was increased to -20 °C and then, the phosphine adduct was rapidly injected to the reaction (entry 8). Under these conditions, the conversion was slightly increased to 82%. When the reaction was performed at 0 °C, the conversion was improved to 90% providing the desired adduct in 56% isolated yield (entry 9). The reaction of the most sterically hindered methyl 3-methylbutanoate (**1d**) under the optimal conditions (used in entry 1) provided the phosphine ester **3d** in 21% isolated yield (entry 10). However, when the reaction was stirred overnight, the desired product was obtained in fair yield (entry 11).

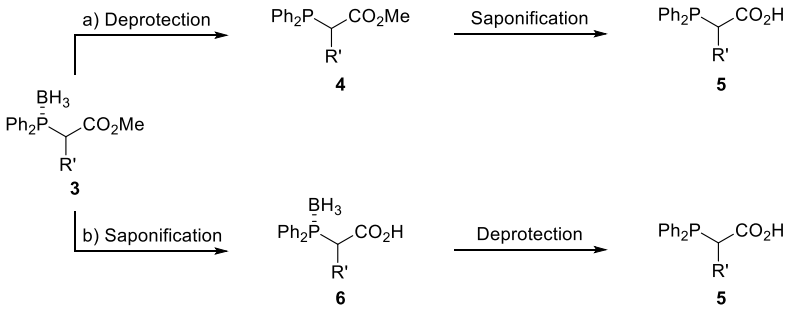
Table 2.1 Synthesis of methyl α-substituted diphenylphosphinoacetate-boranes.



Entry	R'	3	LDA (equiv)	Temp.	Reaction time	Conversion	Isolate yield
1	Et	**3a**	1.2	-78 °C to RT	1 h		73%
2	Et	**3a**	2	-78 °C to RT	1 h		72%
3	Bn	**3b**	1.2	-78 °C to RT	1 h		72%
4	Ph	**3c**	1.2	-78 °C to RT	1 h	53%	
5	Ph	**3c**	1.2	-78 °C to RT	overnight	57%	
6[a]	Ph	**3c**	1.2	-78 °C to RT	1 h	77%	
7[a]	Ph	**3c**	2	-78 °C to RT	1 h	78%	
8[a,b]	Ph	**3c**	1.2	-20 °C to RT	1 h	82%	
9[a,b]	Ph	**3c**	1.2	0 °C to RT	1 h	90%	56%
10	*i*-Pr	**3d**	1.2	-78 °C to RT	1 h		21%
11	*i*-Pr	**3d**	1.2	-78 °C to RT	overnight		52%

[a]Neat methyl ester **1** was directly added to the reaction. [b]The reaction was performed with a fast addition of the phosphine adduct over the enolate.

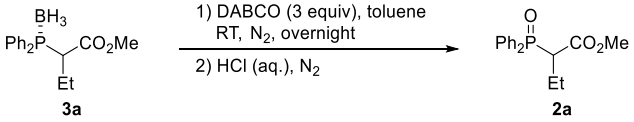
With the protected methyl α-substituted diphenylphosphinoacetate-boranes in hand, the deprotection of the phosphine and hydrolysis of the methyl ester need to be performed to obtain the desired diphenylphosphinoacetic acids **5**. We considered 2 possible routes, a) deprotection of borane and then saponification or b) saponification and then deprotection (Scheme 2.5).



Scheme 2.5 Possible pathways for the synthesis of α-substituted diphenylphosphinocarboxylic acids **5**.

For these steps, methyl 2-ethyl diphenylphosphinoacetate-borane (**3a**) was chosen as a model substrate to optimize the reaction conditions. We first decided to perform the deprotection of borane using 3 equiv of DABCO in degased toluene under an inert atmosphere (Scheme 2.6). However, the corresponding phosphine oxide **2a** was observed

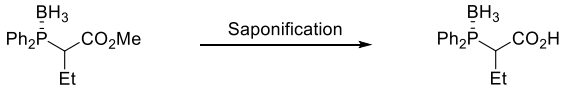
after acidic work up. Due to the easy oxidation of phosphine towards oxygen, we decided to follow pathway b (Scheme 2.5).



Scheme 2.6 Deprotection of methyl 2-ethyl diphenylphosphinoacetate-borane (**3a**).

Hydrolysis of the methyl ester **3a** was carried out under typical reaction conditions using an excess of LiOH in THF:H_2O (10:3) at room temperature and stirring overnight (Table 2.2, entry 1).[11] However, under these conditions, no conversion was observed. We increased the reaction temperature to 60 °C; unfortunately, both hydrolysis and deprotection of the borane took place, providing mainly the oxidized 2-ethyl diphenylphosphinoacetic acid (entry 2). Alternatively, we performed the reaction using NaOH at room temperature but no conversion to the desired product was detected (entry 3), following the same trend than the reaction with LiOH. Encouragingly, by changing the mixture of solvents from THF:H_2O (2:5) to MeOH:H_2O (1:1), the desired product **6a** was obtained in 27% isolated yield together with starting ester **3a** (entry 4). We observed that the ester was not completely dissolved in the solvent system used (MeOH:H_2O). Thus, we decided to use the combination of THF:MeOH:H_2O (1:1:1) as solvent (entry 5), which improved the yield to 53%. To further improve the conversion, we increased the reaction temperature to 30 °C. Under these conditions, full conversion and a mixture of phosphorus species were detected by NMR (entry 6). To balance between the conversion and selectivity towards the desired product **6a**, we shortened the reaction time to 4 h (entry 7), obtaining the product **6a** in 42% yield. Since the yield did not increase by changing temperature or reaction time, we studied the effect of the solvent ratio of the reaction at room temperature. To our delight, the reaction using a higher ratio of MeOH and H_2O respect to THF (2:5:5 of THF:MeOH:H_2O) provided the desired product in 74% isolated yield after stirring the reaction overnight (entry 8). Prolonged reaction time (3 days) improved only slightly the reaction yield (entry 9).

Table 2.2 Synthesis of α-ethyl diphenylphosphinoacetic acid-borane (**6a**).



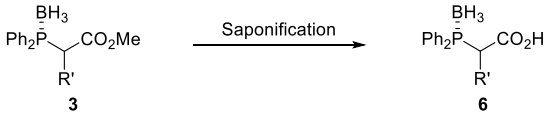
3a **6a**

Entry	Conditions	Temp.	Reaction time	Isolated yield
1	LiOH, THF:H_2O (10:3)	RT	overnight	-[a]
2	LiOH, THF:H_2O (10:3)	60 °C	overnight	-[b]
3	NaOH, THF:H_2O (2:5)	RT	overnight	-[a]
4	NaOH, MeOH:H_2O (1:1)	RT	overnight	27%[c]
5	NaOH, THF:MeOH:H_2O (1:1:1)	RT	overnight	53%[c]
6	NaOH, THF:MeOH:H_2O (1:1:1)	30 °C	overnight	>99% conversion[d]
7	NaOH, THF:MeOH:H_2O (1:1:1)	30 °C	4 h	42%[c]
8	NaOH, THF:MeOH:H_2O (2:5:5)	RT	overnight	74%
9	NaOH, THF:MeOH:H_2O (2:5:5)	RT	3 days	85%

Excess of NaOH and LiOH was used. [a]No conversion. [b]Mainly α-ethyl diphenylphosphanoxideacetic acid was detected. [c]Not full conversion. [d]Other phosphorus species were detected by ^{31}P NMR.

By using the optimal conditions to hydrolyze the methyl ester **3a**, different methyl α-substituted diphenylphosphinoacetates were evaluated (Table 2.3). When compound **3b** was employed, only traces of 2-benzyl diphenylphosphinoacetic acid-borane (**6b**) were obtained along with a large amount of starting material **3b** (entry 1). The hydrolyzed and oxidized 2-benzyl diphenylphosphanoxideacetic acid was formed when the reaction temperature was increased from room temperature to 60 °C (entry 2). Again, to balance between the yield and selectivity, we decreased the reaction temperature to 40 °C (entry 3). A mixture of desired product **6b** and 2-benzyl diphenylphosphanoxideacetic acid was obtained. Taking into account that reactions that were carried out at higher temperatures than room temperature showed the formation of the undesired oxidized product, we decided to perform the reaction at room temperature for longer reaction times. Fortunately, when we stirred the reaction for 4 days, product **6b** was obtained in 54% isolated yield with 85% purity as determined by ^{31}P NMR (entry 4). This protocol was applied also to hydrolyze ester **3c**; however, because of the insolubility of the starting material, we modified the solvent ratio to 1:1:1 of THF:MeOH:H_2O. Under these conditions, 2-phenyl diphenylphosphinoacetic acid-borane (**6c**) was obtained in high yield after 24 h (93% with 87% purity determined by ^{1}H NMR, entry 5). Hydrolysis of methyl 2-isopropyl diphenylphophinoacetate-borane (**3d**) under the optimal conditions (used in entry 1) gave the phosphine oxide ester (entry 6). As expected, when the reaction was performed at higher temperature (60 °C), both removal of the borane and hydrolysis of the ester took place providing mainly 2-isopropyl diphenylphosphanoxideacetic acid (entry 7). Since MeOH could be involved in the deprotection step, we performed several reactions without MeOH at different temperatures and employing LiOH; however, methyl 2-isopropyl diphenylphosphanoxideacetate was obtained in all cases (entries 8–10). We noticed that the deprotection of compound **3d** always occurs before saponification and thus we decided not to pursue further with this substrate.

Table 2.3 Synthesis of α-substituted diphenylphosphinoacetic acid-boranes **6**.

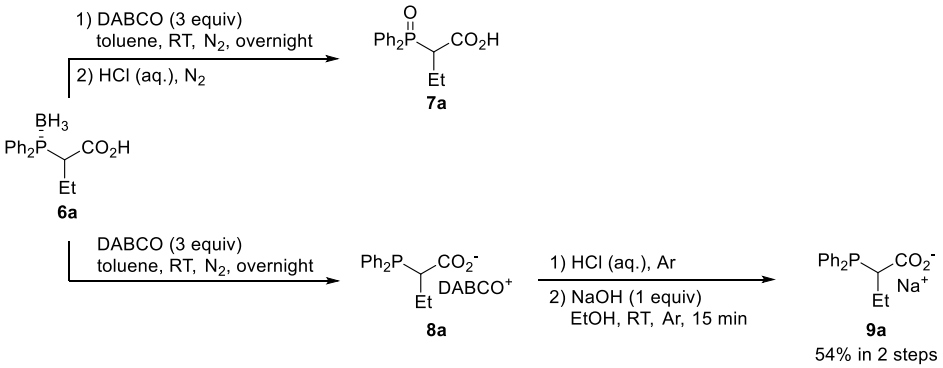


3 **6**

Entry	R'	6	Conditions	Temp.	Reaction time	Isolated yield
1	Bn	**6b**	NaOH, THF:MeOH:H_2O (2:5:5)	RT	overnight	Traces[a]
2	Bn	**6b**	NaOH, THF:MeOH:H_2O (2:5:5)	60 °C	overnight	-[b]
3	Bn	**6b**	NaOH, THF:MeOH:H_2O (2:5:5)	40 °C	overnight	-[c]
4	Bn	**6b**	NaOH, THF:MeOH:H_2O (2:5:5)	RT	4 days	54%[d] (85% purity)
5	Ph	**6c**	NaOH, THF:MeOH:H_2O (1:1:1)	RT	24 h	93%[d] (87% purity)
6	*i*-Pr	**6d**	NaOH, THF:MeOH:H_2O (2:5:5)	RT	overnight	-[e]
7	*i*-Pr	**6d**	NaOH, THF:MeOH:H_2O (2:5:5)	60 °C	overnight	-[b]
8	*i*-Pr	**6d**	NaOH, THF:H_2O (1:1)	60 °C	24 h	-[e]
9	*i*-Pr	**6d**	NaOH, THF:H_2O (1:1)	80 °C	24 h	-[e]
10	*i*-Pr	**6d**	LiOH, THF:H_2O (1:1)	60 °C	24 h	-[e]

Excess of NaOH or LiOH was used. [a]Low conversion. [b]Mainly α-substituted diphenylphosphanoxideacetic acid was obtained. [c]Mixture of the desired product and α-substituted diphenylphosphanoxideacetic acid was obtained. [d]The purity was determined by ^{1}H or ^{31}P NMR. [e]Methyl α-substituted diphenylphosphanoxideacetate was obtained.

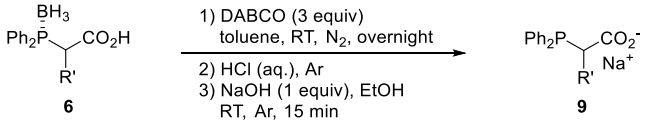
2-Ethyl diphenylphosphinoacetic acid-borane (**6a**) was subsequently subjected to several deprotection procedures to liberate the phosphine from the borane. The deprotection using $HNEt_2$,[10] morpholine,[12] pyrrolidine,[13] TFA[14] or MeOH/toluene[15] showed the formation of the unprotected phosphine together with the phosphine oxide adduct and other impurities. By using 3 equiv of DABCO[16] in degassed toluene at room temperature under nitrogen atmosphere, the reaction cleanly furnished, after acidic workup, 2-ethyl diphenylphosphanoxideacetic acid (**7a**) (Scheme 2.7, above). During this experiment, we noticed that the DABCO salt of 2-ethyl diphenylphosphinoacetic acid (**8a**) was relatively stable towards oxidation, while the free acid was extremely oxygen sensitive. With this in mind, we thought that sodium 2-ethyl diphenylphosphinoacetate (**9a**) could be more stable towards oxidation than the acid. Therefore, we performed an acidic workup of the DABCO salt **8a** under inert atmosphere, followed by the addition of 1 equiv of NaOH in EtOH, providing the corresponding sodium 2-ethyl diphenylphosphinoacetate (**9a**) in 54% yield (2 steps; Scheme 2.7, below). As postulated, this salt is relatively stable towards oxidation and can be stored.



Scheme 2.7 Deprotection of 2-ethyl diphenylphophinoacetic acid-borane (**6a**).

The protocol for the deprotection of the borane and the formation of the sodium salt was applied to other α-substituted diphenylphosphinoacetic acid-boranes (Table 2.4). The reaction of benzyl substrate **6b** provided a mixture of 1:1 ratio of deprotected phosphine and phosphine oxide sodium salts (entry 1). This ratio could be improved to 2.1:1 when the whole process was performed under an Ar atmosphere (entry 2). 2-Phenyl diphenylphosphinoacetic acid-borane (**6c**) also gave a mixture of the deprotected phosphine and the phosphine oxide sodium salts (entry 3). The ratio between the phosphine and phosphine oxide salts changed from step 1 to step 3 and since we know that the salts are relatively stable towards oxidation, we supposed that oxidation took place when the acid was formed after acidic workup (step 2). It must be mentioned, that all these reactions were performed outside a glovebox. We believe that when employing more efficient oxygen free techniques, the sodium α-substituted diphenylphosphinoacetates can be obtained in high purity.

Table 2.4 Deprotection of α-substituted diphenylphophinoacetic acid-boranes **6**.

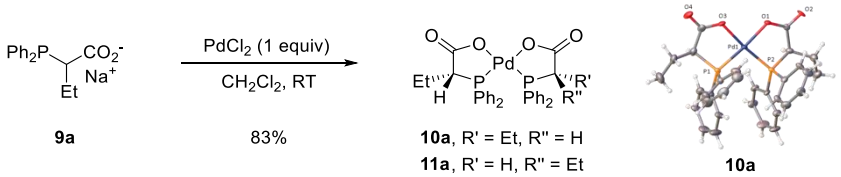


Entry	R'	9	Ratio of deprotected phosphine : phosphine oxide products (after step 1)	Ratio of deprotected phosphine : phosphine oxide products (after step 3)
1	Bn	**9b**	n.d.	1 : 1
2[a]	Bn	**9b**	4.9 : 1	2.1 : 1
3	Ph	**9c**	7.3 : 1	1.6 : 1

The ratio was determined by ^{31}P NMR. n.d = not determined. [a]The deprotection of borane was performed under Ar atmosphere.

With the sodium salt **9a** in hand, we concentrated our efforts towards the synthesis and isolation of P,O-ligand-palladium complexes. The stoichiometric reaction of sodium 2-ethyl diphenylphosphinoacetate (**9a**) with $PdCl_2$ showed the formation of two complexes **10a** and **11a**, as determined by NMR analysis (Scheme 2.8). Complex **10a** was unequivocally

identified by single crystal X-ray diffraction analysis and possesses two molecules of ligands with different stereochemistry attached (i.e. *R*,*S*) in a *cis* geometry. The small differences observed in the NMR spectra between complexes **10a** and **11a** suggest that complex **11a** might be the diastereoisomer of **10a** (i.e. *R*,*R*). The unusual *cis* P-P, square-planar geometry obtained in **10a** and **11a**, has been previously reported on Pd and Pt complexes derivatives from phosphinoacetic acid.[17]



Scheme 2.8 Synthesis of palladium complexes.

Due to the high instability of the prepared α-substituted diphenylphosphinoacetic acids towards oxidation, and taking into account the oxidative conditions generally required in C–H functionalization reactions, we decided not to proceed further with these ligands for C–H functionalization reactions. However, the stable sodium salts or palladium complexes could be applied in some C–H functionalization reactions that do not need strong oxidative conditions.[2-3,5]

2.3 Conclusions

In conclusion, we have developed a general method for the synthesis of α-substituted phosphinoacetic acids in three steps using simple esters and diphenylchlorophosphine-borane as starting materials. The first step consists of phosphonylation of lithium enolates, providing methyl α-substituted diphenylphosphinoacetate-boranes in good yields for both aromatic and aliphatic substrates. Hydrolysis of the esters was successful for ethyl-, benzyl- and phenyl substituted compounds; however, the substrate bearing the isopropyl substituent is problematic due to the easy removal of the borane group. Finally, deprotection of the phosphine is performed in the presence of DABCO. We have observed that α-substituted diphenylphosphinoacetic acids are more sensitive towards phosphine oxidation than the corresponding salts. Two palladium complexes derived from 2-ethyl diphenylphosphinoacetic acid are prepared and one of them has been isolated and characterized by X-ray analysis. Future research should focus on the application of the more stable sodium salts in Pd-catalyzed C–H functionalization reactions.

2.4 Acknowledgements

Dr. Carolina Valderas is kindly acknowledged for her contribution to this chapter. Dr. Wojciech I. Dzik is acknowledged for the provision of X-Ray crystallographic analysis. Ed Zuidinga and Dorette Tromp are thanked for the high-resolution mass measurements.

2.5 Experimental section

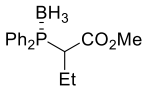
General information

Chromatography: Silicycle Silica Flash P60 size 40–63 µm (230–400 mesh), TLC: Merck silica gel 60 (0.25mm). Visualization of the TLC was performed by UV or phosphomolybdic acid staining. Mass spectra were recorded on a AccuTOF GC v 4g, JMS-T100GCV (for CSI, FD, EI, and FI) and AccuTOF LC, JMS-T100LP (for ESI) mass spectrometers. ^{1}H, ^{13}C, ^{31}P and ^{11}B NMR were recorded on a Bruker DRX 500, Bruker AMX 400 and Bruker DRX 300 using $CDCl_3$ as solvent, unless otherwise mentioned. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 for ^{1}H, δ 77.16 for ^{13}C, acetone-d_6: δ 2.05 for ^{1}H, δ 29.84 for ^{13}C, MeOD-d_4: δ 4.87 for ^{1}H, δ 49.00 for ^{13}C, CD_2Cl_2: δ 5.32 for ^{1}H, δ 54.00 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, td = triplet of doublets, bs = broad singlet, m = multiplet), coupling constants (Hz) and integration. The coupling constants in ^{13}C and ^{31}P NMR are referred to $J_{C\text{-}P}$ and $J_{P\text{-}B}$, respectively. Infrared spectra were recorded on a Bruker IFS 28 FT-spectrophotometer and wavelengths are reported in cm^{-1}. Melting points were measured in a POLYTHERM A Heiztish Mikroskop. Et_2O and THF were dried over sodium/benzophenone and used as freshly distilled. Flame-dried glassware was used for moisture-sensitive reactions. Toluene was dried over CaH_2 and distilled. *i*-Pr_2NH was dried over NaH and distilled. All reagents and solvents that were not mentioned were used as received.

General procedure for the synthesis of methyl α-substituted diphenylphinoacetate-boranes (3)

n-BuLi (1.6 M or 2.5 M solution in hexane, 1.2 equiv) was added to a solution of *i*-Pr_2NH (1.4 equiv) in dry THF at 0 °C under nitrogen atmosphere and stirred for 30 min. Then, the reaction mixture was cooled to -78 °C and a solution of the corresponding ester (1 equiv) in dry THF was added dropwise. The resulting mixture was stirred at -78 °C for 1 h. In a separate flask, a mixture of Ph_2PCl (2.97 equiv) and BH_3·THF (1 M solution in THF, 3 equiv) in dry Et_2O was stirred for 30 min at room temperature and subsequently added dropwise to the reaction mixture at -78 °C or indicated otherwise.[10] The reaction was warmed up to room temperature and stirred over the time period indicated for each substrate. Next, the reaction was quenched with H_2O (0.50 mL) and NEt_3 (0.30 mL) and evaporated to dryness. The resulting crude was dissolved in CH_2Cl_2 (30 mL) and washed with saturated aqueous NaCl solution (30 mL). The organic layer was dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography to obtain the desired product.

Methyl 2-ethyl diphenylphosphinoacetate-borane (3a)

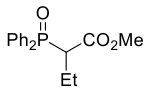


3a

Compound **3a** was prepared following the general procedure using *n*-BuLi (1.6 M, 3.75 mL, 6.00 mmol, 1.2 equiv), *i*-Pr_2NH (0.98 mL, 7.00 mmol, 1.4 equiv) in dry THF (1.5 mL) and methyl butyrate (**1a**) (0.57 mL, 5.00 mmol, 1 equiv) in dry THF (25 mL). A mixture of Ph_2PCl (2.75 mL, 14.85 mmol, 2.97 equiv) and BH_3·THF (15 mL, 15.00 mmol, 3 equiv) in dry Et_2O (9.3 mL) was used. The reaction was stirred for 1 h at room temperature. The crude residue was purified by column chromatography using EtOAc:petroleum ether (1:10 v/v) as an eluent providing the titled

compound as a white solid (1.10 g, 73% yield). ^{1}H NMR (400 MHz) δ = 7.92 – 7.85 (m, 2H), 7.75 – 7.65 (m, 2H), 7.57 – 7.38 (m, 6H), 3.41 (s, 3H), 3.36 (td, *J* = 11.5, 3.1 Hz, 1H), 2.00 – 1.84 (m, 1H), 1.82 – 1.67 (m, 1H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz) δ = 170.8 (d, *J* = 3.6 Hz), 133.8 (d, *J* = 9.5 Hz), 132.8 (d, *J* = 9.1 Hz), 131.9 (d, *J* = 2.5 Hz), 131.6 (d, *J* = 2.5 Hz), 128.9 (d, *J* = 2.5 Hz), 128.7 (d, *J* = 2.6 Hz), 127.9 (d, *J* = 54.4 Hz), 126.3 (d, *J* = 53.9 Hz), 52.0, 46.5 (d, *J* = 26.3 Hz), 21.8, 13.7 (d, *J* = 12.6 Hz); ^{31}P NMR (162 MHz) δ = 23.03 (d, *J* = 72.1 Hz); ^{11}B NMR (128 MHz) δ = -39.00 (bs); IR ν = 2402, 1720, 1435, 1259, 1236, 1062, 741, 692, 478 cm^{-1}; HRMS (FD) calcd for $C_{17}H_{22}BO_2P$ [M]$^{+}$: 300.1445; found: 300.1451; mp 74 – 76 °C.

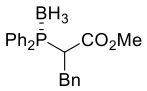
Methyl 2-ethyl diphenylphosphanoxideacetate (2a)



2a

^{1}H NMR (400 MHz) δ = 7.99 – 7.70 (m, 4H), 7.64 – 7.38 (m, 6H), 3.42 (s, 3H), 3.39 – 3.35 (m, 1H), 2.14 – 1.97 (m, 1H), 1.92 – 1.77 (m, 1H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{31}P NMR (162 MHz) δ = 29.53; HRMS (FD) calcd for $C_{17}H_{20}O_3P$ [M+H]$^{+}$: 303.1150; found: 303.1142.

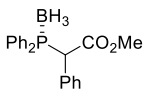
Methyl 2-benzyl diphenylphosphinoacetate-borane (3b)



3b

Compound **3b** was prepared following the general procedure using *n*-BuLi (2.5 M, 2.40 mL, 6.00 mmol, 1.2 equiv), *i*-Pr$_2$NH (0.98 mL, 7.00 mmol, 1.4 equiv) in dry THF (1.5 mL) and methyl 3-phenylpropionate (**1b**) (0.79 mL, 5.00 mmol, 1 equiv) in dry THF (25 mL). A mixture of Ph_2PCl (2.75 mL, 14.85 mmol, 2.97 equiv) and BH_3·THF (15 mL, 15.00 mmol, 3 equiv) in dry Et_2O (9.3 mL) was used. The reaction was stirred for 1 h at room temperature. The crude residue was purified by column chromatography using EtOAc:petroleum ether (1:10 v/v) as an eluent providing the titled compound as a white solid (1.30 g, 72% yield). ^{1}H NMR (400 MHz) δ = 8.02 – 7.95 (m, 2H), 7.85 – 7.77 (m, 2H), 7.63 – 7.46 (m, 6H), 7.32 – 7.12 (m, 5H), 3.77 (td, *J* = 11.7, 2.7 Hz, 1H), 3.31 (s, 3H), 3.26 – 3.17 (m, 1H), 3.08 – 2.99 (m, 1H); ^{13}C NMR (101 MHz) δ = 170.1 (d, *J* = 3.4 Hz), 138.9 (d, *J* = 12.8 Hz), 133.8 (d, *J* = 9.6 Hz), 132.8 (d, *J* = 9.2 Hz), 132.0 (d, *J* = 2.5 Hz), 131.7 (d, *J* = 2.6 Hz), 128.9 (d, *J* = 4.4 Hz), 128.8 (d, *J* = 4.5 Hz), 128.7, 128.6, 127.4 (d, *J* = 54.4 Hz), 126.9, 126.1 (d, *J* = 53.6 Hz), 52.0, 46.8 (d, *J* = 24.1 Hz), 33.8 (d, *J* = 1.9 Hz); ^{31}P NMR (121 MHz) δ = 23.61 (d, *J* = 49.0 Hz); ^{11}B NMR (128 MHz) δ = -39.06 (bs); IR ν = 2386, 1731, 1436, 1151, 1060, 909, 732, 697 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{20}O_2P$ [M-BH_3-H]$^{+}$: 347.1195; found: 347.1184; mp 79 – 81 °C.

Methyl 2-phenyl diphenylphosphinoacetate-borane (3c)

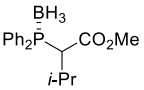


3c

Compound **3c** was prepared following the general procedure using *n*-BuLi (2.5 M, 1.44 mL, 3.60 mmol, 1.2 equiv), *i*-Pr$_2$NH (0.60 mL, 4.20 mmol, 1.4 equiv) in dry THF (1.5 mL). After 30 min, dry THF (15 mL) was added to the reaction. The reaction was cooled down to -78 °C and methyl phenylacetate (**1c**) (0.42 mL, 3.00 mmol, 1 equiv) was added. The reaction was warmed up to 0 °C. A mixture of Ph_2PCl (1.65 mL, 8.91 mmol, 2.97 equiv) and BH_3·THF (9 mL, 9.00 mmol, 3 equiv) in dry Et_2O (5.7 mL) was used. In this case, fast addition of a mixture of Ph_2PCl, BH_3·THF and Et_2O was performed. The reaction was stirred for 1 h at room temperature. The crude residue was purified by column chromatography using EtOAc:petroleum ether (1:5 v/v) as an eluent

providing the titled compound as a white solid (0.58 g, 56% yield). ^{1}H NMR (400 MHz) δ = 7.98 – 7.89 (m, 2H), 7.63 – 7.53 (m, 3H), 7.53 – 7.42 (m, 3H), 7.40 – 7.32 (m, 2H), 7.32 – 7.16 (m, 5H), 4.87 (d, *J* = 12.2 Hz, 1H), 3.59 (s, 3H); ^{13}C NMR (101 MHz) δ = 168.7, 133.6 (d, *J* = 9.2 Hz), 132.9 (d, *J* = 8.9 Hz), 131.8 (d, *J* = 2.5 Hz), 131.3 (d, *J* = 2.4 Hz), 130.6 (d, *J* = 3.1 Hz), 130.1 (d, *J* = 4.4 Hz), 128.5 (d, *J* = 10.3 Hz), 128.4 (d, *J* = 10.0 Hz), 128.1 (d, *J* = 2.5 Hz), 128.0 (d, *J* = 2.0 Hz), 127.2 (d, *J* = 54.4 Hz), 126.3 (d, *J* = 53.5 Hz), 52.4, 51.1 (d, *J* = 25.2 Hz); ^{31}P NMR (162 MHz) δ = 25.66 (d, *J* = 47.7 Hz); ^{11}B NMR (128 MHz) δ = -38.51 (bs); IR v = 2376, 2348, 1733, 1433, 1209, 1100, 1055, 1029, 727, 690, 510 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{19}O_2P$ [M-BH_3]$^+$: 334.1117; found: 334.1116; mp 125 – 127 °C.

Methyl 2-isopropyl diphenylphosphinoacetate-borane (3d)



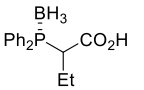
3d

Compound **3d** was prepared following the general procedure using *n*-BuLi (2.5 M, 2.40 mL, 6.00 mmol, 1.2 equiv), *i*-Pr_2NH (0.98 mL, 7.00 mmol, 1.4 equiv) in dry THF (1.5 mL) and methyl isovalerate (**1d**) (0.66 mL, 5.00 mmol, 1 equiv) in dry THF (25 mL). A mixture of Ph_2PCl (2.75 mL, 14.85 mmol, 2.97 equiv) and BH_3·THF (15 mL, 15.00 mmol, 3 equiv) in dry Et_2O (9.3 mL) was used. The reaction was stirred overnight at room temperature. The crude residue was purified by column chromatography using EtOAc:petroleum ether (1:10 v/v) as an eluent providing the titled compound as a white solid (0.82 g, 52% yield). ^{1}H NMR (400 MHz) δ = 8.00 – 7.89 (m, 2H), 7.82 – 7.69 (m, 2H), 7.55 – 7.37 (m, 6H), 3.36 (t, *J* = 9.9 Hz, 1H), 3.25 (s, 3H), 2.51 – 2.37 (m, 1H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz) δ = 170.3 (d, *J* = 3.3 Hz), 133.7 (d, *J* = 9.4 Hz), 132.2 (d, *J* = 9.1 Hz), 131.5 (d, *J* = 2.5 Hz), 131.1 (d, *J* = 2.5 Hz), 128.7 (d, *J* = 54.1 Hz), 128.5 (d, *J* = 8.1 Hz), 128.4 (d, *J* = 8.4 Hz), 126.4 (d, *J* = 53.1 Hz), 52.2 (d, *J* = 26.3 Hz), 51.5, 29.0, 22.4, 22.3; ^{31}P NMR (162 MHz) δ = 18.91 (d, *J* = 68.8 Hz); ^{11}B NMR (128 MHz) δ = -38.63 (bs); IR v = 2966, 2397, 2358, 1736, 1720, 1434, 1292, 1149, 1059, 738, 690, 504 cm^{-1}; HRMS (FI) calcd for $C_{18}H_{21}O_2P$ [M-BH_3]$^+$: 300.1274; found: 300.1222; mp 115 – 116 °C.

General procedure for the hydrolysis of methyl α-substituted diphenylphosphinoacetate-boranes (3)

Methyl α-substituted diphenylphosphinoacetate-borane (**3**) (1 equiv) and NaOH (20 equiv or 40 equiv) were stirred at room temperature in a mixture of THF, MeOH and H_2O. After the indicated time, the reaction was evaporated to dryness. The crude obtained was dissolved in H_2O (10 mL) and washed with CH_2Cl_2 (3 x 10 mL). The aqueous layer was acidified with aqueous HCl solution (1 M) to pH = 1 and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure to afford α-substituted diphenylphosphinoacetic acid-borane (**6**).

2-Ethyl diphenylphosphinoacetic acid-borane (6a)

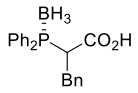


6a

Compound **6a** was prepared following the general procedure using methyl 2-ethyl diphenylphosphinoacetate-borane (**3a**) (100 mg, 0.34 mmol, 1 equiv) and NaOH (272 mg, 6.80 mmol, 20 equiv) in a mixture of THF, MeOH and H_2O (0.2, 0.5 and 0.5 mL, respectively) for 18 h to afford 2-ethyl diphenylphosphinoacetic acid-borane (**6a**) as a white solid (72 mg, 74% yield). ^{1}H NMR (300

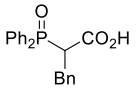
MHz) δ = 9.88 (bs, 1H), 7.86 – 7.77 (m, 2H), 7.77 – 7.66 (m, 2H), 7.57 – 7.38 (m, 6H), 3.35 (td, *J* = 11.6, 3.2 Hz, 1H), 1.98 – 1.81 (m, 1H), 1.80 – 1.65 (m, 1H), 0.98 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz) δ = 175.7, 133.6 (d, *J* = 9.5 Hz), 132.8 (d, *J* = 9.2 Hz), 132.0 (d, *J* = 2.4 Hz), 131.7 (d, *J* = 2.4 Hz), 128.9 (d, *J* = 10.4 Hz), 128.8 (d, *J* = 10.8 Hz), 127.5 (d, *J* = 54.8 Hz), 126.2 (d, *J* = 53.7 Hz), 46.0 (d, *J* = 25.4 Hz), 21.6, 13.6 (d, *J* = 12.4 Hz); ^{31}P NMR (162 MHz) δ = 23.23 (d, *J* = 54.2 Hz); ^{11}B NMR (128 MHz) δ = -39.36 (bs); IR v = 2926, 2389, 1695, 1436, 1279, 1063, 733, 687, 473 cm^{-1}; HRMS (FD) calcd for $C_{16}H_{18}O_2P$ [M-BH_3+H]$^+$: 273.1039; found: 273.1107; mp 133 – 134 °C.

2-Benzyl diphenylphosphinoacetic acid-borane (6b)


6b

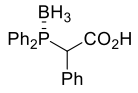
Compound **6b** was prepared following the general procedure using methyl 2-benzyl diphenylphosphinoacetate-borane (**3b**) (50 mg, 0.14 mmol, 1 equiv) and NaOH (224 mg, 5.60 mmol, 40 equiv) in a mixture of THF, MeOH and H_2O (0.1, 0.25 and 0.25 mL, respectively) for 4 days to afford 2-benzyl diphenylphosphinoacetic acid-borane (**6b**) as a white solid (26 mg, 54% yield, 85% purity determined from ^{31}P NMR). ^{1}H NMR (300 MHz) δ = 10.04 (bs, 1H), 7.97 – 7.74 (m, 4H), 7.62 – 7.41 (m, 7H), 7.33 – 7.21 (m, 3H), 7.19 – 7.10 (m, 1H), 3.78 (td, *J* = 11.8, 2.6 Hz, 1H), 3.26 – 3.11 (m, 1H), 3.10 – 2.96 (m, 1H); ^{13}C NMR (75 MHz) δ = 174.8, 138.6 (d, *J* = 12.7 Hz), 133.6 (d, *J* = 9.7 Hz), 132.8 (d, *J* = 9.2 Hz), 132.1 (d, *J* = 2.3 Hz), 131.9 (d, *J* = 2.3 Hz), 129.1, 128.9, 128.8, 128.6, 127.1 (d, *J* = 54.7 Hz), 127.0, 126.0 (d, *J* = 53.3 Hz), 46.3 (d, *J* = 22.9 Hz), 33.5; ^{31}P NMR (121 MHz) δ = 24.33 (s); ^{11}B NMR (96 MHz) δ = -39.63 (bs); IR v = 2932, 2389, 1707, 1437, 1106, 732, 698 cm^{-1}; HRMS (FD) calcd for $C_{21}H_{22}BO_2P$ [M-H]$^+$: 347.1372; found: 347.1386; mp 145 – 146 °C.

2-Benzyl diphenylphosphanoxideacetic acid (7b)


7b

^{1}H NMR (300 MHz) δ = 8.33 (bs, 1H), 7.96 – 7.71 (m, 4H), 7.57 – 7.34 (m, 6H), 7.22 – 7.03 (m, 5H), 3.92 – 3.69 (m, 1H), 3.31 – 3.08 (m, 1H), 3.06 – 2.81 (m, 1H); ^{31}P NMR (121 MHz) δ = 33.64 (s); HRMS (FD) calcd for $C_{21}H_{20}O_3P$ [M+H]$^+$: 351.1150; found: 351.1161.

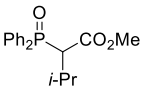
2-Phenyl diphenylphosphinoacetic acid-borane (6c)


6c

Compound **6c** was prepared following the general procedure using methyl 2-phenyl diphenylphosphinoacetate-borane (**3c**) (100 mg, 0.29 mmol, 1 equiv) and NaOH (232 mg, 5.80 mmol, 20 equiv) in a mixture of THF, MeOH and H_2O (0.5, 0.5 and 0.5 mL, respectively) for 1 day to afford 2-phenyl diphenylphosphinoacetic acid-borane (**6c**) as a white solid (91 mg, 93% yield, 87% purity determined from ^{1}H NMR). ^{1}H NMR (300 MHz, Acetone-d_6) δ = 8.09 – 7.97 (m, 2H), 7.67 – 7.48 (m, 5H), 7.47 – 7.40 (m, 1H), 7.40 – 7.29 (m, 4H), 7.22 – 7.10 (m, 3H), 5.19 (d, *J* = 13.9 Hz, 1H); ^{13}C NMR (75 MHz, Acetone-d_6) δ = 169.7, 134.4 (d, *J* = 9.1 Hz), 133.9 (d, *J* = 8.8 Hz), 132.8 (d, *J* = 2.2 Hz), 132.5 (d, *J* = 2.4 Hz), 132.1 (d, *J* = 2.5 Hz), 131.5 (d, *J* = 4.5 Hz), 129.4 (d, *J* = 10.0 Hz), 129.2 (d, *J* = 9.9 Hz), 128.6 (d, *J* = 1.9 Hz), 128.6 (d, *J* = 2.0 Hz), 50.6 (d, *J* = 27.6 Hz); ^{31}P NMR (121 MHz, Acetone-d_6) δ = 23.73 (d, *J* = 65.6 Hz); ^{11}B NMR (96 MHz, Acetone-d_6) δ = -38.80 (bs); IR v = 3058, 2926, 2400, 1723, 1701, 1436, 1267, 1103,

1063, 734, 698 cm^{-1}; HRMS (FD) calcd for $C_{20}H_{19}BO_2P$ $[M-H]^+$: 333.1216; found: 333.1216; mp 142 – 143 °C.

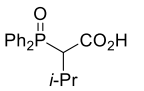
Methyl 2-isopropyl diphenylphosphanoxideacetate (2c)



2c

^{1}H NMR (400 MHz) δ = 8.07 – 7.95 (m, 2H), 7.89 – 7.78 (m, 2H), 7.58 – 7.44 (m, 6H), 3.34 – 3.24 (m, 1H), 3.30 (s, 3H), 2.66 – 2.46 (m, 1H), 1.04 (d, *J* = 6.6 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H); ^{31}P NMR (162 MHz) δ = 26.69 (s); HRMS (EI) calcd for $C_{18}H_{21}O_3P$ $[M]^+$: 316.1228; found: 316.1210.

2-Isopropyl diphenylphosphanoxideacetic acid (7c)



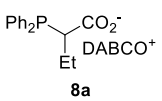
7c

^{1}H NMR (400 MHz) δ = 9.65 (bs, 1H), 8.01 – 7.86 (m, 2H), 7.82 – 7.68 (m, 2H), 7.56 – 7.33 (m, 6H), 3.42 (dd, *J* = 10.2, 8.1 Hz, 1H), 2.41 – 2.29 (m, 1H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H); ^{31}P NMR (162 MHz) δ = 31.99 (s); HRMS (FD) calcd for $C_{17}H_{20}O_3P$ $[M+H]^+$: 303.1150; found 303.1153.

General procedure for the deprotection of α-substituted diphenylphosphinoacetic acid-boranes (6)

α-Substituted diphenylphosphinoacetic acid-borane (**6**) (1 equiv) and DABCO (3 equiv) in dry and degassed toluene were stirred under nitrogen atmosphere at room temperature overnight.[16] The reaction was evaporated to dryness to afford the DABCO salt of the α-substituted diphenylphosphinoacetic acid (**8**).

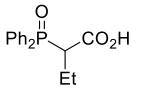
DABCO salt of 2-ethyl diphenylphosphinoacetic acid (8a)



8a

Compound **8a** was prepared following the general procedure using 2-ethyl diphenylphosphinoacetate-borane (**6a**) (100 mg, 0.35 mmol, 1 equiv) and DABCO (118 mg, 1.05 mmol, 3 equiv) in toluene (5 mL) to afford the DABCO salt of 2-ethyl diphenylphosphinoacetic acid (**8a**). ^{1}H NMR (400 MHz) δ = 7.62 – 7.55 (m, 2H), 7.54 – 7.47 (m, 2H), 7.34 – 7.21 (m, 6H), 3.14 – 3.08 (m, 1H), 1.91 – 1.77 (m, 1H), 1.59 – 1.44 (m, 1H), 0.99 (t, *J* = 7.3 Hz, 3H); ^{31}P NMR (121 MHz) δ = -5.27 (s); HRMS (FD) calcd for $C_{16}H_{18}O_2P$ $[R\text{-}CO_2H+H]^+$: 273.1039; found: 273.1031.

2-Ethyl diphenylphosphanoxideacetic acid (7a)

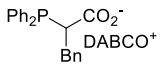


7a

Compound **7a** was obtained following the general procedure using 2-ethyl diphenylphosphinoacetate-borane (**6a**) (100 mg, 0.35 mmol, 1 equiv) and DABCO (118 mg, 1.05 mmol, 3 equiv) in toluene (5 mL). The crude was acidified with aqueous HCl solution (1 M) and extracted with CH_2Cl_2 3 times. The combined organic layers were dried over anh. $MgSO_4$, filtered and concentrated under reduced pressure. ^{1}H NMR (400 MHz) δ = 9.87 (bs, 1H), 7.88 – 7.70 (m, 4H), 7.56 – 7.34 (m, 6H), 3.46 (t, *J* = 11.0 Hz, 1H), 2.02 – 1.87 (m, 1H), 1.74 – 1.60 (m, 1H), 0.97 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz) δ = 170.9 (d, *J* = 3.1 Hz), 131.7 (d, *J* = 3.0 Hz), 131.6 (d, *J* = 3.0 Hz), 131.4 (d, *J* = 10.6 Hz), 130.4 (d, *J* = 4.4 Hz), 129.3 (d, *J* = 4.7 Hz), 128.8 (d, *J* = 3.4 Hz), 128.7 (d, *J* = 3.4 Hz), 128.4 (d, *J* = 13.3 Hz), 50.3 (d, *J* = 59.9 Hz), 20.8 (s), 13.3 (d, *J* = 14.1 Hz); ^{31}P

NMR (162 MHz) δ = 33.97 (s); IR v = 1717, 1437, 1148, 1117, 1090, 725, 692, 547, 519 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{16}OP$ $[M\text{-}HCO_2]^+$: 243.0933; found: 243.0951; mp 74 – 76 °C.

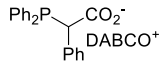
DABCO salt of 2-benzyl diphenylphosphinoacetic acid (8b)



8b

Compound **8b** was prepared following the general procedure using 2-benzyl diphenylphosphinoacetate-borane (**6b**) (28 mg, 0.08 mmol, 1 equiv) and DABCO (27 mg, 0.24 mmol, 3 equiv) in toluene (3 mL) to afford the DABCO salt of 2-benzyl diphenylphosphinoacetic acid (**8b**). ^{1}H NMR (400 MHz) δ = 7.68 – 7.56 (m, 4H), 7.41 – 7.36 (m, 3H), 7.32 – 7.25 (m, 3H), 7.24 – 7.09 (m, 5H), 3.58 (dt, *J* = 11.4, 3.9 Hz, 1H), 3.23 – 3.11 (m, 1H), 2.84 – 2.73 (m, 1H); ^{31}P NMR (162 MHz) δ = -2.26 (s); HRMS (CSI) calcd for $C_{21}H_{18}O_2P$ $[M]^-$: 333.1044; found: 333.1050.

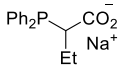
DABCO salt of 2-phenyl diphenylphosphinoacetic acid (8c)



8c

Compound **8c** was prepared following the general procedure using 2-phenyl diphenylphosphinoacetate-borane (**6c**) (30 mg, 0.09 mmol, 1 equiv) and DABCO (30 mg, 0.27 mmol, 3 equiv) in toluene (5 mL) to afford the DABCO salt of 2-phenyl diphenylphosphinoacetic acid (**8c**). ^{1}H NMR (400 MHz) δ = 7.76 – 7.68 (m, 2H), 7.43 – 7.36 (m, 2H), 7.36 – 7.28 (m, 3H), 7.20 – 7.01 (m, 8H), 4.34 (d, *J* = 7.5 Hz, 1H); ^{31}P NMR (162 MHz) δ = -2.71 (s); HRMS (ESI) calcd for $C_{19}H_{16}P$ $[M\text{-}CO_2]^-$: 275.0990; found: 275.0962.

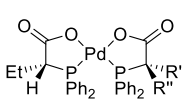
Procedure for the synthesis of sodium 2-ethyl diphenylphosphinoacetate (9a)



9a

DABCO salt of 2-ethyl diphenylphosphinoacetic acid (**8a**) (0.35 mmol, 1 equiv) was dissolved in degassed EtOAc (3 mL) and acidified by using degassed aqueous HCl solution (2 M, 3 mL) under argon atmosphere. The aqueous layer was extracted with degassed EtOAc (2 x 3 mL). The combined EtOAc layers were treated with a degassed solution NaOH in EtOH (1 M, 0.35 mL, 0.35 mmol, 1 equiv) and stirred at room temperature for 15 min. The reaction was evaporated to dryness to afford sodium 2-ethyl diphenylphosphinoacetate (**9a**) as a white solid (57 mg, 54% yield in 2 steps). ^{1}H NMR (400 MHz, MeOD-d_4) δ = 7.55 – 7.39 (m, 4H), 7.30 – 7.14 (m, 6H), 3.08 – 2.98 (m, 1H), 1.79 – 1.66 (m, 1H), 1.40 – 1.25 (m, 1H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, MeOD-d_4) δ = 179.5 (d, *J* = 7.4 Hz), 139.0 (d, *J* = 15.2 Hz), 138.6 (d, *J* = 15.9 Hz), 134.9 (d, *J* = 21.2 Hz), 134.2 (d, *J* = 19.5 Hz), 130.1, 129.6, 129.4 (d, *J* = 7.3 Hz), 129.1 (d, *J* = 6.7 Hz), 50.7 (d, *J* = 14.1 Hz), 25.0 (d, *J* = 18.7 Hz), 13.6 (d, *J* = 12.4 Hz); ^{31}P NMR (162 MHz, MeOD-d_4) δ = -5.49 (s); IR v = 2964, 1687, 1582, 1434, 1375, 1262, 1174, 739, 692, 553, 525 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}Na_2O_2P$ $[M+Na]^+$: 317.0678; found: 317.0671; mp 47 – 49 °C.

Procedure for the synthesis of *cis*-bis(2-ethyl diphenylphosphinoacetate) palladium complexes (10a) and (11a)

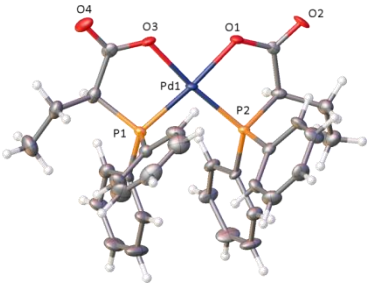


10a, R' = Et, R'' = H
11a, R' = H, R'' = Et

A solution of sodium 2-ethyl diphenylphosphinoacetate (**9a**) (70 mg, 0.24 mmol, 1 equiv) and $PdCl_2$ (43 mg, 0.24 mmol, 1 equiv) in dry and degassed CH_2Cl_2 (5 mL) was stirred at room temperature under nitrogen atmosphere overnight. The reaction was filtrated through a pad of Celite and evaporated to dryness to afford a mixture of two palladium

complexes (*R*,*S*) (**10a**) and (*R*,*R*) (**11a**) in a ratio of 1:1 (66 mg, 83% yield). Single crystal suitable for X-ray crystallography was obtained by crystallization with a two-solvent system (CH_2Cl_2/MeOH). ^{1}H NMR (500 MHz, CD_2Cl_2) δ = 7.82 (bs, 1H), 7.74 (bs, 1H), 7.63 – 7.53 (m, 4H), 7.52 – 7.31 (m, 7H), 7.27 (bs, 1H), 7.24 – 7.08 (m, 4H), 7.03 – 6.94 (m, 2H), 3.57 (bs, 1H, **10a** or **11a**), 3.50 (bs, 1H, **11a** or **10a**), 1.85 – 1.66 (m, 2H), 1.43 – 1.19 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H, **10a** or **11a**), 0.82 (t, *J* = 7.4 Hz, 3H, **11a** or **10a**); ^{31}P NMR (202 MHz, CD_2Cl_2) δ = 30.01 (s), 27.66 (s); HRMS (ESI) calcd for $C_{32}H_{34}O_4P_2Pd$ $[M+2H]^+$: 650.0962; found: 650.1008.

Crystal structure information of (*R*,*S*) *cis*-bis(2-ethyl diphenylphosphinoacetate) palladium complex (**10a**)



CCDC Number	1489246
Empirical formula	$C_{32}H_{32}O_4P_2Pd$
Formula weight	648.91
Temperature/K	150(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.7169(6)
b/Å	19.7933(11)
c/Å	14.8522(8)
α/°	90
β/°	100.15(2)
γ/°	90
Volume/Å^3	2811.8(3)
Z	4
ρ_{calc}g/cm^3	1.533
μ/mm^{-1}	0.811
F(000)	1328.0
Crystal size/mm^3	0.475 x 0.215 x 0.190
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.094 to 50.16
Index ranges	-11 ≤ h ≤ 11, -23 ≤ k ≤ 23, -17 ≤ l ≤ 17
Reflections collected	47408
Independent reflections	9968 [R_{int} = 0.0559, R_{sigma} = 0.0447]
Data/ restraints/ parameters	9968/1/708

Goodness-of-fit on F^2	0.812
Final R indexes [I>2σ (I)]	R_1 = 0.0322, wR_2 = 0.0947
Final R indexes [all data]	R_1 = 0.0396, wR_2 = 0.1023
Largest diff. peak/hole / e $Å^{-3}$	1.19/-0.76
Flack parameter	0.45(3)

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