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Copper-Catalyzed Dehydrative Cyclization of 1-(2-Hydroxyphenyl)propargyl Alcohols with P(O)H Compounds for the Synthesis of 2-Phosphorylmethyl Benzofurans

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Abstract. A $Cu(MeCN)_4BF_4$-catalyzed dehydrative reaction of 1-(2-hydroxyphenyl)propargyl alcohols with diarylphosphine oxides has been developed to provide an efficient synthesis of phosphorylated benzofurans in good to high yields. In the presence of a catalytic amount of an organic base, a variety of H-phosphonates and H-phosphinates can also be employed as good substrates to produce the corresponding products in moderate yields. The reaction has significant economical and ecological advantages since the formation of a new Csp^3–P bond and the benzofuran framework could both be achieved using an inexpensive copper catalyst with water produced as the sole byproduct. The synthetic transformations of the product have also been demonstrated.

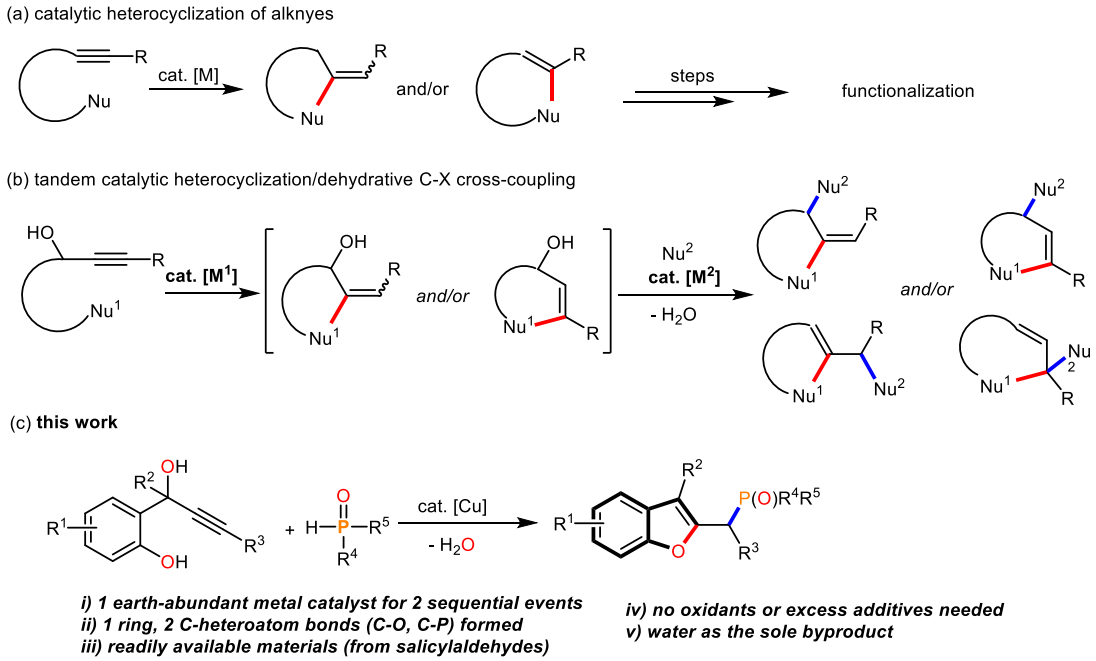
Keywords: copper catalysis; organophosphorus compounds; dehydration; benzofurans; C−P bond formation

Introduction

The development of new and efficient synthetic methods, which hold a high level of atom economy, bond-forming efficiency and selectivity while producing less waste, is highly pursued in modern synthetic chemistry.[1] The dehydrative cross-coupling reaction of a C−OH bond with a Nu−H bond is an appealing protocol for C−C or C−heteroatom formation as it employs the readily available and low-cost alcohols without the need for wasteful pre-functionalization and principally generates water as the sole byproduct.[2,3] Successful combination of this transformation with other bond-forming reactions in one pot can inarguably enhance the efficiency of the method. For example, a tandem cyclization and dehydrative cross-coupling reaction could enable the formation of a heterocyclic core and the installation of an extra functionality in one step with water produced as the byproduct (Scheme 1b). Such a strategy avoids the drawbacks of a traditional synthetic route which often needs the initial heterocyclization followed by pre-functionalization of the hydroxyl group and a substitution reaction to install the second functional group (Scheme 1a). Consequently, it also leads to a minimal use of the reagents and a reduced production of waste, making the whole process more environmentally friendly, particularly when the two steps could be promoted by one catalyst and generate the desired product with high selectivity.[4]

Due to the wide utility of organophosphorus compounds in organic synthesis, biochemistry, pharmaceutical chemistry, agrochemistry and material science, the development of new and efficient C−P bond forming process is in high demand.[5] The synthesis of phosphoryl heterocycles is amongst particularly important as the presence of an organophosphorus functionality could often improve the physical and biological reactivity of the parent heterocycles.[6] While the transition metal catalyzed cross-coupling reaction is a common method to introduce an organophosphorus functionality, this protocol often requires the preparation of the (pseudo)halogenated heterocycles which are not easily accessed.[7] Recently, a lot of new tandem reactions initiated by the addition of phosphoryl radicals to the unsaturated systems have been developed for the synthesis of phosphoryl heterocycles from functionalized alkynes or alkenes.[8] However, the stoichiometric or excess toxic oxidants, noble metal catalysts, expensive ligands and other wasteful additives are often required in these transformations, which limit their further application.

In the course of our interest in developing new C−P bond formation reactions,[9] we propose that the catalytic cyclization/dehydrative cross coupling of alkynyl derivatives with the stable and readily available P(O)H compounds would probably lead to



Scheme 1. Heterocyclization *vs* heterocyclization/ dehydrative cross-coupling reaction of alkynes to produce functionalized heterocycles.

more environmentally friendly and cost-effective methods for the synthesis of phosphoryl heterocycles. As a result, we report here a new copper-catalyzed dehydrative reaction of 1-(2-hydroxyphenyl) propargyl alcohols with P(O)H compounds to provide an efficient and clean method for the synthesis of phosphoryl benzo[*b*]furans (Scheme 1c).[10-12] Notable features of this reaction include the use of an inexpensive copper catalyst, easy availablibity of the starting materials (from commercial chemicals such as salicylaldehydes) and a broad substrate scope. This reaction has significant economical and ecological advantages as the formation of the benzofuran framwork and a new Csp^3–P bond could be efficiently achieved by the same catalyst in a single operation with water produced as the sole byproduct (Scheme 1c). Although several examples have been reported to produce functionalized benzo[*b*]furans from 1-(2-hydroxyphenyl)propargyl alcohols with several other nucleophiles,[4e-4h] to the best of our knowledge, such a process that involves phosphorus nucleophiles and can be promoted by a single catalyst has not been revealed.

Results and Discussion

We commenced the study by examining the reaction of 1-(*o*-hydroxylphenyl)prop-2-yn-1-ol (**1a**) with diphenylphosphine oxide (**2a**) as model substrates in the presence of various Lewis acids. While initial experiments using $ZnCl_2$, $Zn(OTf)_2$ and $Sc(OTf)_3$ all gave negative results (Table 1, entries 1-3), we were pleased to observe that the reaction using $Cu(OTf)_2$ as the catalyst in DCE at 100 °C afforded the expected product **3a** in 61% yield as a white solid (Table 1, entry 4). $Pd(TFA)_2$ could also promote the reaction, but the yield was not satisfactory (Table 1, entry 5). When AgOTf was used, a very low yield was obtained, and the formation of silver mirror was observed in the reaction flask probably due to the reduction of Ag(I) species to Ag(0) by **1a** (Table 1, entry 6). Further optimizations were then made by altering the copper source (Table 1, entries 7-11). The reaction catalyzed by CuCl gave **3a** in a comparable yield with that of $Cu(OTf)_2$ (Table 1, entry 7). The use of CuI unfortunately gave rise to **3a** in a low yield (Table 1, entry 8). Gratifyingly, when $Cu(MeCN)_4PF_6$ was employed, the yield was improved to 86% (Table 1, entry 9). However, the reactions of $Cu(OAc)_2$ and $CuSO_4$ did not give improved results (Table 1, entries 10 and 11). Without a catalyst, no reaction took place (Table 1, entry 12). By using $Cu(MeCN)_4PF_6$ as the catalyst, the solvent effect was then investigated. The results showed that DCE was a suitable choice as all the other solvents we checked gave inferior results. For example, the reactions in toluene and THF produced **3a** in 73% and 64% yield, respectively (Table 1, entries 13 and 14). The use of DMF, MeCN and DMSO all gave **3a** in less than 50% yield (Table 1, entries 15-17). The examination on temperature effect revealed that either a decrease or increase in the reaction temperature (80 °C and 120 °C) led to a reduced product yield (Table 1, entries 18 and 19). Accordingly, we defined the reaction conditions as listed in entry 9 Table 1 as the optimal. The product **3a** was characterized by ^1H, ^{13}C, ^{31}P NMR and HRMS, and the structure was further confirmed by an X-ray crystallographic analysis (Figure 1).[13]

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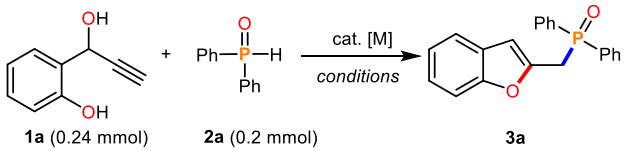
Table 1. Optimization data on reaction conditions [a]



1a (0.24 mmol) **2a** (0.2 mmol) **3a**

entry	[Cu]	solvent	tempt (°C)	yield (%)[b]
1	$ZnCl_2$	DCE	100	trace
2	$Zn(OTf)_2$	DCE	100	trace
3	$Sc(OTf)_3$	DCE	100	ND[c]
4	$Cu(OTf)_2$	DCE	100	61
5	$Pd(TFA)_2$	DCE	100	15
6	AgOTf	DCE	100	<5
7	CuCl	DCE	100	64
8	CuI	DCE	100	46
9	**$Cu(MeCN)_4PF_6$**	**DCE**	**100**	**86**
10	$Cu(OAc)_2$	DCE	100	38
11	$CuSO_4$	DCE	100	60
12	-[d]	DCE	100	ND[c]
13	$Cu(MeCN)_4PF_6$	Toluene	100	73
14	$Cu(MeCN)_4PF_6$	THF	100	64
15	$Cu(MeCN)_4PF_6$	DMF	100	44
16	$Cu(MeCN)_4PF_6$	MeCN	100	45
17	$Cu(MeCN)_4PF_6$	DMSO	100	26
18	$Cu(MeCN)_4PF_6$	DCE	80	70
19	$Cu(MeCN)_4PF_6$	DCE	120	63

[a] Conditions: **1** (0.24 mmol), **2** (0.2 mmol), [M] (10 mol%) in 1 mL of solvent, 4 h.

[b] Isolated yields.

[c] ND: Not detected.

[d] No catalyst.

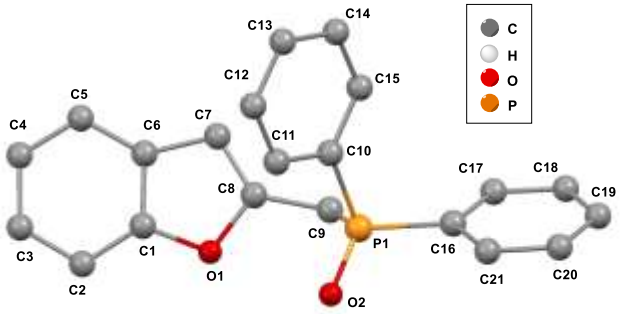
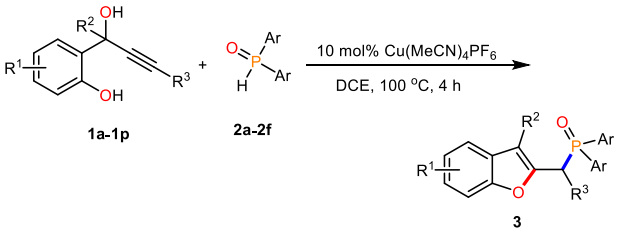


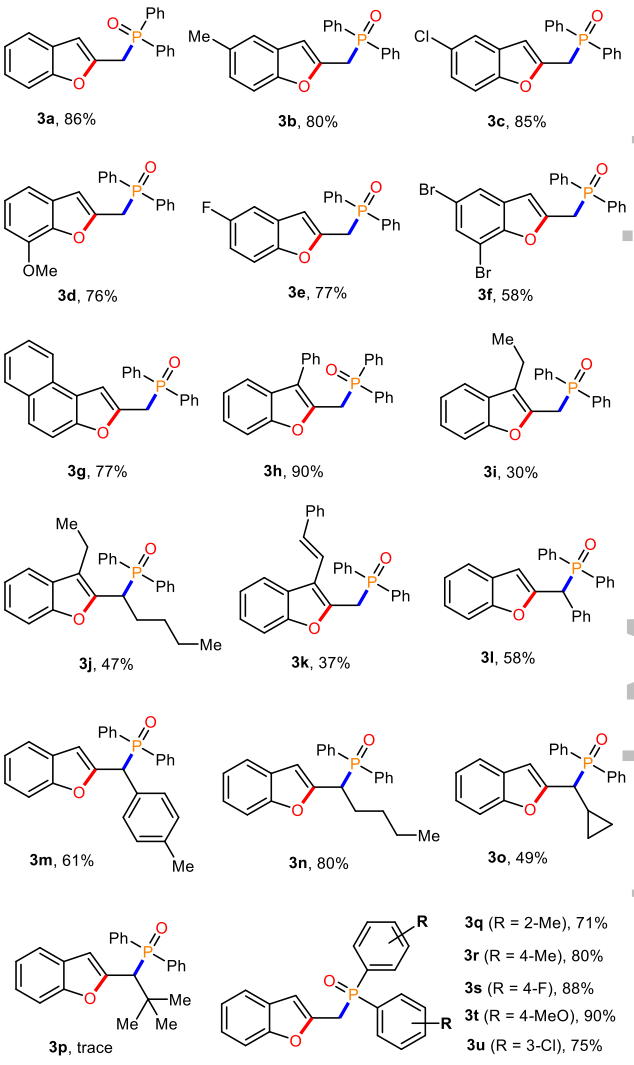
Figure 1. ORTEP presentation of the structure of the product **3a**.

With the optimal conditions in hand, the scope of the reaction was then investigated. As shown in Table 2, A wide range of 1-(*o*-hydroxylphenyl)prop-2-yn-1-ols **1b-1o** were used to react with **2a** to produce the corresponding products **3b-3o** in moderate to high yields. The common functionalities such as chloro, bromo, fluoro and methyloxyl group incorporated at the phenyl rings in substrate **1** are tolerated. The

Table 2. Cu-catalyzed synthesis of phosphorylated benzofurans **3**[a]



1a-1p **2a-2f** **3**



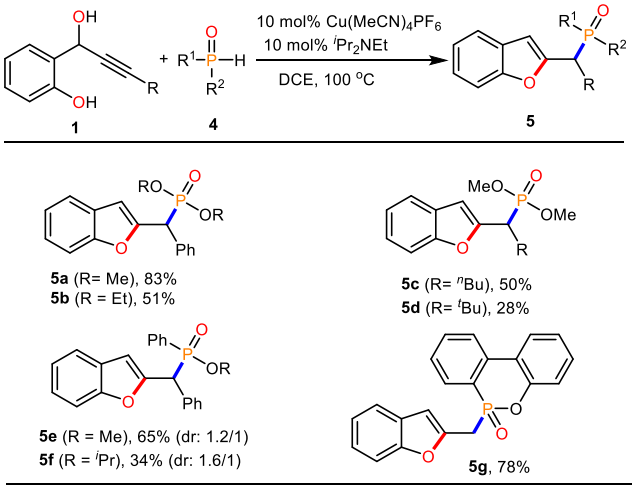
[a] Conditions: **1** (0.24 mmol), **2** (0.2 mmol), [M] (10 mol%) in 1 mL of solvent, 4 h. Isolated yields were given.

reaction could also be performed with 3°-substituted alcohols **1h-1k** to produce the expected products **3h-3k**. The yields varied with the substitute. When R^2 was a phenyl group, the reaction gave the product **3h** in 90% yield, whereas the reactions afforded **3i** and **3j** in low yields wherein R^2 as an ethyl group. It is notable that substrate **1k** bearing an (*E*)-styryl group also reacted with **1a** to give the desired product **3k**, albeit in a low yield. The reactions were also applicable to substrates **1l-1o** bearing internal C≡C triple bonds to produce the corresponding products **3l-3o** in 49-80% yields. Particularly, a cyclopropane

group was found to be tolerated, exemplified by the successful preparation of **3o** in a modest yield. However, only a trace amount of the desired product **3p** was detected from the reaction mixture in case of R^3 as the sterically hindered *tert*-butyl group. With respect to diarylphosphine oxide, typical diarylphosphine oxides bearing electron-donating or electron-withdrawing substitutes on the phenyl rings **2b**-**2f** were also suitable substrates to give the corresponding products **3q**-**3u** in good to high yields.

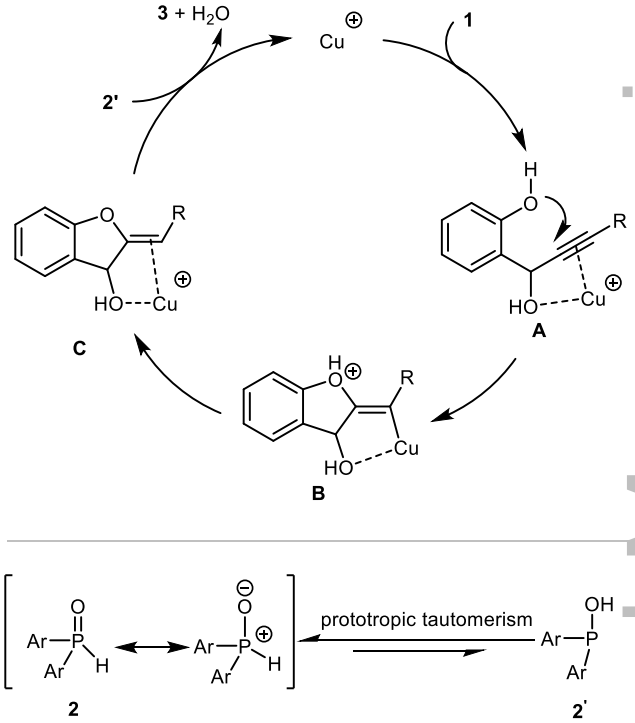
Under similar conditions, the reactions of 1-(*o*-hydroxylphenyl)prop-2-yn-1-ols with H-phosphonates or H-phosphinates unfortunately gave the products in very low yields in most cases probably due to the low reactivity of these P(O)H compounds. While changing the molar ratio of the substrates or adjusting the reaction temperature did not give improved results (<35%), the presence of a catalytic amount of ^{i}Pr$_2$NEt led to improved yields.[14] As shown in Table 3, products **5a**-**5f** were successfully obtained from the corresponding H-phosphonates or H-phosphinates with 1-(*o*-hydroxylphenyl)prop-2-yn-1-ols in the presence of 10 mol% Cu(MeCN)$_4$PF$_6$ and 10 mol% of ^{i}Pr$_2$NEt in DCE at 100 °C. The product yields varied depending on the steric difference of the P(O)H compounds. In general, the less sterically demanding P(O)H compounds gave better yields as exemplified by the preparation of compounds **5a** and **5e** (*vs* **5b** and **5f**). Particularly, the reaction of dimethyl phosphonate (**4a**) with the *tert*-butyl-substituted substrate **1p** also took place to give the corresponding product **5d**, albeit only in 28% yield. In addition, 9,10-dihydro-9-oxa-10-phosphaphenanthrene-10-oxide show a good reactivity and gave **5g** in 78% yield in the absence of the amine.

Table 3. Cu-catalyzed synthesis of phosphorylated benzofurans **5** [a]



[a]Conditions: **1** (1.2-1.5 equiv), **4** (1.0 equiv), Cu(MeCN)$_4$PF$_6$ (10 mol%), ^{i}Pr$_2$NEt (10 mol%) in DCE, 100 °C; Isolated yields were given.

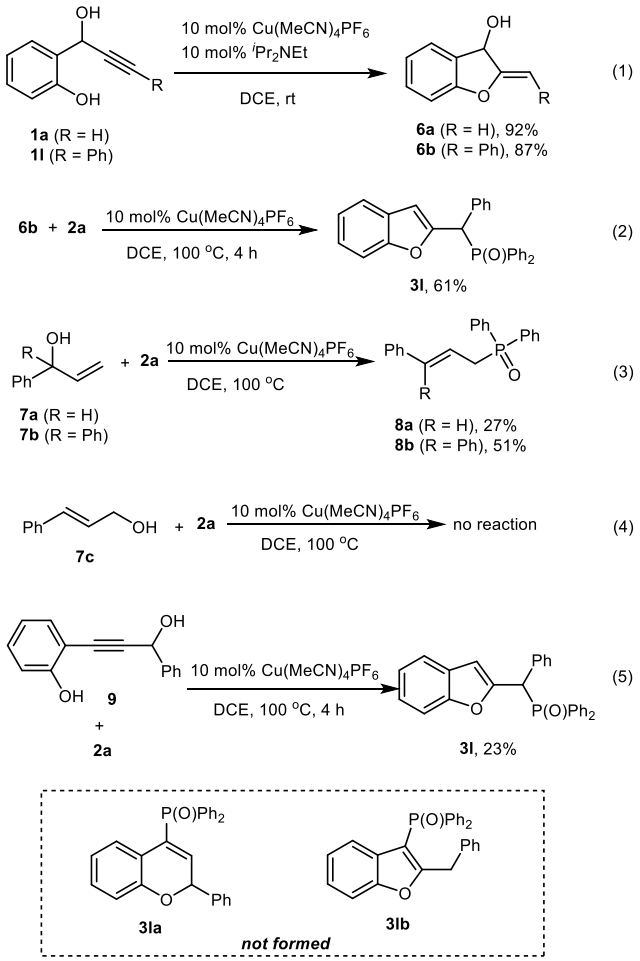
The present reaction is supposed to be the result of a tandem *5-exo-dig* cyclization and the dehydrative C-P cross-coupling process (Scheme 2). Coordination of the Cu(I) species as a Lewis acid to **1** may trigger a highly selective *5-exo-dig* attack of the pendant phenol group to the alkyne moiety to form an exocyclic enol ether-Cu intermediate **B**.[4g] Protonation of **B** then gives an intermediate **C**. The Cu(I) species may further activate the C−OH bond probably as an oxophilic Lewis acid and induce the subsequent SN2'-type substitution by the attack of **2'** (tautomer of **2**) to give the product with the formation the C−P bond and one molecule of water, and regenerate the catalyst.



Scheme 2. The proposed mechanism

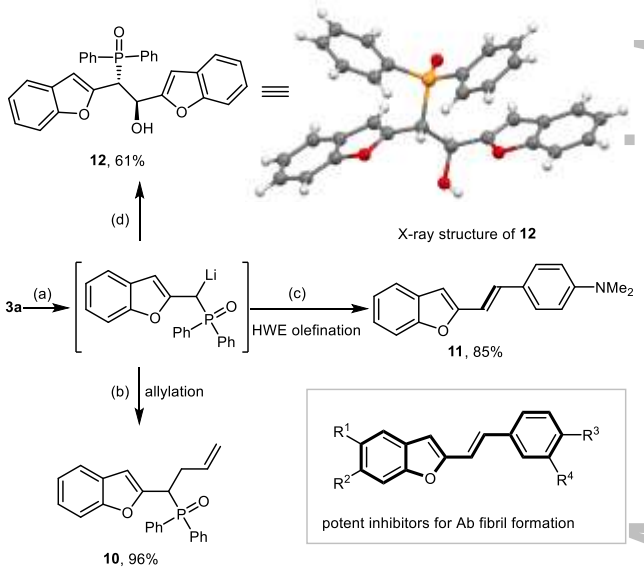
The proposed mechanism was supported by the results of some control experiments (Scheme 3). It was found that the reaction of **1a** with 10 mol% of Cu(MeCN)$_4$PF$_6$ at room temperature proceeded very slowly to give the cyclized product **6a**. When heated to 100 °C, **6a** disappeared and a mixture formed because **6a** was unstable under the conditions. However, the cyclization could be accelerated by the addition of ^{i}Pr$_2$NEt at room temperature, producing **6a** in 92% yield in 3 h (Scheme 3, eq. 1). Similarly, the product **6b** could also be obtained in good yield. The treatment of **6b** and **2a** with 10 mol% of Cu(MeCN)$_4$PF$_6$ gave **3l** in 61% yield, confirming the presumed dehydrative C−P coupling event (Scheme 3, eq. 2). As a matter of fact, our further experiments revealed that such a dehydrative C−P coupling also took place between the allylic alcohol **7a** or **7b** and **2a** to give the corresponding products **8a** and **8b** in the presence of Cu(MeCN)$_4$PF$_6$ (Scheme 3, eq. 3),

whereas the primary allyl alcohol **7c** is inactive for a similar transformation due to its low reactivity (Scheme 3, eq. 4). It is worth mentioning here that such a dehydrative C−P coupling between a nonactive allyl alcohol and $HP(O)R^1R^2$ has not been disclosed before.[15] We suppose that a tendency of the allylic alcohol intermediate like **C** as shown in Scheme 2 to form the aromatic benzofuran motif may facilitate the C−P bond formation process in the present reaction. On the other hand, we noticed that a Cu(OTf)Ph-catalyzed reaction of 2-propynolphenols with diarylphosphine oxides to afford 4-phosphorylated 2H-chromenes has been reported recently.[16] A cascade allenylation followed by an intramolecular cyclization was proposed as the working mechanism. However, under our conditions, the reaction of 2-propynolphenol **9** and **2a** afforded the product **3l** in 23% yield together with the recovery of the unconsumed **1a**, but the possible compounds **3la** or **3lb** from an allenylation reaction followed by the intramolecular cyclization was not detected (Scheme 3, eq. 5).[17] This result showed that the initiation of an intramolecular *5-exo-dig* cyclization was preferred under our conditions and a process involving phosphorylative allenlyation with further cyclization did not take place.



Scheme 3. The mechanism study

Finally, the synthetic transformation of the product was examined (Scheme 4). Metalation of **3a** with *n*-BuLi followed by the addition of allyl bromide afforded the allylation product **10** in 96% yield. The alkenyl benzofuran product **11**, possessing a core structure of the potential inhibitor for Ab fibril formation for the treatment of Alzheimer disease,[18] was readily obtained in high yield from a Horner-Wadsworth-Emmons-type (HWE) reaction of **3a** and 4-(dimethylamino)benzaldehyde. Furthermore, the treatment of the lithiated **3a** with TMSCl resulted in the formation of an interesting product **12** with high diastereoselectivity.[13]



Scheme 4. Synthetic transformations of **3a** (Conditions: (a) *n*-BuLi (1.1 equiv), THF, 0 °C, 5 min; (b) allyl bromide (1.1 equiv), 0 °C-rt, 16 h; (c) 4-(dimethylamino) benzaldehyde (1.2 equiv), 0 °C-rt, overnight; (d) TMSCl (2.0 equiv), 0 °C-rt, overnight).

Conclusion

In summary, we have developed a new Cu-catalyzed dehydrative reaction of 1-(*o*-hydroxylphenyl)prop-2-yn-1-ols and P(O)H compounds. This reaction offers a rapid synthesis of a variety of phosphorylated benzofurans under mild conditions from readily available starting materials with a catalytic system that are low cost, readily available and ecologically benign. Exploration of the methodology for the synthesis of other phosphoryl heterocycles is the next goal.

Experimental Section

General information. Unless otherwise specified, all reactions were performed under dry N_2 atmosphere. Anhydrous solvents were distilled prior to use: THF and toluene were distilled from sodium using benzophenone as the indicator; DCE, DMF, MeCN and DMSO were distilled from CaH_2. 1-(2-Hydroxyphenyl)-propargyl alcohols **1a-1p** were prepared following known

procedures.[19] A typical procedure was given in the Supporting Information. Flash chromatography was performed on silica gel using petroleum ether and EtOAc as eluent. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Chemical shifts are expressed in ppm and *J* values are given in Hz. HRMS analysis of the products was performed at the Analytical Center of the Department of Chemistry of Zhejiang University, China. The X-Ray crystallographic analysis were performed on a Bruker SMART APEX II CCD diffractometer using a graphite-monochromated Mo K_α (λ = 0.71073 Å) radiation.

General procedure for the Cu-catalyzed preparation of phosphoryl benzofurans 3. An oven-dried Schlenk tube containing a Teflon-coated stir bar was charged with $Cu(MeCN)_4PF_6$ (7.4 mg, 10 mol %). The Schlenk tube was sealed and then evacuated and backfilled with N_2 (3 cycles). 0.5 mL of DCE was injected with vigorous stirring (in case of the preparation of **5a-5f**, 10 mol% of ^{i}Pr$_2$NEt was added). Then **1** (0.24 mmol) and **2** (0.2 mmol) dissolved in 0.5 mL of DCE was added. The Schlenk tube was sealed and immersed in an oil bath which was heated to 100 ºC. After the reaction was complete (monitored by TLC, 4 h), removal of the solvent under vacuum left a slurry residue, which was purified by flash chromatography on silica (petroleum ether/ethyl acetate 3/1 to 1/1) to afford the product **3**.

(benzofuran-2-ylmethyl)diphenylphosphine oxide (3a): 58.0 mg (yield 86%), prepared from 35.7 mg of **1a** (0.24 mmol) and 41.2 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.78–7.73 (m, 4H), 7.55–7.41 (m, 7H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.20-7.12 (m, 2H), 6.54 (d, *J* = 3.2 Hz, 1H), 3.88 (d, *J* = 14.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.6, 148.5 (d, J_{P-C} = 8.2 Hz), 132.1 (d, J_{P-C} = 3.1 Hz), 131.7 (d, J_{P-C} = 100.6 Hz), 131.0 (d, J_{P-C} = 9.6 Hz), 128.58 (d, J_{P-C} = 12.1 Hz), 128.56 (d, J_{P-C} = 2.7 Hz), 123.7, 122.6, 120.6, 110.8, 106.0 (d, J_{P-C} = 6.1 Hz), 31.7 (d, J_{P-C} = 67.3 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 27.9. HRMS (ESI-TOF): *m/z* = 333.1026, calcd for $C_{21}H_{18}O_2P$ [MH^+] 333.1044. The structure of this compound was further determined by an X-ray crystallographic analysis. The single crystals were obtained from a hexane-CH_2Cl_2 solution by slow evaporation.

((5-methylbenzofuran-2-yl)methyl)diphenylphosphine oxide (3b): 57.0 mg (yield 80%), prepared from 41.1 mg of **1b** (0.25 mmol) and 41.4 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.77–7.72 (m, 4H), 7.55–7.51 (m, 2H), 7.47-7.43 (m, 4H), 7.21-7.17 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.46 (d, *J* = 3.2 Hz, 1H), 3.86 (d, *J* = 14.4 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.0 (d, J_{P-C} = 1.4 Hz), 148.5 (d, J_{P-C} = 7.5 Hz), 132.0 (d, J_{P-C} = 2.8 Hz), 131.8 (d, J_{P-C} = 100.8 Hz), 131.1 (d, J_{P-C} = 9.4 Hz), 128.7 (d, J_{P-C} = 2.4 Hz), 128.6 (d, J_{P-C} = 11.7 Hz), 124.9, 120.4, 110.3, 105.8 (d, J_{P-C} = 6.9 Hz), 31.8 (d, J_{P-C} = 67.5 Hz), 21.2. ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 27.9; HRMS (ESI-TOF): *m/z* =347.1197, calcd for $C_{22}H_{20}O_2P$ [MH^+]347.1201.

((5-chlorobenzofuran-2-yl)methyl)diphenylphosphine oxide (3c): 62.3 mg (yield 85%), prepared from 41.8 mg of **1c** (0.23 mmol) and 40.4 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.77–7.72 (m, 4H), 7.56–7.52 (m, 2H), 7.48–7.44 (m, 4H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.12 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 6.48 (d, *J* = 2.8 Hz, 1H), 3.86 (d, *J* = 14.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.0, 150.3 (d, J_{P-C} = 7.1 Hz), 132.2 (d, J_{P-C} = 3.2 Hz), 130.5 (d, J_{P-C} = 100.7 Hz), 131.0 (d, J_{P-C} = 9.5 Hz), 129.9 (d, J_{P-C} = 2.4 Hz), 128.7 (d, J_{P-C} = 12.4 Hz), 128.2, 123.9, 120.2, 111.8, 105.7 (d, J_{P-C} = 6.1 Hz), 31.8 (d, J_{P-C} = 67.3 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 27.8. HRMS (ESI-TOF): *m/z* = 367.0636, calcd for $C_{21}H_{17}ClO_2P$ [MH^+] 367.0655.

((7-methoxybenzofuran-2-yl)methyl)diphenylphosphine oxide (3d): 55.0 mg (yield 76%), prepared from 43.0 mg of **1d** (0.24 mmol) and 40.7 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.79–7.73 (m, 4H), 7.53–7.43 (m, 6H), 7.09–7.02 (m, 2H), 6.71 (d, *J* = 7.2 Hz, 1H), 6.63 (d, *J* = 2.8 Hz, 1H), 3.91 (d, *J* = 13.2 Hz, 2H), 3.90 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.5 (d, J_{P-C} = 6.7 Hz), 144.8, 143.7, 132.0 (d, J_{P-C} = 3.1 Hz), 131.8 (d, J_{P-C} = 100.5 Hz), 131.0, 130.9, 130.4 (d, J_{P-C} = 2.3 Hz), 128.7, 128.5, 123.3, 113.1, 106.4, 106.3 (d, J_{P-C} = 5.5 Hz), 56.1, 31.3 (d, J_{P-C} = 68.1 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 27.8. HRMS (ESI-TOF): *m/z* = 363.1157, calcd for $C_{22}H_{20}O_3P$ [MH^+] 363.1150.

((5-fluorobenzofuran-2-yl)methyl)diphenylphosphine oxide (3e): 53.9 mg (yield 77%), prepared from 40.5 mg of **1e** (0.24 mmol) and 40.4 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.78–7.73 (m, 4H), 7.56–7.45 (m, 6H), 7.23-7.20 (m, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.91-6.87 (m, 1H), 6.51 (s, 1H), 3.87 (d, *J* = 14.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.1 (d, J_{F-C} = 237.0 Hz), 150.8, 150.5 (d, J_{P-C} = 7.7 Hz), 132.2 (d, J_{P-C} = 3.1 Hz), 131.2, 131.1, 131.0, 129.4 (d, J_{P-C} = 3.1 Hz), 129.3 (d, J_{P-C} = 2.4 Hz), 128.7, 128.6, 111.4 (d, J_{F-C} = 4.9 Hz), 111.2 (d, J_{F-C} = 11.7 Hz), 106.2 (J_{P-C} = 3.2 Hz), 106.1 (d, J_{F-C} = 25.3 Hz), 31.9 (d, J_{P-C} = 67.1 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 27.8. HRMS (ESI-TOF): *m/z* = 351.0963, calcd for $C_{21}H_{17}FO_2P$ [MH^+] 351.0950.

((5,7-dibromobenzofuran-2-yl)methyl)diphenyl phosphine oxide (3f): 56.8 mg (yield 58%), prepared from 73.6 mg of **1f** (0.24 mmol) and 40.0 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.80–7.75 (m, 4H), 7.58–7.54 (m, 2H), 7.50–7.46 (m, 6H), 6.64 (d, *J* = 2.8 Hz, 1H), 3.91 (d, *J* = 13.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 151.1 (d, J_{P-C} = 7.5 Hz), 150.8, 132.3 (d, J_{P-C} = 2.5 Hz), 131.4 (d, J_{P-C} = 101.3 Hz), 131.1, 131.0 (d, J_{P-C} = 9.4 Hz), 129.0, 128.7 (d, J_{P-C} = 13.0 Hz), 122.5, 115.9, 106.3 (d, J_{P-C} = 5.8 Hz), 104.1, 31.8 (d, J_{P-C} = 66.3 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 27.7. HRMS (ESI-TOF): *m/z* = 490.9238, calcd for $C_{21}H_{16}Br_2O_2P$ [MH^+] 490.9234.

(naphtho[2,1-b]furan-2-ylmethyl)diphenylphosphine oxide (3g): 58.5 mg (yield 77%), prepared from 47.8 mg of **1g** (0.24 mmol) and 40.9 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.79–7.74 (m, 4H), 7.62 (d, *J* = 9.2 Hz, 1H), 7.55–7.42 (m, 9H), 7.05 (d, *J* = 2.8 Hz, 1H), 3.97 (d, *J* = 14.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 152.0 (d, J_{P-C} = 1.1 Hz), 147.7 (d, J_{P-C} = 8.6 Hz), 132.1 (d, J_{P-C} = 3.3 Hz), 131.6 (d, J_{P-C} = 100.0 Hz), 131.1 (d, J_{P-C} = 9.7 Hz), 130.2, 128.6 (d J_{P-C} = 11.8 Hz), 127.3, 126.1, 124.5 (d, J_{P-C} = 1.5 Hz), 131.3 (d, J_{P-C} = 1.5 Hz), 131.2 (d, J_{P-C} = 1.4 Hz), 129.9 (d, J_{P-C} = 5.2 Hz), 128.7, 128.6 (d, J_{P-C} = 11.6 Hz), 124.4, 123.8 (d, J_{P-C} = 2.0 Hz), 123.5, 112.0, 105.2 (d, J_{P-C} = 6.0 Hz), 32.0 (d, *J* = 67.9 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 27.9. HRMS (ESI-TOF): *m/z* = 383.1195, calcd for $C_{25}H_{20}O_2P$ [MH^+] 383.1201.

diphenyl((3-phenylbenzofuran-2-yl)methyl)phosphine oxide (3h):72.4 mg (yield 90%), prepared from 90.2 mg of **1h** (0.4 mmol) and 40.0 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.65 (m, 4H), 7.52–7.31 (m, 12H), 7.33–7.31 (m, 1H), 7.25–7.16 (m, 2H), 3.98 (d, *J* = 14.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.2, 144.8 (d, J_{P-C} = 11.3 Hz), 131.96 (d, J_{P-C} = 2.5 Hz), 131.86 (d, J_{P-C} = 100.0 Hz), 131.6 (d, J_{P-C} = 2.5 Hz), 131.2, 131.1, 129.0 (d, J_{P-C} = 1.4 Hz), 128.8, 128.5, 128.4, 128.2 (d, J_{P-C} = 2.0 Hz), 127.4, 124.2, 122.8, 120.6 (d, J_{P-C} = 7.9 Hz), 119.6, 111.0, 30.6 (d, *J* = 66.2 Hz). ^{1}P NMR ($CDCl_3$, 162 MHz): δ = 28.7; HRMS (ESI-TOF): *m/z* = 409.1367, calcd for $C_{27}H_{22}O_2P$ [MH^+]409.1357.

((3-ethylbenzofuran-2-yl)methyl)diphenylphosphine oxide (3i): 21.5 mg (yield 30%), prepared from 44.1 mg of **1i** (0.23 mmol) and 40.4 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.77–7.72 (m, 4H), 7.53–7.49 (m, 2H), 7.45-7.41 (m, 5H), 7.27-7.25 (m, 1H), 7.18-7.15 (m, 2H), 3.85 (d, *J* = 14.4 Hz, 2H), 2.49-2.43 (m, 2H), 1.05 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.2 (d, J_{P-C} = 1.4 Hz), 143.3 (d, J_{P-C} = 10.5 Hz), 132.0 (d, J_{P-C} = 1.9 Hz), 131.8 (d, J_{P-C} = 98.8 Hz), 131.2 (d, J_{P-C} = 9.5 Hz), 128.8 (d, J_{P-C} = 3.0 Hz), 128.4 (d, J_{P-C} = 12.5 Hz), 123.6, 122.1, 120.0 (d, J_{P-C} = 7.7 Hz), 119.2 (d, J_{P-C} = 1.6 Hz), 110.8, 30.7 (d, J_{P-C} = 68.4 Hz), 16.9 (d, J_{P-C} = 12.1 Hz), 13.9 (d, J_{P-C} = 2.3 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 28.4; HRMS (ESI-TOF): *m/z* = 383.1195, calcd for $C_{23}H_{21}NaO_2P$ [MNa^+] 383.1177.

(1-(3-ethylbenzofuran-2-yl)pentyl)diphenylphosphine oxide (3j): 39.0 mg (yield 47%), prepared from 56.0 mg of

1j (0.24 mmol) and 41.0 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.80–7.75 (m, 2H), 7.70–7.65 (m, 2H), 7.52–7.39 (m, 6H), 7.33–7.29 (m, 2H), 7.25–7.16 (m, 2H), 3.76–3.69 (m, 1H), 2.40–2.34 (m, 2H), 2.30–2.21 (m, 1H), 2.06–1.99 (m, 1H), 1.28–1.17 (m, 4H),0.95 (t, J = 7.6 Hz, 3H), 0.76 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.2, 147.1 (d, J_{P-C} = 9.4 Hz), 131.8 (d, J_{P-C} = 2.0 Hz), 131.6 (d, J_{P-C} = 2.9 Hz), 131.5 (d, J_{P-C} = 94.5 Hz), 131.4 (d, J_{P-C} = 97.6 Hz), 131.38 (d, J_{P-C} = 4.5 Hz), 131.29 (d, J_{P-C} =4.9 Hz), 128.8 (d, J_{P-C} = 1.7 Hz), 128.5 (d, J_{P-C} = 10.9 Hz), 128.1 (d, J_{P-C} = 11.7 Hz), 123.6, 122.1, 120.3 (d, J_{P-C} = 7.9 Hz), 119.2, 111.1, 41.3 (d, J = 67.2 Hz), 30.3 (d, J_{P-C} = 12.8 Hz), 26.6, 22.1, 16.8, 13.84 (d, J_{P-C} = 2.3 Hz), 13.77. ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 31.9; HRMS (ESI-TOF): *m/z* = 417.1981, calcd for $C_{27}H_{30}O_2P$ [MH^+] 417.1983.

(*E*)-diphenyl((3-styrylbenzofuran-2-yl)methyl) phosphine oxide (3k): 32.4 mg (yield 37%), prepared from 60.4 mg of **1k** (0.24 mmol) and 40.8 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.82–7.74 (m, 5H), 7.50–7.32 (m, 11H), 7.27–7.23 (m, 3H), 7.05 (d, J = 16.0 Hz, 1H), 7.12 (dd, J_1 = 16.0 Hz, J_2 = 1.2 Hz, 1H), 4.02 (d, J = 14.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.5, 146.9 (d, J_{P-C} = 11.5 Hz), 137.5, 132.2 (d, J_{P-C} = 2.5 Hz), 132.6 (d, J_{P-C} = 99.7 Hz), 131.2 (d, J_{P-C} = 9.5 Hz), 129.9 (d, J_{P-C} = 3.9 Hz), 128.6 (d, J_{P-C} = 4.3 Hz), 128.5, 127.4, 126.5 (d, J_{P-C} = 2.4 Hz), 126.2, 124.3, 123.0, 120.5, 118.2 (d, J = 3.6 Hz), 117.0 (d, J_{P-C} = 8.0 Hz), 111.2, 31.5 (d, J_{P-C} = 66.4 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 28.1; HRMS (ESI-TOF): *m/z* =435.1518, calcd for $C_{29}H_{24}O_2P$ [MH^+] 435.1514.

(benzofuran-2-yl(phenyl)methyl)diphenylphosphine oxide (3l): 48.0 mg (yield 58%), prepared from 58.0 mg of **1l** (0.26 mmol) and 40.8 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.86–7.82 (m, 2H), 7.51–7.25 (m, 12H), 7.18–7.08 (m, 6H), 5.04 (d, J = 10.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.4, 153.0, 133.4 (d, J_{P-C} = 5.5 Hz), 132.0 (d, J_{P-C} = 2.5 Hz), 131.7 (d, J_{P-C} = 3.4 Hz), 131.6 (d, J_{P-C} = 98.4 Hz), 131.5 (d, J_{P-C} = 101.0 Hz), 131.3 (d, J_{P-C} = 1.5 Hz), 131.2 (d, J_{P-C} = 1.4 Hz), 129.9 (d, J_{P-C} = 5.2 Hz), 128.7, 128.6 (d, J_{P-C} = 11.6 Hz), 128.4 (d, J_{P-C} = 1.9 Hz), 128.2 (d, J_{P-C} = 12.3 Hz), 127.5 (d, J_{P-C} = 2.4 Hz), 123.9, 122.7, 121.1, 110.9, 106.7 (d, J_{P-C} = 2.6 Hz), 47.9 (d, J = 65.0 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 29.6. HRMS (ESI-TOF): *m/z* = 409.1362, calcd for $C_{27}H_{22}O_2P$ [MH^+]409.1357.

(benzofuran-2-yl(p-tolyl)methyl)diphenylphosphine oxide (3m): 52.0 mg (yield 61%), prepared from 57.8 mg of **1m** (0.24 mmol) and 41.0 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.84–7.79 (m, 2H), 7.54–7.37 (m, 7H), 7.33–7.21 (m, 5H), 7.18–7.10 (m, 2H), 7.03–6.98 (m, 3H), 5.03 (d, J = 10.8 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.3, 153.2, 137.2 (d, J_{P-C} = 2.3 Hz), 131.8 (d, J_{P-C} = 2.9 Hz), 131.7 (d, J_{P-C} = 100.0 Hz), 131.61 (d, J_{P-C} = 100.0 Hz), 131.60 (d, J_{P-C} = 2.5 Hz), 131.3 (d, J_{P-C} = 3.5 Hz), 131.2 (d, J_{P-C} = 3.7 Hz), 130.3 (d, J_{P-C} = 5.0 Hz), 129.7 (d, J_{P-C} = 5.0 Hz), 129.1 (d, J_{P-C} = 1.9 Hz), 128.6 (d, J_{P-C} = 1.4 Hz), 128.5 (d, J_{P-C} = 11.7 Hz), 128.1 (d, J_{P-C} = 12.3 Hz), 123.8, 122.6, 120.9, 110.8, 106.5 (d, J_{P-C} = 3.1 Hz), 47.6 (d, J = 65.6 Hz), 21.0. ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 29.5. HRMS (ESI-TOF): *m/z* = 423.1516, calcd for $C_{28}H_{24}O_2P$ [MH^+] 423.1514.

(1-(benzofuran-2-yl)pentyl)diphenylphosphine oxide (3n): 62.0 mg (yield 80%), prepared from 53.9 mg of **1n** (0.26 mmol) and 40.8 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.87–7.82 (m, 2H), 7.64–7.37 (m, 7H), 7.32–7.27 (m, 3H), 7.20–7.14 (m, 2H), 6.59 (d, J = 3.2 Hz, 1H), 3.81 (td, J_1 = 11.2 Hz, J_2 = 3.2 Hz, 1H), 2.15–1.94 (m, 2H), 1.35–1.19 (m, 4H), 0.77 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.4 (d, J_{P-C} = 1.6 Hz), 153.4 (d, J_{P-C} = 5.8 Hz), 131.9 (d, J_{P-C} = 3.4 Hz), 131.7 (d, J_{P-C} = 3.1 Hz), 131.6 (d, J_{P-C} = 95.7 Hz), 131.32 (d, J_{P-C} = 6.5 Hz), 131.28 (d, J_{P-C} = 98.6 Hz), 131.23 (d, J_{P-C} = 9.7 Hz), 128.7 (d, J_{P-C} = 11.2 Hz), 128.6 (d, J_{P-C} = 3.4 Hz), 128.2 (d, J_{P-C} = 11.7 Hz), 123.6, 122.6, 120.7, 110.9, 105.7 (d, J_{P-C} = 6.8 Hz), 41.7 (d, J = 68.0 Hz), 30.2 (d, J_{P-C} = 11.8 Hz), 27.7, 22.2, 13.8. ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 31.2; HRMS (ESI-TOF): *m/z* = 389.1672, calcd for $C_{25}H_{26}O_2P$ [MH^+] 389.1670.

(benzofuran-2-yl(cyclopropyl)methyl)diphenyl phosphine oxide (3o): 36.3 mg (yield 49%), prepared from 50.0 mg of **1o** (0.27 mmol) and 40.2 mg of diphenylphosphine oxide **2a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.88–7.83 (m, 2H), 7.75–7.70 (m, 2H), 7.56–7.26 (m, 8H), 7.20–7.12 (m, 2H), 6.72 (d, J = 2.4 Hz, 1H), 3.25 (t, J = 10.4 Hz, 1H), 1.54–1.47 (m, 1H), 0.57–0.52 (m, 1H), 0.48–0.41 (m, 1H), 0.34–0.28 (m, 1H), -0.01– -0.06 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.3, 153.6 (d, J_{P-C} = 2.8 Hz), 132.1 (d, J_{P-C} = 96.0 Hz), 132.0, 131.7 (d, J_{P-C} = 2.3 Hz), 131.6 (d, J_{P-C} = 3.3 Hz), 131.4 (d, J_{P-C} = 8.8 Hz), 131.1 (d, J_{P-C} = 8.6 Hz), 128.5 (d, J_{P-C} = 1.9 Hz), 128.3 (d, J_{P-C} = 12.7 Hz), 128.2 (d, J_{P-C} = 12.3 Hz), 123.6, 122.5, 120.7, 110.8, 105.6 (d, J_{P-C} = 5.2 Hz), 45.8 (d, J_{P-C} = 68.0 Hz), 10.1, 6.39 (d, J_{P-C} = 1.4 Hz), 4.0 (d, J_{P-C} = 10.0 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 30.5; HRMS (ESI-TOF): *m/z* = 373.1354, calcd for $C_{24}H_{22}O_2P$ [MH^+] 373.1357.

(benzofuran-2-ylmethyl)di-o-tolylphosphine oxide (3q): 51.2 mg (yield 71%), prepared from 35.6 mg of **1a** (0.24 mmol) and 46.0 mg of **2b** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.66 (m, 2H), 7.43–7.38 (m, 3H), 7.31 (d, J = 8.0 Hz, 1H), 7.25–7.12 (m, 6H), 6.59 (dd, J_1 = 3.0 Hz, J_2 = 0.6 Hz, 1H), 3.97 (d, J = 14.0 Hz, 2H), 2.35 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.6, 148.8 (d, J_{P-C} = 6.5 Hz), 142.0 (d, J_{P-C} = 8.4 Hz), 131.96 (d, J_{P-C} = 3.5 Hz), 131.89 (d, J_{P-C} =11.3 Hz), 131.72 (d, J_{P-C} = 11.1 Hz), 130.7 (d, J_{P-C} = 98.1 Hz), 128.7 (d, J_{P-C} = 2.3 Hz), 125.6 (d, J_{P-C} = 12.3 Hz), 123.6, 122.6, 120.6, 110.7, 106.2 (d, J_{P-C} = 5.6 Hz), 31.2 (d, J_{P-C} = 67.3 Hz), 21.2 (d, J_{P-C} = 4.9 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 30.5. HRMS (ESI-TOF): *m/z* = 361.1355, calcd for $C_{23}H_{22}O_2P$ [MH^+] 361.1357.

(benzofuran-2-ylmethyl)di-p-tolylphosphine oxide (3r): 57.6 mg (yield 80%), prepared from 35.6 mg of **1a** (0.24 mmol) and 46.1 mg of **2c** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.43 (d, J = 7.2 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.27–7.24 (m, 4H), 7.20–7.12 (m, 2H), 6.53 (d, J = 3.2 Hz, 1H), 3.84 (d, J = 14.4 Hz, 2H), 2.39 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.6, 148.9 (d, J_{P-C} = 7.3 Hz), 142.5 (d, J_{P-C} = 2.6 Hz), 131.1 (d, J_{P-C} = 9.8 Hz), 129.3 (d, J_{P-C} = 12.4 Hz), 128.8 (d, J_{P-C} = 104.0 Hz), 128.7 (d, J_{P-C} = 3.0 Hz), 123.6, 122.6, 120.6, 110.8, 105.9 (d, J_{P-C} = 5.5 Hz), 31.9 (d, J_{P-C} = 67.6 Hz), 21.6 (d, J_{P-C} = 1.5 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 28.2. HRMS (ESI-TOF): m/z = 361.1360, calcd for $C_{23}H_{22}O_2P$ [MH+]361.1357.

(benzofuran-2-ylmethyl)bis(4-fluorophenyl)phosphine oxide (3s): 65.0 mg (yield 88%), 35.7 mg of **1a** (0.24 mmol) and 47.6 mg of **2d** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.77–7.71 (m, 4H), 7.46–7.44 (m, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.23–7.14 (m, 6H), 6.53 (dd, J_1= 3.2 Hz, J_2= 0.4 Hz, 1H), 3.86 (d, J = 14.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 165.2 (dd, J_{F-C} = 252.5 Hz, J_{P-C} = 3.2 Hz), 154.6, 148.0 (d, J_{P-C} = 8.3 Hz), 133.6 (dd, J_{P-C} = 11.0 Hz, J_{F-C} = 9.0 Hz), 128.4 (d, J_{P-C} = 2.5 Hz), 127.5 (dd, J_{P-C} = 103.1 Hz, J_{F-C} = 3.3 Hz), 124.0, 122.8, 120.7, 116.1 (dd, J_{P-C} = 21.4 Hz, J_{F-C} = 13.1 Hz), 110.8, 106.3 (d, J_{P-C} = 6.7 Hz), 32.2 (d, J_{P-C} = 68.7 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 26.6. HRMS (ESI-TOF): *m/z* = 369.0858, calcd for $C_{21}H_{16}F_2O_2P$ [MH^+] 369.0856.

(benzofuran-2-ylmethyl)bis(4-methoxyphenyl) phosphine oxide (3t): 70.6 mg (yield 90%), prepared from 35.5 mg of **1a** (0.24 mmol) and 52.4 mg of **2e** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.65 (dd, J_1= 11.2 Hz, J_2= 8.8 Hz, 4H), 7.43 (d, J = 6.8 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.20–7.13 (m, 2H), 6.95 (dd, J_1= 8.8 Hz, J_2= 2.4 Hz, 4H), 6.50 (d, J = 2.8 Hz, 1H), 3.83 (s, 6H), 3.82 (d, J= 13.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.5 (d, J_{P-C} = 2.7 Hz), 154.6 (d, J_{P-C} = 1.5 Hz), 149.1 (d, J_{P-C} = 7.0 Hz), 133.0 (d, J_{P-C} = 10.4 Hz), 128.7 (d, J_{P-C} = 3.2 Hz), 123.6, 123.3 (d, J_{P-C} = 107.5 Hz), 122.6, 120.6, 114.2 (d, J_{P-C} = 13.6 Hz), 110.8, 105.8 (d, J_{P-C} = 6.5 Hz), 55.4, 32.3 (d, J_{P-C} = 68.4 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 28.0. HRMS (ESI-TOF): *m/z* = 393.1258, calcd for $C_{23}H_{22}O_4P$ [MH^+] 393.1256.

(benzofuran-2-ylmethyl)bis(3-chlorophenyl)phosphine oxide (3u): 60.0 mg (yield 75%), prepared from 35.7 mg of **1a** (0.24 mmol) and 54.2 mg of **2f** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.78–7.74 (m, 2H), 7.65–7.59 (m, 2H), 7.54–7.51 (m, 2H), 7.46–7.39 (m, 3H), 7.33 (d, J =

8.4 Hz, 1H), 7.23–7.15 (m, 2H), 6.58 (dd, J_1 = 3.2 Hz, J_2 = 0.8 Hz, 1H), 3.89 (d, J = 14.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.7, 147.5 (d, J_{P-C} = 8.3 Hz), 135.3 (d, J_{P-C} = 14.9 Hz), 133.7 (d, J_{P-C} = 98.0 Hz), 132.6 (d, J_{P-C} = 2.0 Hz), 131.0 (d, J_{P-C} = 10.5 Hz), 130.2 (d, J_{P-C} = 12.7 Hz), 129.0 (d, J_{P-C} = 9.2 Hz), 128.4 (d, J_{P-C} = 2.6 Hz), 124.1, 122.9, 120.8, 110.9, 106.6 (d, J_{P-C} = 6.5 Hz), 31.7 (d, J_{P-C} = 68.5 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 25.7. HRMS (ESI-TOF): m/z = 401.0267, calcd for $C_{21}H_{16}Cl_2O_2P$ [MH+] 401.0265.

dimethyl (benzofuran-2-yl(phenyl)methyl)phosphonate (5a): 50.1 mg (yield 83%), prepared from 65.0 mg of **1l** (0.29 mmol) and 21.4 mg of **4a** (0.19 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.55–7.50 (m, 3H), 7.43–7.41 (m, 1H), 7.37–7.28 (m, 3H), 7.26–7.18 (m, 2H), 6.94 (d, J = 2.4 Hz, 1H), 4.69 (d, J = 25.6 Hz, 1H), 3.71 (d, J = 11.2 Hz, 3H), 3.56 (d, J = 10.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.8, 152.6 (d, J_{P-C} = 1.7 Hz), 133.6 (d, J_{P-C} = 6.4 Hz), 129.5 (d, J_{P-C} = 6.6 Hz), 128.8 (d, J_{P-C} = 2.0 Hz), 128.4 (d, J_{P-C} = 1.4 Hz), 127.9 (d, J_{P-C} = 2.6 Hz), 124.2, 122.9, 121.0, 111.1, 105.9 (d, J_{P-C} = 5.1 Hz), 53.8 (d, J_{P-C} = 6.4 Hz), 53.7 (d, J_{P-C} = 7.4 Hz), 45.3 (d, J = 139.7 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 24.0. HRMS (ESI-TOF): m/z = 317.0942, calcd for $C_{17}H_{18}O_4P$ [MH^+] 317.0943.

diethyl (benzofuran-2-yl(phenyl)methyl)phosphonate (5b): 35.1 mg (yield 51%), prepared from 60.4 mg of **1l** (0.27 mmol) and 27.8 mg of **4b** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.55–7.50 (m, 3H), 7.41 (d, J = 8.4 Hz, 1H), 7.36–7.17 (m, 5H), 6.96 (d, J = 2.4 Hz, 1H), 4.66 (d, J = 25.6 Hz, 1H), 4.11–3.96 (m, 3H), 3.82–3.79 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H), 1.12 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.7, 152.9 (d, J_{P-C} = 1.2 Hz), 133.8 (d, J_{P-C} = 6.4 Hz), 129.5 (d, J_{P-C} = 6.1 Hz), 128.6 (d, J_{P-C} = 2.3 Hz), 128.5 (d, J_{P-C} = 1.4 Hz), 127.7 (d, J_{P-C} = 2.6 Hz), 123.9, 122.7, 120.9, 111.0, 105.7 (d, J_{P-C} = 4.5 Hz), 63.2 (d, J_{P-C} = 6.7 Hz), 63.0 (d, J_{P-C} = 7.7 Hz), 45.7 (d, J = 138.7 Hz), 16.3 (d, J_{P-C} = 5.9 Hz), 16.2 (d, J_{P-C} = 5.8 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 21.5. HRMS (ESI-TOF): m/z = 345.1254, calcd for $C_{19}H_{22}O_4P$ [MH^+] 345.1256.

dimethyl (1-(benzofuran-2-yl)pentyl)phosphonate (5c): 29.4 mg (yield 50%), prepared from 52.0 mg of **1n** (0.25 mmol) and 22.0 mg of **4a** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.54–7.46 (m, 2H), 7.27–7.19 (m, 2H),6.65 (d, J = 4.0 Hz, 1H), 3.76 (d, J = 10.8 Hz, 3H), 3.66 (d, J = 10.8 Hz, 3H), 3.39-3.29 (m, 1H), 2.10-1.99 (m, 2H), 1.34-1.21 (m, 4H), 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.9, 153.1 (d, , J_{P-C} = 9.8 Hz), 128.5 (d, J_{P-C} = 2.9 Hz), 123.7 (d, J_{P-C} = 1.4 Hz), 122.7, 120.6 (d, J_{P-C} = 1.4 Hz), 111.1, 105.0 (d, J_{P-C} = 8.6 Hz), 53.3 (d, J_{P-C} = 7.0 Hz), 53.0 (d, J_{P-C} = 7.8 Hz), 38.5 (d, J_{P-C} = 140.0 Hz), 29.9 (d, J_{P-C} = 14.0 Hz), 28.0 (d, J_{P-C} = 3.8 Hz), 22.2, 13.7. ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 28.0. HRMS (ESI-TOF): m/z =297.1249, calcd for $C_{15}H_{22}O_4P$ [MH^+]297.1256.

dimethyl (1-(benzofuran-2-yl)-2,2-dimethylpropyl) phosphonate (5d): 17.9 mg (yield 28%), prepared from 54.1 mg of **1p** (0.26 mmol) and 23.9 mg of **4a** (0.22 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.54 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.27–7.19 (m, 2H), 6.73 (dd, J_1 = 3.0 Hz, J_2 = 0.6 Hz, 1H), 3.72 (d, J = 11.2 Hz, 3H), 3.56 (d, J = 10.8 Hz, 3H), 3.28 (d, J = 24.8 Hz, 1H), 1.17 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.3, 153.0 (d, J_{P-C} = 4.6 Hz), 128.4 (d, J_{P-C} = 2.4 Hz), 123.7, 122.7, 120.7, 111.0, 106.2 (d, J_{P-C} = 6.0 Hz), 53.2 (d, J_{P-C} = 7.8 Hz), 52.1 (d, J_{P-C} = 6.2 Hz), 49.1 (d, J_{P-C} = 137.3 Hz), 34.6, 29.3 (d, J = 6.7 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 27.2. HRMS (ESI-TOF): m/z = 297.1285, calcd for $C_{15}H_{22}O_4P$ [MH^+] 297.1256.

methyl (benzofuran-2-yl(phenyl)methyl)(phenyl) phosphinate (5e): 50.6 mg (yield 65%), prepared from 56.4 mg of **1l** (0.25 mmol) and 33.7 mg of **4c** (0.22 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.66 (m, 1H), 7.57–7.47 (m, 4H), 7.42–7.27 (m, 5.7H), 7.24–7.13 (m, 3.3H), 7.00 (d, J = 2.0 Hz, 0.46H), 6.92 (d, J = 2.0 Hz, 0.54H), 4.76 (d, J = 19.2 Hz, 0.54H), 4.72 (d, J = 19.2 Hz, 0.46H), 3.70 (d, J = 11.2 Hz, 1.37H), 3.56 (d, J = 10.8 Hz, 1.63H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 38.9, 37.5. HRMS (ESI-TOF): m/z = 363.1156, calcd for $C_{22}H_{20}O_3P$ [MH^+] 363.1150.

isopropyl (benzofuran-2-yl(phenyl)methyl)(phenyl) phosphinate (5f): 26.5 mg (yield 34%), prepared from 54.2 mg of **1l** (0.24 mmol) and 36.4 mg of **4d** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.72–7.67 (m, 1H), 7.58–7.14 (m, 10H), 7.21–7.14 (m, 3H), 7.01 (d, J = 2.4 Hz, 0.38H), 6.95 (d, J = 2.4 Hz, 0.62H), 4.68 (d, J = 21.2 Hz, 1H), 4.68–4.50 (m, 1H), 1.26 (d, J = 6.0 Hz, 1.14H), 1.20 (d, J = 6.0 Hz, 1.14H), 1.15 (d, J = 6.0 Hz, 1.86H), 1.08 (d, J = 6.0 Hz, 1.86H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 35.7, 34.4. HRMS (ESI-TOF): m/z = 391.1471, calcd for $C_{24}H_{24}O_3P$ [MH^+] 391.1463.

6-(benzofuran-2-ylmethyl)dibenzo[c,e][1,2]-oxa phosphinine 6-oxide (5g): 54.2 mg (yield 78%), prepared from 37.0 mg of **1a** (0.25 mmol) and 43.7 mg of **4e** (0.2 mmol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.91–7.86 (m, 2H), 7.76 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.69-7.65 (m, 1H), 7.49–7.44 (m, 1H), 7.39–7.29 (m, 2H), 7.24–7.10 (m, 5H), 6.43 (d, J = 4.0 Hz, 1H), 3.63 (d, J = 16.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.7 (d, J_{P-C} = 11.3 Hz), 149.3 (d, J_{P-C} = 9.2 Hz), 147.4 (d, J_{P-C} = 9.2 Hz), 136.0 (d, J_{P-C} = 6.3 Hz), 133.6 (d, J_{P-C} = 2.1 Hz), 130.6, 130.5, 128.4 (d, J_{P-C} = 14.4 Hz), 128.3, 124.9, 124.5, 123.7, 123.6 (d, J_{P-C} = 10.6 Hz), 123.4 (d, J_{P-C} = 122.4 Hz), 122.6, 121.8 (d, J_{P-C} = 11.2 Hz), 120.4 (d, J_{P-C} = 1.6 Hz), 120.3 (d, J_{P-C} = 6.9 Hz), 110.8, 105.9 (d, J_{P-C} = 7.5 Hz), 30.7 (d, J = 94.1 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 30.1. HRMS (ESI-TOF): m/z = 347.0846, calcd for $C_{21}H_{16}O_3P$ [MH^+] 347.0837.

Procedure for the synthesis of (1-(benzofuran-2-yl)but-3-en-1-yl)diphenylphosphine oxide (10): An oven-dried Schlenk tube containing a Teflon-coated stir bar was charged with **3a** (83.0 mg, 0.25 mmol). The Schlenk tube was sealed and then evacuated and backfilled with N_2 (3 cycles). 2 mL of dry THF was injected with stirring. After **3a** was dissolved, the mixture was cooled with an ice-water bath. Then *n*-BuLi (0.11 mL, 2.5 M in hexane, 0.275 mmol) was slowly added. The mixture was kept stirring for another 5 min, followed by the injection of allyl bromide (33.3 mg, 0.275 mmol). The reaction mixture was slowly warmed to room temperature and kept stirring overnight. The mixture was quenched with water and the product was extracted with CH_2Cl_2. Removal of the solvent under vacuum left a solid, which was further purified by flash chromatography on silica (petroleum ether/ethyl acetate 3/1) to afford the product **10** (89.2 mg, 96% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.88–7.83 (m, 2H), 7.64–7.59 (m, 2H), 7.56–7.38 (m, 5H), 7.32–7.27 (m, 3H), 7.19–7.12 (m, 2H), 6.58 (d, J = 3.2 Hz, 1H), 5.75–5.64 (m, 1H), 5.02–4.90 (m, 2H), 3.92 (td, J_1 = 11.6 Hz, J_2 = 3.6 Hz, 1H), 2.89–2.71 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.4 (d, J_{P-C} = 1.3 Hz), 152.5 (d, J_{P-C} = 6.1 Hz), 134.6 (d, J_{P-C} = 13.0 Hz), 132.0 (d, J_{P-C} = 3.1 Hz), 131.7 (d, J_{P-C} = 2.6 Hz), 131.30 (d, J_{P-C} = 94.5 Hz), 131.29 (d, J_{P-C} = 3.7 Hz), 131.20 (d, J_{P-C} = 3.8 Hz), 130.9 (d, J_{P-C} = 99.2 Hz), 128.7 (d, J_{P-C} = 11.9 Hz), 128.4 (d, J_{P-C} = 1.7 Hz), 128.2 (d, J_{P-C} = 11.5 Hz), 123.6, 122.6, 120.6, 117.3, 110.8, 106.1 (d, J_{P-C} = 7.0 Hz), 41.7 (d, J_{P-C} = 67.0 Hz), 32.0. ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 30.9. HRMS (ESI-TOF): m/z = 373.1357, calcd for $C_{24}H_{22}O_2P$ [MH^+] 373.1357.

Procedure for the synthesis of (E)-4-(2-(benzofuran-2-yl)vinyl)-N,N-dimethylaniline (11): this compound was synthesized following a similar procedure for compound **10**. The lithiated **3a** was quenched by 4-(dimethylamino)benzaldehyde (45.0 mg, 0.3 mmol). The reaction mixture was slowly warmed to room temperature and kept stirring overnight. The mixture was quenched with water and the product was extracted with EtOAc. Removal of the solvent under vacuum left a slurry residue, which was further purified by flash chromatography on silica (petroleum ether/ethyl acetate 100/1) to afford the product **11** (55.6 mg, 85% yield). This is a known compound.[18a] ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.49 (d, J = 7.6 Hz, 1H), 7.48–7.42 (m, 3H), 7.28–7.16 (m, 3H), 6.81 (d, J = 16.0 Hz, 1H), 6.72 (d, J = 8.8 Hz, 2H), 6.57 (s, 1H), 3.0 (s, 6H).

Procedure for the synthesis of 1,2-di(benzofuran-2-yl)-2-hydroxyethyl)diphenylphosphine oxide (12): this compound was synthesized following a similar procedure for compound **10**. The lithiated **3a** was quenched by TMSCl (65 μL, 0.5 mmol). The reaction mixture was

slowly warmed to room temperature and kept stirring overnight. The mixture was quenched with water and the product was extracted with CH_2Cl_2. Removal of the solvent under vacuum left a slurry residue, which was further purified by flash chromatography on silica (petroleum ether/ethyl acetate 1/1) to afford the product **12** (36.3 mg, 61% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.06–8.01 (m, 2H), 7.64–7.60 (m, 5H), 7.43–7.33 (m, 4H), 7.26–7.04 (m, 7H), 6.54 (s, 1H), 5.62 (d, J = 6.8 Hz, 1H), 5.32 (s, 1H), 4.50 (dd, J_1 = 9.6 Hz, J_2 = 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.9 (d, J_{P-C} = 12.3 Hz), 154.4, 154.1, 148.5 (d, J_{P-C} = 3.9 Hz), 132.5 (d, J_{P-C} = 3.3 Hz), 132.1 (d, J_{P-C} = 2.7 Hz), 131.2 (d, J_{P-C} = 9.9 Hz), 130.6 (d, J_{P-C} = 9.4 Hz), 130.3 (d, J_{P-C} = 95.6 Hz), 130.2 (d, J_{P-C} = 101.4 Hz), 129.1 (d, J_{P-C} = 11.6 Hz), 128.5 (d, J_{P-C} = 2.2 Hz), 128.3 (d, J_{P-C} = 12.1 Hz), 128.1, 123.8, 123.7, 122.6, 122.5, 121.1, 120.9, 110.9, 110.5, 108.2 (d, J_{P-C} = 5.9 Hz), 104.0, 67.3, 45.0 (d, J_{P-C} = 66.8 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ = 35.1. The structure of this compound was determined by an X-ray crystallographic analysis. The single crystals were obtained from a hexane-CH_2Cl_2 solution by slow evaporation.

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