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Manganese-Catalyzed and Mediated Synthesis of Arylphosphinates and Related Compounds

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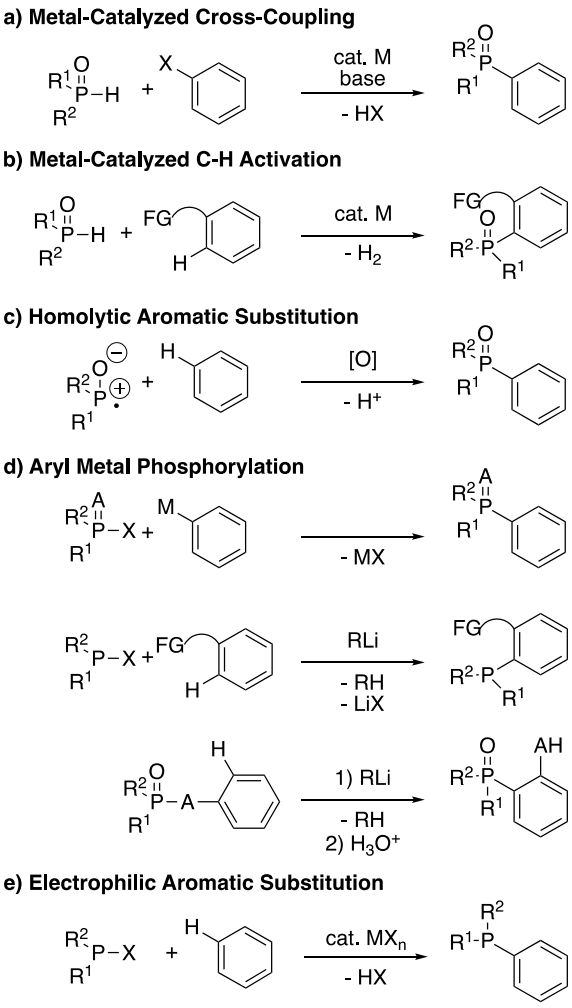
Abstract: The free-radical arylation of *H*-phosphinates and related compounds was examined. A practical catalytic process with air as the oxidant could not be found. However, an inexpensive and robust methodology was developed, using catalytic Mn(II) as the radical initiator and excess Mn(IV) as the stoichiometric oxidant. Using these conditions the inter- and intramolecular arylation of phosphinylidene compounds has a broad scope, including application to the synthesis of *P*-heterocycles. A full account of this methodology is presented including a discussion of its limitations.

Introduction

Synthesizing organophosphorus compounds continues to be of interest because of their importance in various areas. Particularly, arylphosphorus compounds have applications in medicinal chemistry, ligands for catalytic reactions, materials, etc.[1] Several methodologies (Scheme 1) have been reported for the synthesis of arylphosphonates ($R^1 = R^2 = OAlk$), fewer for tertiary phosphine oxides (almost always $R^1 = R^2 = Ph$), and more rarely for phosphinates (R^1 = Alk, Aryl, or H, $R^2 = OAlk$).[2] Of those methodologies, metal-catalyzed cross-couplings using palladium, nickel, and copper catalysts (Scheme 1a) are the most common.[3] More recently, metal-catalyzed C-H activation has been investigated for the preparation of arylphosphorus compounds (Scheme 1b).[4] Free-radical arylation (homolytic aromatic substitution, HAS; Scheme 1c) is a related class of reaction, which also avoids the use of functionalized aromatics such as aryl halides necessary in metal-catalyzed cross-couplings.[5] Other processes that have been employed to prepare arylphosphorus compounds include deprotonation of aryl-C_{sp2}-H (or variations on this theme) followed by reaction with P-Cl reagents (Scheme 1d),[6] and Friedel-Crafts electrophilic aromatic substitution (Scheme 1e).[7]

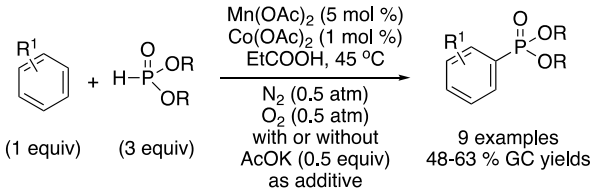
Our laboratory has long been interested in the chemistry of phosphinates.[8] As a result, we have reported several palladium-catalyzed cross-coupling reactions for the synthesis of arylphosphinates. More recently we became interested in investigating the free-radical arylation of *H*-phosphinates, which had been neglected as phosphorus partners.[2] Even though the reactivity of phosphinylidene compounds varies greatly,[9] the published reactions with *H*-phosphonate diesters (or diphenylphosphine oxide) could be used as a starting point. Herein we describe our full study of the free-radical arylation of *H*-phosphinates and related compounds.



Scheme 1. Various methodologies for the preparation of arylphosphorus compounds.

Results and Discussion

Arylation using catalytic oxidants. In reviewing the literature concerning the arylation of *H*-phosphonate diesters, we were intrigued by Ishii's 2004 report concerning a Mn(II)/Co(II)-catalyzed process that uses oxygen as the terminal oxidant (Equation 1).[10]



(1)

Reinvestigating this reaction was our starting point even though we immediately identified three significant issues: 1) the reaction employs a large excess of *H*-phosphonate diesters; 2) the ratio of N_2/O_2 must be carefully controlled; and 3) not a single yield was reported. We chose $(EtO)_2P(O)H$ and mesitylene as the model reagents, and under Ishii's conditions, we obtained a 50% yield of diethyl mesitylphosphonate, undistinguishable from the 48% GC yield he reported.

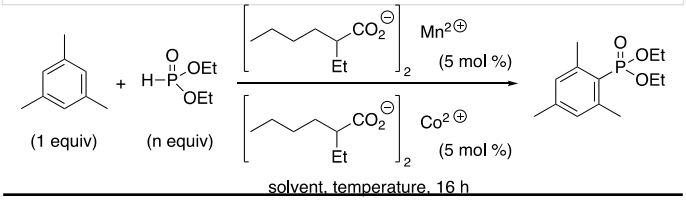
Our main objective was to reduce the amount of $(EtO)_2P(O)H$ (so that ultimately *H*-phosphinates and other valuable compounds could be used) and to find more practical conditions. In order to have a broader range of solvent and conditions, we decided to employ lipophilic Mn(II)- and Co(II)-2-ethylhexanoates (5 mol % each) instead of the acetates, and the results are shown in Table 1. Good results were obtained without any solvent, and in hexanes, ethyl acetate, and acetonitrile (entries 1-2) using compressed air instead of Ishii's 50:50 O_2/N_2 mixture. Unfortunately, decreasing the number of equivalents of the *H*-phosphonate resulted in a drastic loss of yield (entries 2a-2d). Next, oxygen was used in the place of compressed air (entries 3 and 4) and an oxygen balloon gave a yield similar to compressed air, whereas Ishii's 50:50 O_2/N_2 mixture was satisfactory (entry 5), but not air (entry 6).

Interestingly, switching from acetonitrile to ethyl acetate under a flow of oxygen was a significant improvement (entry 7a) and amounts of Mn(II) and/or Co(II) could be lowered (entries 7b-7d) with only a slight drop in yield, but removing the cobalt altogether gave no product at all. Once again but not as sharply as with CH_3CN and compressed air (entry 2), reducing the amount of $(EtO)_2P(O)H$ lowered the yield significantly (entries 8a-8c). Finally, using a balloon of oxygen was virtually identical to the oxygen flow (entries 7a and 9).

Other results not shown in Table 1 are briefly summarized here. Other solvents tested were unsatisfactory (data not shown in Table 1, yield %): DMSO (0), acetone (0), diisobutylketone (0), $CHCl_3$ (0), THF (0), 1,4-dioxane (9), DMF (20), DME (37), perfluorodecalin (41), *t*-AmOH (43).

Several conclusions could be drawn from this study. First, a more convenient terminal oxidant than 50:50 O_2/N_2 could be identified (compressed air, oxygen flow, oxygen balloon). Second, using 2-ethylhexanoate salts allowed reaction in solvents other than acetic or propanoic acids. Third, diethyl mesitylphosphonate could be synthesized in good yield (~70-80%) under various catalytic conditions.

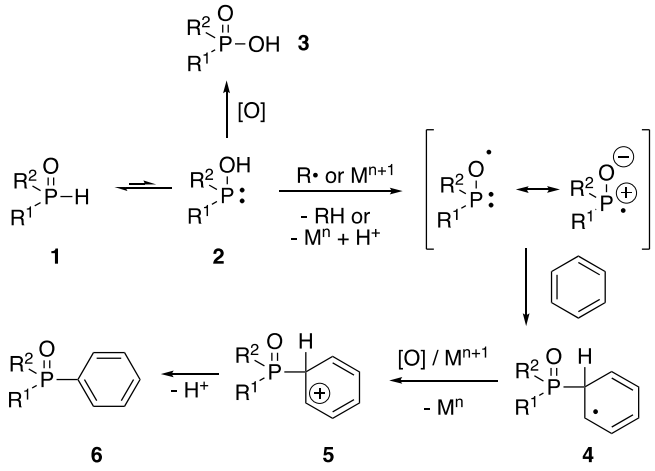
Table 1. Arylation of diethyl *H*-phosphonate with mesitylene



Entry	n (Equiv)	Solvent	Conditions	Yield (%)[a]
1a		none		60
1b	3	hexane(s)	90 °C, compressed air	55
1c		EtOAc		57
2a	3			71
2b	2	CH_3CN	90 °C,	37
2c	1		compressed air	21
2d	0.5			12
3	3	CH_3CN	90 °C, O_2 flow	57
4	3	CH_3CN	90 °C, O_2 balloon	73
5	3	CH_3CN	90 °C, O_2/N_2 1:1	61
6	3	CH_3CN	90 °C, air	33
7a				**78**
7b	**3**	**EtOAc**	**90 °C, O_2 flow**	73[b]
7c				72[c]
7d				65[d]
8a	2			63
8b	1	EtOAc	90 °C, O_2 flow	39
8c	0.2			38
9	3	EtOAc	90 °C, O_2 balloon	77

[a] Yield after purification by chromatography on silica gel. [b] Only 1 mol % of Co(II) 2-ethylhexanoate was employed. [c] Mn(II) and Co(II) 3 mol % each. [d] Mn(II) and Co(II) 1 mol % each.…

A postulated mechanism for the free-radical arylation is shown in Scheme 2. Tautomerization[9] of phosphinylidene **1** to less stable **2** is followed by formation of a free-radical intermediate which adds to the aromatic ring to form resonance-stabilized cyclohexadienyl radical **4**. This radical intermediate is too stable to abstract the hydrogen atom from **1** or **2**. Instead, oxidation of free-radical **4** into cation **5** takes place and then loss of a proton rearomatizes the ring to produce arylphosphorus **6**. A major competing side reaction is the oxidation of **2** into acid **3**.

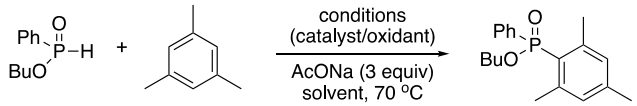


Scheme 2. Proposed mechanism for free-radical phosphinylidene arylation.

Unfortunately, the main goal of reducing the amount of *H*-phosphonate failed, as it leads to losses in yield that are too large. This was a problem because *H*-phosphinates are much more valuable than $(EtO)_2P(O)H$ and sacrificing two equivalents as "antioxidant" would be prohibitive. In fact, with butyl phenyl-*H*-phosphinate and conditions as in Table 1, entries 1a, 2a, and 7a; gave yields of 0 %,12 %, and 0 %, respectively. This once again illustrates the fact that phosphinylidene compounds P(O)H have different reactivities that go back to their tautomeric equilibrium with the P-OH form. In our published study of this equilibrium,[9] we reported that the half-lives of deuteration with D_2O for PhP(O)(OEt)H and $(EtO)_2P(O)H$ are 1.4 h and 21 h, respectively. Because the direct oxidation of the phosphorus reactant takes place via the P-OH tautomer (**2**, Scheme 2), it means that competing background oxidation to acid **3** will be more severe for the *H*-phosphinate than the *H*-phosphonate. But as the mechanism shows, one must walk a tightrope between oxidizing radical **4** efficiently but not oxidizing **2**! To some extent, Ishii accomplished this by employing a 50:50 O_2/N_2 mixture: with air (21:78 O_2/N_2) the reaction did not proceed efficiently (unreacted starting material) and with pure oxygen overoxidation of $(EtO)_2P(O)H$ took place.[10]

Arylation using excess oxidant. Since further studies failed to provide the desired catalytic process, we next turned our attention to conditions that employ a stoichiometric (or excess) oxidant. Whereas Ishii's was the only report of a catalytic free-radical arylation,[10] the literature describing the free-radical arylation of *H*-phosphonate diesters with a stoichiometric excess of oxidants is much more common and it dates back to Effenberger in 1985.[5a] Various oxidants were tested using butyl phenyl-*H*-phosphinate and mesitylene as the model reactants. The results are shown in Table 2. In the literature, mesityl phosphorus compounds have been synthesized through a variety of methods.[5,11,12]

Table 2. Arylation of butyl phenyl-*H*-phosphinate with mesitylene



(1 equiv) (n equiv)

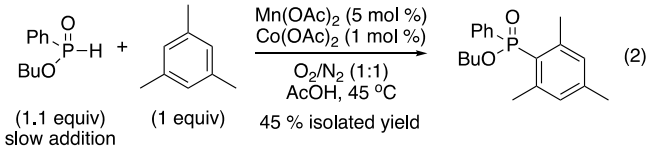
Entry	Solvent	MesH (equiv)	Conditions	Yield[a] (%)
1a	CH_3CN/H_2O	5	$AgNO_3$ (10 mol %)	9[b-e]
1b	2:7	5	$K_2S_2O_8$ (2 equiv)	4[b,c,f]
2	AcOH	5	$Mn(OAc)_3 \cdot 2H_2O$ (3 equiv)	39
3	AcOH	5	air	35[c,g]
4	CH_3CN/H_2O 3:1	5	$AgNO_3$ (10 mol %) MnO_2 (3 equiv)	6
5	AcOH	5	$AgNO_3$ (10 mol %)	78
6a		**5**	**$Mn(OAc)_2$**	**81**
6b		2	**(5 mol %)**	72
6c	**AcOH**	1	**MnO_2 (3 equiv)**	70
6d		5		71[e]
7	AcOH	5	$Mn(OAc)_2$ (5 mol %) MnO_2 (not activated, 3 equiv)	29[c]
8a	AcOH	5	$Mn(OAc)_2$ (5 mol %) Fe_2O_3 (3 equiv)	2[c]
8b			Fe_3O_4 (3 equiv)	0[h]
9	CH_3CN	5	$Mn(OAc)_2$ (5 mol %) MnO_2 (3 equiv)	3[c]

[a] The *H*-phosphinate was slowly added to the reaction mixture under N_2. Yield after purification by chromatography on silica gel, unless otherwise noted. [b] reaction conducted at rt for 48 h. [c] determined by ^{31}P-NMR. [d] 80 % remaining starting material. [e] AcONa was not used. [f] 71 % remaining starting material. [g] 50 % remaining starting material. [h] Unreacted starting material.

Effenberger's conditions[5a] were completely unsatisfactory (Table 2, entry 1). On the other hand using manganese(III) acetate dihydrate, which has been used extensively with *H*-phosphonate diesters, was a significant improvement but still unsatisfactory (entry 2). Replacing $Mn(OAc)_3$ with $Mn(acac)_2$ in air gave a similarly mediocre result (entry 3). When the superstoichiometric oxidant in Effenberger's reaction was replaced with MnO_2, the same result as in entry 1 was observed (entry 4). On the other hand, switching the solvent to acetic acid gave a tremendous improvement to 78 % yield (entry 5). Substituting expensive silver nitrate for manganese(II) acetate gave a similar result (81 %, entry 6a). From these conditions, decreasing the number of equivalents of mesitylene lowered the yield to 72 % and 70 % (entries 6b and 6c, respectively). Omitting the base (AcONa, 3 equiv) gave a 10 % reduction in yield (entry 6d).

If the manganese(IV) oxide was not the "activated" grade, then the yield dropped significantly (entry 7 versus entry 6a). Replacing MnO_2 with iron oxides was unsuccessful (entries 8a-b). Switching the solvent to acetonitrile also failed to deliver the product in acceptable yield (entry 9). Other solvent tried in the place of acetic acid (data not shown in Table 2) were: DME (0), MIBK (0), 1-butanol (0), 1,4-dioxane (0), NMP (0), DMSO (0), TFA (0), and perfluorodecalin (7).

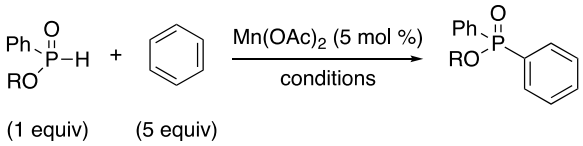
As mentioned above, catalytic conditions were unsuccessful. The best conditions identified were PhP(O)(OBu)H (1.1 equiv) slowly added into an acetic acid solution containing mesitylene (1 equiv), $Mn(OAc)_2$ (5 mol %) and $Co(OAc)_2$ (1 mol %), at 45 °C and under air/N_2 (1:1), which produced a 45 % yield of product (Equation 2).



Additional experiments (Table 3) were conducted, this time using PhP(O)(OR)H with 5 equivalents of benzene, with 5 mol% $Mn(OAc)_2$, 2 equivalents of MnO_2, 16 h, 70 °C, under N_2 gave only 25 % yield under neat conditions (Table 3, entry 1). DMF (entry 2) and other solvents like CH_3CN or DMSO (not shown) were completely unsatisfactory. On the other hand, acetic acid improved to 34 % (entry 3a) but increasing the temperature did not improve the yield (entry 3b). Running the reaction under air gave results worse than under N_2 (entry 4 versus 2). Next, the amount of MnO_2 was increased to 3 equivalents, which produced a significant improvement to 47 % (entry 5a versus 3a). Adding AcONa resulted in a modest improvement (entry 5b). On the other hand, the reaction time was important and adding PhP(O)(OR)H slowly over 2 h in order to minimize background oxidation to acid **3**, followed by an additional 2 h, gave the best result (entry 6a), while adding the reactant more slowly was undistinguishable from the standard 16 h (entry 6b versus 5b). Removing AcONa lowered the yield significantly (entry 7), as did removing the 5 mol% of $Mn(OAc)_2$ (entry 8). Using excess $Mn(OAc)_2$ without MnO_2 similarly decreased the yield (entry 9). Entry 10 shows the influence of the alkyl ester on the yield, with *n*-butyl (entry 6a) still being the best. Concentration plays a role with the standard 0.2 M being the best (entry 6a versus 11). Finally, other oxidants were examined

(entries 12-14), but none gave better results than catalytic Mn(II) with superstoichiometric Mn(IV), which was thus selected for further investigations.

Table 3. Arylation of alkyl phenyl-*H*-phosphinate with benzene



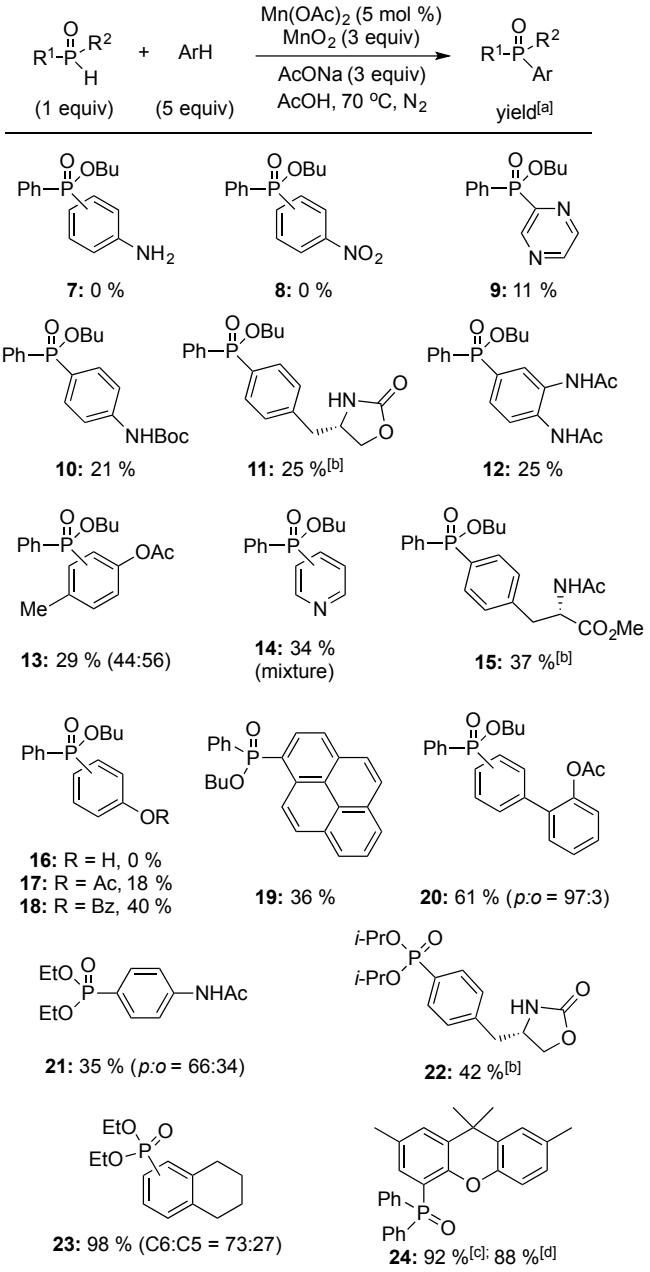
(1 equiv) (5 equiv)

Entry	Solvent	Conditions[a]		Yield[b] (%)
1	none	MnO_2 (2 equiv); no base		25[c,d]
2a	DMF	MnO_2 (2 equiv); no base		0[c,e]
2b		MnO_2 (2 equiv); no base, 120 °C		14[c,f]
3a	AcOH	MnO_2 (2 equiv); no base		34
3b		MnO_2 (2 equiv); no base, 120 °C		27
4	AcOH	MnO_2 (2 equiv); no base, air		13
5a	AcOH	MnO_2 (3 equiv); no base		47
5b		MnO_2 (3 equiv); AcONa (3 equiv)		52
6a	**AcOH**	**MnO_2 (3 equiv); AcONa (3 equiv) 2 h slow addition + 2 h**		**64**
6b		10 h slow addition + 2 h		49
7	AcOH	MnO_2 (3 equiv); no base 2 h slow addition + 2 h		50
8	AcOH	MnO_2 (3 equiv); AcONa (3 equiv) no $Mn(OAc)_2$, 2 h slow addition + 2 h		40
9	AcOH	$Mn(OAc)_2$ (3 equiv); AcONa (3 equiv) no MnO_2, 2 h slow addition + 2 h		36
10a	AcOH	MnO_2 (3 equiv) AcONa (3 equiv) 2 h slow addition + 2 h	R = Et	49
10b			R = *i*-Bu	56
10c			R = Cy	60
11a	AcOH	MnO_2 (3 equiv) AcONa (3 equiv) 2 h slow addition + 2 h	0.4 M	50
11b			0.1 M	44

12a		$KMnO_4$ (n equiv)	n = 2	30
12b	AcOH	AcONa (3 equiv)	n = 1	32
12c		2 h slow addition + 2 h	n = 0.5	29
13a	AcOH	MnO_2 (3 equiv); AcONa (3 equiv)		52[g]
13b		2 h slow addition + 2 h		53[h]
14	AcOH	$BaMnO_4$ (1.5 equiv); AcONa (3 equiv) 2 h slow addition + 2 h		22

[a] Unless otherwise noted, the reactions were conducted with R = Bu, at 70 °C under N_2, for 16 h at 0.2 M concentration. [b] Yield after purification by chromatography on silica gel, unless otherwise noted. [c] ^{31}P-NMR yield. [d] 69 % remaining starting material. [e] unreacted starting material. [f] 86 % remaining starting material. [g] $MnCO_3$ (5 mol %) instead of $Mn(OAc)_2$. [h] $Mn(OAc)_2 \cdot 4H_2O$ (5 mol %) instead of $Mn(OAc)_2$.

Intermolecular arylations. Our communication[12] showed that the reaction has a relatively broad scope in terms of both the phosphinylidene reagent and the aromatic substrate. Here we are presenting additional results to more fully delineate the scope and limitations of our reaction.



Scheme 3. Intermolecular arylation with $R^1R^2P(O)H$. [a] Yield after purification by chromatography on silica gel. [b] Only 1 equivalent of ArH. [c] 10 equiv $Ph_2P(O)H$, 1 equiv ArH. [d] 3 equiv $Ph_2P(O)H$, 1 equiv ArH.

Scheme 3 shows some results not previously reported with various aromatics and heteroaromatics. The reaction does not work on aniline, nitrobenzene, or phenol (**7**, **8**, **16**). It is also sluggish with aniline and phenol derivatives (**10**, **12**, **13**, **17**), although phenyl benzoate gave a moderate 40 % yield of **18**. Chiral aminoacid derivatives were also tried but the yields of **11,** and **15** were rather low, in part due to the fact that only 1 equivalent of the aromatic compound was used. Phosphotyrosine analog **22** could still be prepared easily in acceptable yield.

An attempt at making a precursor of the xantphos ligand[14] was unsuccessful as only one $Ph_2P(O)$ group could be introduced (compound **24**), even when a very large excess of secondary phosphine oxide was employed. Other aromatics that were tried unsuccessfully (not shown) were benzyl alcohol, phenethyl alcohol, phenethyl acetate, 1-phenylethyl acetate, anisole, phenyl acetate, and phenyl benzoate.

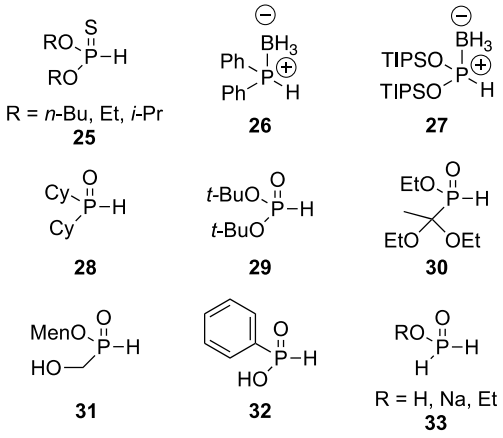
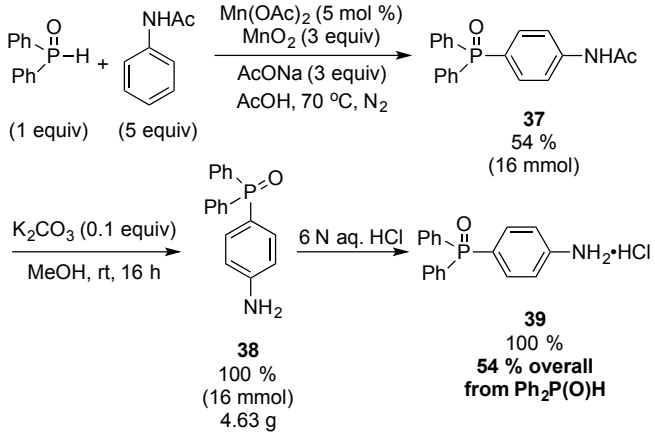


Figure 1. Phosphorus reagents that are unsuccessful (no desired product) in the arylation reaction.

Figure 1 shows phosphorus reagents that were tried unsuccessfully (defined as no product could be obtained from the reaction). In the case of *H*-thiophosphonates **25** the oxidation P=S to P=O was observed. With phosphine-boranes **26** and **27** the free-radical apparently does not form under the manganese conditions, although free-radicals can certainly be obtained using different initiators.[15] Dicyclohexylphosphine oxide **28** also failed presumably because it does not tautomerize easily to **2** (Scheme 2). Di-*tert*-butyl *H*-phosphonate **29** and the Ciba-Geigy *H*-phosphinate **30** did not work because they are cleaved under the acidic conditions. Compound **31** decomposes, but if the hydroxyl is acetylated, then the arylation takes place uneventfully as reported previously.[13] Phenyl-*H*-phosphinic acid **32** and phosphinates **33** do not work because they are rapidly oxidized to acid **3** (Scheme 2).

Synthetic application. (4-Aminophenyl)diphenylphosphine oxide **38** has been synthesized for its second order non-linear optical properties, or as a component of materials with interesting properties.[16] Various literature syntheses of (4-aminophenyl)diphenylphosphine oxide **38**, and the reactions employed are representative of Scheme 1 and feature both cross-couplings and aryl metal phosphorylations.[16]

Our straightforward multigram scale preparation of (4-aminophenyl)diphenylphosphine oxide **38** is shown in Scheme 4. Arylation of diphenylphosphine oxide with acetanilide proceeded regiospecifically in reasonable yield. Deprotection gave the insoluble aniline (which was converted to the hydrochloride salt for full characterization).

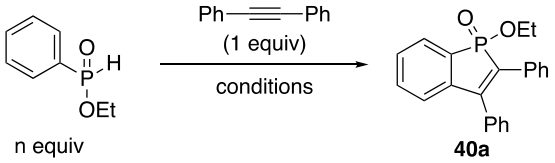


Scheme 4. Multigram-scale preparation of (4-aminophenyl)diphenylphosphine oxide.

Of the literature methods,[16] only the one using the nickel-catalyzed cross-coupling is competitive with ours in terms of cost and simplicity, although the reported scale is small (twenty times smaller than ours) and no scale-up was demonstrated.[16e,f]

Phosphinate-Alkyne Cycloadditions. The reaction of *H*-phosphinates with alkynes under free-radical conditions gives a high energy alkenyl radical intermediate, which can then be cyclized onto an aromatic ring, followed by oxidation and re-aromatization.

Table 4. Literature *H*-Phosphinate-Alkyne Cycloaddition



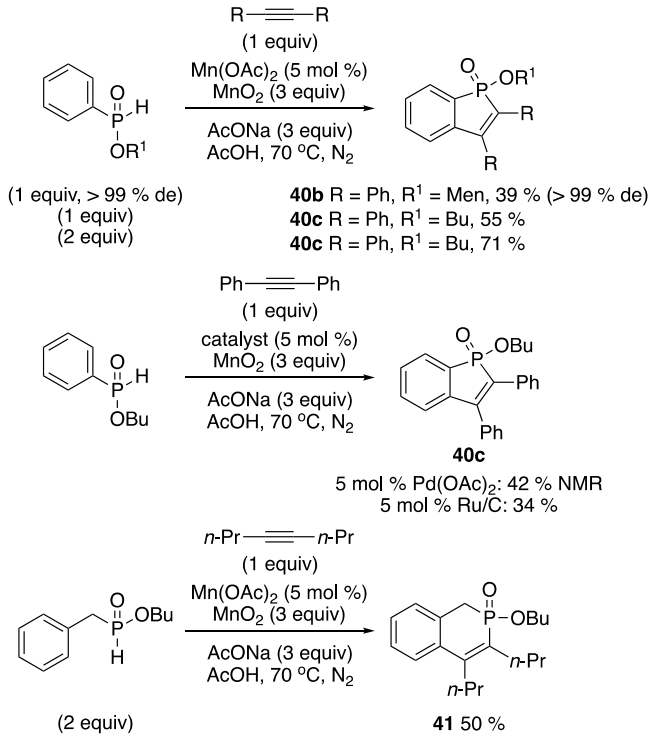
Entry	n	Conditions	Yield[a] (%)
1	2	AgOAc (4 equiv); DMF, 100 °C, N_2, 4 h	53[17a]
2	2	Ag_2O (2 equiv); DMF, 100 °C, N_2, 8 h	60[17b]
3	0.5	AgOAc (2 equiv); DMSO, 120 °C, N_2, 12 h	60[17c]
4	2	*N*-ethoxy-2-methylpyridinium tetrafluoroborate (2 equiv)	43[17d]

$NaHCO_3$ (1.2 equiv); eosin Y (4 mol %), green

LED (525 nm), DMF, 35 °C, N_2, 48 h

[a] Yield after purification by chromatography on silica gel.

Table 4 summarizes the results from other groups with ethyl phenyl-*H*-phosphinate.[17] Miura and coworkers reported the preparation of **40a** using 4 equivalents of AgOAc (Table 4, entry 1).[17a] Chen and Duan also used 4 equivalents of silver(I) (Ag_2O 2 equivalents) in closely related conditions (entry 2).[17b] Ma and Ackerman also reported the silver-promoted synthesis of **40a** but this time using a two-fold excess of diphenylacetylene and silver (Table 4, entry 3).[17c] Finally, Lakhdar and coworkers recently reported a photoredox process (entry 4).[17d]



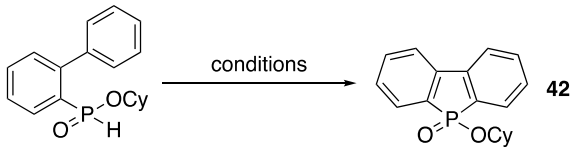
Scheme 5. Phosphinate-Alkyne Cycloaddition.

Scheme 5 summarizes the reactions using our manganese system.[18] From *H*-phosphinate ester starting materials, both 5- and 6-membered rings (Scheme 5, **40b-c** and **41**, respectively) could be obtained in acceptable to good yield. Increasing the amount of *H*-phosphinate resulted in a higher yield of **40c**. Again, Mn(II) was found to be the best catalyst for these reactions. Interestingly, Chen and Duan reported making menthyl ester **40b** under the same conditions as in Table 5, entry 2, in 40 % yield but with very significant racemization, from 99 % de to 50 % de.[17b] In contrast, our method (Scheme 5) uses equimolar amounts of phosphinate and alkyne and is completely stereospecific.[13b] Overall, the various literature methods deliver the

benzo[*b*]phosphole oxide from the *H*-phosphinate in 43-60 % yield, whereas our all-manganese system is rather competitive with 55-71 % yield.

Intramolecular Arylations. The intramolecular reaction of aromatic *H*-phosphinate esters was investigated next. Table 5 shows the results for the preparation of 5-cyclohexyl-5H-benzo[*b*]phosphindole-5-oxide. Catalytic conditions were unsuccessful (Table 5, entries 1 and 2). Palladium acetate was more successful but the reaction did not go to completion (entry 3), however, adding MnO_2 resulted in an excellent yield of cyclized product (entry 4). Nonetheless, our much cheaper all manganese system gave the best result (entry 5).

Table 5. Cyclization of cyclohexyl (2-phenyl)phenyl-*H*-phosphinate



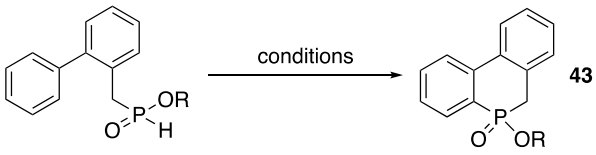
42

Entry	Conditions	Yield[a] (%)
1	$Mn(OAc)_2$ (5 mol %) Cyclohexane, 70 °C, air, 24 h	0
2	$Mn(OAc)_2$ (5 mol %); $Co(OAc)_2 \cdot 4H_2O$ (1 mol %) AcOH, 100 °C, air, 70 h	10[b]
3	$Pd(OAc)_2$ (5 mol %) THF reflux, air, 20 h	48[c]
4	$Pd(OAc)_2$ (5 mol %); MnO_2 (2 equiv) THF, 70 °C, N_2, 12 h	90
5	**$Mn(OAc)_2$ (5 mol %); MnO_2 (3 equiv) AcONa (3 equiv) AcOH, 70 °C, N_2, 2 h slow addition + 2 h**	**98**

[a] Yield after purification by chromatography on silica gel, unless otherwise noted. [b] ^{31}P-NMR yield. [c] 88 % based on recovered starting material, ref. 16e.

The homologous reaction was investigated (Table 6). In this case the Mn(II)/Mn(IV) system was not tried, but standard Mn(III) worked very well (Table 6, entry 3), whereas all catalytic reactions failed (entries 1 and 2).

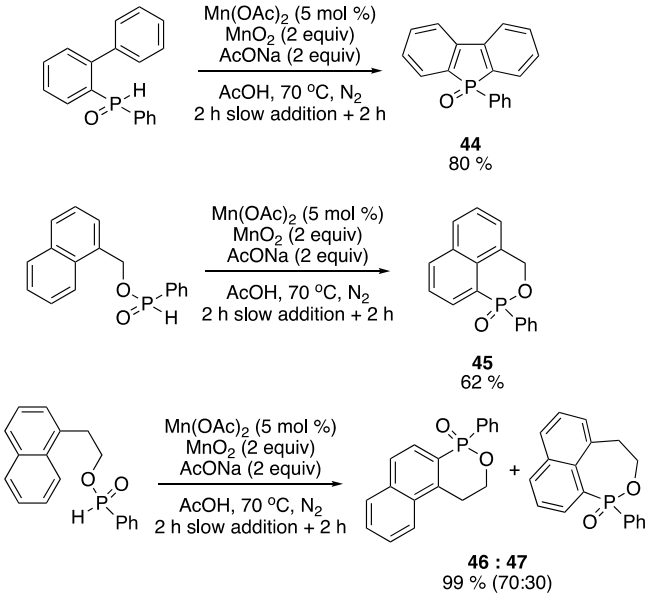
Table 6. Cyclization of alkyl (2-phenyl)benzyl-*H*-phosphinate



Entry	R	Conditions	Yield[a] (%)
1	Bu	$Mn(OAc)_2$ 5 mol %; $Co(OAc)_2•4H_2O$ 1 mol % AcOH, 100 °C, air, 70 h	20[b]
2	Bu	$Pd(OAc)_2$ 5 mol % THF reflux, air, 20 h	0
3	**Cy**	**$Mn(OAc)_3•2H_2O$ 2 equiv; AcONa 2 equiv** **AcOH, 70 °C, N_2, 24 h**	**97**

[a] Yield after purification by chromatography on silica gel, unless otherwise noted. [b] ^{31}P-NMR yield.

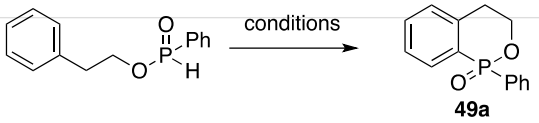
The transformations shown in Scheme 6 are related to the reactions described in Tables 5 and 6. Once again, our Mn(II)/Mn(IV) system gave good results with phosphine oxide **44** and phosphinates **45**-**47**. The last example resulted in the formation of a mixture of isomers favoring the 6-membered ring **46**.



Scheme 6. More cyclizations using the Mn(II)/Mn(IV) system.

More conditions were examined on compound 2-phenethyl phenyl-*H*-phosphinate **48a** and the results are summarized in Table 7.

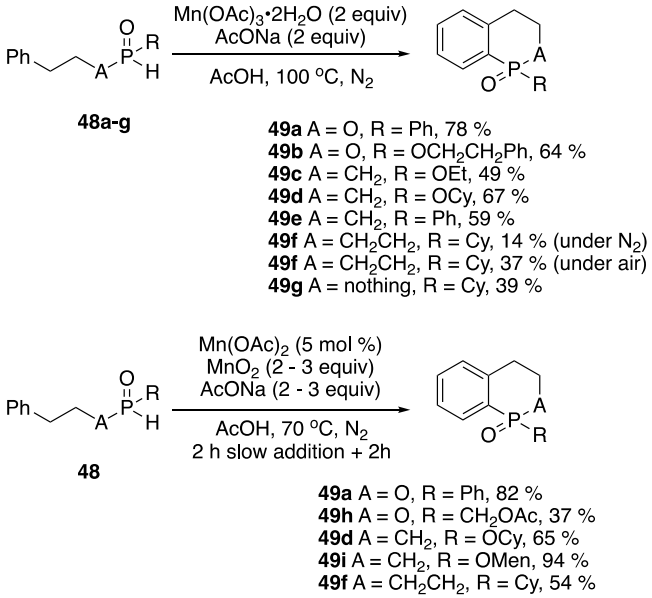
Table 7. Cyclization of 2-phenethyl phenyl-*H*-phosphinate



49a

Entry	Conditions	Yield[a] (%)
1	$Mn(OAc)_2$ (5 mol %); $Cu(OAc)_2$ (2 equiv) AcOH, 70 °C, N_2, 24 h	0
2	$Mn(OAc)_3•2H_2O$ (2 equiv); AcONa (2 equiv) DMSO, 100 °C, N_2, 24 h	42
3a	**$Mn(OAc)_3•2H_2O$ (2 equiv); AcONa (2 equiv)**	**78**
3b	**AcOH, 70 °C, N_2, 24 h**	84[b]
4	$Mn(OAc)_2$ (2 equiv); AcONa (2 equiv) AcOH, 70 °C, air, 24 h	43
5	**$Mn(OAc)_2$ (5 mol %); MnO_2 (2 equiv) AcONa (2 equiv) AcOH, 70 °C, N_2, 2 h slow addition + 2 h**	**82**

[a] Yield after purification by chromatography on silica gel. [b] After regenerating Mn(III) from entry 3a with $KMnO_4$.



Scheme 7. Comparison of the Mn(III) system with our Mn(II)/Mn(IV) system.

Scheme 7 show various examples of phosphonate, secondary phosphine oxides, and phosphinates under two different set of conditions: the Mn(III) and the Mn(II)/Mn(IV) systems. When the same products are synthesized from the two methods, the results can be virtually undistinguishable (Scheme 7, compounds **49a** and **49d**), although 7-membered ring **49f** was formed in significantly better yield using our Mn(II)/Mn(IV) method.

Scheme 8. Cyclization of *para*-substituted *H*-phosphinates.

Scheme 8 shows the results obtained with electron-rich *para*-substituted phenethyl esters. In general, good yields are obtained although the acetamide derivative gave a somewhat lower yield. When the catalytic conditions (5 mol % manganese(II) 2-ethylhexanoate, 5 mol % cobalt(II) 2-ethylhexanoate, EtOAc, O_2, 90 °C; see also Table 1) were tried on **48a** and **48k**, the yields were 37 % and 0 %, respectively.

Conclusions

The direct arylation of various phosphinylidene compounds (and particularly previously under-investigated *H*-phosphinates) via homolytic aromatic substitution was studied. Unfortunately, a practical catalytic version using oxygen as the terminal oxidant was not found. A main requirement imposed from the start was to use the phosphorus species as the limiting reagent instead of using a large excess. This is because the phosphorus component is generally the most valuable, unless simple *H*-phosphonate diesters are used. At the outset, the reaction of *H*-phosphinate was our main objective, especially because it had not been established in the literature.

The desired intra- and inter-molecular transformations could be accomplished using the inexpensive catalytic Mn(II)/superstoichiometric Mn(IV) system. This system is similar or superior to the much more expensive Mn(III) system that has been extensively used in the literature with *H*-phosphonate diesters. The scope and limitations of the arylation was discussed. The reaction appears rather general when the aromatic ring is not electron-deficient, and even hindered mesitylphosphorus compounds could be made more efficiently than via complicated or expensive cross-coupling reactions. On the other hand, certain phosphinylidene compounds failed to undergo arylation and the reason may be specific to each, for example: instability in acidic conditions, rapid oxidation of P-H to P-OH, etc. Overall, the Mn(II)/Mn(IV) system we developed is inexpensive and easily scaled, and therefore it should be useful for the synthesis of various arylphosphorus compounds.

Experimental Section

General Chemistry:

^{1}H NMR spectra were recorded on a 300-MHz Varian INOVA spectrometer or 400-MHz Bruker Avance spectrometer. Chemical shifts for ^{1}H NMR spectra (in parts per million) relative to internal tetramethylsilane (Me_4Si, δ = 0.00 ppm) with deuterated chloroform. $^{13}C\{^{1}H\}$ NMR spectra were recorded at 75.5 or 101 MHz. Chemical shifts for $^{13}C\{^{1}H\}$ NMR spectra are reported (in parts per million) relative to $CDCl_3$ (δ = 77.0 ppm). ^{31}P NMR spectra were recorded at 121.5 or 162 MHz, and chemical shifts reported (in parts per million) relative to external 85% phosphoric acid (δ = 0.0 ppm). Flash chromatography experiments were carried out on Silica Gel premium Rf grade (40−75 μm). Ethyl acetate/hexane mixtures or dichloromethane/acetone were used as the eluent for chromatographic purifications. TLC plates were visualized by UV or immersion in permanganate potassium (3 g $KMnO_4$, 20 g K_2CO_3, 5 mL 5% aq. NaOH and 300 mL of water) followed by heating. High resolution mass spectra (HRMS) were obtained either by direct probe (EI/CI) and analyzed by magnetic sector, or by electrospray using a TOF analyzer.

Reagent and solvents:

All starting materials were purchased from commercial sources and used as received. The solvents were distilled under N_2 and dried according to standard procedures (THF from Na/ benzophenone ketyl; DMF from $MgSO_4$; CH_3CN, toluene and dichloromethane from CaH_2).

Diethyl mesitylphosphonate (Table 1, Entry 7a):[12]

To a solution of Mn(2-ethylhexanoate)$_2$ (42.7 mg, 0.05 mmol, 5 mol%, 40% in mineral oil), Co(2-ethylhexanoate)$_2$ (26.6 mg, 0.05 mmol, 5 mol%, 65% in mineral oil) and mesitylene (0.14 mL, 1 mmol, 1 equiv) in ethyl acetate (2 mL) was added diethylphosphite (414 mg, 3 mmol, 3 equiv) and the reaction mixture was stirred for 16 hours at 90 ^{0}C under a flow of O_2. Ethyl acetate (30 mL) and a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL) were added and stirred vigorously for 10 minutes. The two layers were separated and the organic layer was washed with a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 97:3 to 96:4) to afford the product as a yellow oil (199 mg, 78%).

Butyl mesityl phenylphosphinate (Table 2, Entry 6a):[12]

To a suspension of Mn(OAc)$_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv), sodium acetate (246 mg, 3 mmol, 3 equiv) and mesitylene (0.70 mL, 5 mmol, 5 equiv) in acetic acid (2.5 mL) at 70 ^{0}C under N_2 was added a solution of butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 hours *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 ^{0}C under N_2. Ethyl acetate (30 mL) and a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL) were added. The suspension was stirred vigorously for 5 minutes, filtered through celite and the two layers were separated. The organic layer was washed with a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a colorless oil (257 mg, 81%).

Butyl mesityl phenylphosphinate (Equation 2):[12]

To a solution of butyl phenyl-*H*-phosphinate[19] (220 mg, 1.1 mmol, 1.1 equiv) in acetic acid (1 mL) was added Mn(OAc)$_2$ (8.7 mg, 0.05 mmol, 5 mol%), Co(OAc)$_2$.4H_2O (2.5 mg, 0.01 mmol, 1 mol%) and mesitylene (0.14 mL, 1 mmol, 1 equiv) and the reaction mixture was stirred for 16 hours at 45 ^{0}C under a mixture of O_2 and N_2 1:1. Ethyl acetate (30 mL) and a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL) were added and stirred vigorously for 10 minutes. The two layers were separated and the organic layer was washed with a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford the product as a colorless oil (142 mg, 45%).

Butyl diphenylphosphinate (Table 3, Entry 6a):[11e]

To a suspension of Mn(OAc)$_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv), sodium acetate (246 mg, 3 mmol, 3 equiv) and benzene (0.45 mL, 5 mmol, 5 equiv) in acetic acid (2.5 mL) at 70 ^{0}C under N_2 was added a solution of butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 hours *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 ^{0}C under N_2. Ethyl acetate (30 mL) and a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL) were added. The suspension was stirred vigorously for 5 minutes, filtered through celite and the two layers were separated. The organic layer was washed with a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a white solid (175 mg, 64%).

General procedure for the arylation of *H*-phosphinates and related compounds:

To a suspension of $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv), sodium acetate (246 mg, 3 mmol, 3 equiv) and the appropriate aryl (5 mmol, 5 equiv) in acetic acid (2.5 mL) at 70 ^{0}C via an oil bath and under N_2 was added a solution of the appropriate *H*-phosphinate (1 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 hours *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 ^{0}C using an oil bath and under N_2. Ethyl acetate (30 mL) and a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL) were added. The suspension was stirred vigorously for 5 minutes, filtered through celite and the two layers were separated. The organic layer was washed with a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford the pure product without further purification or after a column chromatography.

Ethyl diphenylphosphinate (Table 3, Entry 10a):[12]

General procedure was used with benzene (0.45 mL, 5 mmol, 5 equiv) and ethyl phenyl-*H*-phosphinate[20] (170 mg, 1 mmol, 1 equiv) to afford the product as a colorless oil (121 mg, 49%).

Isobutyl diphenylphosphinate (Table 3, Entry 10b):[12]

General procedure was used with benzene (0.45 mL, 5 mmol, 5 equiv) and isobutyl phenyl-*H*-phosphinate[12] (198 mg, 1 mmol, 1 equiv) to afford the product as a white solid (153 mg, 56%).

Cyclohexyl diphenylphosphinate (Table 3, Entry 10c):[11e]

General procedure was used with benzene (0.45 mL, 5 mmol, 5 equiv) and cyclohexyl phenyl-*H*-phosphinate[12] (224 mg, 1 mmol, 1 equiv) to afford the product as a white solid (181 mg, 60%).

Butyl 2-pyrazyl phenylphosphinate 9:

General procedure was used with pyrazine (0.39 mL, 5 mmol, 5 equiv) and butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 95:5 to 80:20) to afford the product as an orange oil (30 mg, 11%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.1 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.24 (s, 1H), 8.72 (s, 1H), 8.64-8.69 (m, 1H), 7.92-8.02 (m, 2H), 7.54-7.63 (m, 1H), 7.45-7.54 (m, 2H), 4.05-4.17 (m, 2H), 1.73 (quint., J = 7.1 Hz, 2H), 1.43 (sextuplet, J = 7.5 Hz, 2H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 150.6 (d, J_{PC} = 164 Hz), 148.1 (d, J_{PCNC} = 23.0 Hz), 146.6 (d, J_{PCNCC} = 3.0 Hz), 145.3 (d, J_{PCC} = 16.1 Hz), 133.0 (d, J_{PCCCC} = 2.7 Hz), 132.3 (d, J_{PCCC} = 10.1 Hz, 2C), 129.1 (d, J_{PC} = 141 Hz), 128.7 (d, J_{PCC} = 13.4 Hz, 2C), 65.7 (d, J_{POC} = 6.3 Hz), 32.5 (d, J_{POCC} = 6.4 Hz), 18.8, 13.6; HRMS (EI+) m/z calcd for $C_{14}H_{17}N_2O_2P$ ([M+H]$^+$) 277.1100, found 277.1102.

Butyl p-(tert-butyl-N-phenylcarbamate) phenylphosphinate 10:

General procedure was used with *tert*-butylphenyl carbamate (966 mg, 5 mmol, 5 equiv) and butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford the product as a colorless oil (83 mg, 21%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 35.2 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.14 (s, 1H), 8.31-8.38 (m, 1H), 7.75-

7.84 (m, 2H), 7.39-7.56 (m, 5H), 6.96-7.03 (m, 1H), 4.09 (dm, J = 56.9 Hz, 2H), 1.74 (quint., J = 7.0 Hz, 2H), 1.52 (s, 9H), 1.46 (sextuplet, J = 7.4 Hz, 2H), 0.94 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 153.1, 144.1 (d, J_{PCCC} = 5.8 Hz), 133.6 (d, J_{PCCCC} = 2.0 Hz), 132.4 (d, J_{PCC} = 12.1 Hz), 132.4, 131.7 (d, J_{PC} = 138 Hz), 131.2 (d, J_{PCCC} = 10.3 Hz, 2C), 128.6 (d, J_{PCC} = 13.6 Hz, 2C), 121.7 (d, J_{PCC} = 12.5 Hz), 119.6 (d, J_{PCCC} = 9.1 Hz), 115.6 (d, J_{PC} = 129 Hz), 80.3, 65.2 (d, J_{POC} = 6.0 Hz), 32.5 (d, J_{POCC} = 6.6 Hz), 28.3 (3C), 18.9, 13.6; HRMS (EI+) m/z calcd for $C_{21}H_{28}NO_4P$ ($[M]^+$) 389.1756, found 389.1757.

Butyl [p-((S)-4-benzyl-2-oxazolidinone)] phenylphosphinate 11:

General procedure was used with (S)-4-benzyl-2-oxazolidinone (177 mg, 1 mmol, 1 equiv) and butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 90:10 to 50:50) to afford the product as a colorless oil (93 mg, 25%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 30.9 (s); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.59-7.83 (m, 4H), 7.21-7.53 (m, 5H), 6.64 (s, 1H), 4.29-4.39 (m, 1H), 3.92-4.12 (m, 4H), 2.78-2.98 (m, 2H), 1.68 (quint., J = 6.5 Hz, 2H), 1.39 (sextuplet, J = 7.0 Hz, 2H), 0.89 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 159.5, 140.5 (d, J_{PCCCC} = 2.5 Hz), 133.0 (d, J_{PCCCC} = 2.5 Hz), 132.3 (d, J_{PCCC} = 10.4 Hz), 132.2 (d, J_{PCCC} = 10.4 Hz, 2C), 131.6 (d, J_{PCCC} = 10.1 Hz, 2C), 131.4 (d, J_{PC} = 137 Hz), 130.5 (d, J_{PC} = 139 Hz), 129.4 (d, J_{PCC} = 13.4 Hz, 2C), 128.6 (d, J_{PCC} = 13.1 Hz), 128.6 (d, J_{PCC} = 13.1 Hz), 69.2 (0.5C), 69.2 (0.5C), 64.9 (d, J_{POC} = 6.1 Hz, 0.5C), 64.8 (d, J_{POC} = 6.0 Hz, 0.5C), 53.4, 41.2 (0.5C), 41.0 (0.5C), 32.5 (d, J_{POCC} = 6.6 Hz), 18.8, 13.6; HRMS (EI+) m/z calcd for $C_{20}H_{25}NO_4P$ ($[M+H]^+$) 374.1516, found 374.1520.

Butyl (p-tolylacetate) phenylphosphinate (mixture of ortho and meta isomers) 13:

General procedure was used with *p*-tolylacetate (751 mg, 5 mmol, 5 equiv) and butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford the product as a colorless oil (100 mg, 29%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 30.0 (s, 46%, methyl in meta position) and 27.5 (s, 54%, methyl in ortho position); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84-7.90 (m, 0.5H), 7.71-7.81 (m, 2H), 7.62-7.68 (m, 0.5H), 7.39-7.55 (m, 3H), 7.32-7.38 (m, 0.5H), 7.12-7.22 (m, 1H), 6.94-7.01 (m, 0.5H), 3.89-4.12 (m, 2H), 2.39 (s, 1.5H), 2.36 (s, 1.5H), 2.28 (s, 1.5H), 2.07 (s, 1.5H), 1.71 (quint., J = 6.8 Hz, 2H), 1.42 (sextuplet, J = 7.4 Hz, 2H), 0.91 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 169.3 (0.5C), 169.0 (0.5C), 153.1, 149.9 (d, J_{PCCC} = 3.4 Hz, 0.5C), 148.3 (d, J_{PCC} = 16.5 Hz, 0.5C), 139.3 (d, J_{PCCC} = 10.9 Hz, 0.5C), 135.8 (d, J_{PCC} = 11.4 Hz, 0.5C), 134.6 (d, J_{PCCC} = 6.0 Hz, 0.5C), 134.4 (d, J_{PCCCC} = 2.1 Hz, 0.5C), 132.5 (d, J_{PCC} = 14.3 Hz, 0.5C), 132.4 (d, J_{PC} = 98.8 Hz, 0.5C), 132.1 (d, J_{PCCC} = 5.3 Hz, 0.5C), 132.1 (d, J_{PCCC} = 5.4 Hz, 0.5C), 131.6 (d, J_{PCCC} = 10.5 Hz), 131.6 (d, J_{PC} = 136 Hz, 0.5C), 131.1 (d, J_{PCCC} = 10.7 Hz), 130.9 (d, J_{PC} = 113 Hz, 0.5C), 128.5 (d, J_{PCC} = 13.3 Hz), 128.4 (d, J_{PCC} = 13.8 Hz), 126.1 (d, J_{PCCC} = 9.4 Hz, 0.5C), 125.5 (d, J_{PCCCC} = 2.6 Hz), 123.4 (d, J_{PCCC} = 8.1 Hz, 0.5C), 123.2 (d, J_{PC} = 133 Hz, 0.5C), 64.8 (d, J_{POC} = 5.9 Hz, 0.5C), 64.6 (d, J_{POC} = 5.9 Hz, 0.5C), 32.5 (d, J_{POCC} = 6.6 Hz), 21.0 (0.5H), 20.8 (0.5C), 20.8 (0.5C), 20.5 (d, J_{PCCC} = 3.8 Hz, 0.5C), 18.9 (0.5C), 18.8 (0.5C), 13.6; HRMS (EI+) m/z calcd for $C_{19}H_{24}O_4P$ ($[M+H]^+$) 347.1407, found 347.1402.

Butyl pyridyl phenylphosphinate (mixture of ortho and para derivatives) 14:

General procedure was used with pyridine (0.40 mL, 5 mmol, 5 equiv) and butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv) to afford the product as a colorless oil (93 mg, 34%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 28.0 (s, 38%) and 25.4 (s, 54%); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.67-8.77 (m, 1H), 8.06-8.14 (m, 0.5H), 7.90-7.99 (m, 1H), 7.72-7.83 (m, 1.5H), 7.58-7.66 (m, 1H), 7.39-7.57 (m, 3H), 7.30-7.37 (m, 1H), 3.96-4.09 (m, 2H), 1.63-1.74 (m, 2H), 1.33-1.46 (m, 2H), 0.89 and 0.86 (2t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 154.8 (d, J_{PC} = 168 Hz, 0.6C), 150.5 (d, J_{PCC} = 20.5 Hz, 0.4C), 150.1 (d, J_{PCC} = 10.8 Hz, 0.4C), 150.0 (d, J_{PCCC} = 3.2 Hz, 0.4C), 140.9 (d, J_{PC} = 132 Hz, 0.4C), 136.0 (d, J_{PCC} = 10.1 Hz, 0.6C), 132.8 (d, J_{PCCCC} = 2.6 Hz, 0.4C), 132.3 (d, J_{PCCCC} = 2.6 Hz, 0.6C), 132.3 (d, J_{PCCCC} = 5.0 Hz, 0.6C), 132.2 (d,

J_{PCCC} = 9.8 Hz, 1.2C), 131.7 (d, J_{PCCC} = 10.2 Hz, 0.8C), 130.2 (d, J_{PC} = 139 Hz, 0.4C), 129.9 (d, J_{PC} = 139 Hz, 0.6C), 128.8 (d, J_{PCC} = 13.3 Hz, 0.8C), 128.4 (d, J_{PCC} = 13.2 Hz, 1.2C), 128.2 (d, J_{PCC} = 20.6 Hz, 0.6C), 125.6 (d, J_{PCCCC} = 3.0 Hz, 0.4C), 125.1 (d, J_{PCCC} = 8.2 Hz, 0.6C), 65.3 (d, J_{POC} = 6.2 Hz), 32.5 (d, J_{POCC} = 6.6 Hz, 0.6C), 32.5 (d, J_{POCC} = 6.6 Hz, 0.4C), 18.8 (0.4C), 18.8 (0.6C), 13.6; HRMS (EI+) m/z calcd for $C_{15}H_{18}NO_2P$ ([M+H]$^+$) 276.1148, found 276.1155.

Butyl [4-(D-phenylalanine)] phenylphosphinate 15:

General procedure was used with D-phenylalanine (443 mg, 2 mmol, 1 equiv) and butyl phenyl-*H*-phosphinate[19] (396 mg, 2 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 80:20 to 50:50) to afford the product as a yellow oil (155 mg, 37%, mixture of 2 diastereoisomers 62 : 38). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 31.2 (s, 62%), 31.0 (s, 38%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50-7.77 (m, 4H), 7.22-7.46 (m, 4H), 7.12-7.20 (m, 1H), 6.82-6.99 (m, 1H), 4.69-4.81 (m, 1H), 3.91 (s, 1H), 3.48-3.61 (m, 2H), 2.93-3.14 (m, 2H), 1.85 (s, 3H), 1.60 (quint., *J* = 6.5 Hz, 2H), 1.33 (sextuplet, *J* = 7.0 Hz, 2H), 0.82 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, major diastereiosmer only): δ = 171.9, 170.1, 140.9, 132.2, 131.7 (d, J_{PCCC} = 12.4 Hz, 2C), 131.6 (d, J_{PCCC} = 12.4 Hz, 2C), 131.4 (d, J_{PC} = 112 Hz), 130.0 (d, J_{PC} = 114 Hz), 129.5 (d, J_{PCC} = 13.3 Hz, 2C), 128.6 (d, J_{PCC} = 13.0 Hz, 2C), 64.8 (d, J_{POC} = 6.0 Hz), 53.0, 52.4, 37.6, 32.5 (d, J_{POCC} = 6.4 Hz), 22.9, 18.8, 13.6; HRMS (EI+) m/z calcd for $C_{21}H_{27}NO_5P$ ([M+H]$^+$) 404.1621, found 404.1614.

Butyl 4-(phenylbenzoate) phenylphosphinate 18:

General procedure was used with phenylbenzoate (991 mg, 5 mmol, 5 equiv) and butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 98:2 to 90:10) to afford the product as a colorless oil (158 mg, 40%, mixture of 3 isomers 89 : 7 : 4). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 29.6 (s, 89%, para position); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22-8.30 (m, 2H), 7.93-8.02 (m, 2H), 7.79-7.88 (m, 2H), 7.36-7.56 (m, 5H), 7.22-7.28 (m, 1H), 7.15-7.21 (m, 2H), 4.07 (dt, *J* = 7.1 Hz, 2H), 1.73 (quint., *J* = 7.0 Hz, 2H), 1.44 (sextuplet, *J* = 7.4 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 164.3, 150.7, 137.4 (d, J_{PC} = 134 Hz), 132.7 (d, J_{PCCCC} = 2.6 Hz), 132.5 (d, J_{PCCCC} = 2.6 Hz), 131.8 (d, J_{PCCC} = 10.2 Hz, 2C), 131.7 (d, J_{PCCC} = 10.2 Hz, 2C), 130.8 (d, J_{PC} = 138 Hz), 130.0 (d, J_{PCC} = 13.0 Hz, 2C), 129.6 (2C), 128.7 (d, J_{PCC} = 13.2 Hz, 2C), 126.1, 121.5 (2C), 65.1 (d, J_{POC} = 6.2 Hz), 32.5 (d, J_{POCC} = 6.5 Hz), 18.9, 13.6; HRMS (EI+) m/z calcd for $C_{23}H_{24}O_4P$ ([M+H]$^+$) 395.1407, found 395.1420.

Butyl 1-(pyrenyl) phenylphosphinate 19:

General procedure was used with pyrene (1011 mg, 5 mmol, 5 equiv) and butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 97:3) to afford the product as a colorless oil (175 mg, 44%, mixture of 2 isomers 83 : 17). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 32.6 (s, 83%, C-1 position), 31.8 (s, 17%, C-2 position); ^{1}H NMR (400 MHz, $CDCl_3$, major isomer only): δ = 8.90-8.96 (m, 1H), 8.68-8.76 (m, 1H), 8.05-8.12 (m, 3H), 7.86-8.02 (m, 6H), 7.37-7.48 (m, 3H), 4.11-4.33 (m, 2H), 1.79 (quint., *J* = 7.0 Hz, 2H), 1.48 (sextuplet, *J* = 6.7 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, major isomer only): δ = 138.2 (d, J_{PCCC} = 7.8 Hz), 134.5 (d, J_{PCCCC} = 2.8 Hz), 133.1 (d, J_{PCC} = 11.4 Hz), 133.0 (d, J_{PC} = 137 Hz), 132.0 (d, J_{PCCCC} = 2.5 Hz), 131.6 (d, J_{PC} = 125 Hz), 131.5 (2C), 131.4 (2C), 130.9, 130.2, 129.7, 129.1, 128.6 (d, J_{PCC} = 13.3 Hz, 2C), 127.1, 126.3, 126.3 (d, J_{PCCC} = 9.4 Hz, 2C), 127.3, 125.3 (d, J_{PCCC} = 5.4 Hz), 124.1 (d, J_{PCC} = 13.3 Hz), 64.9 (d, J_{POC} = 5.9 Hz), 32.7 (d, J_{POCC} = 6.7 Hz), 19.0, 13.7; HRMS (EI+) m/z calcd for $C_{26}H_{24}O_2P$ ([M+H]$^+$) 399.1508, found 399.1510.

Butyl [4-(2-acetoxyphenyl)phenyl] phenylphosphinate 20:

General procedure was used with [1,1'-biphenyl]-2-yl acetate (1061 mg, 5 mmol, 5 equiv) and butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv). The crude obtained (mixtures of 4 isomers, 61%) was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford the product as a colorless oil (249 mg, 61%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 31.0 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82-7.95 (m, 4H), 7.46-7.61 (m, 5H), 7.38-7.45 (m, 2H), 7.31-7.37 (m, 1H), 7.13-7.19 (m, 1H), 4.02-4.14 (m, 2H), 2.09 (s, 3H), 1.75 (quint., J = 7.0 Hz, 2H), 1.47 (sextuplet, J = 7.0 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 169.3, 147.7, 141.5 (d, J_{PCCCC} = 2.8 Hz), 133.8, 132.2 (d, J_{PCCCC} = 2.5 Hz), 131.7 (d, J_{PCC} = 12.9 Hz, 2C), 131.6 (d, J_{PCCC} = 13.3 Hz, 2C), 131.5 (d, J_{PC} = 140 Hz), 130.8 (d, J_{PC} = 139 Hz), 130.7, 129.3, 129.0 (d, J_{PCC} = 13.3 Hz, 2C), 128.6 (d, J_{PCCC} = 13.0 Hz, 2C), 126.5, 123.0, 64.8 (d, J_{POC} = 6.0 Hz), 32.6 (d, J_{POCC} = 6.6 Hz), 20.9, 18.9, 13.7; HRMS (EI+) m/z calcd for $C_{24}H_{25}O_4P$ ([M]$^+$) 408.1490, found 408.1502.

Diethyl [4-(acetamido)phenyl]phosphonate 21:[21]

General procedure was used with acetanilide (676 mg, 5 mmol, 5 equiv) and diethyl phosphite (138 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 90:10 to 70:30) to afford the product as a white solid (99 mg, 37%, mixture of 2 isomers 66 : 34). Mp = 142-144 ^{0}C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 19.0 (s, 66%) and 18.3 (s, 34%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.79 (s, 0.34H), 9.70 (s, 0.66H), 7.97-8.06 (m, 0.66H), 7.61-7.79 (m, 2.64H), 7.32-7.47 (m, 0.66H), 3.96-4.13 (m, 4H), 2.17 (s, 1H), 2.16 (s, 2H), 1.27 (t, J = 7.0 Hz, 6H).

diisopropyl [p-((S)-4-benzyl-2-oxazolidinone)]phosphinate 22:

General procedure was used with (S)-4-benzyl-2-oxazolidinone (177 mg, 1 mmol, 1 equiv) and diisopropylphosphite (166 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 85:15 to 50:50) to afford the product as a colorless oil (143 mg, 42%, mixture of 2 isomers). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 16.3 (36%) and 16.2 (64%) (s, 89%, para position), 14.7 and 14.4 (s, 8%, ortho position); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57-7.74 (m, 2H), 7.19-7.38 (m, 2H), 6.81 (s, 1H), 4.56-4.72 (m, 2H), 4.26-4.36 (m, 1H), 3.99-4.11 (m, 2H), 2.89-2.98 (m, 1H), 2.77-2.87 (m, 1H), 1.30 (t, J = 5.7 Hz, 6H), 1.16 (t, J = 6.1 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 159.6, 140.5 (d, J_{PCCCC} = 3.0 Hz, 0.36C), 136.4 (d, J_{PCC} = 15.1 Hz, 0.36C), 133.1 (d, J_{PCCCC} = 3.0 Hz, 0.64C), 132.4 (d, J_{PCCC} = 10.4 Hz, 0.64C), 132.2 (d, J_{PCCC} = 10.2 Hz), 130.4 (d, J_{PC} = 188 Hz, 0.64C), 130.2 (d, J_{PCCC} = 9.3 Hz, 0.36C), 129.2 (d, J_{PCC} = 15.2 Hz), 128.9 (d, J_{PCC} = 15.4 Hz, 0.64C), 128.6 (d, J_{PC} = 191 Hz, 0.36C), 71.0 (dd, J_{POC} = 5.8 and 1.1 Hz, 0.64C), 70.9 (d, J_{POC} = 5.7 Hz, 0.36C), 69.3 (0.36C), 69.1 (0.64C), 53.4 (0.64C), 53.4 (0.36C), 41.2 (0.36C), 40.9 (0.64C), 24.0 (d, J_{POCC} = 4.0 Hz, 2C), 23.8 (d, J_{POCC} = 4.6 Hz, 2C); HRMS (EI+) m/z calcd for $C_{16}H_{25}NO_5P$ ([M+H]$^+$) 342.1465, found 342.1464.

Diethyl tetrahydronaphthalene phosphonate (mixture of isomers C1 and C2 position) 23:[5f]

General procedure was used with tetrahydronaphthalene (0.70 mL, 5 mmol, 5 equiv) and diethyl phosphite (138 mg, 1 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 96:4 to 90:10) to afford the product as an orange oil (262 mg, 98%, mixture of 2 isomers 73 : 27). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 19.9 (s, 73 %, C1-position) and 19.7 (s, 27%, C2-position); ^{1}H NMR (400 MHz, $CDCl_3$, only the major isomer): δ = 7.58-7.67 (m, 1H), 7.07-7.12 (m, 1H), 6.98-7.05 (m, 1H), 3.89-4.08 (m, 4H), 2.61-2.71 (m, 4H), 1.61-1.72 (m, 4H), 1.21 (t, J = 7.1 Hz, 6H).

Diphenyl 4-(2,7,9,9-tetramethyl-9H-xanthenyl) phosphine oxide 24:

General procedure was used with 2,7,9,9-tetramethyl-9*H*-xanthene (120 mg, 0.5 mmol, 1 equiv) and diphenylphosphine oxide (303 mg, 1.5 mmol, 3 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 95:5) to afford the product as a colorless oil (192 mg, 88%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 26.3 (s); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.78-7.86 (m, 4H), 7.68-7.74 (m, 1H), 7.48-7.54 (m, 2H), 7.39-7.46 (m, 5H), 7.12-7.16 (m, 1H), 6.76-6.81 (m, 1H), 5.96-6.01 (m, 1H), 2.38 (s, 3H), 2.29 (s, 3H), 1.59 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 149.6 (d, J_{PCCCC} = 3.1 Hz), 147.6, 133.3 (d, J_{PC} = 108 Hz, 2C), 133.0 (d, J_{PCCC} = 6.0 Hz), 132.8, 132.6 (d, J_{PCC} = 11.7 Hz), 131.8 (d, J_{PCCC} = 10.4 Hz, 4C), 131.6 (d, J_{PCCCC} = 2.0 Hz, 2C), 131.2, 131.0 (d, J_{PCCC} = 6.3 Hz), 129.8, 128.3 (d, J_{PCC}= 12.4 Hz, 4C), 127.8, 125.9, 118.8 (d, J_{PC} = 102 Hz), 115.6, 34.3, 31.6 (2C), 29.3, 21.0; HRMS (EI+) m/z calcd for $C_{29}H_{28}O_2P$ ($[M+H]^+$) 439.1821, found 439.1832.

Diphenyl-4-(aminophenyl) phosphine oxide hydrochloride salt 39:[16e]

General procedure was used with acetanilide (20.3 g, 150 mmol, 5 equiv) and diphenylphosphine oxide (6.1 g, 30 mmol, 1 equiv). The crude obtained was purified by column chromatography (dichloromethane/acetone 80:20 to 40:60) to afford the product as a white solid (5.46 g, 54%).[12] Mp = 150-152 ^{0}C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 29.6 (s); ^1H NMR (400 MHz, $CDCl_3$): δ = 9.16 (s, 1H), 7.62-7.70 (m, 6H), 7.44-7.59 (m, 8H), 2.19 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 169.4, 142.2 (d, J_{PCCCC} = 3.0 Hz), 133.0 (d, J_{PCCC} = 10.7 Hz, 2C), 132.3 (d, J_{PC} = 105 Hz, 2C), 132.1 (d, J_{PCCCC} = 2.5 Hz, 2C), 132.0 (d, J_{PCCC} = 10.1 Hz, 4C), 128.6 (d, J_{PCC} = 12.3 Hz, 4C), 126.3 (d, J_{PC} = 109 Hz), 119.5 (d, J_{PCC} = 12.6 Hz, 2C), 24.5.

To a solution of diphenyl-4-(acetamidophenyl) phosphine oxide (5.3 g, 15.8 mmol, 1 equiv) in methanol (80 mL) was added potassium carbonate (0.22 g, 1.58 mmol, 10 mol %) and the mixture was stirred at rt for 16 hours under N_2. The solvent was removed under vacuum. The residue obtained was solubilized in chloroform and the organic layer was washed with brine. The aqueous layer was then extracted 5 times with chloroform and the combined organic layers was dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a white solid (4.63 g, 100%).[16e] Mp = 204-205 ^{0}C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 32.3 (s).

To a solution of diphenyl-4-(aminophenyl) phosphine oxide (586 mg, 2 mmol, 1 equiv) in methanol (5 mL) was added a solution of HCl 6N (5 mL) and the mixture was stirred at rt for 12 hours under N_2. The solvent was then concentrated under vacuum to afford the product as a yellow solid (656 mg, 100%).[16e] Mp = 148-150 ^{0}C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 29.8 (t, J = 10.8 Hz); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.63-7.71 (m, 4H), 7.50-7.56 (m, 2H), 7.36-7.48 (m, 6H), 6.66-6.72 (m, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 149.9 (d, J_{PCCCC} = 2.5 Hz), 133.8 (d, J_{PCCC} = 11.1 Hz, 2C), 133.3 (d, J_{PC} = 103 Hz, 2C), 132.1 (d, J_{PCCC} = 10.0 Hz, 4C), 131.7 (d, J_{PCCCC} = 2.7 Hz, 2C), 128.4 (d, J_{PCC} = 12.2 Hz, 4C), 119.7 (d, J_{PC} = 114 Hz), 114.3 (d, J_{PCC} = 13.3 Hz, 2C).

(S_p)-1-menthyl-2,3-diphenyl-1-phosphindole 40b:[17b]

To a suspension of $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv), sodium acetate (246 mg, 3 mmol, 3 equiv) and diphenylacetylene (178 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) at 70 ^{0}C under N_2 was added a solution of (R_p)-menthyl phenyl-*H*-phosphinate[13a] (280 mg, 1 mmol, 1 equiv, >99% de) in acetic acid (2.5 mL) over 2 hours *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 ^{0}C under N_2. Ethyl acetate (~ 30 mL) and an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~40 mL) were added. The suspension was stirred vigorously for 5 minutes, filtered through celite and the two layers were separated. The organic layer was washed with an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~40 mL), a saturated aqueous solution of $NaHCO_3$ (~ 40 mL) and brine (~ 40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 98:2) to afford the product as a white solid (175 mg, 39%, > 99% de). Mp = 159-

160 °C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 44.8 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.79 (m, 1H), 7.05-7.56 (m, 13H), 4.29-4.42 (m, 1H), 2.25-2.38 (s, 1H), 1.53-1.76 (m, 3H), 1.38-1.51 (m, 1H), 1.16-1.36 (m, 2H), 0.75-1.10 (m, 2H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.66 (d, *J* = 7.0 Hz, 3H), 0.43 (d, *J* = 6.8 Hz, 3H); $[\alpha]_D^{25}$ = -52.9^0 (chloroform).

1-Butyl-2,3-diphenyl-1-phosphindole 40c:

To a suspension of $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv), sodium acetate (246 mg, 3 mmol, 3 equiv) and diphenylacetylene (178 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) at 70 ^{0}C under N_2 was added a solution of butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 h *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 ^{0}C under N_2. Ethyl acetate (~ 50 mL) and an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~50 mL) were added. The suspension was stirred vigorously for 5 minutes, filtered through celite and the two layers were separated. The organic layer was washed with an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~50 mL), a saturated aqueous solution of $NaHCO_3$ (~ 50 mL) and brine (~ 50 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 97:3) to afford the product as a yellow solid (205 mg, 55%). Mp = 96-97 °C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 45.9 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.76 (m, 1H), 7.32-7.43 (m, 7H), 7.20-7.26 (m, 2H), 7.13-7.20 (m, 3H), 7.06-7.11 (m, 1H), 3.92-4.07 (m, 2H), 1.54 (quint., *J* = 7.0 Hz, 2H), 1.26 (sextuplet, *J* = 7.4 Hz, 2H), 0.78 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 148.6 (d, J_{PCC} = 27.3 Hz), 141.9 (d, J_{PCC} = 34.3 Hz), 133.9 (d, J_{PCC} = 18.0 Hz), 133.1 (d, J_{PCCCC} = 1.7 Hz), 132.5 (d, J_{PCCC} = 9.0 Hz), 130.0 (d, J_{PC} = 125 Hz), 129.1, 129.0 (2C), 128.9 (4C), 128.7, 128.3 (2C), 128.0, 127.7 (d, J_{PCCC} = 8.8 Hz), 127.2 (d, J_{PC} = 134 Hz), 123.9 (d, J_{PCC} = 13.4 Hz), 65.8 (d, J_{POC} = 6.6 Hz), 32.5 (d, J_{POCC} = 6.0 Hz), 18.6, 13.5; HRMS (EI+) m/z calcd for $C_{24}H_{23}O_2P$ ([M]$^+$) 374.1436, found 374.1443.

1-Butyl-2,3-diphenyl-1-phosphindole 40c:

To a suspension of $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv), sodium acetate (246 mg, 3 mmol, 3 equiv) and diphenylacetylene (178 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) at 70 ^{0}C under N_2 was added a solution of butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 h *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 ^{0}C under N_2. Ethyl acetate (~ 50 mL) and an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~50 mL) were added. The suspension was stirred vigorously for 5 minutes, filtered through celite and the two layers were separated. The organic layer was washed with an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~50 mL), a saturated aqueous solution of $NaHCO_3$ (~ 50 mL) and brine (~ 50 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. ^{31}P NMR (162 MHz, $CDCl_3$) of the crude: δ = 46.0 (42%, s).

1-Butyl-2,3-diphenyl-1-phosphindole 40c:

To a suspension of Ru/C (202 mg, 0.05 mmol, 5 mol%, 2.5% wt in water), MnO_2 (261 mg, 3 mmol, 3 equiv), sodium acetate (246 mg, 3 mmol, 3 equiv) and diphenylacetylene (178 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) at 70 ^{0}C under N_2 was added a solution of butyl phenyl-*H*-phosphinate[19] (198 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 h *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 ^{0}C under N_2. Ethyl acetate (~ 50 mL) and an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~50 mL) were added. The suspension was stirred vigorously for 5 minutes, filtered through celite and the two layers were separated. The organic layer was washed with an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~50 mL), a saturated aqueous solution of $NaHCO_3$ (~ 50 mL) and brine (~ 50 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 96:4) to afford the product as a yellow solid (127 mg, 34%). Mp = 96-97 °C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 45.9 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.76 (m, 1H), 7.32-7.43 (m, 7H), 7.20-7.26 (m, 2H), 7.13-7.20 (m, 3H), 7.06-7.11 (m, 1H), 3.92-

4.07 (m, 2H), 1.54 (quint., J = 7.0 Hz, 2H), 1.26 (sextuplet, J = 7.4 Hz, 2H), 0.78 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 148.6 (d, J_{PCC} = 27.3 Hz), 141.9 (d, J_{PCC} = 34.3 Hz), 133.9 (d, J_{PCC} = 18.0 Hz), 133.1 (d, J_{PCCCC} = 1.7 Hz), 132.5 (d, J_{PCCC} = 9.0 Hz), 130.0 (d, J_{PC} = 125 Hz), 129.1, 129.0 (2C), 128.9 (4C), 128.7, 128.3 (2C), 128.0, 127.7 (d, J_{PCCC} = 8.8 Hz), 127.2 (d, J_{PC} = 134 Hz), 123.9 (d, J_{PCC} = 13.4 Hz), 65.8 (d, J_{POC} = 6.6 Hz), 32.5 (d, J_{POCC} = 6.0 Hz), 18.6, 13.5; HRMS (EI+) m/z calcd for $C_{24}H_{23}O_2P$ ($[M]^+$) 374.1436, found 374.1443.

2-butoxy-1,2-dihydro-3,4-dipropyl-2-isophosphinoline-2-oxide 41:[18]

To a solution of butyl benzyl-*H*-phosphinate[18] (212 mg, 1 mmol, 2 equiv) and 4-octyne (55 mg, 0.5 mmol, 1 equiv) in acetic acid (2.5 mL) was added $Mn(OAc)_2$ (4.3 mg, 0.025 mmol, 5 mol %), MnO_2 (85% activated, 154 mg, 1.5 mmol, 3 equiv). The suspension was stirred for 6 h at 70 ^oC under N_2. Ethyl acetate (40 mL) and 0.1 M aqueous solution of $Na_2S_2O_4$ (saturated with NaCl, 20 mL) was added. The mixture was stirred for 5 min and the suspension was filtered over Celite®. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.1M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 7:3 to 3:7) to afford the product as colorless oil (80 mg, 50%).

5-cyclohexyloxy-5H-benzo[b]phosphindole-5-oxide 42:[11e]

To a solution of cyclohexyl 2-(biphenyl)-*H*-phosphinate[12] (150.2 mg, 0.5 mmol, 1 equiv) in tetrahydrofuran (2 ml) was added $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 5.0 mol %) and the mixture was stirred for 20h at 70 °C. The solvent was removed under vacuum and the residue obtained was purified by column chromatography (hexane/ethyl acetate 8:2 to 5:5) to afford the product as a white solid (72 mg, 48%, 88% based on recovered SM).

5-cyclohexyloxy-5H-benzo[b]phosphindole-5-oxide 42:[11e]

To a solution of cyclohexyl 2-(biphenyl)-*H*-phosphinate[12] (300 mg, 1 mmol, 1 equiv) in tetrahydrofuran (10 ml) was added $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 5.0 mol %) and MnO_2 (174 mg, 2 mmol, 2 equiv) and the mixture was stirred for 12h at 70 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 98:2 to 93:7) to afford the product as a white solid (267 mg, 90%).

5-cyclohexyloxy-5H-benzo[b]phosphindole-5-oxide 42:[11e]

To a suspension of $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv) in acetic acid (2.5 mL) at 70 ^0C under N_2 was added a solution of cyclohexyl 2-(biphenyl)-*H*-phosphinate[12] (300 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 h *via* a syringe pump. The reaction mixture was then stirred for an additional 2h at 70 ^0C under N_2. Ethyl acetate (50 mL) and an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (40 mL) were added. The suspension was stirred vigorously for 10 minutes, filtered through celite and the two layers were separated. The organic layer was washed with an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a white solid (291 mg, 98%).

10-cyclohexyloxy-9,10-dihydro-10-phosphaphenanthrene-10-oxide 43:

To a solution of H_3PO_2 (1.32 g, 10 mmol, 2 equiv, concentrated under vacuum for 30 minutes) in *tert*-amylalcohol (25 mL) was added Pd_2dba_3 (23 mg, 0.025 mmol, 0.5 mol %), xantphos (32 mg, 0.055 mmol, 1.1 mol %) and 2-biphenylmethanol (921 mg, 5 mmol, 1 equiv). The mixture

was stirred for 20 hours at reflux under N_2 in a flask equipped with a Dean-Stark trap. After cooling down the reaction to rt, the solvent was removed under vacuum to afford the crude as a brown oil.

The crude obtained was solubilized in toluene (20 mL) and then cyclohexanol (0.53 mL, 5 mmol, 2 equiv) was added. The reaction mixture was stirred for 48 hours at reflux under N_2 in a flask equipped with a Dean-Stark trap. After cooling down the reaction to rt, the solvent was removed under vacuum and the crude obtained was purified by column chromatography (hexane/ethyl acetate 7:3 to 5:5) to afford the product as a colorless oil (421 mg, 27% on two steps). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 33.0 (dm, J = 541 Hz); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24-7.48 (m, 9H), 7.00 (dt, J = 1.9 and 541 Hz), 4.18-4.32 (m, 1H), 3.13-3.34 (m, 2H), 1.14-1.93 (m, 11H).

To a solution of cyclohexyl-2-biphenylmethyl-*H*-phosphinate (400 mg, 1.27 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_3.2H_2O$ (682 mg, 2.54 mmol, 2 equiv) and sodium acetate (208 mg, 2.54 mmol, 2 equiv). The suspension was stirred for 24 h at 100 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a colorless oil (386 mg, 97%). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 30.7 (s); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99-8.10 (m, 1H), 7.74-7.86 (m, 2H), 7.62-7.71 (m, 1H), 7.43-7.52 (m, 1H), 7.34-7.43 (m, 1H), 7.22-7.34 (m, 2H), 4.22-4.36 (m, 1H), 3.15-3.43 (m, 2H), 1.75-1.86 (m, 1H), 1.54-1.67 (m, 1H), 1.32-1.50 (m, 4H), 1.02-1.31 (m, 4H); ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ = 140.7 (d, J_{PCCC} = 7.7 Hz), 133.6 (d, J_{PCC} = 10.3 Hz), 133.1, 131.0 (d, J_{PCC} = 8.4 Hz), 130.3 (d, J_{PC} = 111 Hz), 130.0 (d, J_{PCCCC} = 3.6 Hz), 128.6 (2C), 128.0, 127.7 (d, J_{PCC} = 10.8 Hz), 126.5, 126.2 (d, J_{PCCC} = 9.1 Hz), 74.8 (d, J_{POC} = 3.8 Hz), 33.8, 33.1, 32.4 (d, J_{PC} = 96.7 Hz), 24.9, 23.3, 23.2; HRMS (EI+) m/z calcd for $C_{19}H_{21}O_2P$ ([M]$^+$) 312.1279, found 312.1275.

5-phenyl-5H-benzo[b]phosphoindole-5-oxide 44:[22]

To a solution of cyclohexyl 2-(biphenyl)-*H*-phosphinate[12] (600 mg, 2 mmol, 1 equiv) in tetrahydrofuran (10 mL) was added slowly at 0 °C under N_2 a solution of phenyl magnesium bromide 1M in tetrahydrofuran (3 mL, 3 mmol, 1.5 equiv). The mixture was stirred for 12 hours at rt under N_2. A saturated solution of NH_4Cl was added to neutralize the excess of phenyl magnesium bromide. The two layers were separated and the organic layer was washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 95:5) to afford the product as a colorless oil (460 mg, 83%).[13] ^{31}P NMR (162MHz, $CDCl_3$): δ = 18.8 (d, J = 493 Hz).

To a suspension of $Mn(OAc)_2$ (10.2 mg, 0.059 mmol, 5 mol%), MnO_2 (308 mg, 3.54 mmol, 3 equiv) and sodium acetate (290 mg, 3.54 mmol, 3 equiv) in acetic acid (2.5 mL) at 70 °C under N_2 was added a solution of phenyl 2-(biphenyl)-*H*-phosphine oxide (400 mg, 1.18 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 hours *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 °C under N_2. Ethyl acetate (50 mL) and a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL) were added. The suspension was stirred vigorously for 10 minutes, filtered through celite and the two layers were separated. The organic layer was washed with a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 98:2 to 94:6) to afford the product as a white solid (222 mg, 80%). Mp: 151-153 °C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 33.8 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77-7.83 (m, 2H), 7.60-7.73 (m, 4H), 7.51-7.58 (m, 2H), 7.42-7.49 (m, 1H), 7.30-7.39 (m, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 141.8 (d, J_{PCC} = 21.8 Hz, 2C), 133.4 (d, J_{PCCCC} = 1.1 Hz, 2C), 132.8 (d, J_{PC} = 112 Hz, 2C), 132.2 (d, J_{PCCCC} = 2.3 Hz), 131.2 (d, J_{PCC} = 24.6 Hz, 2C), 130.8 (d, J_{PC} = 104 Hz), 129.9 (d, J_{PCCC} = 9.5 Hz, 2C), 129.5 (d, J_{PCCC} = 11.0 Hz, 2C), 128.7 (d, J_{PCC} = 12.5 Hz, 2C), 121.3 (d, J_{PCC} = 9.9 Hz, 2C).

1-phenyl-2-oxy-3-hydro-[4,5]phenyl-1-phosphinoline-1-oxide 45:

In a flask equipped with a Dean-Stark trap was introduced phenylphosphinic acid (2.84 g, 20 mmol, 1 equiv), 1-naphthylmethanol (6.33 g, 40 mmol, 2 equiv) and toluene (40 ml). After 16 hours at reflux under N_2, the reaction was cooled down to rt and the solvent was concentrated under vacuum. The residue obtained was dissolved in ethyl acetate and the organic layer was washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 9:1 to 5:5) to afford the product as a white solid (4.37 g, 77%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.6 (d, J = 566 Hz); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02-8.10 (m, 1H), 7.65-7.88 (m, 4H), 7.59 (d, J = 566 Hz, 1H), 7.32-7.56 (m, 6H), 5.44-5.62 (m, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ = 133.7, 133.1 (d, J_{PCCCC} = 2.6 Hz), 131.4, 131.0 (d, J_{POCC} = 6.5 Hz), 130.9 (d, J_{PCCC} = 12.1 Hz, 2C), 129.8, 129.6 (d, J_{PC} = 132 Hz), 128.8, 128.7 (d, J_{PCC} = 13.7 Hz, 2C), 127.5, 126.8, 126.2, 125.3, 123.5, 65.7 (d, J_{POC} = 5.9 Hz); HRMS (EI+) m/z calcd for $C_{17}H_{16}O_2P$ ($[M+H]^+$) 283.0882, found 283.0884.

To a solution of 1-naphthylmethyl phenyl-*H*-phosphinate (282 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv). The suspension was stirred for 24 hours at 70 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford the product as a colorless oil (174 mg, 62%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 28.1 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94-8.01 (m, 1H), 7.64-7.85 (m, 4H), 7.42-7.51 (m, 3H), 7.30-7.39 (m, 3H), 5.83-5.92 (m, 1H), 5.32-5.44 (m, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ = 132.8 (d, J_{PCCCC} = 2.6 Hz), 132.7, 132.6 (d, J_{PCCCC} = 3.1 Hz), 132.0 (d, J_{PCCC} = 10.6 Hz, 2C), 130.8 (d, J_{PCCC} = 11.3 Hz), 130.2 (d, J_{PCCC} = 7.5 Hz), 130.1 (d, J_{POCC} = 6.1 Hz), 130.0 (d, J_{PC} = 143 Hz), 128.5 (d, J_{PCC} = 13.8 Hz, 2C), 128.3, 126.1, 125.8 (d, J_{PCC} = 15.3 Hz), 124.9 (d, J_{PC} = 128 Hz), 123.5, 66.9 (d, J_{POC} = 6.8 Hz); HRMS (EI+) m/z calcd for $C_{17}H_{13}O_2P$ ($[M]^+$) 280.0653, found 280.0655.

1-phenyl-3,4-dihydronaphtho-[1,2-c]-[1,2]-oxaphosphinine-1-oxide and 1-phenyl-3,4-dihydronaphtho-[1,8-cd]-[1,2]-oxaphosphepine 1-oxide 46 and 47:

In a flask equipped with a Dean-Stark trap was introduced phenylphosphinic acid (1.42 g, 10 mmol, 1 equiv), 1-naphthalene ethanol (3.44 g, 20 mmol, 2 equiv) and toluene (20 ml). After 16 hours at reflux under N_2, the reaction was cooled down to rt and the solvent was concentrated under vacuum. The residue obtained was dissolved in ethyl acetate and washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 9:1 to 5:5) to afford the product as a colorless oil (2.72 g, 92%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 25.4 (dm, J = 566 Hz); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97-8.05 (m, 1H), 7.86-7.93 (m, 1H), 7.77-7.83 (m, 1H), 7.63-7.73 (m, 2H), 7.53 (d, J = 566 Hz, 1H), 7.38-7.61 (m, 7H), 4.36-4.52 (m, 2H), 3.55 (t, J = 7.0 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (75.46 MHz, $CDCl_3$): δ = 133.8, 133.0 (d, J_{PCCCC} = 2.9 Hz), 132.9, 131.9, 130.8 (d, J_{PCCC} = 11.8 Hz, 2C), 129.6 (d, J_{PC} = 131 Hz), 128.8, 128.6 (d, J_{PCC} = 13.8 Hz, 2C), 127.6, 127.3, 126.2, 125.7, 125.5, 123.4, 65.6 (d, J_{POC} = 6.6 Hz), 34.0 (d, J_{POCC} = 6.1 Hz); HRMS (EI+) m/z calcd for $C_{18}H_{18}O_2P$ ($[M+H]^+$) 297.1044, found 297.1036.

To a solution of 2-[(1-naphthyl)ethyl] phenyl-*H*-phosphinate (296 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv). The suspension was stirred for 24 hours at 70 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained

was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford product **46** as a white solid (204 mg, 70%) and product **47** as a white solid (87 mg, 30%).

For product 46: Mp = 165-166 ^{0}C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 26.3 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02-8.09 (m, 1H), 7.73-7.87 (m, 4H), 7.55-7.67 (m, 3H), 7.45-7.52 (m, 1H), 7.36-7.43 (m, 2H), 4.82-4.93 (m, 1H), 4.61-4.74 (m, 1H), 3.46-3.64 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 139.5 (d, J_{PCCC} = 5.3 Hz), 134.6 (d, J_{PCCCC} = 2.0 Hz), 132.5 (d, J_{PCCCC} = 2.7 Hz), 131.9 (d, J_{PCCC} = 10.6 Hz, 2C), 131.1 (d, J_{PC} = 144 Hz), 130.8 (d, J_{PCCC} = 11.8 Hz), 129.0, 128.5 (d, J_{PCC} = 13.6 Hz, 2C), 128.1, 127.9 (d, J_{PCC} = 13.4 Hz), 127.3, 126.4 (d, J_{PCCC} = 11.6 Hz), 125.0 (d, J_{PC} = 125 Hz), 123.7, 63.8 (d, J_{POC} = 5.9 Hz), 27.7 (d, J_{POCC} = 6.1 Hz); HRMS (EI+) m/z calcd for $C_{18}H_{15}O_2P$ ([M]$^+$) 294.0810, found 294.0805.

For product 47: Mp = 141-142 ^{0}C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 37.3 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93-7.98 (m, 1H), 7.81-7.90 (m, 3H), 7.57-7.64 (m, 1H), 7.46-7.56 (m, 4H), 7.30-7.42 (m, 2H), 4.85-4.93 (m, 1H), 4.73-4.84 (m, 1H), 4.43-4.56 (m, 1H), 3.21-3.31 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 136.9 (d, J_{PCCCC} = 3.1 Hz), 134.3 (d, J_{PCC} = 10.3 Hz), 134.0 (d, J_{PCC} = 14.8 Hz), 133.5 (d, J_{PCCC} = 7.1 Hz), 132.7 (d, J_{PCCCC} = 3.1 Hz), 132.4 (d, J_{PCCC} = 4.7 Hz), 132.3 (d, J_{PCCC} = 9.7 Hz, 2C), 131.9 (d, J_{PC} = 148 Hz), 131.6 (d, J_{PC} = 121 Hz), 129.7, 128.6 (d, J_{PCCCCC} = 1.0 Hz), 128.3 (d, J_{PCC} = 13.5 Hz, 2C), 126.3, 124.2 (d, J_{PCC} = 16.9 Hz), 69.6 (d, J_{POC} = 5.9 Hz), 37.9 (d, J_{POCC} = 3.6 Hz); HRMS (EI+) m/z calcd for $C_{18}H_{15}O_2P$ ([M]$^+$) 294.0810, found 294.0810.

1-phenyl-2-oxy-3,4-dihydro-1-phosphinoline-1-oxide 49a:[18]

In a flask equipped with a Dean-Stark trap was introduced phenylphosphinic acid (3.55 g, 25 mmol, 1 equiv), cyclohexanol (6.11 ml, 50 mmol, 2 equiv) and toluene (50 ml). After 16h at reflux under N_2, the reaction was cooled down to rt and the solvent was concentrated under vacuum. The residue obtained was dissolved in ethyl acetate and washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 9:1 to 5:5) to afford product **48a** as a colorless oil (5.25 g, 85%).

To a solution of 2-phenylethyl phenyl-*H*-phosphinate (246 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_3.2H_2O$ (536 mg, 2 mmol, 2 equiv) and sodium acetate (164 mg, 2 mmol, 2 equiv). The suspension was stirred for 24 h at 100 ^{o}C under N_2. 100 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 8:2 to 5:5) to afford the product as a white solid (189 mg, 78%).

1-phenyl-2-oxy-3,4-dihydro-1-phosphinoline-1-oxide 49a:[18]

To a suspension of $Mn(OAc)_2$ (43.3 mg, 0.25 mmol, 5 mol%), MnO_2 (1.31 g, 15 mmol, 3 equiv) and sodium acetate (1.23 g, 15 mmol, 3 equiv) in acetic acid (15 mL) at 70 ^{0}C under N_2 was added a solution of 2-phenylethyl phenyl-*H*-phosphinate (1.23 g, 5 mmol, 1 equiv) in acetic acid (10 mL) over 2 h *via* a syringe pump. The reaction mixture was then stirred for an additional 2h at 70^{0}C under N_2. Ethyl acetate (100 mL) and a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (100 mL) were added. The suspension was stirred vigorously for 10 minutes, filtered through celite and the two layers were separated. The organic layer was washed with a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (100 mL), a saturated aqueous solution of $NaHCO_3$ (100 mL) and brine (100 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 8:2 to 5:5) to afford the product as a white solid (1.0 g, 82%).

1-(2-phenylethyl)-3,4-tetrahydro-1-phosphonoline-1-oxide 49b:[18]

To a solution of di(2-phenylpropyl)phosphite (290.3 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_3.2H_2O$ (536 mg, 2 mmol, 2 equiv) and sodium acetate (164 mg, 2 mmol, 2 equiv). The suspension was stirred for 24 h at 100 °C under N_2. 100 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 5:5 to 0:10 + 20% acetone) to afford the product as a colorless oil (184 mg, 64%).

1-ethyloxy-1,2,3,4-tetrahydro-1-phosphinoline-1-oxide 49c:[18]

To a solution of ethyl-3-phenylpropyl-*H*-phosphinate (212 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_3.2H_2O$ (536 mg, 2 mmol, 2 equiv) and sodium acetate (164 mg, 2 mmol, 2 equiv). The suspension was stirred for 24 h at 100 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 95:5) to afford the product as a colorless oil (102 mg, 49%).

1-cyclohexyloxy-1,2,3,4-tetrahydro-1-phosphinoline-1-oxide 49d:[18]

To a stock solution of cyclohexyl *H*-phosphinate in toluene (47 mL, 20 mmol, 2 equiv, 0.5M, 85% purity) was added $NiCl_2$ (39 mg, 0.3 mmol, 3 mol %). After 2 hours of stirring at rt under N_2, dppe (136 mg, 0.33 mmol, 3.3 mol %) was added and the mixture was stirred for 30 minutes at rt under N_2. Allylbenzene (1.325 mL, 10 mmol, 1 equiv) was then added and the reaction was stirred for 48 hours at rt. The solvent was removed under vacuum and the residue obtained was solubilized in ethyl acetate. The organic layer was washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The oil obtained was purified by column chromatography (hexane/ethyl acetate 8:2 to 5:5) to afford the product as a colorless oil (1.07 g, 40%).

To a solution of cyclohexyl-3-phenylpropyl-*H*-phosphinate (266 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_3.2H_2O$ (536 mg, 2 mmol, 2 equiv) and sodium acetate (164 mg, 2 mmol, 2 equiv). The suspension was stirred for 24 h at 100 °C under N_2. 100 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 95:5) to afford the product as a colorless oil (177 mg, 67%).

1-cyclohexyloxy-1,2,3,4-tetrahydro-1-phosphinoline-1-oxide 49d:[18]

To a stock solution of cyclohexyl *H*-phosphinate in toluene (47 mL, 20 mmol, 2 equiv, 0.5M, 85% purity) was added $NiCl_2$ (39 mg, 0.3 mmol, 3 mol %). After 2 hours of stirring at rt under N_2, dppe (136 mg, 0.33 mmol, 3.3 mol %) was added and the mixture was stirred for 30 minutes at rt under N_2. Allylbenzene (1.325 mL, 10 mmol, 1 equiv) was then added and the reaction was stirred for 48 hours at rt. The solvent was removed under vacuum and the residue obtained was solubilized in ethyl acetate. The organic layer was washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The oil obtained was purified by column chromatography (hexane/ethyl acetate 8:2 to 5:5) to afford the product as a colorless oil (1.07 g, 40%). To a suspension of $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv) in acetic acid (2.5 mL) at 70 °C under N_2 was added a solution of 2-phenylethyl phenyl-*H*-phosphinate (246 mg, 1 mmol, 1 equiv) in acetic acid (2.5 mL) over 2 h *via* a syringe pump. The reaction mixture was then stirred for an additional 2h at 70°C under N_2. Ethyl acetate (40 mL) and a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL) were added. The suspension was stirred vigorously for 10 minutes, filtered through celite and the two layers were separated. The organic layer was washed with a 0.2M aqueous solution of $Na_2S_2O_4$ saturated with $NaHCO_3$ (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL) and brine (40

mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 95:5) to afford the product as a colorless oil (172 mg, 65%).

1-phenyl-2,3,4-tetrahydro-1-phosphinoline-1-oxide 49e:[18]

To a solution of 3-phenylpropyl-*H*-phosphine oxide (950 mg, 4.48 mmol, 1 equiv) in toluene (5 mL) was added a solution of phenyl magnesium bromide 0.87M in THF (7.72 mL, 6.71 mmol, 1.5 equiv) at 0 °C under N_2. The ice-bath was removed and the mixture was stirred for 2 hours at rt. Saturated NH_4Cl solution was added to neutralize the excess of phenyl magnesium bromide. The two layers were separated and the organic layer was washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum.

To a solution of (3-phenylpropyl)phenyl-*H*-phosphine oxide (244.3 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_3.2H_2O$ (536 mg, 2 mmol, 2 equiv) and sodium acetate (164 mg, 2 mmol, 2 equiv). The suspension was stirred for 24 h at 100 °C under N_2. 100 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 5:5 to 0:10 + 20% acetone) to afford the product as a colorless oil (142 mg, 59%).

In an oven-dried 2 L round-bottom flask, anhydrous $NiCl_2$ (583 mg, 4.5 mmol, 3 mol %) was suspended in 600 mL of a butyl *H*-phosphinate solution in acetonitrile (0.5 M, 300 mmol, 2 equiv). The mixture was heated for 10 minutes until the nickel starts to dissolve, and the reaction mixture was cooled down to rt. Dppe (2.04 g, 4.95 mmol, 3.3 mol %) was added, and after 30 minutes of stirring, 4-phenyl-1-butene (22.5 mL, 150 mmol, 1 equiv) was added, and the mixture was stirred at rt for 24 hours. Upon completion of the first reaction, aqueous NaOH solution (120 mL, 600 mmol, 4 equiv) was poured into the flask and refluxed for 14 hours. The reaction mixture was first extracted with 500 mL of toluene, acidified with saturated $NaHSO_4$ solution until pH < 2, and then extracted with 500 mL of ethyl acetate three times. The combined organic layers was dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a yellow oil (27.35 g, 92%).

The oil obtained (1.982 g, 10 mmol, 1 equiv) was solubilized in toluene (20 mL) and then cyclohexanol (2.11 mL, 20 mmol, 2 equiv) was added. The reaction mixture was stirred for 24 hours at reflux under N_2 in a flask equipped with a Dean-Stark trap. After cooling down the reaction to rt, the solvent was removed under vacuum and the crude obtained was purified by column chromatography (hexane/ethyl acetate 9:1 to 5:5) to afford the product as a colorless oil (2.38 g, 85%).

1-cyclohexyloxy-2,3,4,5-tetrahydrobenzo-[b]-phosphepine-1-oxide 49f:

In an oven-dried 2 L round-bottom flask, anhydrous $NiCl_2$ (583 mg, 4.5 mmol, 3 mol %) was suspended in 600 mL of a butyl *H*-phosphinate solution in acetonitrile (0.5 M, 300 mmol, 2 equiv). The mixture was heated for 10 minutes until the nickel starts to dissolve, and the reaction mixture was cooled down to rt. Dppe (2.04 g, 4.95 mmol, 3.3 mol %) was added, and after 30 minutes of stirring, 4-phenyl-1-butene (22.5 mL, 150 mmol, 1 equiv) was added, and the mixture was stirred at rt for 24 hours. Upon completion of the first reaction, aqueous NaOH solution (120 mL, 600 mmol, 4 equiv) was poured into the flask and refluxed for 14 hours. The reaction mixture was first extracted with 500 mL of toluene, acidified with saturated $NaHSO_4$ solution until pH < 2, and then extracted with 500 mL of ethyl acetate three times. The combined organic layers was dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a yellow oil (27.35 g, 92%). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 38.0 (d, *J* = 540 Hz); ^1H NMR (300 MHz, $CDCl_3$): δ = 10.35 (br, 1H), 7.08 (d, *J* = 540 Hz, 1H), 7.25 (m, 5H), 2.64 (t, *J* = 7.0 Hz, 2H), 1.75 (m, 6H).

The oil obtained (1.982 g, 10 mmol, 1 equiv) was solubilized in toluene (20 mL) and then cyclohexanol (2.11 mL, 20 mmol, 2 equiv) was added. The reaction mixture was stirred for 24 hours at reflux under N_2 in a flask equipped with a Dean-Stark trap. After cooling down the reaction to rt, the solvent was removed under vacuum and the crude obtained was purified by column chromatography (hexane/ethyl acetate 9:1 to 5:5)

to afford the product as a colorless oil (2.38 g, 85%). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 35.4 (d, *J* = 525 Hz); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24-7.33 (m, 2H), 7.12-7.23 (m, 3H), 7.14 (dt, *J* = 1.8 and 525 Hz, 1H), 4.27-4.42 (m, 1H), 2.64 (t, *J* = 7.3 Hz, 2H), 1.86-2.02 (m, 2H), 1.43-1.85 (m, 12H), 1.17-1.42 (m, 3H); ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ = 141.7, 128.3 (4C), 125.8, 75.6 (d, J_{POC} = 7.2 Hz), 35.3, 33.9 (d, J_{POCC} = 2.8 Hz), 32.9 (d, J_{POCC} = 3.4 Hz), 32.1 (d, J_{PCC} = 14.4 Hz), 28.8 (d, J_{PC} = 94.5 Hz), 25.1, 23.5 (2C), 20.4.

To a solution of cyclohexyl-4-phenylbutyl-*H*-phosphinate (280 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_3.2H_2O$ (536 mg, 2 mmol, 2 equiv) and sodium acetate (164 mg, 2 mmol, 2 equiv). The suspension was stirred for 24 h at 100 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (ethyl acetate) to afford the product as a white solid (102 mg, 37%). Mp = 65-66 °C; ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 43.4 (s); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00-8.12 (m, 1H), 7.39-7.447 (m, 1H), 7.27-7.36 (m, 1H), 7.13-7.21 (m, 1H), 4.19-4.33 (m, 1H), 3.06-3.21 (m, 1H), 2.82-2.94 (m, 1H), 1.81-2.22 (m, 5H), 1.68-1.80 (m, 1H), 1.12-1.64 (m, 10H); ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ = 144.7 (d, J_{PCC} = 14.4 Hz), 133.2 (d, J_{PCCC} = 7.7 Hz), 132.5 (d, J_{PCCCC} = 2.8 Hz), 131.2 (d, J_{PC} = 117 Hz), 130.0 (d, J_{PCC} = 13.8 Hz), 125.9 (d, J_{PCCC} = 11.6 Hz), 74.2 (d, J_{POC} = 6.6 Hz), 35.5, 34.3 (d, J_{POCC} = 3.3 Hz), 33.3 (d, J_{POCC} = 3.8 Hz), 29.7 (d, J_{PC} = 95.7 Hz), 27.9, 25.1 (2C), 23.6 (d, J_{PCC} = 15.5 Hz), 23.6 (d, J_{PCCC} = 6.6 Hz); HRMS (EI+) m/z calcd for $C_{16}H_{23}O_2P$ ([M]$^+$) 278.1436, found 278.1437.

1-cyclohexyloxy-2,3,4,5-tetrahydrobenzo-[b]-phosphepine-1-oxide 49f:

To a solution of cyclohexyl-4-phenylbutyl-*H*-phosphinate (280 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol %), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv). The suspension was stirred for 24 hours at 70 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford the product as a colorless oil (149 mg, 54%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 43.1 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88-8.01 (m, 1H), 7.25-7.34 (m, 1H), 7.14-7.23 (m, 1H), 7.01-7.11 (m, 1H), 4.08-4.22 (m, 1H), 3.03 (t, *J* = 12.7 Hz, 1H), 2.71-2.84 (m, 1H), 1.69-2.11 (m, 6H), 1.57-1.67 (m, 1H), 0.98-1.55 (m, 9H); ^{13}C{^{1}H} NMR (75.46 MHz, $CDCl_3$): δ = 144.6 (d, J_{PCC} = 14.0 Hz), 133.1 (d, J_{PCCC} = 7.6 Hz), 132.4 (d, J_{PCCCC} = 2.2 Hz), 131.3 (d, J_{PC} = 117 Hz), 129.9 (d, J_{PCC} = 13.4 Hz), 125.8 (d, J_{PCCC} = 11.4 Hz), 73.9 (d, J_{POC} = 6.6 Hz), 35.4, 34.2 (d, J_{POCC} = 2.8 Hz), 33.2 (d, J_{POCC} = 3.6 Hz), 29.8 (d, J_{PC} = 95.7 Hz), 27.9, 25.1 (2C), 23.6 (d, J_{PCCC} = 9.6 Hz), 23.5 (d, J_{PCC} = 19.3 Hz); HRMS (EI+) m/z calcd for $C_{16}H_{23}O_2P$ ([M]$^+$) 278.1436, found 278.1437.

1-cyclohexyloxy-2,3-dihydro-1-phosphole-1-oxide 49g:

To a stock solution of butyl *H*-phosphinate in acetonitrile (60 mL, 30 mmol, 2 equiv, 0.5M) was added $Pd(OAc)_2$ (67.4 mg, 0.3 mmol, 2 mol %), xantphos (191 mg, 0.33 mmol, 2.2 mol %) and styrene (1.72 mL, 15 mmol, 1 equiv). The mixture was stirred for 24 hours at reflux under N_2. After cooling down the reaction to rt, the solvent was removed under vacuum. The residue obtained was solubilized in ethyl acetate and the organic layer was washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The oil obtained was purified by column chromatography (hexane/ethyl acetate 8:2 to 5:5) to afford the product as a colorless oil (2.9 g, 85%, purity of 94%).[5] ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 37.2 (dm, *J* = 532 Hz); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.18-7.37 (m, 5H), 7.10 (dt, *J* = 1.9 and 532 Hz), 3.94-4.19 (m, 2H), 2.86-3.00 (m, 2H), 2.04-2.18 (m, 2H), 1.69 (quint., *J* = 7.1 Hz), 1.42 (sext., *J* = 7.4 Hz), 0.95 (t, *J* = 7.3 Hz).

To a solution of butyl-2-phenylethyl-*H*-phosphinate (2.8 g, 12.38 mmol, 1 equiv) was added an aqueous solution of NaOH 2N (25 mL, 49.5 mmol, 4 equiv) and then the mixture was refluxed for 20 hours. The reaction mixture was first extracted with 50 mL of toluene twice, acidified

with saturated $NaHSO_4$ solution until pH < 2, and then extracted with 50 mL of dichloromethane three times. The combined organic layers was dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a yellow oil (1.935 g, 92%, 92.3% purity).[6] ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 36.4 (d, J = 547 Hz); ^1H NMR (300 MHz, $CDCl_3$): δ = 12.39 (br, 1H), 7.14-7.36 (m, 5H), 7.10 (d, J = 547 Hz, 1H), 2.85-2.99 (m, 2H), 2.01-2.18 (m, 2H).

The oil obtained (1.87 g, 11 mmol, 1 equiv) was solubilized in toluene (30 mL) and then cyclohexanol (2.32 mL, 22 mmol, 2 equiv) was added. The reaction mixture was stirred for 24 hours at reflux under N_2 in a flask equipped with a Dean-Stark trap. After cooling down the reaction to rt, the solvent was removed under vacuum and the crude obtained was purified by column chromatography (hexane/ethyl acetate 8:2 to 5:5) to afford the product as a colorless oil (2.29 g, 83%, 92.2% purity). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 33.4 (d, J = 530 Hz); ^1H NMR (300 MHz, $CDCl_3$): δ = 7.17-7.38 (m, 5H), 7.17 (dt, J = 1.9 and 530 Hz, 1H), 4.28-4.45 (m, 1H), 2.85-2.99 (m, 2H), 1.88-2.18 (m, 4H), 1.68-1.83 (m, 2H), 1.45-1.64 (m, 3H), 1.18-1.45 (m, 3H); $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ = 140.0 (d, J_{PCCC} = 15.0 Hz), 128.4 (2C), 127.9 (2C), 126.3, 75.6 (d, J_{POC} = 7.1 Hz), 33.7 (d, J_{POCC} = 3.8 Hz), 32.8 (d, J_{POCC} = 3.9 Hz), 30.5 (d, J_{PC} = 93.5 Hz), 26.8 (d, J_{PCC} = 2.2 Hz), 24.9, 23.3, 23.3; HRMS (EI+) m/z calcd for $C_{14}H_{22}O_2P$ ($[M+H]^+$) 253.1352, found 253.1352.

To a solution of cyclohexyl-2-phenylethyl-*H*-phosphinate (252 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_3.2H_2O$ (536 mg, 2 mmol, 2 equiv) and sodium acetate (164 mg, 2 mmol, 2 equiv). The suspension was stirred for 24 h at 100 °C under N_2. 100 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 97.5:2.5) to afford the product as a colorless oil (98 mg, 39%). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 63.9 (s); ^1H NMR (300 MHz, $CDCl_3$): δ = 7.67-7.76 (m, 1H), 7.44-7.54 (m, 1H), 7.26-7.41 (m, 2H), 4.45-4.59 (m, 1H), 3.04-3.25 (m, 2H), 2.11-2.25 (m, 2H), 1.86-2.07 (m, 1H), 1.64-1.90 (m, 3H), 1.14-1.59 (m, 6H); $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ = 146.2 (d, J_{PCC} = 37.6 Hz), 132.5 (d, J_{PCCCC} = 2.8 Hz), 131.1 (d, J_{PC} = 132 Hz), 127.5 (d, J_{PCCC} = 9.4 Hz), 127.3 (d, J_{PCCC} = 11.1 Hz), 126.9 (d, J_{PCC} = 12.7 Hz), 75.0 (d, J_{POC} = 6.7 Hz), 34.1 (d, J_{POCC} = 3.4 Hz), 33.9 (d, J_{POCC} = 3.8 Hz), 26.2 (d, J_{PCC} = 6.7 Hz), 25.1, 24.7 (d, J_{PC} = 96.8 Hz), 23.8, 23.7; HRMS (EI+) m/z calcd for $C_{14}H_{19}O_2P$ ($[M]^+$) 250.1123, found 250.1119.

1-(acetoxymethyl)-2-oxy-3,4-dihydro-1-phosphinoline-1-oxide 49h:

Paraformaldehyde (0.99 g, 33 mmol, 1.1 equiv) and hypophosphorous acid (3.96 g, 30 mmol, 1 equiv, 50% in water) were introduced in a round bottom flask and the reaction mixture was stirred for 24 hours at 75 °C. The reaction mixture was cooled down to rt and the residue was diluted in toluene (40 mL). Phenethyl alcohol (7.2 mL, 60 mmol, 2 equiv) was added and the reaction mixture was stirred for 24 hours at reflux under N_2 in a flask equipped with a Dean-Stark trap. The solvent was then removed under vacuum. To a solution of the residue obtained in dichloromethane (30 mL) at 0 °C under N_2 was added triethylamine (1.75 mL, 12.55 mmol, 1.15 equiv) followed by acetic anhydride (1.13 mL, 12 mmol, 1.1 equiv). The ice-bath was removed and the reaction mixture was stirred for 16 hours at rt. The solvent was removed under vacuum and the residue obtained was solubilized in ethyl acetate. The organic layer was washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product.

To a solution of 2-phenylethyl (acetoxymethyl)-*H*-phosphinate (242 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv), sodium acetate (246 mg, 3 mmol, 3 equiv). The suspension was stirred for 24 hours at 70 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/dichloromethane 60:40 to 0:100) to afford the product as a colorless oil (88 mg, 37%). ^{31}P

NMR (162 MHz, $CDCl_3$): δ = 27.8 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78-7.89 (m, 1H), 7.47-7.56 (m, 1H), 7.35-7.44 (m, 1H), 7.21-7.32 (m, 1H), 4.32-4.64 (m, 4H), 3.11-3.24 (m, 1H), 2.85-3.01 (m, 1H), 1.94 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 169.7 (d, J_{PCOC} = 8.0 Hz), 142.2 (d, J_{PCC} = 5.9 Hz), 133.2 (d, J_{PCCCC} = 2.3 Hz), 132.2 (d, J_{PCCC} = 10.9 Hz), 128.6 (d, J_{PCCC} = 10.3 Hz), 127.8 (d, J_{PCC} = 13.2 Hz), 124.6 (d, J_{PC} = 120 Hz), 65.6 (d, J_{POC} = 6.9 Hz), 59.8 (d, J_{PC} = 125 Hz), 31.5 (d, J_{POCC} = 5.9 Hz), 20.4; HRMS (EI+) m/z calcd for $C_{11}H_{14}O_4P$ ($[M+H]^+$) 241.0624, found 241.0624.

(R_p)-1-Menthyloxy-1,2,3,4-tetrahydro-1-phosphinoline-1-oxide 49i:[13b]

To a solution of cinnamylphosphinic acid (9.11 g, 50 mmol, 1 equiv) in toluene (100 mL) was added L-menthol (7.81 g, 50 mmol, 1 equiv). The reaction mixture was then stirred at reflux for 24 hours under N_2 and in a flask equipped with a Dean-Stark trap. After cooling down the reaction to rt, paraformaldehyde (1.5 g, 50 mmol, 1 equiv) was added and the reaction mixture was stirred at reflux for 24 hours under N_2. The solvent was then removed under vacuum and the crude obtained was recrystallized at rt in a mixture ethyl acetate/diethyl ether (30 mL : 150 mL) to afford the product as a white solid (5.6 g, 32%, > 99% de).

To a suspension of Pd/C (191 mg, 0.18 mmol, 10 mol%) in ethanol (2 mL) flushed with N_2 was added a solution of (R_p)-menthyl cinnamyl(hydroxymethyl)phosphinate (630 g, 1.8 mmol, 1 equiv) in ethanol (8 mL). The tube was placed in a hydrogenator and stirred for 20 hours at 50 psi of H_2. The suspension was then filtered through celite and the solid was washed with ethanol three times. The filtrate was concentrated under vacuum to afford the product as a white solid (633 g, 100%, 98% de).

To a solution of *N*-chlorosuccinimide (721 mg, 5.4 mmol, 3 equiv) in dichloromethane (30 mL) at -78 ^{o}C under N_2 was added dropwise a solution of dimethyl sulfide (0.4 mL, 5.4 mmol, 3 equiv) in dichloromethane (5 mL). After 10 minutes at -78 ^{o}C, a solution of (R_p)-menthyl (3-phenylpropyl)(hydroxymethyl)phosphinate (630 mg, 1.8 mmol, 1 equiv, > 99% de) in dichloromethane (5 mL) was added over 20 minutes. After 1 hour at -78 ^{o}C, triethylamine (1.25 mL, 9 mmol, 5 equiv) was added over 15 minutes and the reaction was allowed to warm to rt. After 1 hour at rt, water was added and the two layers were separated. The aqueous layer was then extracted with dichloromethane (X2). The combined organic layer was dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 99:1 to 97:3) to afford the product as a colorless oil (554 mg, 96%, 96% de).

To a suspension of $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv) in acetic acid (2.5 mL) at 70 ^{0}C under N_2 was added a solution of (S_p)-menthyl (3-phenylpropyl)-*H*-phosphinate (322 mg, 1 mmol, 1 equiv, 96% de) in acetic acid (2.5 mL) over 2 hours *via* a syringe pump. The reaction mixture was then stirred for an additional 2 hours at 70 ^{0}C under N_2. Ethyl acetate (~ 30 mL) and an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~40 mL) were added. The suspension was stirred vigorously for 5 minutes, filtered through celite and the two layers were separated. The organic layer was washed with an aqueous solution of $Na_2S_2O_4$ 0.2M saturated with $NaHCO_3$ (~40 mL), a saturated aqueous solution of $NaHCO_3$ (~ 40 mL) and brine (~ 40 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 95:5) to afford the product as a colorless oil (300 mg, 94%, 96% de).

1-phenyl-2-oxy-3,4-dihydro-7-methoxy-1-phosphinoline-1-oxide 49j:

In a flask equipped with a Dean-Stark trap was introduced phenylphosphinic acid (1.42 g, 10 mmol, 1 equiv), 2-(4-methoxyphenyl)ethanol (3.04 g, 20 mmol, 2 equiv) and toluene (20 ml). After 16h at reflux under N_2, the reaction was cooled down to rt and the solvent was concentrated under vacuum. The residue obtained was dissolved in ethyl acetate and washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 8:2 to 3:7) to afford the product

as a colorless oil (2.49 g, 90%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 25.2 (d, J = 565 Hz); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52-7.63 (m, 2H), 7.39-7.47 (m, 1H), 7.37 (d, J = 565 Hz, 1H), 7.28-7.37 (m, 2H), 6.96-7.04 (m, 2H), 6.68-6.76 (m, 2H), 4.03-4.21 (m, 2H), 3.62 (s, 3H), 2.84 (t, J = 6.6 Hz, 2H); ^{13}C{^{1}H} NMR (75.46 MHz, $CDCl_3$): δ = 158.4, 133.0 (d, J_{PCCCC} = 2.7 Hz), 130.8 (d, J_{PCCC} = 11.8 Hz, 2C), 129.9 (2C), 129.8 (d, J_{PC} = 131 Hz), 129.0, 128.7 (d, J_{PCC} = 13.8 Hz, 2C), 113.9 (2C), 66.4 (d, J_{POC} = 6.7 Hz), 55.1, 36.0 (d, J_{POCC} = 6.3 Hz); HRMS (EI+) m/z calcd for $C_{15}H_{18}O_3P$ ([M+H]$^+$) 277.0994, found 277.0989.

To a solution of 2-[(4-methoxyphenyl)ethyl] phenyl-*H*-phosphinate (276 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv). The suspension was stirred for 24 hours at 70 ^{o}C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford the product as a colorless oil (216 mg, 79%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 25.2 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61-7.72 (m, 2H), 7.25-7.42 (m, 3H), 6.97-7.11 (m, 2H), 6.83-6.91 (m, 1H), 4.46-4.58 (m, 1H), 4.29-4.42 (m, 1H), 3.57 (s, 3H), 3.06-3.19 (m, 1H), 2.74-2.84 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 158.5 (d, J_{PCC} = 16.3 Hz), 133.2 (d, J_{PCCC} = 5.3 Hz), 132.3 (d, J_{PCCCC} = 2.7 Hz), 131.5 (d, J_{PCCC} = 10.6 Hz, 2C), 131.5 (d, J_{PC} = 145 Hz), 130.0 (d, J_{PCC} = 12.3 Hz), 128.6 (d, J_{PC} = 123 Hz), 128.4 (d, J_{PCC} = 13.5 Hz, 2C), 119.2 (d, J_{PCCCC} = 2.3 Hz), 115.4 (d, J_{PCCC} = 12.2 Hz), 65.2 (d, J_{POC} = 6.5 Hz), 55.3, 30.5 (d, J_{POCC} = 5.3 Hz); HRMS (EI+) m/z calcd for $C_{15}H_{15}O_3P$ ([M]$^+$) 274.0758, found 274.0758.

1-phenyl-2-oxy-3,4-dihydro-7-acetylamino-1-phosphinoline-1-oxide 49k:

In a flask equipped with a Dean-Stark trap was introduced phenylphosphinic acid (1.42 g, 10 mmol, 1 equiv), 2-(4-acetylaniline)ethanol (3.04 g, 20 mmol, 2 equiv) and toluene (20 ml). After 16h at reflux under N_2, the reaction was cooled down to rt and the solvent was concentrated under vacuum. The residue obtained was dissolved in ethyl acetate and washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 9:1 to 5:5) to afford the product as a white solid.

To a solution of 2-[(4-acetylaniline)ethyl] phenyl-*H*-phosphinate (302 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv). The suspension was stirred for 24 hours at 70 ^{o}C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 90:10 to 70:30) to afford the product as a white solid (172 mg, 57%). Mp = 227-228 ^{0}C; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 25.6 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.4 (s, 1H), 8.37-8.45 (m, 1H), 7.58-7.72 (m, 3H), 7.44-7.53 (m, 1H), 7.29-7.39 (m, 2H), 7.17-7.26 (m, 1H), 4.48-4.66 (m, 2H), 3.21-3.34 (m, 1H), 2.89-3.01 (m, 1H), 2.12 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 169.8, 139.2 (d, J_{PCC} = 16.0 Hz), 135.4 (d, J_{PCCC} = 5.5 Hz), 132.6 (d, J_{PCCCC} = 2.3 Hz), 131.3 (d, J_{PCCC} = 10.7 Hz, 2C), 131.2 (d, J_{PC} = 146 Hz), 129.4 (d, J_{PCC} = 11.4 Hz), 128.7 (d, J_{PCC} = 13.8 Hz, 2C), 127.1 (d, J_{PC} = 125 Hz), 124.2, 122.1 (d, J_{PCCC} = 12.2 Hz), 65.7 (d, J_{POC} = 6.4 Hz), 30.9 (d, J_{POCC} = 5.4 Hz), 24.2; HRMS (EI+) m/z calcd for $C_{16}H_{16}NO_3P$ ([M]$^+$) 301.0868, found 301.0874.

1-phenyl-2-oxy-3,4-dihydro-7-tertbutyl-1-phosphinoline-1-oxide 49l:

In a flask equipped with a Dean-Stark trap was introduced phenylphosphinic acid (1.42 g, 10 mmol, 1 equiv), 2-(4-*tert*butyl phenyl)ethanol (3.6 g, 20 mmol, 2 equiv) and toluene (20 ml). After 16 hours at reflux under N_2, the reaction was cooled down to rt and the solvent was concentrated under vacuum. The residue obtained was dissolved in ethyl acetate and washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and

concentrated under vacuum. The crude obtained was purified by column chromatography (hexane/ethyl acetate 9:1 to 5:5) to afford the product as a colorless oil (2.95 g, 98%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 25.2 (d, J = 565 Hz); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63-7.72 (m, 2H), 7.52-7.59 (m, 1H), 7.51 (dd, J = 2.1 and 565 Hz, 1H), 7.41-7.49 (m, 2H), 7.30-7.36 (m, 2H), 7.12-7.18 (m, 2H), 4.18-4.36 (m, 2H), 3.00 (t, J = 6.7 Hz, 2H), 1.32 (s, 3H), 1.31 (s, 3H), 1.31 (s, 3H); ^{13}C{^{1}H} NMR (75.46 MHz, $CDCl_3$): δ = 149.6, 134.0, 133.1 (d, J_{PCCCC} = 2.8 Hz), 131.0 (d, J_{PCCC} = 11.8 Hz, 2C), 129.8 (d, J_{PC} = 131 Hz), 128.7 (2C), 128.7 (d, J_{PCC} = 13.8 Hz, 2C), 125.5 (2C), 66.3 (d, J_{POC} = 6.7 Hz), 36.5 (d, J_{POCC} = 6.3 Hz), 34.4, 31.4 (3C); HRMS (EI+) m/z calcd for $C_{18}H_{24}O_2P$ ([M+H]$^+$) 303.1514, found 303.1511.

To a solution of 2-[(4-*tert*butylphenyl)ethyl] phenyl-*H*-phosphinate (302 mg, 1 mmol, 1 equiv) in acetic acid (5 mL) was added $Mn(OAc)_2$ (8.7 mg, 0.05 mmol, 5 mol%), MnO_2 (261 mg, 3 mmol, 3 equiv) and sodium acetate (246 mg, 3 mmol, 3 equiv). The suspension was stirred for 24 hours at 70 °C under N_2. 50 mL of ethyl acetate was added and the suspension was filtered to remove the manganese. The organic layer was washed with aqueous solutions of $Na_2S_2O_4$ 0.5M, $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude obtained was purified by column chromatography (dichloromethane/acetone 100:0 to 90:10) to afford the product as a white solid (218 mg, 73%). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 25.9 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75-7.83 (m, 2H), 7.65-7.72 (m, 1H), 7.50-7.58 (m, 2H), 7.42-7.49 (m, 2H), 7.20-7.26 (m, 1H), 4.67-4.77 (m, 1H), 4.46-4.58 (m, 1H), 3.26-3.37 (m, 1H), 2.95-3.03 (m, 1H), 1.28 (s, 3H), 1.27 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 150.4 (d, J_{PCC} = 12.4 Hz), 138.3 (d, J_{PCCC} = 5.8 Hz), 132.2 (d, J_{PCCCC} = 2.6 Hz), 131.9 (d, J_{PC} = 144 Hz), 131.4 (d, J_{PCCC} = 10.6 Hz, 2C), 129.5 (d, J_{PCCCC} = 2.1 Hz), 128.5 (d, J_{PCCC} = 7.6 Hz), 128.4 (d, J_{PCC} = 13.7 Hz, 2C), 128.4 (d, J_{PCCC} = 7.4 Hz), 127.3 (d, J_{PC} = 124 Hz), 64.9 (d, J_{POC} = 6.5 Hz), 34.5, 31.0 (3C), 30.9 (d, J_{POCC} = 5.6 Hz); HRMS (EI+) m/z calcd for $C_{18}H_{21}O_2P$ ([M]$^+$) 300.1279, found 300.1283.

Supporting Information

Copies of the NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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