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Metal-free oxidative arylphosphination of activated *N*-substituted-*N*-arylacrylamide derivatives using $K_2S_2O_8$

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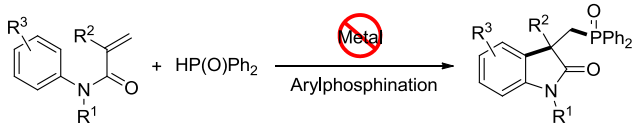
ABSTRACT

A novel metal-free oxidative arylphosphination of activated *N*-substituted-*N*-arylacrylamide derivatives by phosphorylation and C–H functionalization cascade process has been developed. This methodology provides an efficient way to construct a variety of phosphorus-containing oxindole moieties.

1. Introduction

Organophosphorus compounds can be found in a wide range of medicinal chemistry, biochemistry, photoelectric materials, catalysis, and organic synthesis.[1] Therefore, the development of new and efficient C–P bond-forming method for the construction of phosphorus compounds that are not readily available by classic methods is urgent and very important.[2] A great deal of recent effort has focused on two general strategies: (1) transition-metal-catalyzed coupling reactions[3] and (2) alkenes or alkynes functionalization.[4] For the latter, up to now, most of the transformations were focussed on the simple addition reactions, while less work was reported on the phosphorus-containing difunctionalization of alkenes,[5] although the difunctionalization may offer more environmentally benign and atom-economical processes.

Difunctionalization of alkenes is among the most powerful transformation in organic synthesis.[6] The catalytic difunctionalization of acrylamides via direct C–H bond functionalization has attracted much attention in the past few years and has been applied successfully for the synthesis of various functionalized oxindoles.[7] In particular, metal-free oxidative coupling/cyclization reactions were also discovered.[8] Very recently, we reported a novel silver-catalyzed oxidative arylphosphination of alkenes.[5b] This approach provided a new entry to more valuable phosphorus-containing oxindoles with high atom economy and high efficiency. We envisaged that this transformation might be accomplished by more simple oxidant-promoted radical cyclization. Herein we report a metal-free $K_2S_2O_8$-mediated oxidative arylphosphination of activated alkenes to form phosphorus-containing oxindoles by using readily available diphenylphosphine oxide as coupling partners (Scheme 1). Over the past several years, the development of transition-metal-free processes has become a topic of great interest in chemical synthesis.[9] Such protocols are very valuable as an attractive alternative and beneficial complements for transition-metal-catalyzed transformations. In particular, from a practical aspect, metal-free syntheses are preferred, as the removal of metal contamination can render a process quite expensive.



Scheme 1. Arylphosphination of alkenes.

2. Results and discussions

We initiated our study on the reaction of *N*-methyl-*N*-phenylmethacrylamide (**1a**) with $HP(O)Ph_2$ and an oxidant in CH_3CN at

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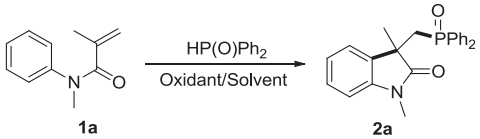
80 °C. To our delight, the desired product **2a** was obtained in 58% yield when the reaction employed 2.0 equiv $K_2S_2O_8$ (Table 1, entry 1). With regard to the optimal amount of the oxidant, the reaction with 3.0 equiv $K_2S_2O_8$ provided the best results (entries 2–3). The concentration of substrate **1a** was important. Decreasing the concentration of **1a** from 0.1 M to 0.067 M, the yield of **2a** improved to 88% (entry 2 vs entry 4). Further decreasing the substrate concentration resulted in a decrease in yield (entry 5). Subsequently, different solvents, CH_3CN, toluene, DMF, DMSO, and NMP were screened, and among them CH_3CN exhibited unmatched efficacy for the transformation (entry 4 vs entries 6–10). Among the reaction temperatures examined, it turned out that the reaction at 90 °C gave the best results (entries 11–13). Finally, a series of oxidants, such as oxone, benzoyl peroxide (BPO), *tert*-butyl peroxybenzoate (TBPB), *tert*-butyl hydroperoxide (TBHP, anhydrous, about 5.5 M in decane), and di-*tert*-butyl peroxide (DTBP), were examined, and $K_2S_2O_8$ was found to be the best choice (entry 4 vs entries 14–18).

Table 1
Optimization of reaction conditions[a]

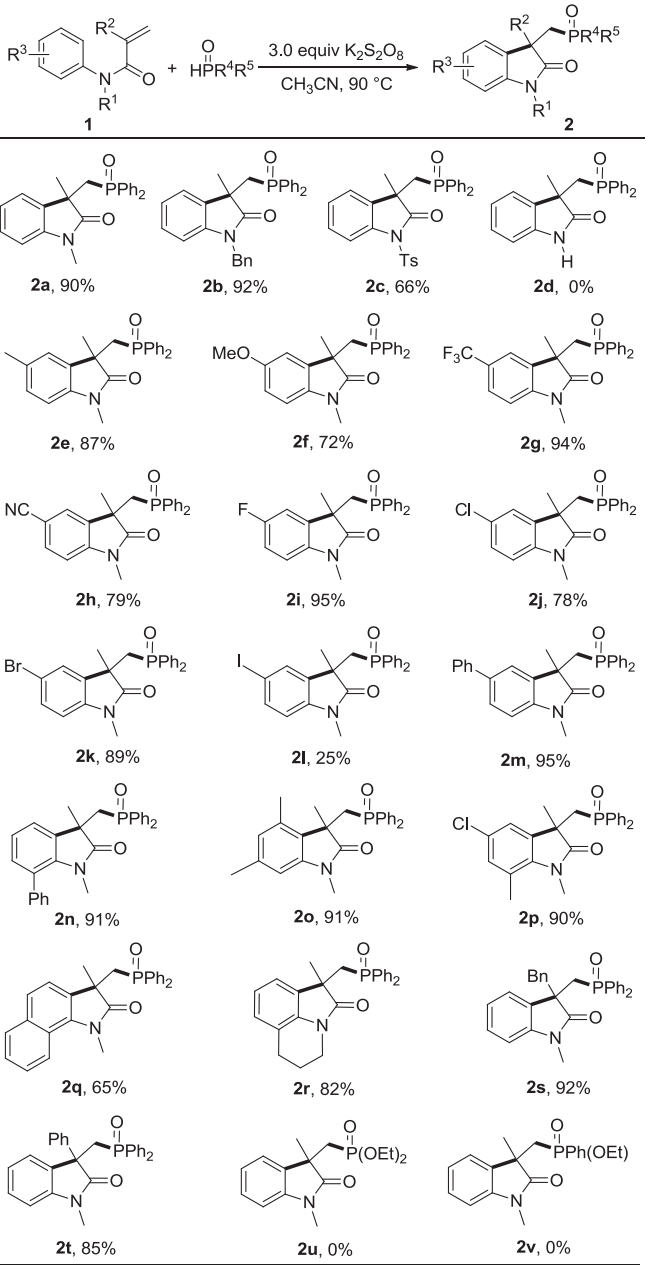


Entry	Oxidant (equiv)	Temp (°C)	Solvent	Yield[b] (%)
1[c]	$K_2S_2O_8$ (2)	80	CH_3CN	58
2[c]	$K_2S_2O_8$ (3)	80	CH_3CN	72
3[c]	$K_2S_2O_8$ (4)	80	CH_3CN	63
4	$K_2S_2O_8$ (3)	80	CH_3CN	88
5[d]	$K_2S_2O_8$ (3)	80	CH_3CN	86
6	$K_2S_2O_8$ (3)	80	THF	30
7	$K_2S_2O_8$ (3)	80	Toluene	70
8	$K_2S_2O_8$ (3)	80	DMF	Trace
9	$K_2S_2O_8$ (3)	80	DMSO	25
10	$K_2S_2O_8$ (3)	80	NMP	Trace
11	$K_2S_2O_8$ (3)	60	CH_3CN	75
12	$K_2S_2O_8$ (3)	90	CH_3CN	90
13	$K_2S_2O_8$ (3)	100	CH_3CN	78
14	Oxone (3)	90	CH_3CN	26
15	BPO (3)	90	CH_3CN	83
16	TBPB (3)	90	CH_3CN	50
17	TBHP (3)	90	CH_3CN	73
18	DTBP (3)	90	CH_3CN	41

[a] Reaction conditions: **1a** (0.3 mmol), $HP(O)Ph_2$ (0.9 mmol), and oxidant in dry solvent (4.5 mL) under argon for 20 h.
[b] Isolated yield.
[c] CH_3CN (3 mL) was used.
[d] CH_3CN (6 mL) was used.

With the optimized reaction conditions, the substrate scope was then investigated as shown in Table 2. Substrates **1a**–**c** bearing methyl, benzyl or tosyl protecting groups on the nitrogen were good for this transformation, but unprotected *N*–H acrylamide failed to give the desired product **2d**. It indicated that nitrogen protecting group was essential under the oxidative environment. The effect of substituents at the *N*-aryl moiety was subsequently examined (**2e**–**p**). Screening showed that *N*-arylacrylamides bearing electron-donating or -withdrawing substituents on aniline moieties could be successfully converted into the desired products in good to excellent yields (**2e**–**i**). Gratifyingly, Cl, Br, and I groups were also well tolerated, thereby facilitating possible additional modifications at the halogenated positions (**2j**–**l**). *N*-arylacrylamide substrates with phenyl group at the *para* or *ortho* position displayed high reactivity in this transformation, provided the corresponding oxindoles in excellent yields (**2m**, **2n**). Substrates

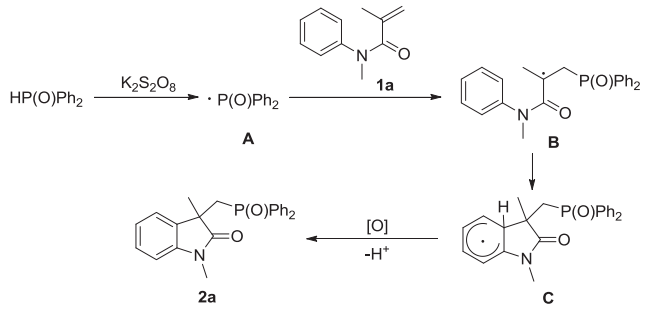
Table 2
Scope of arylphosphination[a,b]



[a] All the reactions were carried out in the presence of 0.3 mmol of **1a**–**v**, $HP(O)R^4R^5$ (3.0 equiv), $K_2S_2O_8$ (3.0 equiv) in 4.5 mL CH_3CN at 90 °C.
[b] Isolated yield.

having two substituents on the phenyl rings also reacted well with $HP(O)Ph_2$ (**2o**, **2p**). When the benzene ring of the substrates was changed to naphthalene, the reaction successfully provided the product (**2q**). Tetrahydroisoquinoline structural motif is commonly encountered in many biologically active compounds. Acrylamides prepared from this amine provided the corresponding tricyclic oxindole derivative in excellent yield under the developed reaction conditions (**2r**). In addition, a series of α-substituted olefins bearing different functional groups, such as benzyl (**2s**) and phenyl (**2t**) could also be converted into the corresponding oxindoles in good yields. Finally, various phosphonyl radicals were evaluated. However, under the same conditions, other phosphorus species, such as diethyl phosphate and ethyl phenylphosphinate failed to afford the desired products (**2u**, **2v**).

Based on the previous mechanistic studies,[5b,8] a plausible mechanism for our methodology is depicted in Scheme 2. Initially, potassium peroxydisulphate may be decomposed to sulfate radical anion upon heating.[10] Then $HP(O)Ph_2$ reacts with sulfate radical anion to form phosphoryl radical **A**, followed by addition to the carbon–carbon double bond of amide **1a** affording radical intermediate **B**.[4b,d] The resulting alkyl radical **B** participates in an intramolecular radical substitution reaction. Addition of radical to the aromatic ring generates intermediate **C**, followed by oxidation of **C** into the corresponding carbocation, which loses H^+ to produce the oxindole **2a**.



Scheme 2. Proposed mechanisms.

3. Conclusion

In summary, we have developed a novel metal-free oxidative arylphosphination of activated alkenes by phosphorylation and C–H functionalization cascade process using $K_2S_2O_8$ oxidant. This reaction creates an opportunity to construct a variety of phosphorus-containing oxindole moieties. Further investigations toward the reaction scope, and applications in organic synthesis are currently ongoing in our laboratory.

4. Experimental section

4.1. General

^1H and ^{13}C NMR spectra were recorded on a Bruker advance III 400 spectrometer in $CDCl_3$ with TMS as internal standard. ^{31}P NMR spectra and ^{19}F NMR were recorded on the same instrument. IR spectra were recorded on a Nexus 670 FT-IR spectrometer and only major peaks are reported in cm^{-1}. HRMS data were determined on a Bruker Daltonics APEXII 47e FT-ICR spectrometer. The starting materials were purchased from Aldrich, Acros Organics, J&K Chemicals or TCI and used without further purification. Solvents were dried and purified according to the procedure from 'Purification of Laboratory Chemicals book'. Column chromatography was carried out on silica gel (particle size 200–400 mesh ASTM).

4.2. General procedures for arylphosphination of alkenes

In a Schlenk tube, amide **1** (0.30 mmol), $HP(O)Ph_2$ (182 mg, 0.90 mmol), $K_2S_2O_8$ (243 mg, 0.90 mmol) were added and charged with Ar three times. Then, anhydrous CH_3CN (4.5 mL) were added. The mixture was allowed to stir at 90 °C for 20 h. The reaction was cooled to room temperature and diluted with CH_3CN, then filtering through a bed of Celite. The filtered reaction mixture was concentrated by rotary evaporation and purified by column chromatography (hexane/isopropanol=10:1) to give the product **2**.

*4.2.1. Compound **2a**.* This compound was prepared by the general procedures. Yield=90%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.60–7.55 (m, 2H), 7.51–7.44 (m, 2H), 7.43–7.27 (m, 6H), 7.18–7.14 (m, 2H), 6.79 (t, J=7.6 Hz, 1H), 6.67 (d, J=7.6 Hz, 1H), 3.09 (dd, d, J=10.4, 15.2 Hz, 1H), 3.01 (s, 1H), 2.86 (dd, J=10.8, 15.2 Hz, 1H), 1.43 (d, J=1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.4 (d, J_{C-P}=4.1 Hz), 142.9, 133.8 (d, J_{C-P}=98.5 Hz), 133.0 (d, J_{C-P}=97.9 Hz), 131.4 (d, J_{C-P}=2.5 Hz), 131.3 (d, J_{C-P}=2.0 Hz), 131.2 (d, J_{C-P}=2.6 Hz), 130.7 (d, J_{C-P}=9.2 Hz), 130.4 (d, J_{C-P}=9.1 Hz), 128.3 (d, J_{C-P}=11.7 Hz), 128.1 (d, J_{C-P}=11.6 Hz), 127.9, 127.8, 122.1, 107.8, 45.4 (d, J_{C-P}=3.7 Hz), 37.8 (d, J_{C-P}=71.4 Hz), 26.8 (d, J_{C-P}=11.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.71. IR (film) ν_{max}: 3407, 3054, 2931, 1712, 1612, 1491, 1439, 1376, 1188, 1119, 861, 748, 696, 537, 501 cm^{-1}. HRMS calcd for $C_{23}H_{22}NO_2P$ $(M+Na)^+$, 398.1280; found, 398.1286.

*4.2.2. Compound **2b**.* This compound was prepared by the General procedures. Yield=92%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.63–7.53 (m, 4H), 7.43 (t, J=7.2 Hz, 2H), 7.38–7.34 (m, 4H), 7.31–7.22 (m, 4H), 7.20 (d, J=7.2 Hz, 2H), 7.03 (t, J=7.6 Hz, 1H), 6.73 (t, J=7.6 Hz, 1H), 6.55 (d, J=8.0 Hz, 1H), 5.04 (d, J=16.0 Hz, 1H), 4.40 (d, J=16.0 Hz, 1H), 3.09 (dd, J=10.8, 19.2 Hz, 1H), 2.93 (dd, J=10.0, 14.6 Hz, 1H), 1.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.7 (d, J_{C-P}=5.1 Hz), 142.1, 136.2, 133.7 (d, J_{C-P}=98.9 Hz), 133.3 (d, J_{C-P}=98.3 Hz), 131.6 (d, J_{C-P}=2.7 Hz), 131.5 (d, J_{C-P}=2.8 Hz), 131.3 (d, J_{C-P}=2.7 Hz), 130.7 (d, J_{C-P}=9.4 Hz), 130.6 (d, J_{C-P}=9.3 Hz), 128.7, 128.4 (d, J_{C-P}=11.7 Hz), 128.3 (d, J_{C-P}=11.7 Hz), 127.8, 127.4, 127.1, 125.0, 122.2, 108.9, 45.7 (d, J_{C-P}=4.5 Hz), 44.0, 37.3 (d, J_{C-P}=71.1 Hz), 27.0 (d, J_{C-P}=11.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.20. IR (film) ν_{max}: 3427, 3055, 2923, 1710, 1611, 1489, 1437, 1354, 1176, 1116, 999, 744, 696, 536 cm^{-1}. HRMS calcd for $C_{29}H_{26}NO_2P$ $(M+Na)^+$, 474.1593; found, 474.1603.

*4.2.3. Compound **2c**.* This compound was prepared by the General procedures. Yield=66%. ^1H NMR (400 MHz, $CDCl_3$): δ 8.48 (s, 1H), 7.67–7.63 (m, 2H), 7.48–7.42 (m, 5H), 7.39–7.32 (m, 3H), 7.25–7.20 (m, 3H), 7.09 (d, J=8.0 Hz, 2H), 7.04 (t, J=7.2 Hz, 1H), 6.81 (d, J=8.4 Hz, 1H), 3.26 (dd, J=12.4, 15.6 Hz, 1H), 3.10 (dd, J=8.8, 15.6 Hz, 1H), 2.18 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4 (d, J_{C-P}=9.3 Hz), 138.3, 138.2, 136.9, 134.2 (d, J_{C-P}=100.0 Hz), 132.9 (d, J_{C-P}=99.0 Hz), 131.3 (d, J_{C-P}=2.7 Hz), 130.7 (d, J_{C-P}=2.8 Hz), 130.5, 130.4, 130.3, 130.2, 128.9, 128.7, 128.4 (d, J_{C-P}=11.6 Hz), 128.1 (d, J_{C-P}=11.7 Hz), 127.0, 123.9, 119.7, 50.5 (d, J_{C-P}=2.8 Hz), 39.2 (d, J_{C-P}=70.8 Hz), 25.8 (d, J_{C-P}=4.9 Hz), 20.8 (d, J_{C-P}=1.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 28.69. IR (film) ν_{max}: 3441, 3285, 3051, 2932, 1662, 1599, 1533, 1436, 1315, 1246, 1184, 1114, 753, 695, 526 cm^{-1}. HRMS calcd for $C_{29}H_{26}NO_4PS$ $(M+Na)^+$, 538.1212; found, 538.1211.

*4.2.4. Compound **2e**.* This compound was prepared by the General procedures. Yield=87%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.56–7.46 (m, 4H), 7.40 (t, J=7.2 Hz, 1H), 7.35–7.28 (m, 4H), 6.93 (d, J=7.6 Hz, 1H), 6.78 (s, 1H), 6.59 (d, J=8.0 Hz, 1H), 3.11–3.05 (m, 4H), 2.82 (dd, J=9.6, 15.2 Hz, 1H), 2.06 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.3 (d, J_{C-P}=4.1 Hz), 140.3, 133.6 (d, J_{C-P}=98.6 Hz), 133.3 (d, J_{C-P}=100.8 Hz), 131.3 (d, J_{C-P}=2.6 Hz), 131.2, 131.1 (d, J_{C-P}=2.7 Hz), 130.9 (d, J_{C-P}=2.7 Hz), 130.5 (d, J_{C-P}=9.4 Hz), 130.4 (d, J_{C-P}=9.2 Hz), 128.1 (d, J_{C-P}=1.9 Hz), 128.1, 128.0 (d, J_{C-P}=1.9 Hz), 125.4, 107.5, 45.3 (d, J_{C-P}=5.0 Hz), 37.5 (d, J_{C-P}=71.2 Hz), 26.6 (d, J_{C-P}=12.1 Hz), 26.3, 20.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.71. IR (film) ν_{max}: 3402, 3071, 2928, 1709, 1622, 1495, 1436, 1353, 1190, 1113, 751, 694, 538, 506 cm^{-1}. HRMS calcd for $C_{24}H_{24}NO_2P$ $(M+Na)^+$, 412.1437; found, 412.1437.

*4.2.5. Compound **2f**.* This compound was prepared by the General procedures. Yield=72%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.57–7.50 (m, 4H), 7.44–7.39 (m, 2H), 7.37–7.31 (m, 4H), 6.75 (d, J=2.4 Hz, 1H), 6.70 (dd, J=2.4, 8.4 Hz, 1H), 6.59 (d, J=8.4 Hz, 1H), 3.64 (s, 3H),

3.11–3.04 (m, 4H), 2.82 (dd, J=10.4, 15.2 Hz, 1H), 1.43 (d, J=1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.9, 155.5, 136.6, 133.7 (d, J_{C-P}=98.4 Hz), 133.2 (d, J_{C-P}=98.1 Hz), 132.6 (d, J_{C-P}=2.6 Hz), 131.4 (d, J_{C-P}=2.5 Hz), 131.2 (d, J_{C-P}=2.6 Hz), 130.6 (d, J_{C-P}=9.4 Hz), 130.5 (d, J_{C-P}=9.3 Hz), 128.3 (d, J_{C-P}=6.9 Hz), 128.2 (d, J_{C-P}=6.9 Hz), 113.2, 111.5, 108.2, 55.6, 46.0 (d, J_{C-P}=3.8 Hz), 37.5 (d, J_{C-P}=71.6 Hz), 26.7 (d, J_{C-P}=12.3 Hz), 26.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.01. IR (film) ν_{max}: 3398, 3054, 2934, 1707, 1599, 1497, 1435, 1236, 1189, 1116, 1041, 750, 695, 540, 509 cm^{-1}. HRMS calcd for $C_{24}H_{24}NO_3P$ $(M+Na)^+$, 428.1386; found, 428.1388.

4.2.6. Compound ***2g****.* This compound was prepared by the General procedures. Yield=94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.55 (m, 2H), 7.45–7.34 (m, 7H), 7.31–7.27 (m, 2H), 7.08 (s, 1H), 6.82 (d, J=8.4 Hz, 1H), 3.20–3.13 (m, 4H), 2.86 (dd, J=8.0, 15.2 Hz, 1H), 1.46 (d, J=1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.5 (d, J_{C-P}=3.2 Hz), 146.4, 133.5 (d, J_{C-P}=98.9 Hz), 132.7 (d, J_{C-P}=99.0 Hz), 132.2, 131.6 (d, J_{C-P}=2.5 Hz), 131.5 (d, J_{C-P}=2.7 Hz), 130.3 (d, J_{C-P}=9.4 Hz), 130.1 (d, J_{C-P}=9.3 Hz), 128.4 (d, J_{C-P}=6.8 Hz), 128.3 (d, J_{C-P}=7.0 Hz), 125.8 (d, J_{C-F}=3.8 Hz), 124.0 (d, J_{C-F}=270.0 Hz), 123.9 (d, J_{C-F}=32.6 Hz), 121.1 (d, J_{C-F}=3.8 Hz), 107.7, 45.2 (d, J_{C-P}=4.0 Hz), 37.7 (d, J_{C-P}=71.2 Hz), 26.7, 26.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.36. ^{19}F NMR (376 MHz, $CDCl_3$): δ −61.10. IR (film) ν_{max}: 3429, 3057, 2908, 1724, 1624, 1398, 1328, 1182, 1119, 743, 695, 533 cm^{-1}. HRMS calcd for $C_{24}H_{21}F_3NO_2P$ $(M+Na)^+$, 466.1154; found, 466.1146.

4.2.7. Compound ***2h****.* This compound was prepared by the General procedures. Yield=79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.59 (m, 2H), 7.53–7.30 (m, 9H), 6.92 (d, J=12.1 Hz, 1H), 6.83 (d, J=8.0 Hz, 1H), 3.22 (s, 3H), 3.15 (dd, J=12.4, 14.8 Hz, 1H), 2.48 (dd, J=6.8, 14.8 Hz, 1H), 1.45 (d, J=1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.1 (d, J=2.9 Hz), 147.3, 133.2 (d, J=99.2 Hz), 133.1, 132.5 (d, J=98.6 Hz), 131.8 (d, J=2.7 Hz), 131.7 (d, J=2.8 Hz), 131.7, 130.2 (d, J=10.1 Hz), 130.1 (d, J=9.6 Hz), 128.4 (d, J=9.1 Hz), 128.3 (d, J=9.1 Hz), 127.5, 118.8, 108.3, 104.7, 44.9 (d, J=4.0 Hz), 37.7 (d, J=71.1 Hz), 26.7, 26.2 (d, J=12.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.24. IR (film) ν_{max}: 3429, 3043, 2960, 2219, 1723, 1612, 1450, 1347, 1190, 1118, 827, 755, 697, 547, 494 cm^{-1}. HRMS calcd for $C_{24}H_{21}N_2O_2P$ $(M+Na)^+$, 423.1233; found, 423.1223.

4.2.8. Compound ***2i****.* This compound was prepared by the General procedures. Yield=95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.51 (m, 4H), 7.46–7.4 (m, 2H), 7.39–7.32 (m, 4H), 7.10 (dd, J=2.0, 8.4 Hz, 1H), 6.83 (d, J=2.0 Hz, 1H), 6.65 (d, J=8.0 Hz, 1H), 3.12–3.06 (m, 5H), 2.79 (dd, J=8.4, 14.8 Hz, 1H), 1.42 (d, J=1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.0 (d, J=4.3 Hz), 158.6 (d, J_{C-F}=238.7 Hz), 139.0 (d, J_{C-F}=1.8 Hz), 133.2 (d, J=98.6 Hz), 133.1 (d, J=98.6 Hz), 132.9 (dd, J=2.6, 8.3 Hz), 131.4 (d, J=2.7 Hz), 131.3 (d, J=2.7 Hz), 130.4 (d, J=9.4 Hz), 130.3 (d, J=9.2 Hz), 128.3 (d, J=6.5 Hz), 128.2 (d, J=6.5 Hz), 114.1 (d, J_{C-F}=23.5 Hz), 112.7 (d, J_{C-F}=25.2 Hz), 108.1 (d, J_{C-F}=8.1 Hz), 45.8 (d, J=2.2 Hz), 37.4 (d, J=71.3 Hz), 26.4, 26.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.59. ^{19}F NMR (376 MHz, $CDCl_3$): δ −121.22. IR (film) ν_{max}: 3414, 3057, 2902, 1716, 1497, 1178, 1119, 748, 693, 542 cm^{-1}. HRMS calcd for $C_{23}H_{21}FNO_2P$ $(M+Na)^+$, 416.1186; found, 416.1193.

4.2.9. Compound ***2j****.* This compound was prepared by the General procedures. Yield=78%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.56 (m, 2H), 7.48–7.42 (m, 4H), 7.39–7.32 (m, 4H), 7.10 (dd, J=2.0, 8.4 Hz, 1H), 8.63 (d, J=2.0 Hz, 1H), 6.65 (d, J=8.0 Hz, 1H), 3.12 (m, 5H), 2.79 (dd, J=8.4, 14.8 Hz, 1H), 1.42 (d, J=1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.0 (d, J_{C-P}=3.7 Hz), 141.9, 133.3 (d, J_{C-P}=98.8 Hz), 132.9 (d, J_{C-P}=98.7 Hz), 132.8 (d, J_{C-P}=2.7 Hz), 131.6 (d, J_{C-P}=2.7 Hz), 131.5 (d, J_{C-P}=2.8 Hz), 130.5 (d, J_{C-P}=9.4 Hz), 130.3 (d, J_{C-P}=9.3 Hz), 128.4 (d, J_{C-P}=6.0 Hz), 128.3 (d, J_{C-P}=6.0 Hz), 127.9, 127.2, 125.0, 108.8, 45.5 (d, J_{C-P}=4.0 Hz), 37.6 (d, J_{C-P}=70.8 Hz), 26.6, 26.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.51. IR (film) ν_{max}: 3417, 3058, 2983, 1715, 1609, 1488, 1435, 1189, 1118, 808, 743, 695, 542 cm^{-1}. HRMS calcd for $C_{23}H_{21}ClNO_2P$ $(M+Na)^+$, 432.0891; found, 432.0883.

4.2.10. Compound ***2k****.* This compound was prepared by the General procedures. Yield=89%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.56 (m, 2H), 7.48–7.42 (m, 4H), 7.39–7.32 (m, 4H), 7.26–7.23 (m, 1H), 6.94 (d, J=2.0 Hz, 1H), 6.61 (d, J=8.3 Hz, 1H), 3.13–3.06 (m, 4H), 2.78 (dd, J=8.4, 15.2 Hz, 1H), 1.42 (d, J=1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.9 (d, J_{C-P}=3.5 Hz), 142.4, 133.3 (d, J_{C-P}=98.8 Hz), 133.12, 133.10, 132.8 (d, J_{C-P}=99.0 Hz), 131.6, 130.8, 130.4 (d, J_{C-P}=9.3 Hz), 130.2 (d, J_{C-P}=9.1 Hz), 128.4 (d, J_{C-P}=6.1 Hz), 128.3 (d, J_{C-P}=6.2 Hz), 127.7, 114.6, 109.3, 45.4 (d, J_{C-P}=4.0 Hz), 37.6 (d, J_{C-P}=70.7 Hz), 26.54, 26.53 (d, J_{C-P}=12.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.42. IR (film) ν_{max}: 3397, 3057, 2985, 2229, 1710, 1604, 1488, 1190, 1118, 912, 739, 540 cm^{-1}. HRMS calcd for $C_{23}H_{21}BrNO_2P$ $(M+Na)^+$, 476.0385; found, 476.0372.

4.2.11. Compound ***2l****.* This compound was prepared by the General procedures. Yield=25%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.57 (m, 2H), 7.50–7.29 (m, 9H), 7.07 (d, J=1.2 Hz, 1H), 6.53 (d, J=4.4 Hz, 1H), 3.14–3.02 (m, 4H), 2.77 (dd, J=7.6, 14.8 Hz, 1H), 1.41 (d, J=1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.1 (d, J_{C-P}=3.2 Hz), 143.2, 140.6, 134.4 (d, J_{C-P}=2.8 Hz), 133.6 (d, J_{C-P}=99.0 Hz), 132.2 (d, J_{C-P}=97.7 Hz), 131.6 (d, J_{C-P}=2.5 Hz), 131.4 (d, J_{C-P}=2.5 Hz), 130.8 (d, J_{C-P}=9.5 Hz), 130.5 (d, J_{C-P}=9.0 Hz), 128.4 (d, J_{C-P}=11.7 Hz), 128.2 (d, J_{C-P}=11.7 Hz), 124.7, 123.9, 71.3, 45.0 (d, J_{C-P}=3.7 Hz), 37.7 (d, J_{C-P}=70.3 Hz), 30.2, 27.4 (d, J_{C-P}=12.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.42. IR (film) ν_{max}: 3403, 3063, 2896, 1715, 1601, 1485, 1342, 1190, 1118, 744, 696, 540 cm^{-1}. HRMS calcd for $C_{23}H_{21}INO_2P$ $(M+Na)^+$, 524.0247; found, 524.0241.

4.2.12. Compound ***2m****.* This compound was prepared by the General procedures. Yield=95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.47 (m, 4H), 7.42–7.35 (m, 6H), 7.33–7.26 (m, 7H), 6.75 (d, J=8.0 Hz, 1H), 3.20 (dd, J=10.8, 15.2 Hz, 1H), 3.09 (s, 3H), 2.93 (dd, J=10.4, 15.2 Hz, 1H), 1.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.5 (d, J_{C-P}=3.4 Hz), 142.6, 140.7, 135.3, 133.0 (d, J_{C-P}=99.2 Hz), 132.5 (d, J_{C-P}=98.8 Hz), 131.7 (d, J_{C-P}=2.8 Hz), 131.5 (d, J_{C-P}=2.6 Hz), 131.5 (d, J_{C-P}=2.5 Hz), 130.7 (d, J_{C-P}=9.5 Hz), 130.4 (d, J_{C-P}=9.3 Hz), 120.5, 128.3 (d, J_{C-P}=7.5 Hz), 128.2 (d, J_{C-P}=7.4 Hz), 126.9, 126.8, 126.7, 123.8, 108.1, 45.5 (d, J_{C-P}=3.7 Hz), 37.4 (d, J_{C-P}=71.2 Hz), 27.1 (d, J_{C-P}=12.3 Hz), 26.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.40. IR (film) ν_{max}: 3431, 3056, 2926, 2219, 1892, 1713, 1619, 1486, 1437, 1352, 1190, 1119, 907, 721, 695, 544 cm^{-1}. HRMS calcd for $C_{29}H_{26}NO_2P$ $(M+H)^+$, 452.1774; found, 452.1788.

4.2.13. Compound ***2n****.* This compound was prepared by the General procedures. Yield=91%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.53 (m, 4H), 7.44–7.34 (m, 11H), 7.13 (d, J=6.8 Hz, 1H), 6.97 (d, J=8.0 Hz, 1H), 6.75 (t, J=7.6 Hz, 1H), 3.15 (dd, J=10.8, 15.2 Hz, 1H), 2.88 (dd, J=10.8, 15.2 Hz, 1H), 2.55 (s, 3H), 1.48 (d, J=1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.3 (d, J_{C-P}=3.7 Hz), 139.8, 139.0, 133.7 (d, J_{C-P}=98.5 Hz), 133.1 (d, J_{C-P}=97.8 Hz), 132.2, 131.3 (d, J_{C-P}=2.4 Hz), 131.1 (d, J_{C-P}=2.7 Hz), 130.9, 130.7 (d, J_{C-P}=9.4 Hz), 130.4 (d, J_{C-P}=9.0 Hz), 128.3 (d, J_{C-P}=11.7 Hz), 128.1 (d, J_{C-P}=11.7 Hz), 127.6, 127.4, 125.0, 123.7, 121.4, 44.7 (d, J_{C-P}=3.8 Hz), 38.0 (d, J_{C-P}=70.8 Hz), 30.3, 27.2 (d, J_{C-P}=12.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.61. IR (film) ν_{max}: 3404, 3055, 2926, 1711, 1601, 1458, 1438, 1372, 1340, 1194, 1119, 1064, 859, 741, 699, 543, 505 cm^{-1}. HRMS calcd for $C_{29}H_{26}NO_2P$ $(M+H)^+$, 452.1774; found, 452.1788.

4.2.14. Compound ***2o****.* This compound was prepared by the General procedures. Yield=91%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.38 (m, 6H), 7.33–7.28 (m, 4H), 6.41 (s, 1H), 6.34 (s, 1H), 3.27 (dd, J=10.4, 15.2 Hz, 1H), 2.93–2.87 (m, 4H), 2.32 (s, 3H), 2.08 (s, 3H), 1.47 (d,

J=2.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.3, 143.5, 137.9, 135.2, 133.4 (d, J_{C-P}=100.3 Hz), 132.4 (d, J_{C-P}=97.6 Hz), 131.3 (d, J_{C-P}=2.6 Hz), 131.0 (d, J_{C-P}=2.6 Hz), 130.9 (d, J_{C-P}=9.4 Hz), 130.5 (d, J_{C-P}=9.1 Hz), 128.0 (d, J_{C-P}=11.7 Hz), 127.9 (d, J_{C-P}=11.8 Hz), 125.6 (d, J_{C-P}=2.9 Hz), 125.3, 106.5, 45.2 (d, J_{C-P}=3.6 Hz), 36.8 (d, J_{C-P}=70.1 Hz), 26.2, 25.3 (d, J_{C-P}=14.4 Hz), 21.5, 18.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.08. IR (film) ν_{max}: 3398, 3080, 3015, 2962, 1909, 1708, 1620, 1596, 1439, 1337, 1205, 1192, 1120, 1047, 881, 828, 753, 722, 697, 549, 534, 507 cm^{-1}. HRMS calcd for $C_{25}H_{26}NO_2P$ $(M+H)^+$, 404.1774; found, 404.1759.

4.2.15. Compound ***2p***. This compound was prepared by the General procedures. Yield=90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.54 (m, 2H), 7.49–7.44 (m, 4H), 7.40–7.34 (m, 4H), 6.84 (s, 1H), 6.67 (d, J=1.6 Hz, 1H), 3.35 (s, 3H), 3.14 (dd, J=11.6, 15.2 Hz, 1H), 2.77 (dd, J=8.8, 14.8 Hz, 1H), 2.47 (s, 3H), 1.39 (d, J=1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.7 (d, J_{C-P}=2.7 Hz), 139.8, 133.3 (d, J_{C-P}=2.5 Hz), 132.7 (d, J_{C-P}=99.0 Hz), 132.5 (d, J_{C-P}=99.3 Hz), 131.7, 131.6 (d, J_{C-P}=2.9 Hz), 131.3, 130.6 (d, J_{C-P}=9.5 Hz), 130.3 (d, J_{C-P}=9.3 Hz), 128.4 (d, J_{C-P}=1.9 Hz), 128.3 (d, J_{C-P}=1.8 Hz), 126.9, 122.6, 121.0, 44.9 (d, J_{C-P}=3.9 Hz), 37.9 (d, J_{C-P}=71.0 Hz), 29.8, 27.1 (d, J_{C-P}=12.7 Hz), 18.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.77. IR (film) ν_{max}: 3424, 3024, 2928, 1720, 1597, 1463, 1437, 1354, 1331, 1192, 1122, 815, 743, 694, 547, 531, 508 cm^{-1}. HRMS calcd for $C_{24}H_{23}ClNO_2P$ $(M+H)^+$, 424.1228; found, 424.1210.

4.2.16. Compound ***2q***. This compound was prepared by the General procedures. Yield=65%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J=8.0 Hz, 1H), 7.49–7.41 (m, 3H), 7.37–7.19 (m, 9H), 7.11–7.07 (m, 2H), 6.79 (d, J=7.6 Hz, 1H), 3.83 (dd, J=10.0, 15.2 Hz, 1H), 3.34 (s, 3H), 2.99 (dd, J=11.2, 15.2 Hz, 1H), 1.74 (d, J=2.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3 (d, J_{C-P}=2.1 Hz), 136.5, 135.3 (d, J_{C-P}=2.4 Hz), 133.5 (d, J_{C-P}=98.1 Hz), 133.0, 132.9 (d, J_{C-P}=97.5 Hz), 131.0 (d, J_{C-P}=2.5 Hz), 131.0, 130.9, 130.8, 130.5 (d, J_{C-P}=9.1 Hz), 128.0 (d, J_{C-P}=11.7 Hz), 127.6 (d, J_{C-P}=11.7 Hz), 126.3 (d, J_{C-P}=4.2 Hz), 126.1, 124.1, 122.2, 119.1, 108.4, 45.2 (d, J_{C-P}=3.3 Hz), 42.2 (d, J_{C-P}=69.4 Hz), 34.8 (d, J_{C-P}=13.5 Hz), 29.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.29. IR (film) ν_{max}: 3439, 3052, 2923, 1668, 1586, 1378, 1315, 1178, 1120, 740, 695, 544 cm^{-1}. HRMS calcd for $C_{27}H_{24}NO_2P$ $(M+Na)^+$, 448.1437; found, 448.1449.

4.2.17. Compound ***2r***. This compound was prepared by the General procedures. Yield=82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.58 (m, 2H), 7.53–7.48 (m, 2H), 7.45–7.29 (m, 6H), 7.03 (d, J=7.4 Hz, 1H), 6.90 (d, J=7.7 Hz, 1H), 6.70 (t, J=7.6 Hz, 1H), 3.65–3.59 (m, 1H), 3.38–3.32 (m, 1H), 3.08 (dd, J=10.1, 15.2 Hz, 1H), 2.87 (dd, J=11.1, 15.2 Hz, 1H), 2.71–2.60 (m, 2H), 1.95–1.84 (m, 2H), 1.43 (d, J=1.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.3 (d, J_{C-P}=4.5 Hz), 138.6, 133.8 (d, J_{C-P}=98.7 Hz), 133.0 (d, J_{C-P}=97.9 Hz), 131.3 (d, J_{C-P}=2.7 Hz), 131.2 (d, J_{C-P}=2.4 Hz), 130.8 (d, J_{C-P}=9.4 Hz), 130.5 (d, J_{C-P}=9.2 Hz), 130.0 (d, J_{C-P}=2.8 Hz), 128.3 (d, J_{C-P}=11.6 Hz), 128.1 (d, J_{C-P}=11.7 Hz), 126.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.10. IR (film) ν_{max}: 3414, 3054, 2963, 2891, 1707, 1627, 1483, 1357, 1189, 1118, 745, 697, 537 cm^{-1}. HRMS calcd for $C_{25}H_{24}NO_2P$ $(M+Na)^+$, 424.1437; found, 424.1438.

4.2.18. Compound ***2s***. This compound was prepared by the General procedures. Yield=92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.58 (m, 2H), 7.48–7.40 (m, 3H), 7.38–7.33 (m, 3H), 7.30–7.25 (m, 2H), 7.13 (d, J=7.2 Hz, 1H), 7.08 (dd, J=0.8, 7.6 Hz, 1H), 7.05–6.96 (m, 3H), 6.79 (dd, J=0.8, 7.6 Hz, 1H), 6.74 (m, 2H), 6.35 (d, J=7.6 Hz, 1H), 3.26–2.95 (m, 2H), 2.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.8 (d, J_{C-P}=3.7 Hz), 143.4, 134.6, 133.8 (d, J_{C-P}=98.7 Hz), 132.8 (d, J_{C-P}=98.1 Hz), 131.2 (d, J_{C-P}=2.7 Hz), 130.8 (d, J_{C-P}=9.4 Hz), 130.5 (d, J_{C-P}=9.0 Hz), 129.9, 128.5, 128.4, 128.3, 128.0, 127.9 (d, J_{C-P}=4.4 Hz), 127.3, 126.6, 125.8, 121.6, 107.4, 50.9 (d, J_{C-P}=93.6 Hz), 46.2 (d, J_{C-P}=12.2 Hz), 36.4 (d, J_{C-P}=70.8 Hz), 25.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.93. IR (film) ν_{max}: 3411, 3051, 2900, 1713, 1610, 1493, 1436, 1380, 1186, 1121, 744, 697, 541, 500 cm^{-1}. HRMS calcd for $C_{29}H_{26}NO_2P$ $(M+Na)^+$, 474.1593; found, 474.1583.

4.2.19. Compound ***2t***. This compound was prepared by the General procedures. Yield=85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57–7.43 (m, 4H), 7.41–7.23 (m, 8H), 7.25–7.16 (m, 4H), 7.04 (d, J=7.2 Hz, 1H), 6.75–6.71 (m, 2H), 3.71 (dd, J=11.2, 15.2 Hz, 1H), 3.23 (dd, J=10.0, 14.8 Hz, 1H), 3.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5 (d, J_{C-P}=2.1 Hz), 144.2, 140.6 (d, J_{C-P}=12.3 Hz), 133.5 (d, J_{C-P}=99.2 Hz), 133.2 (d, J_{C-P}=98.1 Hz), 131.3 (d, J_{C-P}=2.7 Hz), 131.0 (d, J_{C-P}=2.6 Hz), 130.7 (d, J_{C-P}=9.2 Hz), 130.4 (d, J_{C-P}=9.1 Hz), 129.0 (d, J_{C-P}=3.3 Hz), 128.5, 128.3 (d, J_{C-P}=7.9 Hz), 128.2 (d, J_{C-P}=5.1 Hz), 128.1, 127.4, 126.9, 126.4, 121.8, 108.1, 52.5 (d, J_{C-P}=2.9 Hz), 38.5 (d, J_{C-P}=69.6 Hz), 26.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.90. IR (film) ν_{max}: 3406, 3056, 2930, 1714, 1612, 1493, 1373, 1188, 1119, 744, 696, 542, 514 cm^{-1}. HRMS calcd for $C_{28}H_{24}NO_2P$ $(M+Na)^+$, 460.1437; found, 460.1427.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.01.065.

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