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Coupling Reactions of Heteroarenes with Phosphites under Silver Catalysis

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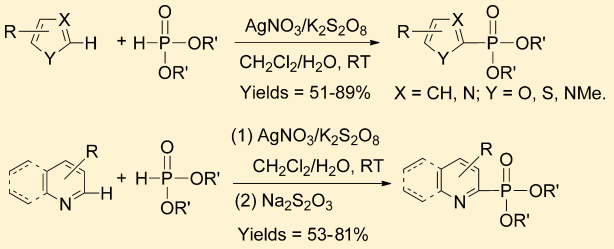
Supporting Information

ABSTRACT: A silver-catalyzed dehydrogenative cross-coupling reaction of substituted furans, thiophene, thioazole, and pyrrole **1a−e** with dialkyl phosphites **2** was first developed to afford corresponding phosphonated products **3a−h** with up to 89% yield and good regioselectivities. Moreover, an unprecedented coupling of various substituted pyridines **1f−k** with dialkyl phosphites **2** using $AgNO_3$ as a catalyst and $K_2S_2O_8$ as an oxidant, followed by reduction with $Na_2S_2O_3$, was also realized to furnish desired pyridine phosphonates **3i−q** in satisfactory yields with good regioselectivities.



Many heteroaryl phosphonates are a class of biologically important compounds.[1] Among various methods for the synthesis of them, transition-metal-catalyzed coupling reactions are becoming a most widely used method.[2] However, these coupling reactions required functionalized reactants, such as functionalized heteroarenes. In order to avoid prefunctionalization of reactants, the dehydrogenative cross-coupling reaction of heteroarene with phosphites should become an efficient and promising strategy for the synthesis of heteroaryl phosphonates. In relation to heteroaryl phosphonate, the synthesis of aryl phosphonates through the dehydrogenative cross-coupling reaction of arenes with tri- or dialkyphosphites was realized by Effenberger et al. using peroxodisulfate/$AgNO_3$ as an oxidative system in AcOH.[3] In 2006, Ishii et al. reported that, under the catalysis of $Mn(OAc)_2/Co(OAc)_2$ and using O_2 as an oxidant, dialkyl phosphites reacted with various arenes to give arylphosphonates in good yields.[4]

In view of the synthesis of heteroaryl phosphonates through a dehydrogenative cross-coupling reaction,[5] Zou et al. found that, when mediated by $Mn(OAc)_3$ (3 equiv), thiazoles, furans, or pyrroles reacted smoothly with dialkylphosphites to give phosphonated heteroarenes in high yields and good regioselectivities.[1a] Very recently, Li et al. disclosed their work on the dehydrogenative cross-coupling of benzoazoles with dialkyl phosphites under the catalysis of $Pd(OAc)_2$ and in the presence of ligand via a Pd(II)/Pd(IV)mechanism.[6] However, there is still no report on the dehydrogenative cross-coupling reactions of substituted furans, thiophenes, pyrroles, or pyridines with phosphites under the catalysis of transition metal. Herein we wish to report our results on the coupling reactions of heteroarenes including substituted furans, thiophene, thioazole, pyrrole, and pyridines with phosphites under silver catalysis.

Initially, the reaction of acetylfuran **1a** with diethyl phosphite **2a** was chosen as a model reaction to explore and optimize the reaction conditions. Gratifyingly, when Ag_2CO_3 and $K_2S_2O_8$ were used as a catalyst and an oxidant, respectively, their dehydrogenative cross-coupling reaction occurred in the mixed solvent of CH_2Cl_2/H_2O, affording desired 5-acetylfuran-2-yl phosphonate **3a** in 81% yield without the observation of its isomer of 5-acetylfuran-3-yl phosphonate (entry 1, Table 1). Then, various silver catalysts and other transition-metal catalysts were screened in the reaction (entries 2−6, Table 1; also see Supporting Information). It was found that only some silver salts were effective in this transformation. Among them, $AgNO_3$ proved to be best to give **3a** in 89% yield (entry 4, Table 1). Other oxidants, such as H_2O_2, MnO_2, TBHP, TBP, and BPO, were also examined in the reaction. Our experiment demonstrated that they were not effective (entries 7−10, Table 1; also see Supporting Information). Solvents were crucial for this reaction, as well. Using CH_3CN/H_2O, DMF/H_2O, or $EtOH/H_2O$ led to a trace amount of **3a**, while acetone/H_2O led to a moderate yield (entries 11−13, Table 1; also see Supporting Information). Further study indicated that the yields of **3a** were decreased when the amounts of the oxidant were below 4 equiv (entries 14 and 15, Table 1).

After screening of reaction conditions, it can be concluded that the optimized reaction should be performed under the catalysis of 20 mol % of $AgNO_3$ using $K_2S_2O_8$ as an oxidant in the mixed solvent of CH_2Cl_2/H_2O (v/v = 1/1) at room temperature. Under the optimal conditions, we examined the scope of the dehydrogenative cross-coupling reaction of five-

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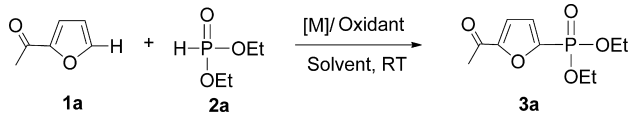
Table 1. Optimization of Dehydrogenative Cross-Coupling Reaction of Furan 1a with Diethyl Phosphite 2a[a]



1a 2a 3a

entry	[M]	oxidant (equiv)	mixed solvent	yield (%)[b]
1	Ag_2CO_3	$K_2S_2O_8$ (4)	CH_2Cl_2/H_2O	81
2	AgOAc	$K_2S_2O_8$ (4)	CH_2Cl_2/H_2O	69
3	Ag_2O	$K_2S_2O_8$ (4)	CH_2Cl_2/H_2O	63
4	$AgNO_3$	$K_2S_2O_8$ (4)	CH_2Cl_2/H_2O	89
5	CAN	$K_2S_2O_8$ (4)	CH_2Cl_2/H_2O	trace
6	SmI_2	$K_2S_2O_8$ (4)	CH_2Cl_2/H_2O	trace
7	$AgNO_3$	H_2O_2 (4)	CH_2Cl_2/H_2O	0
8	$AgNO_3$	MnO_2 (4)	CH_2Cl_2/H_2O	trace
9	$AgNO_3$	TBHP (4)	CH_2Cl_2/H_2O	0
10	$AgNO_3$	TBP (4)	CH_2Cl_2/H_2O	0
11	$AgNO_3$	$K_2S_2O_8$ (4)	CH_3CN/H_2O	trace
12	$AgNO_3$	$K_2S_2O_8$ (4)	DMF/H_2O	trace
13	$AgNO_3$	$K_2S_2O_8$ (4)	acetone/H_2O	79
14	$AgNO_3$	$K_2S_2O_8$ (3)	CH_2Cl_2/H_2O	85
15	$AgNO_3$	$K_2S_2O_8$ (2)	CH_2Cl_2/H_2O	76

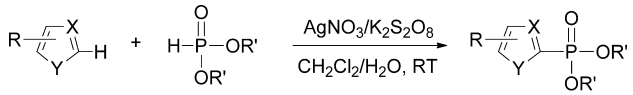
[a]The mixture of **1a** (0.25 mmol), diethyl phosphite **2a** (0.38 mmol), [M] (0.05 mmol, 20 mol %), and an oxidant in a mixed solvent (3 mL, v/v = 1/1) was stirred at rt for 6 h. [b]Isolated yields.

membered heteroarenes **1a−e** with dialkyl phosphites **2**. The experiment indicated that 2-acetylfuran **1a** could react with dialkyl phosphites **2** smoothly to give furan-2-yl phosphonates **3a,b** in excellent yields with good regioselectivities (entries 1 and 2, Table 2). Moreover, furan-2-carbaldehyde **1b** was also a good substrate and led to desired coupling product **3c** in a good yield (entry 3, Table 2). Thiophene **1c** can also undergo the coupling reaction with dialkyl phosphites **2** to give thiophen-2-yl phosphonates **3d,e** in comparatively lower yields (entries 4 and 5, Table 2). Different from thiophene **1c**, thiazole **1d** resulted in thiazol-2-yl phosphonate **3f** in good yield (entry 6, Table 2). Similar to furan **1a**, pyrrol **1e** also performed the coupling reaction expediently to furnish pyrrole phosphonates **3g,h** in good yields with good regioselectivities (entries 7 and 8, Table 2).

To examine the practical value of the dehydrogenative cross-coupling reaction, a gram-scale (2.75 g, 25 mmol, 100-fold scale) reaction of 2-acetylfuran **1a** with diethyl phosphate was conducted. The experiment showed that the reaction proceeded efficiently to give the desired furan-2-yl phosphonate **3a** in 88% yield, which was similar to that in the small-scale reaction (entry 1, Table 2). The reaction was performed at room temperature with no requirement of strict water- and oxygen-free conditions and completed after stirring for 6 h. Therefore, this synthetic method for heteroarene-2-phosphonates **3a−h** should have potential industrial application in the future.

When pyridine **1f** was subjected to the above optimized conditions for five-membered heteroarenes, we obtained the desired pyridine-2-yl phosphonate **3i**, albeit in lower yield (entry 1, Table 3). By MS analysis of the reaction mixture, a minor amount of *N*-oxide of pyridine-2-phosphonate **3i** was probably formed as a side product (see Supporting Information). The successive study showed that adding 4 equiv of $Na_2S_2O_3$ to the mixture after the coupling enhanced the yield of **3i** remarkably. Thus, in order to improve the yields

Table 2. Dehydrogenative Cross-Coupling Reaction of Five-Membered Heteroarenes 1a−e with Dialkyl Phosphites 2[a]



1a-e X = CH, N; Y = O, S. NMe. **2** **2a**: R' = Et **2b**: R' = Me **3a-h**

entry	heteroarene **1**	product **3**	time (hr)	yield (%)[b]
1	**1a**	**3a**	6	89
2	**1a**	**3b**	6	87
3	**1b**	**3c**	6	83
4	**1c**	**3d**	8	51
5	**1c**	**3e**	8	61
6	**1d**	**3f**	6	81
7	**1e**	**3g**	10	83
8	**1e**	**3h**	10	85

[a]The mixture of **1a−e** (0.25 mmol), dialkyl phosphite (0.38 mmol), $AgNO_3$ (0.05 mmol), and $K_2S_2O_8$ (1.0 mmol) in the mixed solvent of CH_2Cl_2/H_2O (v/v = 1/1) was stirred at rt for 6−10 h. [b]Isolated yields.

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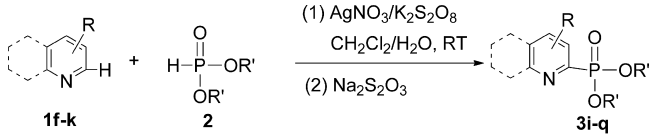
Table 3. Silver-Catalyzed Coupling Reaction of Pyridines 1f–j or Quinoline 1k with Dialkyl Phosphites 2[a]



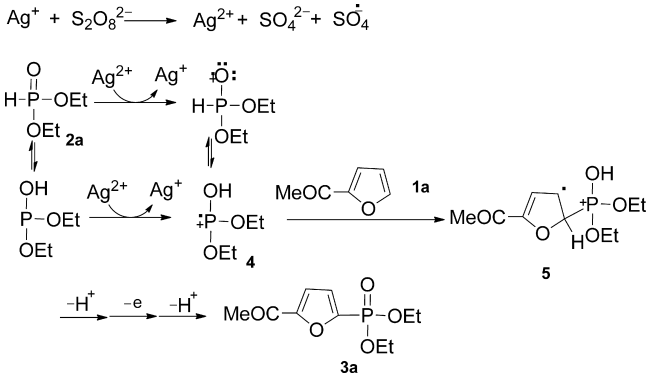
entry	pyridine **1**	product **3**	time (hr)	yield (%)[b]
1	**1f**	**3i**	6	58[c]
2	**1f**	**3i**	6	81
3	**1f**	**3j**	0.25	68
4	**1g**	**3k**	0.25	61
5	**1h**	**3l**	0.25	71
6	**1i**	**3m**	6	78
7	**1j**	**3n**	10	55
8	**1j**	**3o**	10	70
9	**1k**	**3p**	8	53
10	**1k**	**3q**	8	55

[a]The mixture of **1f–k** (0.25 mmol), dialkyl phosphite (0.38 mmol), $AgNO_3$ (0.05 mmol), and $K_2S_2O_8$ (1.0 mmol) in the mixed solvent of CH_2Cl_2/H_2O (v/v = 1/1) was stirred at rt for 0.25–10 h. After the reaction, 4 equiv of $Na_2S_2O_3$ was added and the mixture was stirred for 15 min at rt. [b]Isolated yields. [c]Without using $Na_2S_2O_3$.

of phosphonated pyridines, the reduction step with $Na_2S_2O_3$ was added, becoming a partial one-pot coupling reaction. Then, a series of substituted pyridines were examined in the coupling reaction. The experiment demonstrated that when using $AgNO_3$ as a catalyst and $K_2S_2O_8$ as an oxidant, various substituted pyridines **1f–k** could undergo the coupling reaction with dialkyl phosphites **2** smoothly under mild conditions, furnishing the desired pyridine-2-yl phosphonates **3i–q** in 53–81% yields with good regioselectivities (entries 2–10, Table 3). Methyl- or ethyl-substituted pyridines, whether the substituent was at the 2- or 4-position, were good substrates to lead to the desired coupling products **3k–m** in satisfactory yields (entries 4–6, Table 3). When 2-aminopyridine **1j** was employed in the reaction, diethyl phosphonite **2a** resulted in better yield of coupling product than dimethyl phosphonite **2b** (compare entry 8 with 7, Table 3). In addition, quinoline **1k** was also suitable for this phosphonation to give quinolin-2-yl phosphonates **3p,q** (entries 9 and 10, Table 3).

If tetramethylpiperidinyloxy (TEMPO), a radical scavenger, was added into the reaction system, the dehydrogenative cross-coupling reaction of acetylfuran **1a** with diethyl phosphite **2a** was quenched. This result suggests that the reaction may undergo a radical mechanism. The plausible mechanism of the dehydrogenative cross-coupling reaction may be as follows (Scheme 1), which is similar to that proposed by Effenberger et al.[3] Initially, silver(I) cation is oxidized to silver(II) cation by peroxodisulfate. Then, diethyl phosphite **2a** is deprived of an electron by the silver(II) ion to form cation radical **4**. Its electrophilic addition to furan **1a** leads to intermediate **5**, which

Scheme 1. Plausible Mechanism of the Coupling Reaction of Heteroarene 1 with Dialkyl Phophite 2



may lose a hydrogen cation, an electron, and another hydrogen cation successively, giving desired furan-2-yl phosphonate **3a**.

In conclusion, we have developed a silver-catalyzed dehydrogenative cross-coupling reaction of substituted furans, thiophene, thioazole, and pyrrole **1a–e** with dialkyl phosphites **2** under mild conditions, affording the corresponding phosphonated products **3a–h** with up to 89% yield and good regioselectivities. Moreover, an unprecedented coupling of various substituted pyridines **1f–k** with dialkyl phosphites **2** was also realized using $AgNO_3$ as a catalyst and $K_2S_2O_8$ as an oxidant in CH_2Cl_2/H_2O, followed by reduction with $Na_2S_2O_3$, which furnished desired pyridine-2-yl phosphonates **3i–q** in satisfactory yields and good regioselectivities.

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EXPERIMENTAL SECTION

General Procedure for the Dehydrogenative Cross-Coupling Reaction of Five-Membered Heteroarenes with Phosphites. The mixture of five-membered heteroarenes **1a−e** (0.25 mmol), dialkyl phosphite (0.38 mmol), $AgNO_3$ (8.5 mg, 0.05 mmol, 20 mol %), and $K_2S_2O_8$ (0.27 g, 1.0 mmol) in the mixed solvent of CH_2Cl_2 and H_2O (3 mL, v/v = 1/1) was stirred at rt for 6−10 h. The mixture was evaporated, and the residue was purified by TLC (silica gel, ethyl acetate/petroleum ether = 2/1 to 3/1 as an eluent) to afford the desired heteroaryl phosphates **3a−h**.

Diethyl 5-acetylfuran-2-ylphosphonate ***3a*** *(ref 7):* Yield 89%; ethyl acetate/petroleum ether = 2/1 as an eluant, R_f = 0.45; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.18−7.17 (m, 2H), 4.24−4.16 (m, 4H), 2.53 (s, 3H), 1.36 (t, J = 7.1 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_{10}H_{16}O_5P$ 247.07, found 247.05.

Dimethyl 5-acetylfuran-2-ylphosphonate ***3b*** *(ref 1a):* Yield 87%; ethyl acetate/petroleum ether = 2/1 as an eluant, R_f = 0.40; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.21−7.19 (m, 2H), 3.88−3.82 (m, 6H), 2.54 (d, J = 4.8 Hz, 3H); MS (ESI) m/z $[M + H]^+$ calcd for $C_8H_{12}O_5P$ 219.03, found 218.95.

Dimethyl 5-formylfuran-2-ylphosphonate ***3c*** *(ref 1a):* Yield 83%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.56; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.78 (d, J = 3.6 Hz, 1H), 7.27 (d, J = 1.5 Hz, 2H), 3.86 (d, J = 11.7 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_7H_{10}O_5P$ 205.02, found 205.00.

Dimethyl thiophen-2-ylphosphonate ***3d*** *(ref 8):* Yield 51%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.70; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.74−7.65 (m, 2H), 7.21−7.17 (m, 1H), 3.78 (d, J = 11.4 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_6H_{10}O_3PS$ 193.00, found 193.00.

Diethyl thiophen-2-ylphosphonate ***3e*** *(ref 9):* Yield 61%; ethyl acetate/petroleum ether = 2/1 as an eluant, R_f = 0.63; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.71−7.65 (m, 2H), 7.20−7.16 (m, 1H), 4.19−4.09 (m, 4H), 1.34 (t, J = 7.2 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_8H_{14}O_3PS$ 221.03, found 221.00.

Diethyl 4-methylthiazol-2-ylphosphonate ***3f*** *(ref 1a):* Yield 81%; ethyl acetate/petroleum ether = 2/1 as an eluant, R_f = 0.68; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.18 (s, 1H), 4.17 (q, J = 8.4 Hz, 4H), 2.48 (s, 3H), 1.31−1.24 (m, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_8H_{15}NO_3PS$ 236.04, found 236.05.

Dimethyl 5-acetyl-1-methyl-1H-pyrrol-2-ylphosphonate ***3g*** *(ref 1a):* Yield 83%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.62; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.90 (t, J = 4.2 Hz, 1H), 6.74 (t, J = 3.6 Hz, 1H), 4.06 (s, 3H), 3.76 (d, J = 11.1 Hz, 6H), 2.46 (s, 3H); MS (ESI) m/z $[M + H]^+$ calcd for $C_9H_{15}NO_4P$ 232.07, found 232.05.

Diethyl 5-acetyl-1-methyl-1H-pyrrol-2-ylphosphonate ***3h:*** Yield 85%; ethyl acetate/petroleum ether = 2/1 as an eluant, R_f = 0.63; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.90 (t, J = 4.2 Hz, 1H), 6.77−6.74 (m, 1H), 4.14 (q, J = 7.5 Hz, 4H), 4.08 (s, 3H), 2.47 (s, 3H), 1.33 (t, J = 6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 189.9, 135.5 (d, J = 12.0 Hz), 127.9 (d, J = 218.0 Hz), 119.5 (d, J = 16.7 Hz), 118.0 (d, J = 13.6 Hz), 62.7 (d, J = 4.8 Hz), 45.9, 28.2, 16.3 (d, J = 6.6 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ (ppm) 8.4; MS (ESI) m/z $[M + H]^+$ calcd for $C_{11}H_{19}NO_4P$ 260.10, found 260.10; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{11}H_{18}NNaO_4P$ 282.0871, found 282.0872.

General Procedure for the Coupling Reaction of Pyridines with Phosphites. The mixture of substituted pyridines **1f−j** or quinoline **1k** (0.25 mmol), dialkyl phosphite **2** (0.38 mmol), $AgNO_3$ (8.5 mg, 0.05 mmol, 20 mol %), and $K_2S_2O_8$ (0.27 g, 1.0 mmol) in the mixed solvent of CH_2Cl_2 and H_2O (3 mL, v/v = 1/1) was stirred for 0.25−10 h at rt. After the reaction, $Na_2S_2O_3$ (0.25 g, 1 mmol) was added, and the reaction mixture was stirred at rt for 15 min. The resulting mixture was evaporated, and the residue was purified by TLC (silica gel, ethyl acetate/petroleum ether = 2/1 to 3/1 as an eluent) to afford the desired pyridin-2-yl phosphate **3i−o** or quinolin-2-yl phosphonate **3p**,**q**.

Diethyl pyridin-2-yl-2-phosphonate ***3i*** *(ref 10):* Yield 82%; ethyl acetate/petroleum ether = 2/1 as an eluant, R_f = 0.36; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.78 (d, J = 2.1 Hz, 1H), 7.95 (t, J = 6.9 Hz, 1H), 7.91−7.75 (m, 1H), 7.41 (d, J = 2.6 Hz, 1H), 4.21 (q, J = 7.8 Hz, 4H), 1.33 (t, J = 6.9 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_9H_{15}NO_3P$ 216.07, found 215.95.

Dimethyl pyridin-2-yl-2-phosphonate ***3j*** *(ref 11):* Yield 68%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.35; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.82 (d, J = 2.1 Hz, 1H), 7.98 (t, J = 7.1 Hz, 1H), 7.86−7.80 (m, 1H), 7.46 (s, 1H), 3.87 (d, J = 5.4 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_7H_{11}NO_3P$ 188.04, found 187.95.

Dimethyl 6-methylpyridin-2-ylphosphonate ***3k:*** Yield 61%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.45; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.78 (t, J = 7.2 Hz, 1H), 7.72−7.77 (m, 1H), 7.30 (d, J = 4.2 Hz,1H), 3.87 (d, J = 5.4 Hz, 6H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 159.8 (d, J = 22.8 Hz), 149.9 (d, J = 226.7 Hz), 136.2 (d, J = 12.2 Hz), 126.2 (d, J = 4.1 Hz), 125.6 (d, J = 25.2 Hz), 53.4 (d, J = 6.2 Hz), 24.6; ^{31}P NMR (202 MHz, $CDCl_3$) δ (ppm) 13.71; MS (ESI) m/z $[M + H]^+$ calcd for $C_8H_{13}NO_3P$ 202.06, found 202.05; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_8H_{13}NO_3P$ 202.0633, found 202.0648.

Dimethyl 6-ethylpyridin-2-ylphosphonate ***3l:*** Yield 72%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.53; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.76−7.64 (m, 2H), 7.29−7.26 (m, 1H), 3.83 (d, J = 10.8 Hz, 6H), 2.87 (q, J = 7.8 Hz, 2H), 1.28 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 164.7 (d, J = 22.0 Hz), 150.0 (d, J = 226.3 Hz), 136.3 (d, J = 13.1 Hz), 125.7 (d, J = 32.3 Hz), 124.9 (d, J = 4.2 Hz), 53.6 (d, J = 6.2 Hz), 31.4, 13.8; ^{31}P NMR (202 MHz, $CDCl_3$) δ (ppm) 13.6; MS (ESI) m/z $[M + H]^+$ calcd for $C_9H_{15}NO_3P$ 216.07, found 215.95; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_9H_{15}NO_3P$ 216.0790, found 216.0794.

Diethyl 4-methylpyridin-2-ylphosphonate ***3m*** *(ref 12):* Yield 78%; ethyl acetate/petroleum ether = 2/1 as an eluant, R_f = 0.46; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.62 (d, J = 2.4 Hz, 1H), 7.79 (d, J = 6.6 Hz, 1H), 7.21 (d, J = 2.6 Hz, 1H), 4.19 (q, J = 9.6 Hz, 4H), 2.38 (s, 3H), 1.32 (t, J = 7.2 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_{10}H_{17}NO_3P$ 230.09, found 230.05.

Dimethyl 6-aminopyridin-2-ylphosphonate ***3n:*** Yield 55%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.33; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.19−8.18 (m, 1H), 7.74−7.65 (m, 1H), 6.65−6.60 (m, 1H), 5.97 (s, 2H), 3.73 (d, J = 11.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 160.4 (d, J = 10.5 Hz), 153.3, 147.0, 142.8 (d, J = 44.2 Hz), 138.1, 52.8 (d, J = 4.73 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ (ppm) 21.8; MS (ESI) m/z $[M + H]^+$ calcd for $C_7H_{12}N_2O_3P$ 203.05, found 203.00; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_7H_{12}N_2O_3P$ 203.0586, found 203.0581.

Diethyl 6-aminopyridin-2-ylphosphonate ***3o:*** Yield 70%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.54; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.16−8.14 (m, 1H), 7.74−7,67 (m, 1H), 6.63−6.58 (m, 1H), 6.22 (s, 2H), 4.16−4.00 (m, 4H), 1.29 (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 160.2 (d, J = 11.1 Hz), 152.8, 142.7 (d, J = 6.4 Hz), 112.7 (d, J = 10.2 Hz), 103.9 (d, J = 185.4 Hz), 62.3 (d, J = 5.4 Hz), 16.2 (d, J = 6.6 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ (ppm) 18.8; MS (ESI) m/z $[M + H]^+$ calcd for $C_9H_{16}N_2O_3P$ 231.08, found 231.05; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_9H_{15}N_2NaO_3P$ 253.0718, found 253.0719.

Dimethyl quinolin-2-ylphosphonate ***3p*** *(ref 13):* Yield 51%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.56; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.30−8.25 (m, 2H), 8.01 (dd, J = 8.3, 4.8 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.80 (t, J = 7.8 Hz, 1H), 7.66 (t, J = 7.4 Hz, 1H), 3.94 (d, J = 10.8 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_{11}H_{13}NO_3P$ 238.06, found 238.05.

Diethyl quinolin-2-ylphosphonate ***3q*** *(ref 14):* Yield 53%; ethyl acetate/petroleum ether = 3/1 as an eluant, R_f = 0.58; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.03 (t, J = 4.8 Hz, 1H), 8.48 (d, J = 8.1 Hz, 1H), 8.27−8.17 (m, 1H), 8.03−7.96 (m, 1H), 7.79 (t, J = 6.9 Hz,1H), 7.66 (t, J = 6.90 Hz, 1H), 4.29−4.13 (m, 4H), 1.33 (t, J = 3.9 Hz, 6H); MS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{17}NO_3P$ 266.09, found 266.05.

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■ ASSOCIATED CONTENT

Supporting Information

Screening experiments, spectra of ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, MS, and HRMS. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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