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Graphical abstract

A quantum chemical study on the mechanism and energetics of the direct esterification, thioesterification and amidation of 1-hydroxy-3-methyl-3-phospholene 1-oxide

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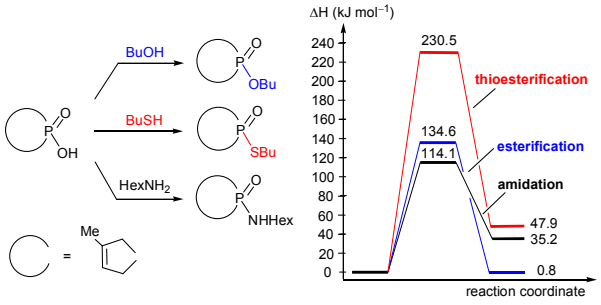

The derivatization of a phosphinic acid, that is possible only on microwave irradiation, was evaluated by B3LYP/6-31G(d,p) calculations using the solvent model.

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ARTICLE TYPE

A "green" variation of the Hirao reaction: the P–C coupling of diethyl phosphite, alkyl phenyl-*H*-phosphinates and secondary phosphine oxides with bromoarenes using P-ligand-free $Pd(OAc)_2$ catalyst under microwave and solvent-free conditions[1]

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The P–C coupling of diethyl phosphite, alkyl phenyl-*H*-phosphinates, diphenylphosphine oxide and dialkylphosphine oxides with bromoarenes may be performed in the presence of P-ligand-free $Pd(OAc)_2$ catalyst and triethylamine under microwave-assisted (MW) and, in almost all cases, solvent-free conditions to afford diethyl arylphosphonates, alkyl diphenylphosphinates, aryldiphenylphosphine oxides and dialkylphenylphosphine oxides, respectively. This is the "greenest" accomplishment of the well-known Hirao reaction that has now been found to have general application for a broad spectrum of >P(O)H species with different reactivity and a great variety of substituted bromobenzenes. The alkyl phenyl-*H*-phosphinates were prepared by the MW-promoted alkylation of phenyl-*H*-phosphinic acid in the absence of any solvent.

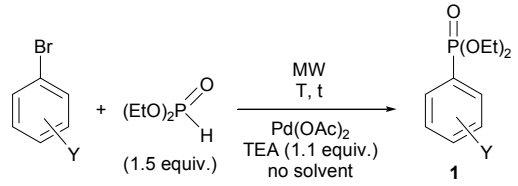
Introduction

The synthesis of aryl phosphonates and related derivatives is in a focus of interest these days.[2] The preparation of aryl phosphonates by the Arbuzov reaction of trialkyl phosphites and aryl halides is possible only under special conditions due to the lower reactivity of aryl halides.[3,4] The most suitable method for the synthesis of aryl phosphonates is the Hirao reaction comprising a P–C coupling between a dialkyl phosphite (*H*-phosphonate) and an aryl or vinyl halide (or another aryl derivative) in the presence of $Pd(PPh_3)_4$ as the catalyst, and in most cases, triethylamine as the base in different solvents.[5–12] The first examples of the Hirao reaction included also the preparation of vinyl phosphates from vinyl halides. Many variations and applications of the Hirao reaction have been described; the coupling was extended to *H*-phosphinates, secondary phosphine oxides and other P-reactants, as well as to other Pd(0) complexes and Pd(II) salts applied in the presence of suitable P-ligands.[2] According to one method, the P–C coupling was enhanced by microwave (MW) irradiation, but this method did not bring a breakthrough, as $Pd(PPh_3)_4$ and THF had to be used.[13] In another case,[14] MW irradiation also had only an accelerating effect. It was a milestone, when attempts were made to replace $Pd(PPh_3)_4$ with $Pd(dba)_2$ (dba = dibenzylideneacetone), $Pd(OAc)_2$ or $PdCl_2$. The most efficient catalytic system was formed from $Pd(OAc)_2$ in the presence of triphenylphosphine as the P-ligand.[15] There have been attempts to apply bidentate P-ligands, such as dppf [1,1'-bis(diphenylphosphino)ferrocene], xantphos [4,5-bis(diphenylphosphino)-9,9-dimethylxanthene], dppp [1,3-bis(diphenylphosphino)propane], dppb [1,4-bis(diphenylphosphino)butane], and BINAP [2,2'-bis(diphenylphosphino)-1,1'-binaphthyl] together with $Pd(OAc)_2$, instead of triphenylphosphine, to establish *in situ* catalysts.[16–18] In another variation, a Pd(II) salt was used with triphenylphosphine, but the base was K_2CO_3, and the reaction was performed in the presence of triethylbenzylammonium chloride (TEBAC) as the phase transfer catalyst.[19–22] It was observed that the phosphinylation of aryl iodides took place in the presence of 'phosphine-free Pd', but aryl bromides underwent the coupling reaction only in the presence of triphenylphosphine as the P-ligand.[19–22] Diphenylphosphine may also be the subject of an analogous coupling reaction using $Pd(OAc)_2$ catalyst under MW irradiation. However, this kind of P-C coupling has been limited only to iodobenzene as the reactant.[23] The high ability of Ph_2PH towards oxidation means another disadvantage, and this reaction was not described as a general method. It is noteworthy that reductive Hirao couplings were also described using $NiBr_2$ and Mg,[24] or $NiCl_2$ and Zn along with 2,2'bipyridine and K_3PO_4 in a suitable solvent.[25]

We experienced that in certain alkylation reactions, the catalysts could be substituted by MW irradiation,[26–30] or it influenced positively the effect of a catalyst.[4,31,32] For this reason, we wished to investigate the role of MW irradiation in the Hirao reaction. We envisaged that the catalyst system may be simplified. It was a question of whether it might be possible to omit the P-ligand under certain conditions in the coupling reaction of bromoarenes. If the simplification of the catalytic system is possible, for which >P(O)H reagents might it be relevant? Our preliminary results on a limited scope of the P-C coupling reactions have been published in a communication.[1]

Results and discussion

Our model reaction was the P–C coupling between bromoarenes and, in most cases, 1.5–1 equivalents of diethyl phosphite, alkyl phenyl-*H*-phosphinates and secondary phosphine oxides using $Pd(OAc)_2$ as the catalyst without any P-ligand and 1.1 equivalents of triethylamine as the base in the absence of any solvent on MW irradiation. The basic model was the coupling of diethyl phosphite with bromoarenes (Scheme 1).



Y = H (**a**), 4-MeO (**b**), 3-MeO (**c**), 4-Pr (**d**), 4-Et (**e**), 4-Me (**f**) 4-Cl (**g**), 3-Cl (**h**), 4-F (**i**), 3-F (**j**), 4-CO_2Et (**k**), 3-CO_2Et (**l**), 4-C(O)Me (**m**), 3-C(O)Me (**n**)

Scheme 1 P–C coupling reaction of bromoarenes with diethyl phosphite.

First, the reaction of diethyl phosphite (DEP) with bromobenzene was investigated. The coupling was complete in the presence of 5 mol% of $Pd(OAc)_2$ at 150 °C, after an irradiation of 5 min, and diethyl phenylphosphonate **1a** was obtained in a yield of 93% (Table 1, entry 1).[1] The comparative thermal reaction led to a conversion of only 47% (Table 1, entry 2).

Then, DEP was reacted with a series of substituted aryl bromides. Using 4-methoxybromobenzene at 150 °C in the presence of 5 mol% and 10 mol% $Pd(OAc)_2$, incomplete conversions of 57% and 67%, respectively, were observed and the compositions did not change on extending the reaction times of 10/5 min (Table 1, entries 3 and 4). A comparative thermal experiment carried out in the presence of 10 mol% of $Pd(OAc)_2$ at 150 °C for 5 min led to a conversion of only 38% (Table 1, entry 5), that was increased to 62% after a heating of 15 min, but than the conversion could not be increased further (Table 1, entry 6). Increasing the temperature to 175 °C and 200 °C, and applying reaction times of 5 min and 2 min, the conversions were 77% and 80%, respectively, and decomposition was observed on further irradiation (Table 1, entries 7 and 8). Hence, the last two experiments were the best giving diethyl arylphosphonates **1b** in yields of 66% and 69%, respectively (Table 1, entries 7 and 8). It is obvious that the 4-methoxybromobenzene is significantly less reactive in the reaction under discussion than bromobenzene. The 3-methoxybromobenzene was, however, somewhat more reactive than the 4-methoxy substituted analogue, as measuring in 10 mol% of the catalyst and applying conditions of 150 °C/5 min, 175 °C/5 min and 200 °C/2 min, the conversions were 78%, 81% and 93%, respectively (Table 1, entries 9–11). The preparative yield of 3-methoxyphenylphosphonate **1c** from the best experiment was 79% (Table 1, entry 11). At 150/175 °C, the conversions remained incomplete even on prolonged heating, while at 200 °C, decomposition was observed after a reaction time of 2 min. In the next experiments 4-alkyl substituted bromobenzenes were the model compounds in reaction with 1.5 equivalents of DEP. First, 4-propylbromobenzene was used as the starting material. Applying a combination of 150 °C/15 min, 175 °C/5 min and 200 °C/2 min in the presence of 10 mol% of $Pd(OAc)_2$, the conversions were 70%, 77% and 86%, respectively (Table 1, entries 12–14). The conversions were incomplete and the prolonged heating had a negative effect on the yield. From the best experiment, the 4-propylphenylphosphonate (**1d**) was isolated in a yield of 71% (Table 1, entry 14). In respect of the 4-ethyl- and 4-methylbromobenzenes, a reaction temperature of 175 °C seemed to be the optimum to afford products **1e** and **1f** in conversions of 93% and 86%, respectively, after reaction times of 15 min and 10 min, respectively (Table 1, entries 16 and 17). The 4-ethylphenylphosphonate (**1e**) was isolated in a yield of 85%, while the 4-methyl counterpart (**1f**) in a yield of 73% (Table 1, entries 16 and 17). It can be seen that the 4-alkyl substituted bromobenzenes are also less reactive than bromobenzene. Above 175 °C, the phosphonates with electron-donating substituents in the aromatic ring (*eg.* **1b-f**) were not entirely stable and decomposed partially to give the corresponding benzene derivative as a minor by-product.

The next experiments embraced the reactions of halogeno-substituted bromobenzenes. The coupling reactions of 4-chlorobromobenzene and the 3-chloro analogue were quite efficient in the presence of 10 mol% of the catalyst at 175 °C after an irradiation of 10 min, as chlorophenylphosphonates **1g** and **1h** were obtained in conversions of 95% for both cases, and in yields of 83% and 87%, respectively (Table 1, entries 18 and 20). At 150 °C, the conversion was lower (73%), while at 200 °C it remained practically the same (92%) as that detected at 175 °C (Table 1, entries 19 and 21). The fluoro-substituted bromobenzenes were the most efficient reagents after bromobenzene. Both the 4-fluoro- and the 3-fluorobromobenzene took part in a quantitative reaction with DEP in the presence of 5 mol% of $Pd(OAc)_2$ as the catalyst at 175 °C after a reaction time of 5 min and 10 min, respectively, to furnish fluorophenylphosphonates **1i** and **1j** in 91% and 88% yields, respectively (Table 1, entries 22 and 24). In respect of the 3-fluoro starting material, the coupling was incomplete at 150 °C for 5 min, while using more (10 mol%) of the catalyst, the shorter reaction time of 5 min was enough (Table 1, entries 23 and 25). It was a noteworthy observation that the coupling reaction of the bromo-function of the dihalogenobenzenes with the >P(O)H species was entirely selective, the chloro- and fluoro-moieties remained intact under the MW-assisted P-ligand-free and solvent-free conditions.

The next experiments involved a study with the ethyl 4- and 3-bromobenzoates. The 4-ethoxycarbonyl- and 3-(ethoxycarbonyl)bromobenzene could be involved in quite efficient couplings using 5 mol% of $Pd(OAc)_2$ at 175 °C for 15 min and 10 mol% of the catalyst at 200 °C for 2 min, respectively, to provide products **1k** and **1l** in yields of 89% and 81%, respectively (Table 1, entries 26 and 29). Regarding the reaction of ethyl 3-bromobenzoate, lower temperatures than 200 °C were less efficient (Table 1, entries 27 and 28). At 150 °C incomplete conversions occurred, while at 175 °C/200 °C decomposition of the product (**1l**) was observed (Table 1, entries 27–29). It can be seen that the ethyl bromobenzoates are less reactive than bromobenzene.

Finally, the 4- and 3-bromoacetophenones were tested. The coupling reaction of 4-bromoacetophenone with DEP was complete using 5 mol% of $Pd(OAc)_2$ at 175 °C for 5 min, but a

partial dehalogenation of the starting material was also observed (Table 1, entry 30). At the same time, the reaction of the 3-bromoacetophenone took place quantitatively in the presence of 10 mol% of catalyst at 175 °C after 5 min, or applying 5 mol% of catalyst at 200 °C after 2 min (Table 1/Entries 33 and 34). At 150 °C/15 min in the presence of 10 mol% of $Pd(OAc)_2$, or 175 °C/10 min using 5 mol% of the catalyst, the conversions were 76% and 81%, respectively (Table 1, entries 31 and 32). The 3-acetylbromobenzene was found to reveal a comparable reactivity with that of the 4 bromobenzoate.

Table 1 P–C coupling reaction of bromoarenes with diethyl phosphite

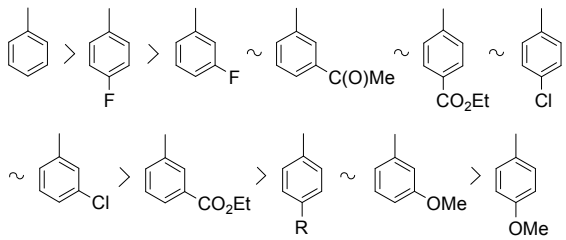
Entry	Y	$Pd(OAc)_2$ (%)	T (°C)	t (min)	Mode of heating	Conversion[a] (%)	Yield (%)	Ref.
1	H	5	150	5	MW	99	93 (**1a**)	1
2	H	5	150	5	Δ[c]	47	27 (**1a**)	
3	4-MeO[b]	5	150	10	MW	57[d,e]	50	
4	4-MeO	10	150	5	MW	67[d,e]	56	
5	4-MeO	10	150	5	Δ[c]	38[d]	30	
6	4-MeO	10	150	15	Δ[c]	62[e]	53	
7	4-MeO	10	175	5	MW	77[d,f]	66	
8	4-MeO	10	200[g]	2	MW	80[f]	69 (**1b**)	
9	3-MeO[b]	10	150	5	MW	78[e]		
10	3-MeO	10	175	5	MW	81[e]	73	
11	3-MeO	10	200[g]	2	MW	93[f]	79 (**1c**)	
12	4-Pr	10	150	15	MW	70		
13	4-Pr	10	175	5	MW	77[f]		
14	4-Pr	10	200[g]	2	MW	86[f]	71 (**1d**)	
15	4-Et	10	150	15	MW	61		
16	4-Et	10	175	15	MW	93[f]	85 (**1e**)	
17	4-Me	10	175	10	MW	86[f]	73 (**1f**)	1
18	4-Cl	10	175	10	MW	95	83 (**1g**)	1
19	3-Cl	10	150	10	MW	73[e]		
20	3-Cl	10	175	10	MW	95	87 (**1h**)	
21	3-Cl	10	200[g]	2	MW	92		
22	4-F	5	175	5	MW	99	91 (**1i**)	1
23	3-F	5	150	5	MW	70		
24	3-F	5	175	10	MW	100	88 (**1j**)	
25	3-F	10	175	5	MW	95		
26	4-CO_2Et	5	175	15	MW	100	89 (**1k**)	1
27	3-CO_2Et	10	150	15	MW	66[e]		
28	3-CO_2Et	10	175	5	MW	83[f]	74	
29	3-CO_2Et	10	200[g]	2	MW	93[f]	81 (**1l**)	
30	4-C(O)Me	5	175	5	MW	96[h]	71 (**1m**)	1
31	3-C(O)Me	10	150	15	MW	76		
32	3-C(O)Me	5	175	10	MW	81		
33	3-C(O)Me	10	175	5	MW	100	92	
34	3-C(O)Me	5	200[g]	2	MW	100	89 (**1n**)	

[a] On the basis of GC analysis $\left(\text{conversion} = \frac{I_{(EtO)_2P(O)Ar}}{I_{(EtO)_2P(O)Ar} + I_{ArBr}}\right)$. [b] In this case 3 equiv. DEP were used. [c] Conventional heating. [d] Average of two reactions. The deviation is ±1.5%. [e] No change on further irradiation. [f] On further irradiation, the product decomposed. [g] Quasi-isothermal reaction. [h] The starting material was partially.

It is worthy to mention that the reaction mixtures formed a homogeneous liquid phase. Due to the stirring, there could not have been a temperature gradient in the mixtures.

It was found that the addition of 10 mol% of PPh_3 (1 equivalent to the catalyst) to the reaction mixture was without any effect. Repeating the experiment marked by entry 4 of Table 1 in the presence of PPh_3, the yield of arylphosphonate **1b** was 57%.

It can be seen that with the exception of 4-methoxybromobenzene, all bromoarenes investigated could be converted into the corresponding diethyl arylphosphonates (**1**) in conversions ≥ 86%, although the optimum conditions were somewhat different. The overall reactivity of the aromatic substrates was the following:



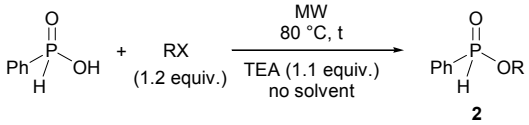
One may conclude that the presence of substituents in general decreases the reactivity of the bromoarenes and that electron-donating (methoxy and alkyl) substituents have a more significant effect in this respect than electron-withdrawing (halogeno, acetyl and ethoxycarbonyl) substituents. In the case of electron-donating substituents, the conversions were incomplete and the best yields

were 69–85%. 4-Methoxybromobenzene revealed the lowest reactivity among the aromatic substrates used.

The main message of our finding is that, first in the literature, the Hirao reaction of bromoarenes could be performed in the presence of P-ligand-free $Pd(OAc)_2$ that now proved to be general for a wide variety of substituted bromobenzenes. This was possible only under MW irradiation, as shown by the result of comparative thermal experiments. Moreover, our procedure can be carried out under solvent-free conditions. The explanation for the beneficial influence of MW irradiation may be that the statistically occurring local overheating effect promotes the P-C coupling in the absence of P-ligands.[33] This experience augments the number of cases, when MW irradiation simplifies the realization of catalytic reactions.[4,26–32]

From among the diethyl arylphosphonates (**1a-n**) synthesized, **1a-c**, **1e-g**, **1i-k**, **1m** and **1n** prepared are known compounds.[1,3,34–39] All arylphosphonates (**1**) were characterized by ^{31}P, ^{13}C ,^{1}H NMR, and HR-MS.

In the next part of our work, we wished to utilize alkyl phenyl-*H*-phosphinates in the Hirao reaction. First we had to prepare the phenylphosphinates (**2**). This was done essentially on the basis of our previous method involving the alkylating esterification of phosphinic acids under MW- and solvent-free conditions.[40,41] According to this, phenyl-*H*-phosphinic acid was reacted with alkyl halides in the presence of triethylamine at 80 °C for 5–15 min with MW irradiation without the use of any solvent (Scheme 2, Table 2). In our original procedure, K_2CO_3 was used as the base together with a phase transfer catalyst.[40,41] Now, triethylamine was applied in a homogeneous medium for the synthesis of never representatives.



RX = EtI (**a**), ^{n}PrBr (**b**), ^{i}PrBr (**c**), ^{n}BuBr (**d**), ^{i}BuBr (**e**), ^{i}PentBr (**f**)

Scheme 2 Alkylating esterification of phenyl-*H*-phosphinic acid with alkyl halides.

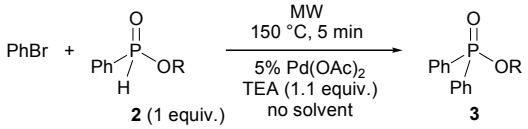
Table 2 Alkylating esterification of phenyl-*H*-phosphinic acid with alkyl halides

Entry	RX	t (min)	Mode of heating	Yield (%)
1	EtI	5	MW	97 (**2a**)
2	^{n}PrBr	12	MW	94 (**2b**)
3	^{i}PrBr	15	MW	76 (**2c**)
4	^{i}PrBr	15	Δ[a]	26 (**2c**)
5	^{i}PrBr	30	Δ[a]	53 (**2c**)
6	^{n}BuBr	15	MW	96 (**2d**)
7	^{n}BuBr	15	Δ[a]	69 (**2d**)
8	^{n}BuBr	30	Δ[a]	94 (**2d**)
9	^{i}BuBr	15	MW	79 (**2e**)
10	^{i}PentBr	15	MW	91 (**2f**)

[a] Conventional heating.

One may see from Table 2 that using ethyl iodide, *n*-propyl bromide, isopropyl bromide, *n*-butyl bromide, isobutyl bromide and isopentyl bromide, the corresponding alkyl phenyl-*H*-phosphinates (**2a-f**) were obtained in yields of 76–97% after flash column chromatography. In these *O*-alkylation reactions the effect of MW is noteworthy, if the results are compared with those of the comparative thermal experiments. In the alkylation with isopropyl bromide at 80 °C for 15 min, the MW-assisted reaction gave phenylphosphinate **2c** in a yield of 76% (Table 2, entry 3). As the same time, the outcome of the comparative thermal experiment was only 26% (Table 2, entry 4). Increasing the reaction time to 30 min, the yield was doubled (53%) Table 2, entry 5). In the alkylation with butyl bromide, the effect of MW was also considerable, but after a prolonged reaction time, almost the same yield (94%) could be achieved on conventional heating, as that in the MW variation (96%) (Table 2, entries 6–8). From among the *H*-phosphinates (**2a-e**) prepared, the isopentyl ester (**2f**) was new.

Then, the alkyl phenyl-*H*-phosphinates **2a-f** were tested in reaction with bromobenzene at 150 °C using 5 mol% $Pd(OAc)_2$ as the catalyst and triethylamine as the base under solvent-free conditions (Scheme 3, Table 3).



R = Et (**a**), ^{n}Pr (**b**), ^{i}Pr (**c**), ^{n}Bu (**d**), ^{i}Bu (**e**), ^{i}Pent (**f**)

Scheme 3 P–C coupling reaction of alkyl phenyl-*H*-phosphinates (**2a-f**) with bromobenzene.

Table 3 P–C coupling reaction of alkyl phenyl-*H*-phosphinates (**2a-f**) with bromobenzene

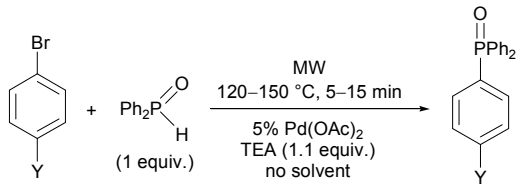
Entry	R	Yield (%)
1	Et	85 (**3a**)
2	^{n}Pr	91 (**3b**)
3	^{i}Pr	68 (**3c**)
4	^{n}Bu	87 (**3d**)
5	^{i}Bu	76 (**3e**)
6	^{i}Pent	92 (**3f**)

The P–C couplings were complete after a 5 min reaction time. Flash chromatography afforded alkyl diphenylphosphinates **3a**, **3b** and **3d-f** in yields of 76–92% (Table 3, entries 1, 2, 4–6). The sterically hindered isopropyl derivative (**3c**) was obtained only in a yield of 68% (Table 3, entry 3).

It can be seen, that the alkyl phenyl-*H*-phosphinates (with the exception of the isopropyl derivative **3c**) were as reactive, as dialkyl phosphites in the $Pd(OAc)_2$-catalyzed, P-ligand-free Hirao reaction with bromobenzene. Hence, the P-ligand-free coupling seems to be rather general.

Most of the alkyl diphenylphosphinates (**3a**, **3c**, **3d** and **3f**) prepared have been described in the literature.[1,42–47] All phosphinates (**3a-f**) were identified by ^{31}P, ^{13}C, ^{1}H NMR, and HR-MS.

As another extension, the coupling of diphenylphosphine oxide with bromobenzene and a few 4-substituted derivatives was also investigated under the standard conditions applied above (Scheme 4). Due to the enhanced reactivity of $Ph_2P(O)H$, the reactions were complete at 120 °C after 15 min, or, using bromobenzene, at 150 °C within 5 min, to afford aryldiphenylphosphine oxides (**4a-d**) in yields of 83-90% (Table 4). All aryldiphenylphosphine oxides (**4a-d**) have been known from the literature.[48–51]



Scheme 4 P–C coupling reaction of diphenylphosphine oxide with bromoarenes.

Table 4 P–C coupling reaction of diphenylphosphine oxide with bromoarenes

Entry	Y	T (°C)	t (min)	Yield (%)
1	H	120	15	90 (**4a**)
2	H	150	<5	88 (**4a**)
3	4-Me	150	5	83 (**4b**)
4	4-Cl	150	5	89 (**4c**)
5	4-F	150	5	87 (**4d**)

Finally, a few dialkylphenylphosphine oxides (**6a-c**) were synthesized by the reaction of dialkylphosphine oxides (**5a-c**) with bromobenzene under the conditions of the P-ligand-free Hirao reaction at 175 °C. It was advantageous to use acetonitrile as the solvent to avoid the decomposition observed under solvent-free conditions. Using acetonitrile, completion of the reactions required 1.5 h.

Scheme 5 P–C coupling of dialkylphosphine oxides (**5a-c**) with bromobenzene.

This series of couplings proves the more general value of the P-ligand-free P–C coupling reaction developed by us.

It is noted that the starting secondary phosphines oxides (**5a-c**)[52–55] were also prepared by us.

The dialkylphenylphosphine oxides (**6a-c**)[56–59] prepared are known compounds.

The most striking feature of the newer developments of our work is the broad scope of the possible applications of the new method, since an impressive range of >P(O)H reagents could be used with similar efficiencies. It can be said that the hydrogen atom on the P=O moiety of diphenylphosphine oxide is significantly more acidic, than the similar proton in diethyl phosphite, as suggested by the pK_a values of 14.5 (predicted by the program Marvin Sketch, Version 5.4.1.1) and 20.8,[60] respectively. At the same time, the acidity of the P-*H* of dialkylphosphine oxides is comparable with that of diethyl phosphite or in general dialkyl phosphites. However, the acidity of the P-*H* has not much role in the efficiency of the couplings studied.

In conclusion, the first P-ligand-free accomplishment of the Hirao reaction has been developed and extended to the synthesis of a wider range of derivatives, such as diethyl arylphosphonates, alkyl diphenylphosphinates and different tertiary phosphine oxides demonstrating the general value of the MW-assisted, P-ligand-free and, in almost all cases, solvent-free conditions for this reaction. The omission of the P-ligand in the Pd-catalyzed Hirao coupling under MW conditions means an enormous advantage from the point of view environmentally friendly conditions and costs. It can be expected that this novel method will have further impact on the development of P-ligand-free methodologies including also other model compounds, such as, among others, (2-bromovinyl)benzenes.

Experimental

General

The reactions were carried out in a 300W CEM Discover focused microwave reactor equipped with a pressure controller applying 30–50 W under isothermal conditions. Standard 5 mL glass reaction vessels were used distributed by the supplier of the CEM reactor, and the reaction mixtures were stirred magnetically.

The ^{13}C and ^{1}H NMR spectra were obtained in $CDCl_3$ solution on a Bruker DRX-500 spectrometer operating at 125.7, and 500.1 MHz, respectively. The ^{13}C and ^{1}H chemical shifts are referred to TMS. ^{31}P NMR spectra were obtained on a Bruker AV-300 spectrometer. Chemical shifts are downfield relative to 85% H_3PO_4. Mass spectrometry was performed on a ZAB-2SEQ instrument.

1.) Synthesis of the non-commercial starting materials

1.1.) General procedure for the preparation alkyl-phenyl-*H*-phosphinates

To phenyl-*H*-phosphinic acid (0.28 g, 2.0 mmol) was added the alkyl bromide (2.4 mmol: 0.19 mL of ethyl iodide, 0.22 mL of propyl bromide, 0.23 mL of isopropyl bromide, 0.26 mL of butyl bromide, 0.26 mL of isobutyl bromide or 0.29 mL of isopentyl bromide) and TEA (0.31 mL, 2.2 mmol) and the resulting mixture was irradiated in a closed vial in the microwave reactor at 80 °C for the time shown in Table **2**. The reaction mixture was passed through a thin (*ca.* 1–1.5 cm) layer of silica gel using ethyl acetate as the eluent. The products (**2a-f**) were obtained as colourless oils.

Selected spectral data for alkyl phenyl-*H*-phosphinates

Entry	Product	δ_P ($CDCl_3$) (ppm)	δ[46] (ppm)	$[M+H]^+_{found}$	$[M+H]^+_{requires}$
1	**2a**	22.7	24.7	171.0575	171.0575
2	**2b**	25.7	24.9	185.0733	185.0731
3	**2c**	20.6	22.3	185.0733	185.7310
4	**2d**	25.1	24.9	199.0888	199.0888
5	**2e**	25.7	25.0	199.0887	199.0888

Isopentyl phenyl-*H*-phosphinate (2f): ^{31}P NMR ($CDCl_3$) δ 24.9; ^{13}C NMR ($CDCl_3$) δ 22.4 (CH_3), 24.6 (CH), 39.2 (d, J = 6.4, OCH_2CH_2), 64.5 (d, J = 6.6, OCH_2), 128.8 (d, J = 13.8, C_2)*, 130.0 (d, J = 132.1, C_1), 130.9 (d, J = 11.8, C_3)*, 133.1 (d, J = 2.9, C_4), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 6H, J = 6.1, 2×CH_3), 1.50–1.61 (m, 2H, OCH_2CH_2), 1.62–1.79 (m, 1H, CH), 4.00–4.15 (m, 2H, OCH_2), 7.54 (d, 1H, J = 562.5, P–H), 7.41–7.61 (m, 3H, ArH), 7.69–7.80 (m, 2H, ArH); $[M+H]^+$ = 213.1042, $C_{11}H_{18}O_2P$ requires 213.1044.

1.2.) General procedure for the preparation of the dialkylphosphine oxides (5a-c)

The Grignard reagent (40.0 mmol) formed from (0.97 g ,40.0 mmol) of magnesium and alkyl halide (40.0 mmol: 3.6 mL of bromopropane, 4.2 mL chlorobutane or 4.6 mL of benzyl chloride) in diethyl ether (50 mL) was added dropwise to the diethyl phosphite (1.7 ml, 13.0 mmol) in diethyl ether (10 mL) at 0°C. The resulting mixture was stirred at 26 °C for 1.5 hours. The mixture was hydrolyzed with 10% HCl solution (40 mL) and the aqueous phase was extracted with diethyl ether (2×50 mL). The combined organic phases were dried (Na_2SO_4). Evaporation of the solvent provided a residue that was purified by column chromatography using silica gel, 1% methanol in dichloromethane as the eluent to give products **5a-c** as white crystals.

Dipropylphosphine Oxide (5a): Yield: 71%; white crystals; mp.: 47–48 °C, mp.[52]: 48–50 °C; ^{31}P NMR ($CDCl_3$) δ 35.3, δ_P ($CDCl_3$)[53] 32.5; $[M+H]^+$ = 135.0930, $C_6H_{16}OP$ requires 135.0933.

Dibutylphosphine Oxide (5b): Yield: 65%; white crystals; mp.: 55–56 °C, mp.[54]: 55–56 °C; ^{31}P NMR ($CDCl_3$) δ 33.9, δ_P ($CDCl_3$)[54] 36.09; $[M+H]^+$ = 163.1249, $C_8H_{20}OP$ requires 163.1246.

Dibenzylphosphine Oxide (5c): Yield: 78%; white crystals; mp.: 109–110 °C, mp.[55]: 106–107 °C; ^{31}P NMR ($CDCl_3$) δ 36.2, δ_P ($CDCl_3$)[55] 35.5; $[M+H]^+$ = 231.0937, $C_{14}H_{16}OP$ requires 231.0933.

2.) General procedures for P–C couplings

2.1.) General procedure for the reaction of bromoarenes and diethyl phosphite

To the bromoarene (2.0 mmol: 0.21 mL of bromobenzene, 0.25 mL of 4-bromoanisole, 0.25 mL of 3-bromoanisole, 0.31 mL of 4-propyl bromobenzene, 0.28 mL of 4-ethyl bromobenzene, 0.34 g of 4-bromotoluene, 0.38 g of 4-bromo-chlorobenzene, 0.24 mL of 3-bromo-chlorobenzene, 0.22 mL of 4-bromo-fluorobenzene, 0.22 mL of 3-bromo-fluorobenzene, 0.32 mL of ethyl 4-bromobenzoate, 0.32 mL of 3 ethyl 3-bromobenzoate, 0.40 g of 4-bromoacetophenone and 0.26 mL of 3-bromoacetophenone) was added diethyl phosphite 0.39 mL (3.0 mmol) [or in the case of 4-bromoanisole, diethyl phosphite (6.0 mmol, 0.79 mL)] triethylamine (0.31 mL, 2.2 mmol) and palladium acetate (0.022 g, 0.10 mmol or 0.044 g, 0.20 mmol – see Table 1.) and the resulting mixture was irradiated in a closed vial in the microwave reactor at the temperature and for the time shown in Table 1. The reaction mixture was passed through a thin (*ca.* 1.5–2 cm) layer of silica gel using ethyl acetate as the eluent. The products **1a-n** were obtained as colourless oils.

Diethyl 4-methoxyphenylphosphonate (1b): ^{31}P NMR ($CDCl_3$) δ 19.8, δ_P ($CDCl_3$)[34] 18.8; ^{13}C NMR ($CDCl_3$) δ 16.3 (d, J = 6.6, CH_2CH_3), 55.3 (OCH_3), 62.9 (d, J = 5.3, OCH_2), 114.0 (d, J = 16.0, C_2)*, 119.6 (d, J = 194.9, C_1), 133.8 (d, J = 11.4, C_3)*, 162.8 (d, J = 3.3, C_4), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 1.31 (t, 6H, J = 7.0, CH_3), 3.83 (OCH_3), 3.96–4.21 (m, 4H, OCH_2), 6.89–7.02 (m, 2H, ArH), 7.65–7.85 (m, 2H, ArH); $[M+H]^+$ = 245.0945, $C_{11}H_{18}O_4P$ requires 245.0943.

Diethyl 3-methoxyphenylphosphonate (1c): ^{31}P NMR ($CDCl_3$) δ 18.8; δ_P ($CDCl_3$)[35] 18.7; ^{13}C NMR ($CDCl_3$) δ 16.3 (d, J = 6.5, CH_2CH_3), 55.4 (OCH_3), 62.2 (d, J = 5.4, OCH_2), 116.4 (d, J = 11.4, C_2), 118.8 (d, J = 3.2, C_4), 124.0 (d, J = 9.2, C_6), 129.6 (d, J = 186.8, C_1), 129.8 (d, J = 17.6, C_5), 159.5 (d, J = 18.9, C_3); ^{1}H NMR ($CDCl_3$) δ 1.30 (t, 6H, J = 7.1, CH_3), 3.82 (OCH_3), 3.96–4.20 (m, 4H, OCH_2), 7.00–7.10 (m, 1H, ArH), 7.26–7.41 (m, 3H, ArH); $[M+H]^+$ = 245.0939, $C_{11}H_{18}O_4P$ requires 245.0943.

Diethyl 4-propylphenylphosphonate (1d): ^{31}P NMR ($CDCl_3$) δ 20.5; ^{13}C NMR ($CDCl_3$) δ 13.8 ($CH_2CH_2CH_3$), 16.4 (d, J = 6.5, CH_2CH_3), 24.3 (C_4–CH_2CH_2), 38.1 (C_4–CH_2), 62.0 (d, J = 5.4, OCH_2), 125.4 (d, J = 189.9, C_1), 128.7 (d, J = 15.4, C_2)*, 131.9 (d, J = 10.3, C_3)*, 147.6 (d, J = 3.1, C_1), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 0.95 (t, 3H, J = 7.3, $CH_2CH_2CH_3$), 1.32 (t, 6H, J = 7.0, OH_2CH_3), 1.57–1.75 (m, 2H, C_4–CH_2CH_2), 2.63 (t, 2H, J = 7.6, C_4–CH_2), 4.00–4.23 (m, 4H, OCH_2), 7.23–7.30 (m, 2H, ArH), 7.65–7.78 (m, 2H, ArH); $[M+H]^+$ = 257.1302, $C_{13}H_{22}O_3P$ requires 257.1301.

Diethyl 4-ethylphenylphosphonate (1e): ^{31}P NMR ($CDCl_3$) δ 19.6, δ_P (MeOH)[3] 19.4; ^{13}C NMR ($CDCl_3$) δ 15.2 (C_4–CH_2CH_3), 16.4 (d, J = 6.5, OCH_2CH_3), 24.3 (C_4–CH_2CH_3), 61.0 (d, J = 5.3, OCH_2), 125.3 (d, J = 190.0, C_1), 128.1 (d, J = 15.4, C_2)*, 131.9 (d, J = 10.3, C_3)*, 149.1 (d, J = 3.1, C_4), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 1.24 (t, 3H, J = 7.6, C_4–CH_2CH_3), 1.30 (t, 6H, J = 7.0, OH_2CH_3), 2.68 (q, 2H, J = 7.6, C_4–CH_2), 3.97–4.20 (m, 4H, OCH_2), 7.21–7.35 (m, 2H, ArH), 7.64–7.80 (m, 2H, ArH); $[M+H]^+$ = 243.1146, $C_{12}H_{20}O_3P$ requires 243.1145.

Diethyl 3-chlorophenylphosphonate (1h): ^{31}P NMR ($CDCl_3$) δ 17.5; ^{13}C NMR ($CDCl_3$) δ 16.2 (d, J = 6.4, CH_3), 62.3 (d, J = 5.5, CH_2), 129.69 (d, J = 9.2, C_5), 129.74 (d, J = 16.3, C_6), 130.7 (d, J = 187.9, C_1), 131.6 (d, J = 10.7, C_3), 132.4 (d, J = 3.0, C_4), 134.7 (d, J = 20.3, C_2); ^{1}H NMR ($CDCl_3$) δ 1.30 (t, 6H, J = 7.1, CH_3), 3.96–4.20 (m, 4H, OCH_2), 7.40–7.31 (m, 1H, ArH), 7.43–7.51 (m, 1H, ArH), 7.59–7.81 (m, 2H, ArH); $[M+H]^+$ = 249.0448, $C_{10}H_{15}O_3P^{35}Cl$ requires 249.0447.

Diethyl 3-fluorophenylphosphonate (1j): ^{31}P NMR ($CDCl_3$) δ 16.7 (d, J = 8.7); δ_P ($CDCl_3$)[37] 17.4; ^{13}C NMR ($CDCl_3$) δ 16.3 (d, J_1 = 6.4, CH_3), 62.4 (d, J_1 = 5.5, CH_2), 118.6 (dd, J_1 = 10.5, J_2 = 22.3, C_2), 119.5 (dd, J_1 = 3.1, J_2 = 21.1, C_4), 127.5 (dd, J_1 = 9.2, J_2 = 3.3, C_6), 130.5 (dd, J_1 = 17.5, J_2 = 7.5, C_5), 131.0 (dd, J_1 = 188.9, J_2 = 6.2, C_1), 162.4 (dd, J_1 = 21.4, J_2 = 249.4, C_3); ^{1}H NMR ($CDCl_3$) δ 1.29 (t, 6H, J = 7.0, CH_3), 3.99–4.20 (m, 4H, OCH_2), 7.13–7.23 (m, 1H, ArH), 7.33–7.60 (m, 3H, ArH); $[M+H]^+$ = 233.0743, $C_{10}H_{15}O_3PF$ requires 233.0743.

Diethyl 3-ethoxycarbonylphenylphosphonate (1l): ^{31}P NMR ($CDCl_3$) δ 17.4; ^{13}C NMR ($CDCl_3$) δ 14.4 ($COCH_2CH_3$), 16.4 (d, J = 6.4, $POCH_2CH_3$), 61.4 ($COCH_2$), 62.4 (d, J = 5.5, $POCH_2$), 128.7 (d, J = 15.0, C_2), 129.3 (d, J = 189.7, C_1), 130.9 (d, J = 15.1, C_6), 132.8 (d, J = 10.9, C_5), 133.3 (d, J = 3.0, C_4), 135.9 (d, J = 10.0, C_3), 165.7 (d, J = 2.2, C=O); ^{1}H NMR ($CDCl_3$) δ 1.33 (t, 6H, J = 7.1, $POCH_2CH_3$), 1.40 (t, 3H, J = 7.1, $COCH_2CH_3$), 4.00–4.28 (m, 4H, $POCH_2$), 4.35–4.46 (m, 2H, $COCH_2$), 7.49–7.60 (m, 1H, ArH), 7.94–8.08 (m, 1H, ArH), 8.22 (d, 1H, J = 7.8, C_4–H), 8.46 (d, 1H, J = 13.8, C_2–H), $[M+H]^+$ = 287.1048, $C_{13}H_{20}O_5P$ requires 287.1048.

Diethyl 3-acetylphenylphosphonate (1n): ^{31}P NMR ($CDCl_3$) δ 18.1, δ_P ($CDCl_3$)[39] 18.1; ^{13}C NMR ($CDCl_3$) δ 16.4 (d, J = 6.4, CH_2CH_3), 26.0 ($C(O)CH_3$), 62.4 (d, J = 5.6, OCH_2), 129.0 (d, J = 14.8, C_6), 129.5 (d, J = 189.4, C_1), 131.7 (d, J = 10.6 C_5), 131.9 (d, J = 3.0, C_4), 136.0 (d, J = 10.0, C_3), 137.2 (d, J = 13.9, C_2),

197.2 (d, J = 1.4, C=O); ^{1}H NMR ($CDCl_3$) δ 1.35 (t, 6H, J = 7.0, CH_2CH_3), 2.65 (3H, $C(O)CH_3$), 4.07–4.28 (m, 4H, OCH_2), 7.55–7.66 (m, 1H, ArH), 7.94–8.03 (m, 1H, ArH), 8.15 (d, 1H, J = 7.5, C_4–H), 8.38 (d, 1H, J = 13.8, C_2-H); $[M+H]^+$ = 257.0943, $C_{12}H_{18}O_4P$ requires 257.0943.

2.2.) General procedure for the reaction of bromobenzene and alkyl phenyl-*H*-phosphinates (2a-f)

To the bromobenzene (0.11 mL, 1.0 mmol) was added alkyl phenyl-*H*-phosphinate [1.0 mmol: 0.15 mL of ethyl phenylphosphinate (**2a**), 0.17 mL of propyl phenylphosphinate (**2b**), 0.17 mL of isopropyl phenylphosphinate (**2c**), 0.18 mL of butyl phenylphosphinate (**2d**), 0.19 mL of isobutyl phenylphosphinate (**2e**), 0.21 g isopentyl phenylphosphinate (**2f**)], triethylamine (0.16 mL, 1.1 mmol)) and $Pd(OAc)_2$ (0.011 g, 0.05 mmol) and the resulting mixture was irradiated by microwave as above (2.1) at 150 °C for 5 min. The mixture was purified as above using hexane - ethyl acetate 1:1 as the eluent. The products (**3a-f**) were obtained as white crystals.

Ethyl diphenylphosphinate (3a): white crystals; mp.: 43–44 °C, mp.[42]: 39–41 °C, ^{31}P NMR ($CDCl_3$) δ 32.2, δ_P ($CDCl_3$)[43] 31.5; ^{13}C NMR ($CDCl_3$) δ 16.5 (d, J = 6.6, CH_3), 61.1 (d, J = 5.9, OCH_2), 128.4 (d, J = 13.1, C_2)*, 131.6 (d, J = 10.1, C_3)*, 131.7 (d, J = 137.0, C_1), 132.0 (d, J = 2.8, C_4), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 1.36 (t, 3H, J = 7.1, CH_3), 4.01–4.16 (m, 2H, OCH_2), 7.39–7.58 (m, 6H, ArH), 7.75–7.88 (m, 4H, ArH); $[M+H]^+$ = 247.0888, $C_{14}H_{16}O_2P$ requires 247.0888.

Propyl diphenylphosphinate (3b): white crystals; mp.: 92–93 °C, mp.[44]: 89–91 °C; ^{31}P NMR ($CDCl_3$) δ 33.5; ^{13}C NMR ($CDCl_3$) δ 10.3 (CH_2CH_3), 24.0 (d, J = 6.7, OCH_2CH_2), 66.4 (d, J = 6.1, OCH_2), 128.6 (d, J = 13.1, C_2)*, 131.7 (d, J = 10.1, C_3)*, 131.8 (d, J = 137.2, C_1), 132.2 (d, J = 2.8, C_4), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 0.94 (t, 3H, J = 7.4, CH_3), 1.71–1.80 (m, 2H, OCH_2CH_2), 3.99 (q, 2H, J = 6.7, OCH_2), 7.39–7.53 (m, 6H, ArH), 7.79–7.88 (m, 4H, ArH); $[M+H]^+$ = 261.1040, $C_{15}H_{18}O_2P$ requires 261.1039.

Isopropyl diphenylphosphinate (3c): white crystals; mp.: 101–102 °C, mp.[43]: 98–100 °C; ^{31}P NMR ($CDCl_3$) δ 30.0, δ_P ($CDCl_3$)[43] 31.4; ^{13}C NMR ($CDCl_3$) δ 24.4 (d, J = 4.2, CH_3), 70.3 (d, J = 6.0, OCH), 128.5 (d, J = 13.1, C_2)*, 131.7 (d, J = 10.1, C_3)*, 132.0 (d, J = 2.8, C_4), 132.4 (d, J = 137.3, C_1), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 1.34 (d, 6H, J = 6.1, CH_3), 4.57–4.74 (m, 1H, OCH), 7.36–7.56 (m, 6H, ArH), 7.75–7.90 (m, 4H, ArH); $[M+H]^+$ = 261.1040, $C_{15}H_{18}O_2P$ requires 261.1039.

Butyl diphenylphosphinate (3d): white crystals; mp.: 95–96 °C, mp.[45]: 90–92 °C; ^{31}P NMR ($CDCl_3$) δ 31.2, δ_P ($CDCl_3$)[46] 31.2; ^{13}C NMR ($CDCl_3$) δ 13.7 (CH_3), 18.9 (CH_2CH_3), 32.7 (d, J = 6.6, OCH_2CH_2), 64.8 (d, J = 6.1, OCH), 128.5 (d, J = 13.1, C_2)*, 131.7 (d, J = 10.1, C_3)*, 131.8 (d, J = 2.8, C_4), 132.1 (d, J = 137.0, C_1), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, 3H, J = 7.3, CH_3), 1.35–1.55 (d, 2H, CH_2CH_3), 1.62–1.80 (m, 2H, OCH_2CH_2), 4.03 (t, 2H, J = 6.6, OCH_2), 7.35–7.61 (m, 6H, ArH), 7.71–7.94 (m, 4H, ArH); $[M+H]^+$ = 275.1196, $C_{16}H_{20}O_2P$ requires 275.1195.

Isobutyl diphenylphosphinate (3e): white crystals; mp.: 82–83 °C, mp.[44]: 79–80 °C; ^{31}P NMR ($CDCl_3$) δ 31.0; ^{13}C NMR ($CDCl_3$) δ 19.0 (CH_3), 29.4 (d, J = 6.9, CH), 70.9 (d, J = 6.3, OCH_2), 128.6 (d, J = 13.1, C_2)*, 131.8 (d, J = 10.1, C_3)*, 131.9 (d, J = 2.8, C_4), 132.2 (d, J = 137.2, C_1), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 0.96 (d, 6H, J = 6.7, CH_3), 1.89–2.07 (m, 1H, CH), 3.78 (t, 2H, J = 6.3, OCH_2), 7.34–7.56 (m, 6H, ArH), 7.65–7.88 (m, 4H, ArH); $[M+H]^+$ = 275.1197, $C_{16}H_{20}O_2P$ requires 275.1195.

Isopentyl diphenylphosphinate (3f): white crystals; mp.: 55–56 °C, mp.[47]: 55–57 °C; ^{31}P NMR ($CDCl_3$) δ 31.2, δ_P ($CDCl_3$)[47] 30.1; ^{13}C NMR ($CDCl_3$) δ 22.3 (CH_3), 24.6 (CH), 39.2 (d, J = 6.6, OCH_2CH_2), 63.4 (d, J = 6.1, OCH_2), 128.4 (d, J = 13.1, C_2)*, 131.5 (d, J = 10.1, C_3)*, 131.6 (d, J = 137.0, C_1), 132.0 (d, J = 2.8, C_4), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 0.88 (d, 6H, J = 6.5, CH_3), 1.60 (q, 2H, J = 6.7, OCH_2CH_2), 1.68–1.85 (m, 1H, CH), 4.04 (q, 2H, J = 6.5, OCH_2), 7.34–7.56 (m, 6H, ArH), 7.65–7.85 (m, 4H, ArH); $[M+H]^+$ = 289.1353, $C_{17}H_{22}O_2P$ requires 289.1352.

2.3.) General procedure for the reaction of secondary phosphine oxides with bromoarenes

The tertiary phosphine oxides (**4a-d** and **6a-c**) were prepared from the corresponding bromoarene (2.0 mmol: 0.21 mL of bromobenzene, 0.34 g of 4-bromotoluene, 0.38 g 4-bromo-chlorobenzene and 0.22 mL 4-bromo-fluorobenzene) and the secondary phosphine oxide [2.0 mmol: 0.40 g of diphenylphosphine oxide, 0.27 g of dipropylphosphine oxide (**5a**), 0.32 g of dibutylphosphine oxide (**5b**) and 0.46 g of dibenzylphosphine oxide (**5c**)] [in the case of dialkylphosphine oxides in acetonitrile (1 ml)], as above (2.1). The only difference is that, in the case of dialkylphosphine oxides (**5a-c**), the solvent was removed after the reaction. The products **4a-d** and **6a-c** were obtained as white or pale yellow crystals.

Triphenylphosphine Oxide (4a): white crystals; mp.: 156–157 °C, mp.[48]: 156–157 °C; ^{31}P NMR ($CDCl_3$) δ 30.6, δ_P ($CDCl_3$)[48] 29.5.

4-Methylphenyl diphenylphosphine Oxide (4b): white crystals; mp.: 118–119 °C, mp.[49]: 119–123°C; ^{31}P NMR ($CDCl_3$) δ 29.3, δ_P ($CDCl_3$)[49] 29.1; ^{13}C NMR ($CDCl_3$) δ 21.6 (CH_3), 128.4 (d, J = 12.1, C_2')[a], 129.1 (d, J = 106.4, C_1), 129.2 (d, J = 12.6, C_2)[b], 131.8 (d, J = 2.7, C_4'), 132.0 (d, J = 9.9, C_3')[a], 132.1 (d, J = 10.2, C_3)[b], 132.8 (d, J = 105.9, C_1'), 142.4 (d, J = 2.8, C_4), [a,b]may be reversed; ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H, CH_3), 7.11–7.29 (m, 2H, ArH), 7.40–7.80 (m, 12H, ArH); $[M+H]^+$ = 293.1085, $C_{19}H_{18}OP$ requires 293.1090.

4-Chlorophenyl diphenylphenylphosphine Oxide (4c): pale yellow crystals; mp.: 142–143 °C, mp.[49]: 141–142 °C; ^{31}P NMR ($CDCl_3$) δ 28.5, δ_P ($CDCl_3$)[49] 28.8; ^{13}C NMR ($CDCl_3$) δ 128.6 (d, J = 12.2, C_2')[a], 128.8 (d, J = 12.7, C_2)[b], 131.1 (d, J = 104.7, C_1), 131.96 (d, J = 10.0, C_3')[a], 132.02 (d, J = 105.0, C_1'), 132.1 (d, J = 2.7, C_4'), 133.4 (d, J = 10.7, C_3)[b], 138.5 (d, J = 3.4, C_4), [a,b]may be reversed; ^{1}H NMR ($CDCl_3$) δ 7.20–7.87 (m, ArH); $[M+H]^+$ = 313.0551, $C_{18}H_{15}OP^{35}Cl$ requires 313.0544.

4-Fluorophenyl diphenylphosphine Oxide (4d): pale yellow crystals; mp.: 134–135 °C, mp.[50]: 134–135 °C; ^{31}P NMR ($CDCl_3$) δ 28.5, δ_P ($CDCl_3$)[51] 28.3; ^{13}C NMR ($CDCl_3$) δ, 115.8 (dd, J_1 = 13.2, J_2 = 21.4, C_2)[a], 128.52 (dd, J_1 =106.5, J_2 = 3.4, C_1), 128.53 (d, J =12.2, C_2')[b], 132.0 (d, J =12.2, C_3')[b], ~132.1 (d, J ~ 3.0, C_4'), 132.3 (d, J =105.0, C_1'), 134.5 (dd, J_1 = 11.3, J_2 = 8.8, C_3)[a], 165.0 (dd, J_1 = 3.2, J_2 = 253.6, C_4), [a,b]may be reversed; ^{1}H NMR ($CDCl_3$) δ 7.06–7.20 (m, 2H, ArH), 7.37–7.75 (m, 12H, ArH), $[M+H]^+$ = 297.0846, $C_{18}H_{15}OPF$ requires 297.0839.

Dipropylphenylphosphine Oxide (6a): Yield: 80%; pale

yellow crystals; mp.: 41–42 °C , mp.[56]: 43 °C; ^{31}P NMR ($CDCl_3$) δ 40.5; ^{13}C NMR ($CDCl_3$) δ 15.4 (d, J = 4.1, CH_3), 15.9 (d, J = 14.9, CH_2CH_3), 32.3 (d, J = 68.3, PCH_2), 128.8 (d, J = 11.1, C_2)*, 130.6 (d, J = 8.8, C_3)*, 131.6 (d, J = 2.7, C_4), 132.8 (d, J = 91.7, C_1), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 0.95 (t, 6H, J = 7.3, CH_3), 1.37–1.69 (m, 4H, CH_2CH_3), 1.75–2.01 (m, 4H, PCH_2), 7.40–7.51 (m, 3H, ArH), 7.61–7.73 (m, 2H, ArH); $[M+H]^+$ = 211.1247, $C_{12}H_{20}OP$ requires 211.1246.

Dibutylphenylphosphine Oxide (6b): Yield: 88%; pale yellow crystals; mp.: 58–59 °C, mp.[57]: 55–57 °C; ^{31}P NMR ($CDCl_3$) δ 39.1, δ_P ($CDCl_3$)[58] 42.8; ^{13}C NMR ($CDCl_3$) δ 13.5 (CH_3), 23.4 (d, J = 4.1, CH_2CH_3), 24.0 (d, J = 14.5, PCH_2CH_2), 29.6 (d, J = 68.5, PCH_2), 128.5 (d, J = 11.1, C_2)*, 130.3 (d, J = 8.7, C_3)*, 131.3 (d, J = 2.7, C_4), 132.6 (d, J = 91.8, C_1), *may be reversed; ^{1}H NMR ($CDCl_3$) δ 0.83 (t, 6H, J = 6.8, CH_3), 1.23–1.69 (m, 8H, CH_2CH_2), 1.74–2.05 (m, 4H, PCH_2), 7.37–7.54 (m, 3H, ArH), 7.59–7.75 (m, 2H, ArH); $[M+H]^+$ = 239.1554, $C_{14}H_{24}OP$ requires 239.1559.

Dibenzylphenylphosphine Oxide (6c): Yield: 95%; white crystals; mp.: 179–180 °C, mp.[59]: 178–181 °C; ^{31}P NMR ($CDCl_3$) δ 35.0, δ_P ($CDCl_3$)[59] 35.2; ^{13}C NMR ($CDCl_3$) δ 37.4 (d, J = 63.4, PCH_2), 126.7 (d, J = 2.9, C_4'), 128.2 (d, J = 11.4, C_2)[a], 128.4 (d, J = 2.5, C_3')[b], 129.9 (d, J = 5.2, C_2')[b], 130.9 (d, J = 94.8, C_1), 131.0 (d, J = 8.5, C_3)[a], 131.4 (d, J = 7.6, C_1'), 131.6 (d, J = 2.7, C_4), [a,b]may be reversed; ^{1}H NMR ($CDCl_3$) δ 3.49 (d, 4H, J = 13.9, PCH_2), 7.20–7.71 (m, 15H, ArH); $[M+H]^+$ = 307.1241, $C_{20}H_{20}OP$ requires 307.1246.

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Graphical abstract

A “green” variation of the Hirao reaction: the P–C coupling of diethyl phosphite, alkyl phenyl-*H*-phosphinates and secondary phosphine oxides with bromoarenes using P-ligand-free $Pd(OAc)_2$ catalyst under microwave and solvent-free conditions

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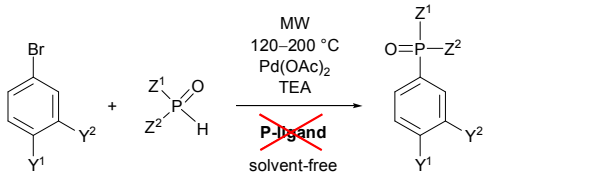

Y^1	Y^2
Q	H
H	Q

Z^1	Z^2
EtO	EtO
R^1O	Ph
Ph	Ph
R^2	R^2

Q = H, MeO, Pr, Et, Me, Cl, F, CO_2Et, C(O)Me

R^1 = Et, ^{n}Pr, ^{i}Pr, ^{n}Bu, ^{i}Bu, ^{i}Pent

R^2 = ^{n}Pr, ^{n}Bu, Bn

The general value of the title reaction affording diethyl arylphosphonates, alkyl diphenylphosphinates and tertiary phosphine oxides was demonstrated.