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Electrochemical Dehydrogenative Phosphorylation of Alcohols for the Synthesis of Organophosphinates

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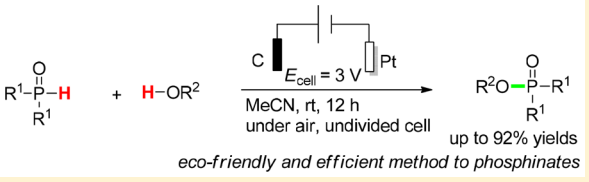
Supporting Information

ABSTRACT: An eco-friendly and efficient method for the synthesis of organophosphinates via an electrochemical cross-dehydrogenative-coupling reaction between alcohols and secondary phosphine oxides has been developed. This electrochemical reaction was conducted at room temperature without the addition of any oxidant, metal catalyst, or additive, which provides a new strategy for the synthesis of organophosphinates.

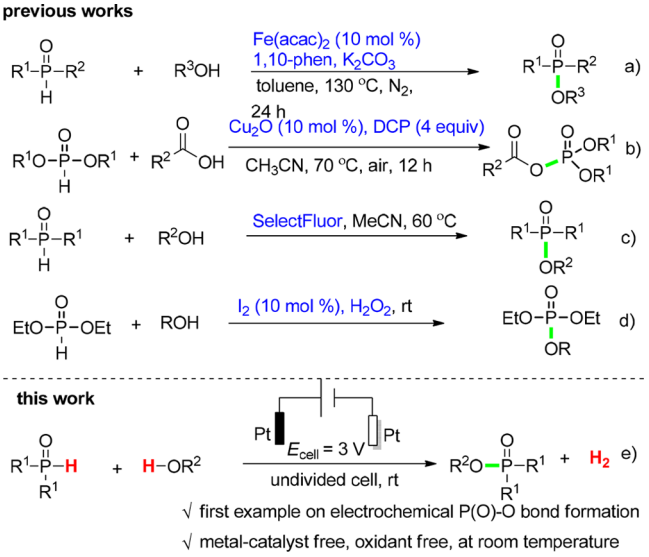


INTRODUCTION

The organophosphinates belong to an extremely important type of organic compounds in organic, biological, and medicinal chemistries, which have been demonstrated to show high bioactivity. This structural unit is also found to exist in many natural products.[1] Furthermore, they have been developed as efficient chiral phosphorus ligands in many asymmetric catalytic reactions.[2] Thus, development of a synthetic method for the preparation of organophosphinates has become a compelling interest and attracted wide research attention. The traditional method for the preparation of these compounds is the direct esterification of alcohols, which relies on the use of toxic and moisture-sensitive phosphoryl halides.[3,4] In the past few years, direct cross-dehydrogenative coupling (CDC) reactions between hydrogen phosphoryl compounds and alcohols have been developed for the synthesis of these compounds.[5] In 2016, the Chen and Han group reported a synthetic method for the preparation of phosphoryl compounds via a Fe(acac)$_2$/1,10-phen-catalyzed CDC reaction of P(O)−H compounds with alcohols at high temperature (Scheme 1a).[6] In 2017, the Li group developed a Cu-catalyzed oxidative CDC reaction of *H*-phosphonates with carboxylic acids at 70 °C with 4 equiv of dicumyl peroxide as the oxidant (Scheme 1b).[7] Although the metal-free methods for the preparation of phosphoryl compounds via CDC reaction have also been developed, an additional oxidant, such as SelectFluor or H_2O_2, is needed for the transformation (Scheme 1c,d).[8]

Electrochemical synthesis is a very special type of organic transformation and has emerged as an active research area in the past few years.[9] Different from the traditional oxidative reaction, electrosynthesis is regarded as a green transformation, as it does not require the use of chemical oxidant. Several types of electroorganic oxidative transformations, such as dehydrogenation cross-coupling reactions,[10] functionalization of unsaturated C−C bonds,[11] cascade cyclization,[12] and other reactions,[13] have been developed, which achieved the C−X (X = C, O, N, S), N−S, N−N, N−P, and S−S bond formations.[10−13]

Scheme 1. Synthesis of Organophosphinates



Inspired by recent developments in the area of synthetic electrochemistry[9−13] and challenged by the problems in the previous systems,[6−8] we herein report the first example of electrochemical cross-dehydrogenative coupling of alcohols with phosphine oxides for the P(O)−O bond formation (Scheme 1e). Notably, Torii and co-workers reported a related work on the electrochemical cross-dehydrogenative coupling of dialkyl phosphites with amines for the P−N bond formation.[14] To the best of our knowledge, the construction of the P−O bond via the electrochemical method has never been reported.

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This electrochemical reaction was conducted at room temperature without the use of any oxidant and metal catalyst, which provides a new strategy for the synthesis of organophosphinates.

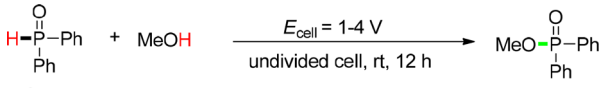
RESULTS AND DISCUSSION

Initially, diphenylphosphine oxide **1a** and methanol **2a** were selected as the model compounds for the electrochemical CDC reaction, and the results are summarized in Table 1. The reaction occurred when it was carried out in acetonitrile by the use of platinum-plate anode and cathode with H_4NI as an electrolyte, at 3.0 V cell potential at room temperature under air for 12 h, affording the corresponding coupling product **3a** in 40% isolated yield (entry 1). Other electrolytes, such as $LiClO_4$, were tried but did not work for this reaction (entry 2). The reaction proceeded smoothly with Bu_4NBr (entry 3) or Bu_4NI (entry 4) as electrolyte, and the desired product **3a** was obtained in dramatically increased yields (84% and 86%, respectively). Performing the reaction under an argon atmosphere did not provide any improvement of the chemical yield (56%, entry 5). To further improve the yield, several types of electrodes, such as nickel, graphite and copper plates, were scanned for this reaction (entries 6–9). The best result was obtained when the graphite electrode was used for the anode and the platinum plate was used for the cathode (92% yield, entry 9). Solvent showed a great effect on this reaction. The use of dichloromethane, DMF, and 1,4-dioxane (entries 10–12) also afforded the desired product but in lower chemical yields. Variation of the voltage from 1.0 to 4.0 V was carried out (entries 13–18), and no improvement on the reaction yield was found, which indicated 3.0 V voltage was the best reaction condition. Finally, the addition of additives into the system was demonstrated to be unsuccessful, and almost the same level of chemical yield was obtained (entries 19–20).

After obtaining the optimized reaction conditions, we then investigated the substrate generality of this electrochemical coupling reaction (Scheme 2). The reaction tolerated a wide range of diarylphosphine oxides bearing electron-donating and -withdrawing groups at different positions on the phenyl ring and proceeded smoothly to give the corresponding organophosphinates **3a–l** in good to excellent yields (59–92%). For example, a series of methyl-substituted derivatives **1b–d** reacted with methanol **2a** well, and the chemical yields ranged from 59 to 84%. Notably, the substrate-bearing dimethyl-substituted phenyl **1e** could also work well in this system, affording the desired product **3e** in 73% yield. The electronic properties of the substituent had almost no noticeable effect on the reaction efficiency. For example, the substrates with a *para*-substituted phenyl group, **2d**, **2f–i**, either with a strong electron-withdrawing group (**1f,g**) or with an electron-donating group (**1i**) could be well tolerated in the reaction resulting in good yields (76–83% yields, **3f–i**). Taking into account the great value of alkyl phosphinates, we were curious to develop the alkyl phosphine oxides as the substrates for this reaction. We were pleased that the alkyl phosphine oxides, such as dibenzylphosphine oxide **1j**, dicyclohexylphosphine oxide **1k**, and dicyclopentylphosphine oxide **1l**, were also suitable substrates for this reaction, resulting in the desired products in 60–82% yields (**3j–l**). Dibutyl phosphonate **1m** could participate in this reaction, and the desired product was isolated in 30% yield (**3m**).

Then another part of the substrate scope study with regard to the alcohols was carried out, and the results are shown in Scheme 3. Almost all of the examined linear alcohols were

Table 1. Optimization of the Reaction Conditions[a]

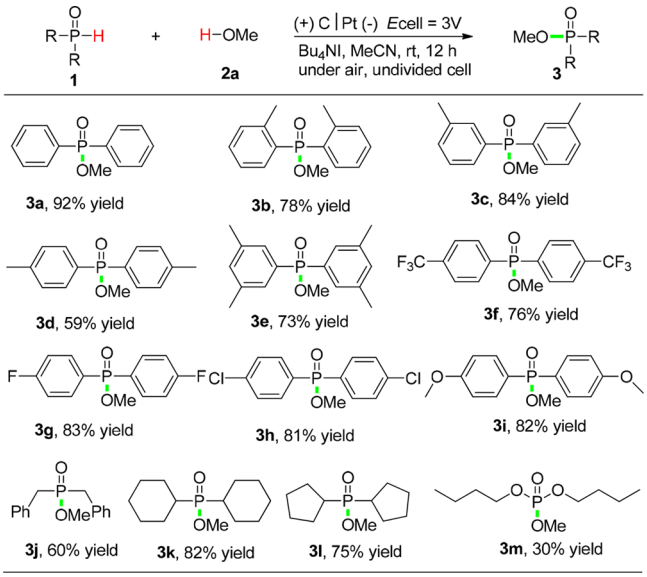


1a **2a** **3a**

entry	anode/cathode	solvent	electrolyte	voltage (V)	yield[b] (%)
1	Pt/Pt	MeCN	NH_4I	3	40
2	Pt/Pt	MeCN	$LiClO_4$	3	nr
3	Pt/Pt	MeCN	Bu_4NBr	3	84
4	Pt/Pt	MeCN	Bu_4NI	3	86
5	Pt/Pt	MeCN	Bu_4NI	3	56[c]
6	C/Ni	MeCN	Bu_4NI	3	55
7	C/C	MeCN	Bu_4NI	3	88
8	C/Cu	MeCN	Bu_4NI	3	50
9	C/Pt	MeCN	Bu_4NI	3	92
10	C/Pt	DCM	Bu_4NI	3	86
11	C/Pt	DMF	Bu_4NI	3	76
12	C/Pt	dioxane	Bu_4NI	3	11
13	C/Pt	MeCN	Bu_4NI	1	6
14	C/Pt	MeCN	Bu_4NI	1.5	12
15	C/Pt	MeCN	Bu_4NI	2	75
16	C/Pt	MeCN	Bu_4NI	2.5	82
17	C/Pt	MeCN	Bu_4NI	3.5	84
18	C/Pt	MeCN	Bu_4NI	4	80
19	C/Pt	MeCN	Bu_4NI	3	78[d]
20	C/Pt	MeCN	Bu_4NI	3	84[e]

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (1 mL), solvent (4 mL), electrolyte (2.0 equiv) in an undivided cell at room temperature for 12 h. [b]Isolated yield based on **1a**. [c]Argon atmosphere. [d]K_2CO_3 (2.0 equiv) was added. [e]Et_3N (2.0 equiv) was added.

Scheme 2. Substrate Scope Study of P(O)–H Compounds[a,b]



[a]Reaction conditions: graphite anode (1 cm × 1 cm × 0.3 cm), Pt cathode (1 cm × 1 cm × 0.2 mm), at 3.0 V cell potential, **1** (0.2 mmol), **2a** (1 mL), MeCN (4 mL), Bu_4NI (2 equiv) under air at room temperature for 12 h. [b]Isolated yield based on **1**.

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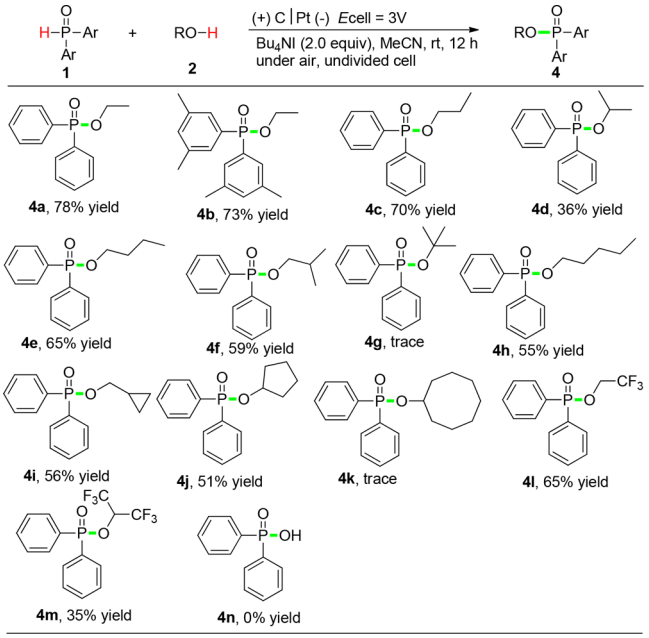
Scheme 3. Substrate Scope Study of Alcohols[a,b]

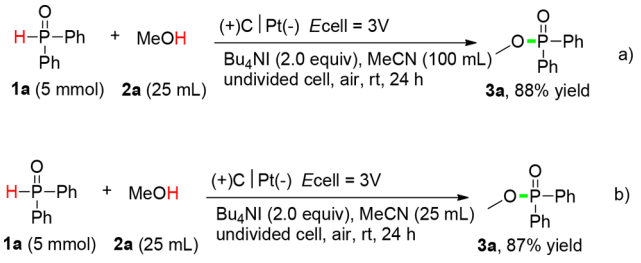


[a]Reaction conditions: graphite anode (1 cm × 1 cm × 0.3 cm), Pt cathode (1 cm × 1 cm × 0.2 mm), at 3.0 V cell potential, **1** (0.2 mmol), **2** (120 equiv), MeCN (4 mL), Bu_4NI (2 equiv) under air at room temperature for 12 h. [b]Isolated yield based on **1**.

suitable substrates and reacted very well with diphenylphosphine oxide **1a**, affording the corresponding products in moderate to good chemical yields (36−78%). It should be mentioned that the isolated yields for the primary alcohols became lower when the length of alkyl chain increased (**4a**, **4c**, **4e** and **4h**). A moderate yield (55%, **4h**) was obtained when pentan-1-ol was used as a coupling partner. An obvious steric effect of this reaction was observed when secondary and tertiary alcohols were used as substrates. For example, the reaction of 2-propanol also proceeded, giving the desired product with only 36% yield (**4d**). Unfortunately, the reaction with the tertiary alcohol did not happen at all (**4g**). Then, three cyclic alcohols were investigated in this electrochemical system, and a similar trend was also found from these reactions. It was obvious that the alcohols bearing larger alkyl membered ring gave lower chemical yields (**4i−k**). Two fluorinated alcohols, 2,2,2-trifluoroethanol and 1,1,1,3,3,3-hexafluoropropan-2-ol, were also examined in this reaction. These two fluorinated substrates worked very well in the coupling reactions, yielding the products **4l**,**m** in moderate yields. Finally, we tried to use water as a coupling partner in this electrochemical coupling reaction with diphenylphosphine oxide. However, the reaction was unsuccessful and failed to give the desired product after 12 h (**4n**).

As another synthetic objective of this study, we tried to demonstrate the possibility of the large-scale synthesis of this electrochemical reaction (Scheme 4). The reaction was conducted with the use of 5 mmol of diphenylphosphine oxide **1a** and methanol. The reaction proceeded smoothly, and the desired product **3a** was obtained in 88% isolated yield after the reaction time was prolonged to 24 h (Scheme 4a). Also, 87% yield was obtained when the reaction was conducted in 25 mL of acetonitrile (Scheme 4b). This result clearly indicates the high potential of this electrochemical coupling reaction as

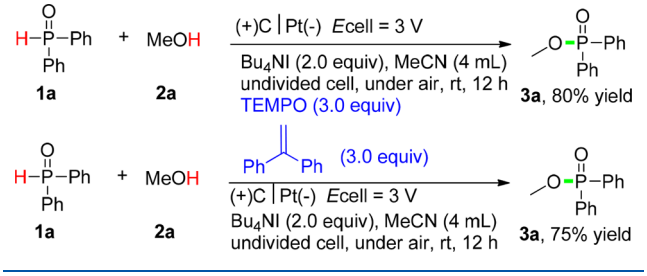
Scheme 4. Large-Scale Synthesis



an efficient and eco-friendly way for the synthesis of organophosphinates.

The final goal of this study was the mechanism investigation (Scheme 5). The reaction also proceeded smoothly when a

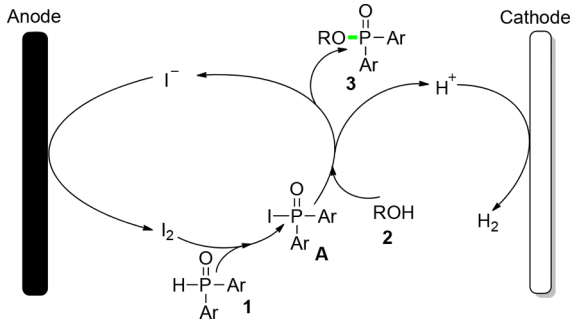
Scheme 5. Control Experiments



radical inhibitor TEMPO (3.0 equiv) was added to the system under the standard reaction conditions, and the desired product **3a** was obtained in 80% yield. A similar result was also found when a radical trapping reagent 1,1-diphenylethylene was added into the reaction under standard conditions, and the desired coupling product **3a** was isolated in 75% yield. These results clearly disclose that this is not a radical process.

On the basis of the above results and the previous reports,[8b] a possible mechanism has been provided in Scheme 6 for this

Scheme 6. Possible Mechanism



electrochemical transformation. Initially, iodide anion is oxidized at the anode to generate iodide.[15] Then, electrophilic iodination of *H*-phosphite **1** provides the phosphoryl iodide intermediate **A**. Subsequently, the nucleophilic substitution happens between intermediate **A** and alcohol **2**, affording the final coupling product **3**, iodine anion for the next cycle, and proton. At the same time, the proton is reduced to release hydrogen gas at the cathode.

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CONCLUSION

In summary, an electrochemical cross-dehydrogenative-coupling reaction between alcohols and secondary phosphine oxides has been reported. Using this eco-friendly method, we were able to synthesize the organophosphinates from readily available starting materials under oxidant-free conditions. This work represents the first example on the P−O bond formation under electrochemical conditions, also provides a new and green access to organophosphinates.

EXPERIMENTAL SECTION

General Procedures for the Synthesis of Phosphine Oxides 1. All of the phosphine oxides are known compounds, and the commercially unavailable phosphine oxides were prepared according to the previous reports.[16] Aryl bromide (16.5 mmol, 3.3 equiv) in THF (10 mL) was added slowly to a suspension of magnesium turnings (600 mg, 25 mmol, 5.0 equiv) in THF (15 mL) containing a catalytic amount of I_2 (cat.) and refluxed for 1 h. A solution of diethyl phosphate (690 mg, 5.0 mmol, 1.0 equiv) in THF (5 mL) was added slowly at 0 °C. Then the mixture was warmed to room temperature and stirred over 3 h. After ammonium chloride solution quenching, the precipitated solid was removed by filtration. The filtrate was extracted with ethyl acetate, washed with sodium chloride solution, and dried over Na_2SO_4. After filtration and concentration, the pure product was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1:1).

*Di-o-tolylphosphine oxide (**1b**):*[16a] white solid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.20 (d, J = 477.3 Hz, 1H), 7.76−7.67 (m, 2H), 7.47 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.27−7.22 (m, 2H), 2.38 (s, 6H).

*Di-m-tolylphosphine oxide (**1c**):*[16a] colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.01 (d, J = 479.2 Hz, 1H), 7.58−7.42 (m, 4H), 7.40−7.34 (m, 4H), 2.38 (s, 6H).

*Bis(4-(trifluoromethyl)phenyl)phosphine oxide (**1f**):*[16b] pale yellow oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.19 (d, J = 491.3 Hz, 1H), 7.92−7.78 (m, 8H).

*Bis(4-fluorophenyl)phosphine oxide (**1g**):*[16a] colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.10 (d, J = 485.9 Hz, 1H), 7.78−7.66 (m, 4H), 7.19−7.21 (m, 4H).

*Bis(4-chlorophenyl)phosphine oxide (**1h**):*[16a] white solid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.07 (d, J = 487.0 Hz, 1H), 7.69−7.60 (m, 4H), 7.55−7.46 (m, 4H).

*Bis(4-methoxyphenyl)phosphine oxide (**2i**):*[16a] white solid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.03 (d, J = 477.4 Hz, 1H), 7.65−7.56 (m, 4H), 7.00−7.10 (m, 4H), 3.85 (s, 6H).

*Dibenzylphosphine oxide (**1j**):*[16b] white solid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.39−7.19 (m, 8H), 6.96 (dp, J = 468.8, 3.3 Hz, 1H), 3.18 (dt, J = 14.5, 3.6 Hz, 4H).

*Dicyclohexylphosphine oxide (**2k**):*[16a] white solid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 6.31 (dt, J = 434.3, 2.9 Hz, 1H), 2.14−1.16 (m, 22H).

*Dicyclopentylphosphine oxide (**1l**):*[16c] colorless oil; ^{1}H NMR (400 MHz, chloroform-*d*) δ 6.54 (dt, J = 440.2, 3.3 Hz, 1H), 2.18−1.53 (m, 18H).

Large-Scale Synthesis. The reaction took place in an oven-dried beaker (250 mL) equipped with a stir bar and Bu_4NI (10 mmol). The bottle was equipped with carbon electrodes (10× 10× 3 mm) as the anode and platinum electrodes (10× 10× 0.2 mm) as the cathode under air. *H*-Phosphine oxide **1** (5 mmol) was added into bottle. Then 100 mL of MeCN and 25 mL of CH_3OH were added into bottle by syringe. The reaction mixture was stirred and electrolyzed at a constant voltage of 3 V (the dual display potentiostat was operating in constant voltage mode) under room temperature for 24 h. When the reaction was finished, the solution was removed with a rotary evaporator. The pure product **3a** was obtained in 88% yield (1.02 g) by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1).

Control Experiment with the Addition of TEMPO. The reaction took place in an oven-dried undivided three-necked bottle (10 mL) equipped with a stir bar and Bu_4NI (0.4 mmol). The bottle was equipped with carbon electrodes (10× 10× 3 mm) as the anode and platinum electrodes (10× 10× 0.2 mm) as the cathode under air. *H*-Phosphine oxides (0.2 mmol) and TEMPO (3 equiv) were added into bottle. Then 4 mL of MeCN and 1 mL of CH_3OH were added into the bottle by syringe. The reaction mixture was stirred and electrolyzed at a constant voltage of 3 V (the dual display potentiostat was operating in constant voltage mode) under room temperature for 12 h. When the reaction was finished, the solution was removed with a rotary evaporator. The pure product **3a** was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1).

Control Experiment with the Addition of 1,1-Diphenylethylene. The reaction took place in an oven-dried undivided three-necked bottle (10 mL) equipped with a stir bar and Bu_4NI (0.4 mmol). The bottle was equipped with carbon electrodes (10× 10× 3 mm) as the anode and platinum electrodes (10× 10× 0.2 mm) as the cathode under air. *H*-Phosphine oxides (0.2 mmol) were added into the bottle. Then 4 mL of MeCN, 1 mL of CH_3OH, and 1,1-diphenylethylene (3 equiv) were added into the bottle by syringe. The reaction mixture was stirred and electrolyzed at a constant voltage of 3 V (the dual display potentiostat was operating in constant voltage mode) under room temperature for 12 h. When the reaction was finished, the solution was removed with a rotary evaporator. The pure product **3a** was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1).

General Procedure for the Electrochemical CDC Reaction. The reaction took place in an oven-dried undivided three-necked bottle (10 mL) equipped with a stir bar and Bu_4NI (0.4 mmol). The bottle was equipped with carbon electrodes (10 × 10 × 3 mm) as the anode and platinum electrodes (10 × 10 × 0.2 mm) as the cathode under air. *H*-Phosphine oxides **1** (0.2 mmol) was added into bottle. Then MeCN (4 mL) and alcohols **2** (120 equiv) were added into the bottle by syringe. The reaction mixture was stirred and electrolyzed at a constant voltage of 3 V (the dual display potentiostat was operating in constant voltage mode) under room temperature for 12 h. When the reaction was finished, the solution was removed on a rotary evaporator. The pure product **3** or **4** was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1).

*Methyl diphenylphosphinate (**3a**):* colorless oil, 43 mg (92% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.86−7.78 (m, 4H), 7.56−7.42 (m, 6H), 3.76 (d, J = 11.2 Hz, 3H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 132.2 (d, J = 2.8 Hz), 131.7 (d, J = 10.1 Hz), 131.0 (d, J = 137.8 Hz), 128.6 (d, J = 13.1 Hz), 51.6 (d, J = 6.0 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 33.28; HRMS (TOF MS ESI) calcd for $C_{13}H_{14}O_2P^+$ $[M + H]^+$ 233.0726, found 233.0728; IR (cm^{-1})

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3057, 3013, 2947, 2920, 2848, 1646, 1591, 1439, 1226, 1182, 1130, 1113, 1035.

*Methyl di-o-tolylphosphinate (**3b**):* colorless oil, 41 mg (78% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.94−7.86 (m, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.28 (td, *J* = 7.2, 2.6 Hz, 2H), 7.23−7.17 (m, 2H), 3.75 (d, *J* = 11.1 Hz, 3H), 2.36 (s, 6H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 141.7 (d, *J* = 11.1 Hz), 133.6 (d, *J* = 9.9 Hz), 132.3 (d, *J* = 2.7 Hz), 131.4 (d, *J* = 12.6 Hz), 129.5 (d, *J* = 132.5 Hz), 125.5 (d, *J* = 12.7 Hz), 51.0 (d, *J* = 5.8 Hz), 21.1 (d, *J* = 4.2 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 34.12; HRMS (TOF MS ESI) calcd for $C_{15}H_{18}O_2P^+$ [M + H]$^+$ 261.1039, found 261.1042; IR (cm^{-1}) 3058, 3014, 2947, 2846, 1738, 1595, 1455, 1382, 1279, 1219, 1143, 1078, 1031.

*Methyl di-m-tolylphosphinate (**3c**):* colorless oil, 44 mg (84% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.69−7.55 (m, 4H), 7.37−7.30 (m, 4H), 3.75 (d, *J* = 11.1 Hz, 3H), 2.37 (s, 6H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 138.4 (d, *J* = 13.1 Hz), 133.0 (d, *J* = 2.9 Hz), 132.1 (d, *J* = 10.2 Hz), 130.9 (d, *J* = 136.4 Hz), 128.7 (d, *J* = 10.1 Hz), 128.5 (d, *J* = 13.9 Hz), 51.5 (d, *J* = 6.0 Hz), 21.4; ^{31}P NMR (162 MHz, chloroform-*d*) δ 33.96; HRMS (TOF MS ESI) calcd for $C_{15}H_{18}O_2P^+$ [M + H]$^+$ 261.1039, found 261.1042; IR (cm^{-1}) 3016, 2947, 2923, 2847, 2736, 1738, 1597, 1581, 1479, 1455, 1410, 1378, 1236, 1214, 1120, 1032.

*Methyl di-p-tolylphosphinate (**3d**):* colorless oil, 31 mg (59% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.69 (dd, *J* = 12.0, 8.0 Hz, 4H), 7.28−7.23 (m, 4H), 3.73 (d, *J* = 11.1 Hz, 3H), 2.38 (s, 6H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 142.7 (d, *J* = 2.7 Hz), 131.6 (d, *J* = 10.5 Hz), 129.3 (d, *J* = 13.5 Hz), 127.9 (d, *J* = 139.9 Hz), 51.4 (d, *J* = 6.0 Hz), 21.6. ^{31}P NMR (162 MHz, chloroform-*d*) δ 34.32; HRMS (TOF MS ESI) calcd for $C_{15}H_{18}O_2P^+$ [M + H]$^+$ 261.1039, found 261.1042; IR (cm^{-1}) 3023, 2947, 2923, 2868, 2846, 2732, 1924, 1814, 1726, 1603, 1503, 1451, 1401, 1380, 1310, 1228, 1209, 1185, 1128, 1111, 1034, 1018.

*Methyl bis(3,5-dimethylphenyl)phosphinate (**3e**):* colorless oil, 42 mg (73% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.42 (d, *J* = 12.5 Hz, 4H), 7.14 (s, 2H), 3.74 (d, *J* = 11.1 Hz, 3H), 2.33 (s, 12H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 138.2 (d, *J* = 13.7 Hz), 133.9 (d, *J* = 2.9 Hz), 130.8 (d, *J* = 135.6 Hz), 129.2 (d, *J* = 10.1 Hz), 51.4 (d, *J* = 6.1 Hz), 21.2; ^{31}P NMR (162 MHz, chloroform-*d*) δ 34.49; HRMS (TOF MS ESI) calcd for $C_{17}H_{22}O_2P^+$ [M + H]$^+$ 289.1352, found 289.1353; IR (cm^{-1}) 3029, 2998, 2946, 2919, 2860, 2734, 1805, 1736, 1601, 1456, 1422, 1379, 1277, 1224, 1131, 1034, 994.

*Methyl bis(4-(trifluoromethyl)phenyl)phosphinate (**3f**):* colorless oil, 56 mg (76% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.97 (dd, *J* = 12.0, 8.0 Hz, 4H), 7.75 (dd, *J* = 8.2, 2.7 Hz, 4H), 3.84 (d, *J* = 11.2 Hz, 3H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 134.6 (d, *J* = 138.0 Hz), 134.4 (dd, *J* = 32.9, 3.0 Hz), 132.2 (d, *J* = 10.5 Hz), 125.7 (dq, *J* = 13.3, 3.7 Hz), 123.4 (q, *J* = 273.7 Hz), 52.0 (d, *J* = 6.1 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 29.35; HRMS (TOF MS ESI) calcd for $C_{15}H_{12}F_6O_2P^+$ [M + H]$^+$ 369.0474, found 369.0473; IR (cm^{-1}): 3046, 2954, 2853, 1938, 1738, 1679, 1614, 1505, 1461, 1401, 1324, 1238, 1171, 1131, 1107, 1063, 1036, 1017.

*Methyl bis(4-fluorophenyl)phosphinate (**3g**):* colorless oil, 45 mg (83% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.86−7.77 (m, 4H), 7.16 (tq, *J* = 9.3, 2.5 Hz, 4H), 3.77 (d, *J* = 11.2 Hz, 3H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 165.3 (dd, *J* = 254.0, 3.5 Hz), 134.2 (dd, *J* = 11.6, 8.9 Hz), 126.8 (dd, *J* = 142.0, 3.5 Hz), 116.0 (dd, *J* = 21.5, 14.4 Hz), 51.6 (d, *J* = 6.0 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 31.41; HRMS (TOF MS ESI) calcd for $C_{13}H_{12}F_2O_2P^+$ [M + H]$^+$ 269.0537, found 269.0537; IR (cm^{-1}) 3100, 3063, 3037, 2970, 2950, 2850, 1738, 1659, 1592, 1500, 1400, 1365, 1301, 1226, 1160, 1129, 1112, 1033, 1014.

*Methyl bis(4-chlorophenyl)phosphinate (**3h**):* yellow oil, 49 mg (81% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.76−7.70 (m, 4H), 7.48−7.43 (m, 4H), 3.77 (d, *J* = 11.2 Hz, 3H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 139.1 (d, *J* = 3.6 Hz), 133.0 (d, *J* = 11.0 Hz), 129.2 (d, *J* = 141.4 Hz), 129.1 (d, *J* = 13.9 Hz), 51.7 (d, *J* = 6.0 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 31.23; HRMS (TOF MS ESI) calcd for $C_{13}H_{12}Cl_2O_2P^+$ [M + H]$^+$ 300.9946, found 300.9944; IR (cm^{-1}): 3082, 3052, 3021, 2948, 2847, 1738, 1585, 1482, 1391, 1231, 1130, 1087, 1034, 1013.

*Methyl bis(4-methoxyphenyl)phosphinate (**3i**):* colorless oil, 48 mg (82% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.76−7.69 (m, 4H), 6.95 (dq, *J* = 9.3, 2.5 Hz, 4H), 3.82 (s, 6H), 3.72 (d, *J* = 11.2 Hz, 3H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 162.6 (d, *J* = 3.1 Hz), 133.5 (d, *J* = 11.4 Hz), 122.6 (d, *J* = 144.7 Hz), 114.1 (d, *J* = 14.1 Hz), 55.3, 51.3 (d, *J* = 5.9 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 34.14; HRMS (TOF MS ESI) calcd for $C_{15}H_{18}O_4P^+$ [M + H]$^+$ 293.0937, found 293.0941; IR (cm^{-1}) 3068, 3005, 2970, 2947, 2841, 1738, 1598, 1571, 1505, 1462, 1442, 1409, 1365, 1296, 1256, 1218, 1179, 1130, 1116, 1028.

*Methyl dibenzylphosphinate (**3j**):* white solid; mp 68−73 °C, 31 mg (60% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.35−7.20 (m, 10H), 3.56 (d, *J* = 10.5 Hz, 3H), 3.08 (d, *J* = 16.3 Hz, 4H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 131.3 (d, *J* = 7.6 Hz), 129.9 (d, *J* = 5.8 Hz), 128.7 (d, *J* = 2.6 Hz), 127.0 (d, *J* = 3.1 Hz), 51.9 (d, *J* = 7.0 Hz), 35.6 (d, *J* = 86.9 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 49.22; HRMS (TOF MS ESI) calcd for $C_{15}H_{18}O_2P^+$ [M + H]$^+$ 261.1039, found 261.1042; IR (cm^{-1}) 3086, 3062, 3029, 3005, 2970, 2950, 2907, 2848, 1738, 1602, 1496, 1455, 1403, 1365, 1229, 1217, 1130, 1039.

*Methyl dicyclohexylphosphinate (**3k**):* colorless oil, 40 mg (82% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.72 (d, *J* = 9.8 Hz, 3H), 2.01−1.14 (m, 22H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 52.0 (d, *J* = 7.0 Hz), 36.0 (d, *J* = 88.5 Hz), 26.3 (d, *J* = 13.6 Hz), 25.9 (d, *J* = 1.1 Hz), 25.3 (dd, *J* = 5.5, 3.4 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 59.90; HRMS (TOF MS ESI) calcd for $C_{13}H_{26}O_2P^+$ [M + H]$^+$ 245.1665, found 245.1672; IR (cm^{-1}) 2929, 2853, 1738, 1449, 1365, 1277, 1223, 1191, 1120, 1051, 1036.

*Methyl dicyclopentylphosphinate (**3l**):* colorless oil, 33 mg (75% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.74 (d, *J* = 9.8 Hz, 3H), 2.18−2.02 (m, 2H), 1.96−1.53 (m, 16H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 51.9 (d, *J* = 6.9 Hz), 37.1 (d, *J* = 92.9 Hz), 26.8−26.5 (m), 26.4 (dd, *J* = 10.3, 2.4 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 63.18; HRMS (TOF MS ESI) calcd for $C_{11}H_{22}O_2P^+$ [M + H]$^+$ 217.1352, found 217.1355; IR (cm^{-1}) 2955, 2870, 2620, 1718, 1634, 1618, 1452, 1365, 1262, 1201, 1039.

*Dibutyl methyl phosphate (**3m**):* white solid; mp 66−69 °C, 14 mg (30% yield); ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.05 (q, *J* = 6.7 Hz, 4H), 3.76 (d, *J* = 11.1 Hz, 3H), 1.71−1.63 (m, 4H), 1.48−1.36 (m, 4H), 0.94 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR {^{1}H} (101 MHz, chloroform-*d*) δ 67.5 (d, *J* = 6.0 Hz), 54.1 (d, *J* = 6.0 Hz), 32.3 (d, *J* = 6.8 Hz), 18.7, 13.6; ^{31}P NMR

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(162 MHz, chloroform-*d*) δ 0.37; HRMS (TOF MS ESI) calcd for $C_9H_{22}O_4P^+$ $[M + H]^+$ 225.1250, found 225.1249; IR (cm^{-1}) 2960, 2875, 1738, 1464, 1365, 1281, 1230, 1217, 1120, 1030.

*Ethyl diphenylphosphinate (**4a**):* colorless oil, 38 mg (78% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.86−7.78 (m, 4H), 7.54−7.41 (m, 6H), 4.11 (p, J = 7.1 Hz, 2H), 1.37 (t, J = 7.0 Hz, 3H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.1 (d, J = 2.7 Hz), 131.6 (d, J = 137.4 Hz), 131.6 (d, J = 10.1 Hz), 128.5 (d, J = 13.1 Hz), 61.1 (d, J = 5.8 Hz), 16.5 (d, J = 6.6 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 31.38; HRMS (TOF MS ESI) calcd for $C_{14}H_{16}O_2P^+$ $[M + H]^+$ 247.0882, found 247.0883; IR (cm^{-1}) 3077, 3058, 2982, 2855, 1737, 1678, 1592, 1485, 1392, 1227, 1130, 1114, 1034.

*Ethyl bis(3,5-dimethylphenyl)phosphinate (**4b**):* white solid; mp 74−79 °C, 44 mg (73% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.43 (d, J = 12.4 Hz, 4H), 7.12 (s, 2H), 4.13−4.04 (m, 2H), 2.33 (s, 12H), 1.37 (t, J = 7.0 Hz, 3H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 138.2 (d, J = 13.7 Hz), 133.8 (d, J = 2.9 Hz), 131.5 (d, J = 135.4 Hz), 129.1 (d, J = 10.1 Hz), 61.0 (d, J = 5.8 Hz), 21.3, 16.6 (d, J = 6.5 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 32.62; HRMS (TOF MS ESI) calcd for $C_{18}H_{24}O_2P^+$ $[M + H]^+$ 303.1508, found 303.1513; IR (cm^{-1}) 3030, 2979, 2921, 2861, 1738, 1601, 1443, 1276, 1163, 1097, 993.

*Propyl diphenylphosphinate (**4c**):* white solid; mp 80−84 °C, 37 mg (70% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.86−7.78 (m, 4H), 7.54−7.41 (m, 6H), 3.99 (q, J = 6.7 Hz, 2H), 1.81−1.70 (m, 2H), 1.01−0.95 (m, 2H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.1 (d, J = 2.8 Hz), 131.7 (d, J = 137.4 Hz), 131.6 (d, J = 10.1 Hz), 128.5 (d, J = 13.1 Hz), 66.5 (d, J = 6.1 Hz), 23.9 (d, J = 6.7 Hz), 10.2; ^{31}P NMR (162 MHz, chloroform-*d*) δ 31.14; HRMS (TOF MS ESI) calcd for $C_{15}H_{18}O_2P^+$ $[M + H]^+$ 261.1039, found 261.1039; IR (cm^{-1}) 3058, 3015, 2969, 1738, 1592, 1484, 1365, 1227, 1113, 1058.

*Isopropyl diphenylphosphinate (**4d**):* white solid; mp 86−89 °C, 19 mg (36% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.86−7.78 (m, 4H), 7.53−7.40 (m, 6H), 4.74−4.62 (m, 1H), 1.35 (d, J = 6.1 Hz, 6H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.4 (d, J = 138.4 Hz), 131.9 (d, J = 2.7 Hz), 131.6 (d, J = 10.0 Hz), 128.4 (d, J = 13.0 Hz), 70.2 (d, J = 6.0 Hz), 24.3 (d, J = 4.1 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 29.80; HRMS (TOF MS ESI) calcd for $C_{15}H_{18}O_2P^+$ $[M + H]^+$ 261.1039, found 261.1038; IR (cm^{-1}) 3058, 3015, 2972, 2929, 1738, 1592, 1465, 1440, 1386, 1219, 1178, 1118, 1100, 1002.

*Butyl diphenylphosphinate (**4e**):* colorless oil, 36 mg (65% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.85−7.78 (m, 4H), 7.54−7.41 (m, 6H), 4.03 (q, J = 6.6 Hz, 2H), 1.75−1.67 (m, 2H), 1.49−1.38 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.1 (d, J = 2.6 Hz), 131.7 (d, J = 137.4 Hz), 131.6 (d, J = 10.0 Hz), 128.5 (d, J = 13.1 Hz), 64.7 (d, J = 6.0 Hz), 32.6 (d, J = 6.6 Hz), 18.9, 13.6; ^{31}P NMR (162 MHz, chloroform-*d*) δ 31.14; HRMS (TOF MS ESI) calcd for $C_{16}H_{20}O_2P^+$ $[M + H]^+$ 275.1195, found 275.1195; IR (cm^{-1}) 3016, 2970, 2874, 1739, 1591, 1441, 1365, 1218, 1114, 1063, 985.

*Isobutyl diphenylphosphinate (**4f**):* white solid; mp 64−68 °C, 32 mg (59% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.85−7.78 (m, 4H), 7.55−7.42 (m, 6H), 3.79 (t, J = 6.3 Hz, 2H), 2.07−1.96 (m, 1H), 0.97 (d, J = 6.7 Hz, 6H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.1 (d, J = 2.8 Hz), 131.6 (d, J = 137.4 Hz), 131.6 (d, J = 10.1 Hz), 128.5 (d, J = 13.1 Hz), 70.7 (d, J = 6.3 Hz), 29.3 (d, J = 6.9 Hz), 18.9; ^{31}P NMR (162 MHz, chloroform-*d*) δ 30.96; HRMS (TOF MS ESI) calcd for $C_{16}H_{20}O_2P^+$ $[M + H]^+$ 275.1195, found 275.1195; IR (cm^{-1}) 3077, 3015, 2961, 2875, 1738, 1592, 1470, 1367, 1228, 1130, 1071.

*Pentyl diphenylphosphinate (**4h**):* colorless oil, 32 mg (55% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.84−7.76 (m, 4H), 7.53−7.40 (m, 6H), 4.01 (q, J = 6.7 Hz, 2H), 1.76−1.67 (m, 2H), 1.42−1.23 (m, 4H), 0.87 (t, J = 7.1 Hz, 3H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.1 (d, J = 2.8 Hz), 131.6 (d, J = 138.4 Hz), 131.6 (d, J = 10.1 Hz), 128.5 (d, J = 13.1 Hz), 65.0 (d, J = 6.1 Hz), 30.2 (d, J = 6.6 Hz), 27.7, 22.2, 14.0; ^{31}P NMR (162 MHz, chloroform-*d*) δ 31.20; HRMS (TOF MS ESI) calcd for $C_{17}H_{22}O_2P^+$ $[M + H]^+$ 289.1352, found 289.1351; IR (cm^{-1}) 3077, 3058, 2956, 2931, 1738, 1592, 1466, 1378, 1229, 1113, 1071.

*Cyclopropylmethyl diphenylphosphinate (**4i**):* colorless oil, 31 mg (56% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.87−7.79 (m, 4H), 7.55−7.41 (m, 6H), 3.89 (t, J = 7.4 Hz, 2H), 1.23−1.14 (m, 1H), 0.58−0.52 (m, 2H), 0.29−0.24 (m, 2H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.1 (d, J = 2.8 Hz), 131.8 (d, J = 137.4 Hz), 131.7 (d, J = 10.1 Hz), 128.5 (d, J = 13.1 Hz), 69.9 (d, J = 5.8 Hz), 11.5 (d, J = 7.2 Hz), 3.6; ^{31}P NMR (162 MHz, chloroform-*d*) δ 31.13; HRMS (TOF MS ESI) calcd for $C_{16}H_{18}O_2P^+$ $[M + H]^+$ 273.1039, found 273.1037; IR (cm^{-1}) 3058, 3010, 2945, 2885, 1737, 1592, 1485, 1365, 1280, 1130, 1071.

*Cyclopentyl diphenylphosphinate (**4j**):* white solid; mp 108−113 °C, 29 mg (51% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.85−7.76 (m, 4H), 7.54−7.40 (m, 6H), 4.92−4.85 (m, 1H), 1.96−1.87 (m, 2H), 1.85−1.73 (m, 4H), 1.64−1.53 (m, 2H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.3 (d, J = 137.4 Hz), 132.0 (d, J = 2.8 Hz), 131.6 (d, J = 10.1 Hz), 128.4 (d, J = 13.1 Hz), 78.9 (d, J = 6.3 Hz), 34.3 (d, J = 4.2 Hz), 23.1; ^{31}P NMR (162 MHz, chloroform-*d*) δ 30.07; HRMS (TOF MS ESI) calcd for $C_{17}H_{20}O_2P^+$ $[M + H]^+$ 287.1195, found 287.1193; IR (cm^{-1}) 3077, 3014, 2963, 2872, 1737, 1592, 1484, 1366, 1220, 1168, 1114, 1073.

*2,2,2-Trifluoroethyl diphenylphosphinate (**4l**):* white solid; mp 89−94 °C, 39 mg (65% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.85−7.78 (m, 4H), 7.59−7.44 (m, 6H), 4.33 (qd, J = 8.1, 6.7 Hz, 2H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 132.9 (d, J = 2.9 Hz), 131.6 (d, J = 10.6 Hz), 129.8 (d, J = 137.3 Hz), 128.8 (d, J = 13.5 Hz), 123.0 (qd, J = 278.6, 10.4 Hz), 60.9 (qd, J = 37.7, 4.7 Hz); ^{31}P NMR (162 MHz, chloroform-*d*) δ 35.19; HRMS (TOF MS ESI) calcd for $C_{14}H_{13}F_3O_2P^+$ $[M + H]^+$ 301.0600, found 301.0600; IR (cm^{-1}) 3061, 3016, 2970, 2855, 1738, 1593, 1486, 1440, 1366, 1286, 1132, 1080.

*1,1,1,3,3,3-Hexafluoropropan-2-yl diphenylphosphinate (**4m**):* white solid; mp 58−63 °C, 26 mg (35% yield); ^1H NMR (400 MHz, chloroform-*d*) δ 7.82−7.74 (m, 4H), 7.63−7.46 (m, 6H), 5.49−5.34 (m, 1H); ^{13}C NMR $\{^1H\}$ (101 MHz, chloroform-*d*) δ 133.2 (d, J = 2.9 Hz), 131.5 (d, J = 11.2 Hz), 129.6 (d, J = 137.2 Hz), 128.7 (d, J = 13.9 Hz), 120.7(q, J = 282.8 Hz), 69.2−67.7 (m); ^{31}P NMR (162 MHz, chloroform-*d*) δ 39.90; HRMS (TOF MS ESI) calcd for $C_{15}H_{11}F_6NaO_2P^+$ $[M+ Na]^+$ 391.0293, found 391.0293; IR (cm^{-1}) 3063, 3017, 2946, 2856, 1738, 1594, 1486, 1440, 1382, 1293, 1199, 1133, 1109.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b02882.

Full spectroscopic data for compounds **3** and **4**; copies of ^{1}H NMR and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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