JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Nickel-Catalyzed One-Pot Tandem 1,4-1,2-Addition of P(O)H Compounds to 1,10-Phenanthrolines

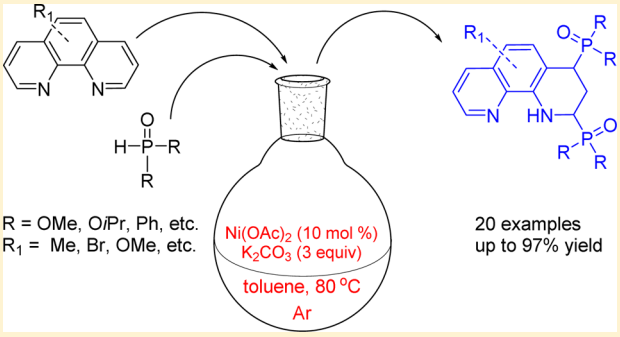
Yuxing Gao,*[,†] Honggui Deng,[†] Shanshan Zhang,[†] Wanhua Xue,[†] Yile Wu,[†] Hongwei Qiao,[†] Pengxiang Xu,*[,†] and Yufen Zhao[†,‡]

[†]Department of Chemistry and Key Laboratory for Chemical Biology of Fujian Province, College of Chemistry and Chemical Engineering, Xiamen University, Xiamen 361005, Fujian, China

[‡]Key Laboratory of Bioorganic Phosphorus Chemistry and Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, China

Supporting Information

ABSTRACT: A novel and efficient nickel-catalyzed tandem 1,4-1,2-addition of P(O)H compounds to 1,10-phenanthrolines forming various 2,4-diphosphono-1,2,3,4-tetrahydro-1,10-phenanthrolines has been developed. This reaction breaks up the aromatic stabilization and directly introduces two phosphorus moieties in one single step. This finding is the first example of transition-metal-catalyzed double hydrophosphonylation of 1,10-phenanthrolines.



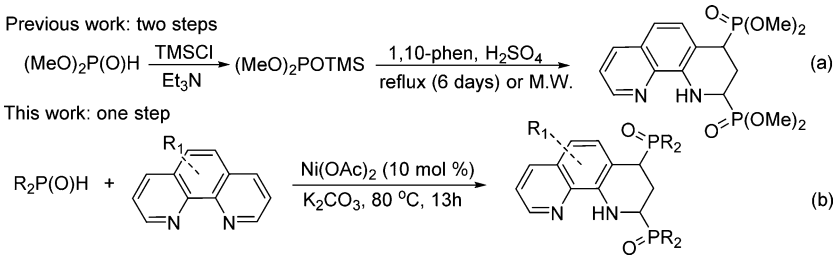
Transition-metal-catalyzed additions of a heteroatom compound to the carbon−carbon and carbon−heteroatom unsaturated bonds have become one of the most powerful and practical tools for the preparation of heteroatom compounds in organic synthesis and industrial processes.[1] Azaheterocyclic phosphonates containing a P−C bond are important classes of valuable phosphorus-containing compounds in organic chemistry, and agrochemical and medicinal chemistry.[2] For example, dialkyl phosphonate diesters bearing a 2-pyridyl moiety have broad applications as corrosion inhibitors, antistatics and lubricant additives, and dispersing and emulsifying agents in various fields.[3] Furthermore, some phosphonylated pyridines themselves are endowed with wide-ranging biological activities, which are successfully used as potent insecticides, fungicides, and herbicides.[4] Several P−C bond-containing quinolylphosphonic acid derivatives have been studied intensively for potential use as therapeutic agents in the acute treatment of stroke and head trauma.[5]

A large number of methods for the preparation of azaheterocyclic phosphonates have continuously emerged over the years,[6] but known literature methods for the synthesis of azaheterocyclic diphosphonates and diphosphonic acids, especially for diphosphonylated diazaheterocycles which probably exhibit numerous interesting biological properties, are scarce. Through a Reissert-type reaction, phthalazine, 1,8-naphthyridine, and 1,7-phenanthroline activated by various sulfonyl or acyl chlorides could react with trialkyl phosphites in the presence of sodium iodide, respectively, affording the corresponding monophosphonylated 1,2-adducts or 1,4-adducts.[7] In addition, 1,7-phenanthroline, 1,5- or 1,8-naphthyridine could be activated using simple methyl iodide to undergo nucleophilic attack from trimethyl phosphite or dimethyl sodiophosphonate with the formation of their corresponding α- or γ-phosphonylated diazaheterocycles.[8] Besides this regioselective 1,2- or 1,4-addition of phosphites to azaheterocycles, for 4,7-phenanthroline, the diphosphonylated adducts were obtained in a Reissert-type reaction, but 1,10-phenanthroline was recovered under similar reaction conditions.[7b,9] Recently, a general protocol for the Pd-catalyzed coupling of dihalo-1,10-phenanthrolines with diethyl phosphite forming the corresponding diphosphonylated adducts was reported.[10] Very recently, Stevens and co-workers[11] developed the only current tandem 1,4-1,2 addition of dimethyl trimethylsilyl phosphite (DMPTMS) to several diazaheterocycles, including 1,5-naphthyridine, 1,10-phenanthroline, 1,7-phenanthroline, and 4,7-phenanthroline, leading to the corresponding diphosphonylated products (Scheme 1a), but this method needed microwave and strong acidic conditions, as well as previous preparation of unstable[12] DMPTMS, which was obtained by O-silylation of dimethyl phosphonate with trimethylsilyl chloride and triethylamine in dry dichloromethane[13] and stored for only 1 month at −30 °C in a well-closed bulb.[14] Herein, we reported the first Ni-catalyzed one-pot tandem 1,4-1,2-addition of commercially available P(O)H compounds to 1,10-phenanthrolines, leading to various diphosphonylated 1,10-phenanthrolines, which are both α-aminophosphonates and unnatural

Received: August 9, 2014
Published: December 8, 2014

   dx.doi.org/10.1021/jo501842p | J. Org. Chem. 2015, 80, 1192−1199

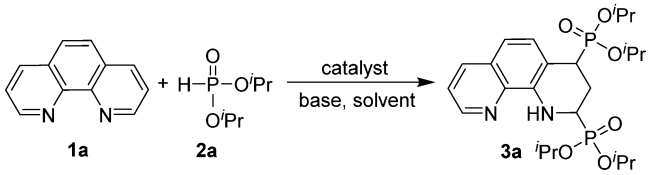
Scheme 1. Synthesis of 2,4-Diphosphono-1,2,3,4-tetrahydro-1,10-phenanthrolines



amino acid analogues that exhibited a wide range of biological activities,[15] through direct hydrophosphonylation to introduce two phosphorus moieties in one step.

To optimize reaction conditions, the 1,4-1,2-addition of diisopropyl phosphonate **2a** to 1,10-phenanthroline **1a** was selected as the model reaction, and some representative results were presented in Table 1. A screening of the catalysts showed

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	base	solvent	yield (%)[b]
1	$NiCl_2(PPh_3)_2$	K_2CO_3	toluene	85
2	$NiCl_2$	K_2CO_3	toluene	93
3	**$Ni(OAc)_2$**	**K_2CO_3**	**toluene**	**97**
4	$FeCl_3$	K_2CO_3	toluene	6
5	$Cu(OAc)_2$	K_2CO_3	toluene	21
6	$Ni(OAc)_2{\cdot}4H_2O$	K_2CO_3	toluene	91
7		K_2CO_3	toluene	0
8	$Ni(OAc)_2$		toluene	0
9	$Ni(OAc)_2$	K_3PO_4	toluene	47
10	$Ni(OAc)_2$	Et_3N	toluene	0
11	$Ni(OAc)_2$	K_2CO_3	DCE	76
12	$Ni(OAc)_2$	K_2CO_3	CH_3CN	61
13	$Ni(OAc)_2$	K_2CO_3	1,4-dioxane	78
14[c]	$Ni(OAc)_2$	K_2CO_3	DMF	55

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1.5 mmol), base (1.5 mmol), catalyst (0.05 mmol), solvent (2.0 mL), 80 °C, 13 h, under argon. [b]Yields based on **1a**. The product **3a** was separated as a mixture of (2S, 4S)- and (2R, 4R)-enantiomers through silica gel column chromatography. [c]Run at 45 °C.

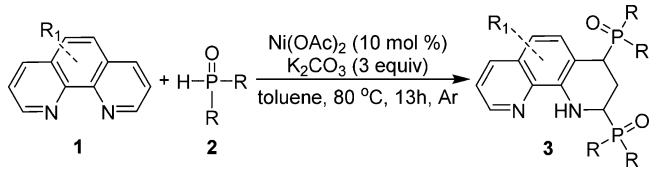
that Ni(II) salts, especially $Ni(OAc)_2$, was found to be the most effective catalyst to generate **3a** in an excellent yield of 97% (entry 3). Analysis by ^{31}P NMR spectroscopy revealed the formation of the double addition product **3a** as one major pair of enantiomers. Other catalysts and corresponding yields of **3a** were as follows: $NiCl_2(PPh_3)_2$, 85% (entry 1); $NiCl_2$, 93% (entry 2); $FeCl_3$, 6% (entry 4); and $Cu(OAc)_2$, 23% (entry 5). Note that $Ni(OAc)_2{\cdot}4H_2O$ containing water of crystallization instead of anhydrous $Ni(OAc)_2$ resulted in a slight decrease of the yield, demonstrating that water was unfavorable for the reaction (entry 6). Without $Ni(OAc)_2$, the reaction did not occur (entry 7), indicating that a $Ni(OAc)_2$ catalyst was vital to achieve a high yield of **3a**. The addition of base was essential to the success of this double phosphorylation reaction, and no product was detected in the absence of base (entry 8). Among the various bases screened, K_2CO_3 turned out to be the best choice, whereas K_3PO_4 and Et_3N were less effective (entries 3, 9, 10). The type of solvent also highly affected the yield of this reaction. We investigated various solvents and found that toluene was the best suitable solvent for this procedure (entries 11−13). Decreasing the reaction temperature led to a significant decrease of yield (entry 14).

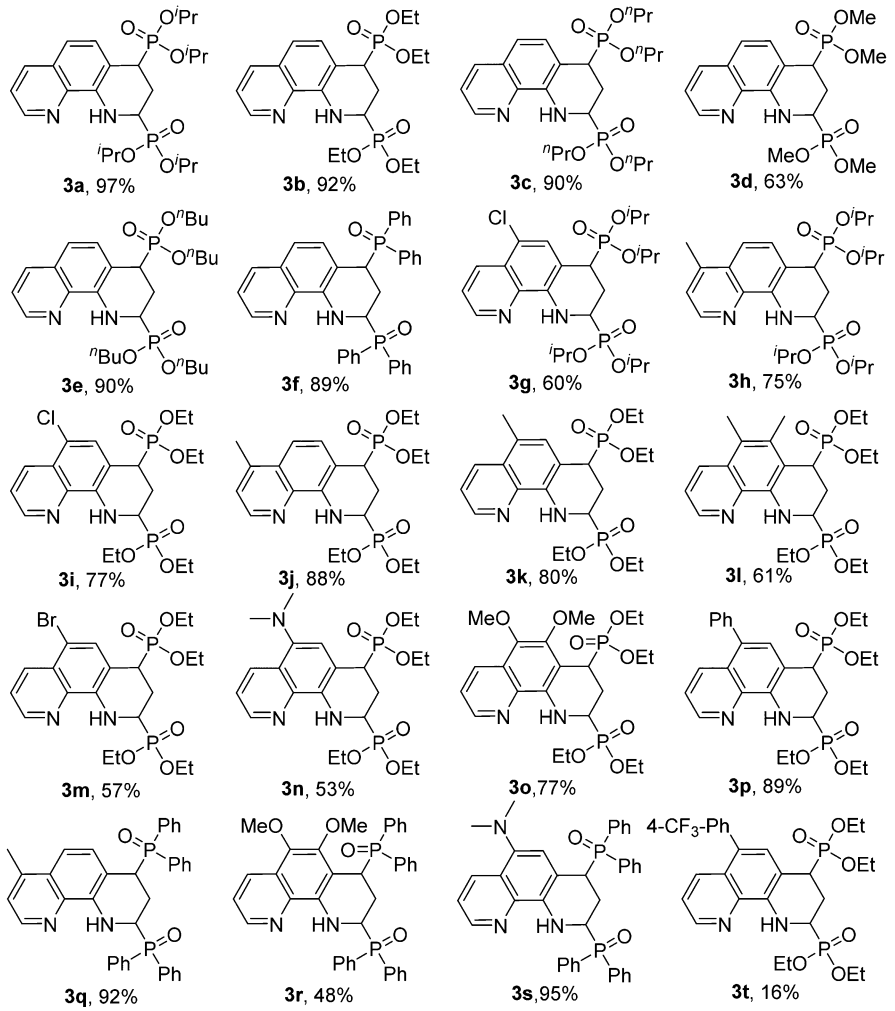
Under the optimized conditions shown in footnote *a* in Table 2, we next surveyed the tandem 1,4-1,2-addition reaction of various substituted 1,10-phenanthrolines with several *H*-phosphonates to understand the substrate scope. As demonstrated in Table 2, a variety of valuable 2,4-diphosphono-1,2,3,4-tetrahydro-1,10-phenanthrolines could be conveniently and efficiently obtained in moderate to excellent yields by this novel Ni-catalyzed double phosphorylation reaction of 1,10-phenanthrolines. Unsurprisingly, in addition to diisopropyl **2a**, other aliphatic dialkyl *H*-phosphonates, such as diethyl **2b**, di-*n*-propyl **2c**, dimethyl **2d**, and di-*n*-butyl *H*-phosphonates **2e**, were all suitable substrates and generated the corresponding products (**3b**−**3e**) in 92, 90, 63, and 90% yields, respectively. Besides, diphenylphosphine oxide (**2f**) also reacted smoothly with various 1,10-phenanthrolines to afford the desired diphosphinylated products (**3f**, **3q**−**3s**), which might be used as a class of valuable bidentate phosphorus ligands in catalyst science after their reduction.

A variety of functionalities on the 1,10-phenanthrolines, such as methyl (**3h**, **3j**, **3k**, **3l**, and **3q**), chloro (**3g** and **3i**), bromo (**3m**), dimethylamino (**3n** and **3s**), methoxy (**3o** and **3r**), and phenyl (**3p**) groups, were all tolerated. It is noticeable that the preferred direction of attack on 1,10-phenanthroline was from the sterically less-hindered side, leading to **3** as the major product. The electron-neutral 4-methyl-1,10-phenanthroline and electron-rich 5,6-dimethoxy-1,10-phenanthroline reacted well with **2b** to give 88% and 77% yields, respectively (**3j** and **3o**), but no desired product was detected by ^{31}P NMR spectroscopy using electron-deficient 5-nitro-1,10-phenanthroline as the substrate. The results illustrated that electronic effects played key roles in this reaction. In addition, the reaction of 5-phenyl-1,10-phenanthroline with **2b** afforded the product **3p** in a high yield of 89%, but the 5-phenyl-1,10-phenanthroline derivative modified by the strong election-withdrawing trifluoromethyl group reacted with **2b** to give product **3t** in only 16% yield, also demonstrating that this system was relatively sensitive to small changes of electronic effects in the phenanthrolines. Notably, the double addition of 5-methyl-1,10-phenanthroline afforded an 80% yield of **3k**, whereas sterically hindered 5,6-dimethyl-1,10-phenanthroline showed lower reactivity and provided a lower yield of 61% (**3l**), indicating that this reaction was also influenced markedly by the steric effects. Interestingly, 5-bromo-1,10-phenanthroline was also compatible with this reaction and the bromo group was

dx.doi.org/10.1021/jo501842p | J. Org. Chem. 2015, 80, 1192−1199

Table 2. Ni-Catalyzed 1,4-1,2-Addition of Various 1,10-Phenanthrolines with P(O)-H Compounds[a]





[a]Conditions: **1** (0.5 mmol), **2** (1.5 mmol), K_2CO_3 (1.5 mmol), $Ni(OAc)_2$ (0.05 mmol), toluene (2.0 mL), 80 °C, 13 h, under argon. The product **3** was separated as a mixture of (2S,4S)- and (2R,4R)-enantiomers through silica gel column chromatography.

retained (**3m**). Thus, the chemoselectivity may be applied for the preparation of more complex molecules through further coupling reaction of halides. Nevertheless, using 2,2′-bipyridine, quinoline, benzo[*h*]quinoline, *N*,*N*-dimethylquinolin-8-amine, 1,7-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, and 2,9-dimethyl-1,10-phenanthroline as the substrates, this 1,4-1,2-addition reaction did not occur, clearly revealing that the 1,10-phenanthroline backbone was indispensable and the position of substituents greatly influenced this reaction.

The double addition product **3f** was recrystallized from a $CHCl_3$/ethyl acetate mixture solvent as yellow crystals. The molecular structure of **3f** having molecules of both enantiomers in a single crystalline cell was confirmed by single-crystal X-ray diffraction (Figure 1).

In summary, we have successfully developed a simple and efficient method for the preparation of various 2,4-diphosphono-1,2,3,4-tetrahydro-1,10-phenanthrolines through a novel Ni-

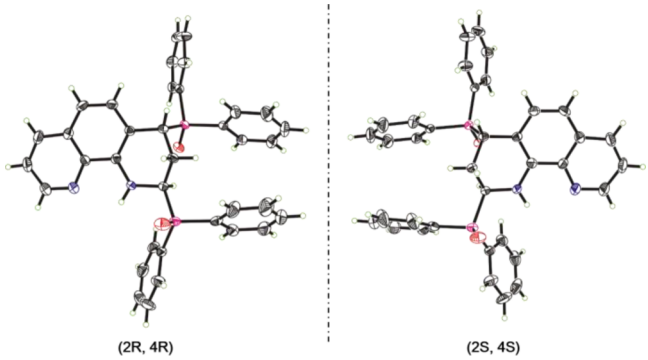


Figure 1. Crystal structure of (2S,4S)- and (2R,4R)-isomers of compound **3f**. Displacement ellipsoids are drawn at the 50% probability level, and H atoms are shown as small spheres of arbitrary radii.

dx.doi.org/10.1021/jo501842p | *J. Org. Chem.* 2015, 80, 1192−1199

catalyzed tandem 1,4-1,2-addition of readily available *H*-phosphonates and diphenylphosphine oxide to 1,10-phenanthrolines under relatively mild reaction conditions. Notably, using commercially available and inexpensive $Ni(OAc)_2$ as catalyst, this double addition is first performed under transition-metal catalysis. Moreover, this reaction results in the breakup of the aromatic stabilization and regeneration of two P−C bonds in a simple one-pot process. More attractively, in contrast, direct use of stable *H*-phosphonates without the need to simultaneously prepare the unstable silylated phosphites, improving greatly the reaction efficiency, represents a prominent advantage of the method. Preliminary mechanistic studies indicated that this reaction might involve a tandem 1,4-1,2-addition (see the Supporting Information for details).

EXPERIMENTAL SECTION

All reactions were carried out under dry argon. ^{31}P, ^{1}H, and $^{13}C\{^{1}H\}$ NMR spectra were measured on a 400 MHz spectrometer. ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$ as the internal standard (^{1}H NMR: TMS at 0.00 ppm, $CHCl_3$ at 7.26 ppm; $^{13}C\{^{1}H\}$ NMR: $CDCl_3$ at 77.0 ppm), and 85% H_3PO_4 as external standard for ^{31}P NMR. All coupling constants (J values) were reported in hertz (Hz). All compounds were further characterized by HRMS. Column chromatography was performed on silica gel 300−400 mesh. The reactions for mechanism studies in the Supporting Information were also carried out under dry argon, and ^{31}P, ^{1}H, and $^{13}C\{^{1}H\}$ NMR spectra were also measured on a 400 MHz spectrometer. MS spectra for mechanism studies were recorded on an ESI-MS apparatus.

Typical Procedure for the Preparation of 2,4-Diphosphono-1,2,3,4-tetrahydro-1,10-phenanthrolines. An oven-dried Schlenk tube containing 1,10-phenanthrolines (0.5 mmol, 1.0 equiv), $Ni(OAc)_2$ (0.05 mmol, 10 mol %), and K_2CO_3 (1.5 mmol, 3.0 equiv) was evacuated and purged with dry argon three times. Then, a mixture of freshly distilled toluene (2.0 mL) and *H*-phosphonates or $Ph_2P(O)H$ (1.5 mmol, 3 equiv) was added by a syringe to the reaction system at room temperature. The reaction mixture was stirred at 80 °C for 13 h. The mixture was cooled to room temperature and then was concentrated under vacuum. The desired products were obtained in the corresponding yields after purification by flash chromatography on silica gel using dichloromethane/methanol (or ethyl acetate/petroleum ether) as the eluent.

Spectral Data of the Compounds. *Tetraisopropyl (1,2,3,4-Tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3a**, New Compound).* Yellow oil; 248 mg, 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 (dd, J = 4.1, 1.5 Hz, 1H), 7.96 (dd, J = 8.2, 1.4 Hz, 1H), 7.41 (dd, J = 8.4, 1.5 Hz, 1H), 7.29 (dd, J = 8.2, 4.2 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 6.52 (d, J = 5.0 Hz, 1H), 4.74−4.89 (m, 2H), 4.54−4.67 (m, 1H), 4.39−4.52 (m, 1H), 4.16 (ddd, J = 11.4, 7.9, 3.3 Hz, 1H), 3.42 (dt, J = 24.3, 4.4 Hz, 1H), 2.53−2.74 (m, 1H), 2.07−2.31 (m, 1H), 1.39 (d, J = 6.2 Hz, 3H), 1.35 (d, J = 6.2 Hz, 6H, overlap), 1.264 (d, J = 6.1 Hz, 3H), 1.262 (d, J = 6.2 Hz, 3H), 1.256 (d, J = 6.2 Hz, 3H), 1.23 (d, J = 6.2 Hz, 3H), 0.91 (d, J = 6.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 147.0, 140.1 (dd, $J_{C\text{-}P}$ = 10.3, 6.9 Hz), 137.4 (d, $J_{C\text{-}P}$ = 2.2 Hz), 135.4, 129.4 (d, $J_{C\text{-}P}$ = 3.5 Hz), 127.5 (d, $J_{C\text{-}P}$ = 2.1 Hz), 121.0, 113.4 (d, $J_{C\text{-}P}$ = 2.2 Hz), 108.9 (d, $J_{C\text{-}P}$ = 7.1 Hz), 71.3 (d, $J_{C\text{-}P}$ = 6.9 Hz), 71.1 (d, $J_{C\text{-}P}$ = 8.6 Hz), 71.0 (d, $J_{C\text{-}P}$ = 7.6 Hz), 70.3 (d, $J_{C\text{-}P}$ = 7.7 Hz), 45.6 (d, $J_{C\text{-}P}$ = 160.9 Hz), 35.4 (dd, $J_{C\text{-}P}$ = 143.2, 14.1 Hz), 24.09 (d, $J_{C\text{-}P}$ = 5.3 Hz), 24.06 (d, $J_{C\text{-}P}$ = 5.7 Hz), 24.0 (d, $J_{C\text{-}P}$ = 4.7 Hz), 23.9 (d, $J_{C\text{-}P}$ = 4.9 Hz), 23.84 (d, $J_{C\text{-}P}$ = 5.3 Hz), 23.78 (d, $J_{C\text{-}P}$ = 5.2 Hz), 23.2 (d, $J_{C\text{-}P}$ = 5.4 Hz), 22.4 (dd apparent t, $J_{C\text{-}P}$ = 5.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 23.14, 24.72; IR (film) υ_{max}: 3398, 2978, 2933, 2873, 1570, 1513, 1480, 1452, 1424, 1385, 1319, 1294, 1240, 1176, 1142, 1106, 982, 886, 801, 826, 766, 724 cm^{-1}; HRMS (ESI-Q-TOF): m/z 513.2280 ([M + H]$^+$, $C_{24}H_{39}N_2O_6P_2^+$ calcd. 513.2278).

*Tetraethyl (1,2,3,4-Tetrahydro-1,10-phenanthroline-2,4-diyl)bis-(phosphonate) (**3b**, New Compound).* Yellow oil; 210 mg, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.65 (dd, J = 4.2, 1.5 Hz, 1H), 7.94 (dd, J = 8.2, 1.4 Hz, 1H), 7.33 (dd, J = 8.5, 1.5 Hz, 1H), 7.27 (dd, J = 8.0, 4.0 Hz, 1H), 6.98(d, J = 8.4 Hz, 1H), 6.50 (d, J = 5.0 Hz, 1H), 4.14−4.28 (m, 5H), 3.92−4.00 (m, 3H), 3.82−3.91 (m, 1H), 3.40−3.50 (m, 1H), 2.56−2.70 (m, 1H), 2.12−2.31 (m, 1H), 1.33 (t, J = 7.0 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 1.13 (t, J = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 147.2, 140.0 (dd, $J_{C\text{-}P}$ = 10.1, 7.0 Hz), 137.5 (d, $J_{C\text{-}P}$ = 2.4 Hz), 135.4, 129.1 (d, $J_{C\text{-}P}$ = 3.5 Hz), 127.6 (d, J_{C-P} = 2.0 Hz), 121.2, 113.8 (d, $J_{C\text{-}P}$ = 2.3 Hz), 108.6 (d, $J_{C\text{-}P}$ = 7.1 Hz), 62.8 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.5 (d, $J_{C\text{-}P}$ = 7.5 Hz, overlap), 62.4 (d, $J_{C\text{-}P}$ = 8.0 Hz, overlap), 62.1 (d, $J_{C\text{-}P}$ = 7.2 Hz), 45.3 (d, $J_{C\text{-}P}$ = 159.3 Hz), 34.8 (dd, $J_{C\text{-}P}$ = 141.7, 14.2 Hz), 22.1 (dd apparent t, $J_{C\text{-}P}$ = 5.1 Hz), 16.38 (d, $J_{C\text{-}P}$ = 5.2 Hz, overlap), 16.36 (d, $J_{C\text{-}P}$ = 5.3 Hz, overlap), 16.26 (d, $J_{C\text{-}P}$ = 5.8 Hz, overlap), 16.23 (d, $J_{C\text{-}P}$ = 5.3 Hz, overlap); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 24.79, 26.55; IR (film) υ_{max}: 3398, 2982, 2931, 2908, 2868, 1571, 1514, 1478, 1446, 1387, 1317, 1237, 1164, 1021, 967, 827, 793, 733 cm^{-1}; HRMS (ESI-Q-TOF): m/z 457.1656 ([M + H]$^+$, $C_{20}H_{31}N_2O_6P_2^+$ calcd. 457.1652).

*Tetrapropyl (1,2,3,4-Tetrahydro-1,10-phenanthroline-2,4-diyl)-bis(phosphonate) (**3c**, New Compound).* Yellow oil; 230 mg, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.69 (dd, J = 4.2, 1.6 Hz, 1H), 7.99 (dd, J = 8.2, 1.6 Hz, 1H), 7.38 (dd, J = 8.5, 1.7 Hz, 1H), 7.30−7.34 (m, 1H), 7.02 (d, J = 8.4 Hz, 1H), 6.54 (d, J = 4.9 Hz, 1H), 4.29 (ddd, J = 11.7, 8.1, 3.5 Hz, 1H), 4.05−4.18 (m, 4H), 3.85−3.93 (m, 3H), 3.73−3.81 (m, 1H), 3.47−3.56 (m, 1H), 2.62−2.73 (m, 1H), 2.19−2.35 (m, 1H), 1.49−1.78 (m, 8H), 0.97 (t, J = 7.4 Hz, 3H, overlap), 0.94 (t, J = 7.4 Hz, 3H, overlap), 0.90 (t, J = 7.4 Hz, 3H, overlap), 0.82 (t, J = 7.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 147.3, 140.1 (dd, $J_{C\text{-}P}$ = 10.2, 6.8 Hz), 137.6 (d, $J_{C\text{-}P}$ = 2.5 Hz), 135.6, 129.3 (d, $J_{C\text{-}P}$ = 3.4 Hz), 127.8 (d, $J_{C\text{-}P}$ = 1.9 Hz), 121.3, 113.9 (d, $J_{C\text{-}P}$ = 2.6 Hz), 108.8 (d, $J_{C\text{-}P}$ = 7.1 Hz), 68.4 (d, $J_{C\text{-}P}$ = 6.8 Hz), 68.2 (d, $J_{C\text{-}P}$ = 7.4 Hz), 68.1 (d, $J_{C\text{-}P}$ = 7.3 Hz), 67.7 (d, $J_{C\text{-}P}$ = 7.5 Hz), 45.5 (d, $J_{C\text{-}P}$ = 160.8 Hz), 35.0 (dd, $J_{C\text{-}P}$ = 141.9, 14.3 Hz), 23.99 (d, $J_{C\text{-}P}$ = 6.1 Hz, overlap), 23.98 (d, $J_{C\text{-}P}$ = 6.3 Hz, overlap), 23.92 (d, $J_{C\text{-}P}$ = 6.0 Hz, overlap), 23.88 (d, $J_{C\text{-}P}$ = 5.7 Hz, overlap), 22.4 (dd apparent t, $J_{C\text{-}P}$ = 5.3 Hz), 10.04, 10.02, 10.01, 10.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ = 26.43, 24.70; IR (film) υ_{max}: 3397, 2968, 2940, 2894, 1570, 1514, 1479, 1386, 1318, 1263, 1238, 1163, 1063, 994, 905, 854, 827, 801, 749 cm^{-1}; HRMS (ESI-Q-TOF): m/z 513.2283 ([M + H]$^+$, $C_{24}H_{39}N_2O_6P_2^+$ calcd. 513.2278).

*Tetramethyl (1,2,3,4-Tetrahydro-1,10-phenanthroline-2,4-diyl)-bis(phosphonate) (**3d**, CAS 1426583-37-0).* Yellow oil; 126 mg, 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.59 (dd, J = 4.2, 1.5 Hz, 1H), 7.88 (dd, J = 8.3, 1.5 Hz, 1H), 7.17−7.26 (m, 2H), 6.93 (d, J = 8.4 Hz, 1H), 6.40 (d, J = 4.8 Hz, 1H), 4.22 (ddd, J = 11.7, 8.1, 3.5 Hz, 1H), 3.77 (d, J = 10.5 Hz, 3H), 3.76 (d, J = 10.6 Hz, 3H), 3.55 (d, J = 10.6 Hz, 3H), 3.54 (d, J = 10.6 Hz, 3H), 3.37−3.48 (m, 1H), 2.49−2.64 (m, 1H), 2.03−2.30 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 147.1, 139.5 (dd, $J_{C\text{-}P}$ = 9.9, 7.0 Hz), 137.2 (d, $J_{C\text{-}P}$ = 2.1 Hz), 135.4, 128.7 (d, $J_{C\text{-}P}$ = 3.4 Hz), 127.5 (d, $J_{C\text{-}P}$ = 2.0 Hz), 121.2, 114.0 (d, $J_{C\text{-}P}$ = 2.1 Hz), 108.1 (d, $J_{C\text{-}P}$ = 7.3 Hz), 53.3 (d, $J_{C\text{-}P}$ = 6.7 Hz), 53.0 (d, $J_{C\text{-}P}$ = 7.3 Hz), 52.9 (d, $J_{C\text{-}P}$ = 7.4 Hz), 52.8 (d, $J_{C\text{-}P}$ = 7.3 Hz), 44.8 (d, $J_{C\text{-}P}$ = 159.8 Hz), 34.1 (dd, $J_{C\text{-}P}$ = 141.8, 14.4 Hz), 21.7 (dd apparent t, $J_{C\text{-}P}$ = 5.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 28.76, 26.90; IR (film) υ_{max}: 3398, 2954, 2852, 1571, 1513, 1479, 1386, 1319, 1238, 1180, 1028, 963, 858, 826, 801, 772, 738 cm^{-1}; HRMS (ESI): m/z 423.0841 ([M + Na]$^+$, $C_{16}H_{22}N_2NaO_6P_2^+$ calcd. 423.0845).

*Tetrabutyl (1,2,3,4-Tetrahydro-1,10-phenanthroline-2,4-diyl)bis-(phosphonate) (**3e**, New Compound).* Yellow oil; 256 mg, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.68 (dd, J = 4.2, 1.6 Hz, 1H), 7.99 (dd, J = 8.2, 1.5 Hz, 1H), 7.37 (dd, J = 8.5, 1.6 Hz, 1H), 7.32 (dd, J = 8.2, 4.2 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 6.53 (d, J = 5.0 Hz, 1H), 4.22−4.29 (m, 1H), 4.10−4.20 (m, 4H), 3.87−3.97 (m, 3H), 3.76−3.84 (m, 1H), 3.46−3.55 (m, 1H), 2.62−2.71 (m, 1H), 2.16−2.35 (m, 1H), 1.56−1.73 (m, 6H), 1.31−1.50 (m, 8H), 1.18−1.27 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.4 Hz, 6H), 0.76 (t, J = 7.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 147.2, 140.0 (dd, $J_{C\text{-}P}$ = 10.0, 7.0 Hz), 137.6 (d, $J_{C\text{-}P}$ = 2.5 Hz), 135.5, 129.2 (d, $J_{C\text{-}P}$ = 3.4 Hz), 127.7 (d, $J_{C\text{-}P}$ = 2.1 Hz), 121.3, 113.9 (d, $J_{C\text{-}P}$ = 2.4 Hz), 108.7 (d, $J_{C\text{-}P}$ = 7.2 Hz), 66.7 (d, $J_{C\text{-}P}$ = 6.8 Hz), 66.4 (d, $J_{C\text{-}P}$ = 8.5 Hz, overlap), 66.3

dx.doi.org/10.1021/jo501842p | J. Org. Chem. 2015, 80, 1192−1199

(d, $J_{C\text{-}P}$ = 7.6 Hz, overlap), 65.8 (d, $J_{C\text{-}P}$ = 7.5 Hz), 45.4 (d, $J_{C\text{-}P}$ = 159.2 Hz), 34.9 (dd, $J_{C\text{-}P}$ = 141.7, 14.1 Hz), 32.6 (d, $J_{C\text{-}P}$ = 5.9 Hz, overlap), 32.5 (d, $J_{C\text{-}P}$ = 6.1 Hz, overlap), 32.4 (d, $J_{C\text{-}P}$ = 5.6 Hz), 22.3 (dd apparent t, $J_{C\text{-}P}$ = 5.3 Hz), 18.7 (overlap), 18.6 (overlap), 18.5, 13.6, 13.53, 13.52 (overlap), 13.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ = 26.46, 24.75; IR (film) υ_{max}: 3396, 2960, 2933, 2872, 1570, 1514, 1478, 1385, 1318, 1262, 1163, 1065, 1024, 980, 896, 826, 780, 749 cm^{-1}; HRMS (ESI): m/z 591.2727 ([M + Na]$^+$, $C_{28}H_{46}N_2NaO_6P_2^+$ calcd. 591.2723).

*(1,2,3,4-Tetrahydro-1,10-phenanthroline-2,4-diyl)bis(diphenylphosphine oxide) (**3f**, New Compound).* Yellow solid; 260 mg, 89% yield. mp: 236−237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.54 (dd, J = 4.2, 1.6 Hz, 1H), 7.76−7.96 (m, 7H), 7.59−7.64 (m, 2H), 7.44−7.58 (m, 8H), 7.34−7.41 (m, 4H), 7.23 (dd, J = 8.2, 4.1 Hz, 1H), 6.60 (d, J = 8.4 Hz, 1H), 6.44 (d, J = 4.3 Hz, 1H), 6.25 (dd, J = 8.5, 1.2 Hz, 1H), 5.12 (dt, J = 11.9, 2.6 Hz, 1H), 3.88−3.96 (m, 1H), 2.46−2.56 (m, 1H), 2.20−2.38 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 147.2, 141.2 (dd, $J_{C\text{-}P}$ = 7.7, 5.1 Hz), 137.7 (d, $J_{C\text{-}P}$ = 2.0 Hz), 135.3, 132.2 (d, $J_{C\text{-}P}$ = 2.2 Hz), 131.9 (d, $J_{C\text{-}P}$ = 2.4 Hz), 131.8 (d, $J_{C\text{-}P}$ = 96.6 Hz), 131.8 (d, $J_{C\text{-}P}$ = 3.0 Hz), 131.7 (d, $J_{C\text{-}P}$ = 9.3 Hz), 131.6 (d, $J_{C\text{-}P}$ = 9.1 Hz), 131.3 (d, $J_{C\text{-}P}$ = 8.7 Hz), 131.2 (d, $J_{C\text{-}P}$ = 8.2 Hz), 131.1 (d, $J_{C\text{-}P}$ = 93.7 Hz), 130.32 (d, $J_{C\text{-}P}$ = 97.2 Hz), 129.5 (d, $J_{C\text{-}P}$ = 97.2 Hz), 128.8 (d, $J_{C\text{-}P}$ = 11.5 Hz), 128.7 (d, $J_{C\text{-}P}$ = 10.9 Hz), 128.6 (d, $J_{C\text{-}P}$ = 5.1 Hz), 128.5 (d, $J_{C\text{-}P}$ = 11.2 Hz), 128.3 (d, $J_{C\text{-}P}$ = 11.4 Hz), 127.5 (d, $J_{C\text{-}P}$ = 1.9 Hz), 121.2, 113.1 (d, $J_{C\text{-}P}$ = 1.9 Hz), 108.0 (d, $J_{C\text{-}P}$ = 5.9 Hz), 47.3 (d, $J_{C\text{-}P}$ = 80.1 Hz), 38.2 (dd, $J_{C\text{-}P}$ = 68.2, 11.3 Hz), 21.7 (br s); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 31.41, 30.44; IR (film) υ_{max}: 3382, 3054, 2964, 2924, 2858, 1591, 1569, 1512, 1478, 1437, 1386, 1342, 1319, 1262, 1191, 1149, 1117, 1072, 1029, 997, 956, 825, 799, 726, 698 cm^{-1}; HRMS (ESI-Q-TOF): m/z 585.1857 ([M + H]$^+$, $C_{36}H_{31}N_2O_2P_2^+$ calcd. 585.1855).

*Tetraisopropyl (6-Chloro-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3g**, New Compound).* Yellow oil; 164 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.67 (dd, J = 4.1, 1.5 Hz, 1H), 8.32 (dd, J = 8.5, 1.4 Hz, 1H), 7.44 (d, J = 1.5 Hz, 1H), 7.34−7.41 (m, 1H), 6.53 (d, J = 5.1 Hz, 1H), 4.72−4.87 (m, 2H), 4.46 4.65(m, 2), 4.16 (ddd, J = 11.6, 8.3, 3.3 Hz, 1H), 3.33 (dt, J = 24.3, 4.4 Hz, 1H), 2.51−2.65 (m, 1H), 2.03−2.27 (m, 1H), 1.36 (d, J = 6.2 Hz, 3H), 1.32 (d, J = 6.2 Hz, 6H, overlap), 1.25 (d, J = 6.2 Hz, 3H), 1.24 (d, J = 6.2 Hz, 3H), 1.23 (d, J = 6.2 Hz, 3H), 1.22 (d, J = 6.2 Hz, 3H), 1.04 (d, J = 6.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 147.5, 139.6 (dd, $J_{C\text{-}P}$ = 10.4, 6.9 Hz), 137.9 (d, $J_{C\text{-}P}$ = 2.3 Hz), 132.4, 129.1 (d, $J_{C\text{-}P}$ = 3.3 Hz), 125.4 (d, $J_{C\text{-}P}$ = 1.9 Hz), 121.8, 115.8 (d, $J_{C\text{-}P}$ = 3.2 Hz), 109.0 (d, $J_{C\text{-}P}$ = 7.1 Hz), 71.4 (d, $J_{C\text{-}P}$ = 6.9 Hz), 71.1 (d, $J_{C\text{-}P}$ = 7.3 Hz), 71.0 (d, $J_{C\text{-}P}$ = 7.7 Hz), 70.8 (d, $J_{C\text{-}P}$ = 7.6 Hz), 45.6 (d, $J_{C\text{-}P}$ = 160.9 Hz), 35.1 (dd, $J_{C\text{-}P}$ = 143.9, 13.9 Hz), 24.1 (d, $J_{C\text{-}P}$ = 7.2 Hz), 24.03 (d, $J_{C\text{-}P}$ = 7.1 Hz), 23.99 (d, $J_{C\text{-}P}$ = 6.4 Hz), 23.9 (d, $J_{C\text{-}P}$ = 5.1 Hz), 23.8 (d, $J_{C\text{-}P}$ = 4.6 Hz), 23.7 (d, $J_{C\text{-}P}$ = 5.3 Hz), 23.5 (d, $J_{C\text{-}P}$ = 5.1 Hz), 22.2 (dd apparent t, $J_{C\text{-}P}$ = 5.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 22.74, 24.22; IR (film) υ_{max}: 3397, 2979, 2933, 2869, 1569, 1512, 1472, 1380, 1317, 1245, 1175, 1141, 983, 937, 886, 790, 764, 677, 596, 567 cm^{-1}; HRMS (ESI): m/z 569.1717 ([M + Na]$^+$, $C_{24}H_{37}ClN_2NaO_6P_2^+$ calcd. 569.1708).

*Tetraisopropyl (7-Methyl-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3h**, New Compound).* Yellow oil; 197 mg, 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.51 (d, J = 4.3 Hz, 1H), 7.42 (dd, J = 8.7, 1.4 Hz, 1H), 7.07−7.16 (m, 2H), 7.07 (d, J = 4.1 Hz, 1H), 6.60 (d, J = 5.0 Hz, 1H), 4.74−4.88 (m, 2H), 4.55−4.68 (m, 1H), 4.37−4.49 (m, 1H), 4.15 (ddd, J = 11.5, 8.0, 3.4 Hz, 1H), 3.42 (dt, J = 24.2, 4.4 Hz, 1H), 2.59−2.68 (m, 1H), 2.58 (s, 3H), 2.09−2.26 (m, 1H), 1.38 (d, J = 6.2 Hz, 3H), 1.34 (d, J = 6.2 Hz, 6H, overlap), 1.27 (d, J = 6.2 Hz, 3H), 1.26 (d, J = 6.6 Hz, 3H), 1.25 (d, J = 6.8 Hz, 3H), 1.22 (d, J = 6.2 Hz, 3H), 0.91 (d, J = 6.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 146.6, 143.6, 140.4 (dd, $J_{C\text{-}P}$ = 10.3, 7.1 Hz), 137.0 (d, $J_{C\text{-}P}$ = 1.5 Hz), 129.0 (d, $J_{C\text{-}P}$ = 3.4 Hz), 127.4 (d, $J_{C\text{-}P}$ = 2.0 Hz), 121.9, 109.5 (d, $J_{C\text{-}P}$ = 1.9 Hz), 108.6 (d, $J_{C\text{-}P}$ = 6.9 Hz), 71.2 (d, $J_{C\text{-}P}$ = 6.8 Hz), 71.0 (d, $J_{C\text{-}P}$ = 7.4 Hz), 70.9 (d, $J_{C\text{-}P}$ = 7.2 Hz), 70.2 (d, $J_{C\text{-}P}$ = 7.6 Hz), 45.6 (d, $J_{C\text{-}P}$ = 160.9 Hz), 35.3 (dd, $J_{C\text{-}P}$ = 142.8, 14.2 Hz), 24.1 (d, $J_{C\text{-}P}$ = 7.1 Hz), 24.0 (d, $J_{C\text{-}P}$ = 7.6 Hz), 23.90 (d, $J_{C\text{-}P}$ = 5.1 Hz), 23.86 (d, $J_{C\text{-}P}$ = 4.7 Hz), 23.8 (d, $J_{C\text{-}P}$ = 3.9 Hz), 23.7 (d, $J_{C\text{-}P}$ = 4.9 Hz), 23.2 (d, $J_{C\text{-}P}$ = 5.4 Hz), 22.3 (dd apparent t, $J_{C\text{-}P}$ = 5.4 Hz), 18.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ = 23.23, 24.79; IR (film) υ_{max}: 3396, 2978, 2933, 2873, 1568, 1522, 1481, 1452, 1410, 1376, 1359, 1315, 1241, 1176, 1142, 1106, 983, 894, 839, 765, 699 cm^{-1}; HRMS (ESI): m/z 549.2237 ([M + Na]$^+$, $C_{25}H_{40}N_2NaO_6P_2^+$ calcd. 549.2254).

*Tetraethyl (6-Chloro-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3i**, New Compound).* Yellow oil; 188 mg, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.74 (dd, J = 4.2, 1.5 Hz, 1H), 8.39 (dd, J = 8.5, 1.5 Hz, 1H), 7.43−7.47 (m, 2H), 6.56 (d, J = 5.0 Hz, 1H), 4.18−4.31 (m, 5H), 3.98−4.09 (m, 4H), 3.38−3.48 (m, 1H), 2.60−2.79 (m, 1H), 2.13−2.33 (m, 1H), 1.38 (t, J = 7.0 Hz, 3H), 1.34 (t, J = 7.0 Hz, 3H), 1.28 (t, J = 7.2 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 147.7, 139.5 (dd, $J_{C\text{-}P}$ = 10.4, 6.6 Hz), 138.0 (d, $J_{C\text{-}P}$ = 2.3 Hz), 132.6, 128.8 (d, $J_{C\text{-}P}$ = 3.6 Hz), 125.6 (d, $J_{C\text{-}P}$ = 2.1 Hz), 122.0, 116.4 (d, $J_{C\text{-}P}$ = 3.2 Hz), 108.8 (d, $J_{C\text{-}P}$ = 7.2 Hz), 63.0 (d, $J_{C\text{-}P}$ = 6.6 Hz), 62.7 (d, $J_{C\text{-}P}$ = 7.1 Hz), 62.6 (d, $J_{C\text{-}P}$ = 7.6 Hz, overlap), 62.5 (d, $J_{C\text{-}P}$ = 7.5 Hz, overlap), 45.3 (d, $J_{C\text{-}P}$ = 160 Hz), 34.6(dd, $J_{C\text{-}P}$ = 142.6, 14.3 Hz), 22.1 (dd apparent t, $J_{C\text{-}P}$ = 4.9 Hz), 16.49 (d, $J_{C\text{-}P}$ = 5.1 Hz), 16.46 (d, $J_{C\text{-}P}$ = 5.4 Hz), 16.4 (d, $J_{C\text{-}P}$ = 5.7 Hz, overlap), 16.3 (d, $J_{C\text{-}P}$ = 5.6 Hz, overlap); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 24.48, 26.06; IR (film) υ_{max}: 3396, 2982, 2907, 2866, 1611, 1569, 1512, 1474, 1444, 1378, 1246, 1162, 1096, 1048, 1024, 968, 793, 763, 675, 619, 594, 562 cm^{-1}; HRMS (ESI): m/z 513.1079 ([M + Na]$^+$, $C_{20}H_{29}ClN_2NaO_6P_2^+$ calcd. 513.1082).

*Tetraethyl (7-Methyl-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3j**, New Compound).* Yellow oil; 207 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.53 (d, J = 4.4 Hz, 1H), 7.37 (dd, J = 8.7, 1.4 Hz, 1H), 7.13−7.16 (m, 2H), 6.58 (d, J = 4.9 Hz, 1H), 4.16−4.27 (m, 5H), 3.93−4.04 (m, 3H), 3.85−3.92 (m, 1H), 3.42−3.52 (m, 1H), 2.60−2.71 (m, 1H), 2.58 (s, 3H), 2.13−2.32 (m, 1H), 1.35 (t, J = 7.0 Hz, 3H), 1.32 (t, J = 7.0 Hz, 3H), 1.26 (t, J = 7.0 Hz, 3H), 1.15 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 146.9, 143.9 (d, $J_{C\text{-}P}$ = 1.5 Hz), 140.4 (dd, $J_{C\text{-}P}$ = 10.0, 7.0 Hz), 137.1 (d, $J_{C\text{-}P}$ = 2.4 Hz), 128.8 (d, $J_{C\text{-}P}$ = 3.3 Hz), 127.6 (d, $J_{C\text{-}P}$ = 2.1 Hz), 122.1, 110.0 (d, $J_{C\text{-}P}$ = 2.4 Hz), 108.4 (d, $J_{C\text{-}P}$ = 7.1 Hz), 62.9 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.6 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.5 (d, $J_{C\text{-}P}$ = 7.2 Hz), 62.1 (d, $J_{C\text{-}P}$ = 7.3 Hz), 45.4 (d, $J_{C\text{-}P}$ = 159.1 Hz), 34.7 (dd, $J_{C\text{-}P}$ = 141.6, 14.4 Hz), 22.1 (dd apparent t, $J_{C\text{-}P}$ = 5.2 Hz), 18.7, 16.44 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.41 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.33 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.30 (d, $J_{C\text{-}P}$ = 5.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 24.92, 26.63; IR (film) υ_{max}: 3395, 2981, 2931, 2907, 2866, 1568, 1522, 1480, 1445, 1410, 1380, 1315, 1242, 1164, 1096, 1050, 1024, 967, 840, 787, 752 cm^{-1}; HRMS (ESI): m/z 493.1634 ([M + Na]$^+$, $C_{21}H_{32}N_2NaO_6P_2^+$ calcd. 493.1628).

*Tetraethyl (6-Methyl-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3k**, New Compound).* Yellow oil; 188 mg, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.70 (dd, J = 4.1, 1.5 Hz, 1H), 8.14 (dd, J = 8.4, 1.5 Hz, 1H), 7.36 (dd, J = 8.4, 4.1 Hz, 1H), 7.20 (br s, 1H), 6.40 (d, J = 4.7 Hz, 1H), 4.17−4.28 (m, 5H), 3.87−4.05 (m, 4H), 3.39−348 (m, 1H), 2.61−2.70 (m, 1H), 2.50 (s, 3H), 2.16−2.32 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.1 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 146.9, 138.5 (dd, $J_{C\text{-}P}$ = 10.4, 7.5 Hz), 138.1 (d, $J_{C\text{-}P}$ = 2.7 Hz), 132.2, 129.3 (d, $J_{C\text{-}P}$ = 2.7 Hz), 127.1, 120.9, 120.1, 108.3 (d, $J_{C\text{-}P}$ = 7.4 Hz), 62.9 (d, $J_{C\text{-}P}$ = 6.6 Hz), 62.6 (d, $J_{C\text{-}P}$ = 6.3 Hz), 62.5 (d, $J_{C\text{-}P}$ = 6.6 Hz), 62.2 (d, $J_{C\text{-}P}$ = 7.0 Hz), 45.4 (d, $J_{C\text{-}P}$ = 159.6 Hz), 34.8 (dd, $J_{C\text{-}P}$ = 141.7, 14.2 Hz), 22.4 (dd apparent t, $J_{C\text{-}P}$ = 6.0 Hz), 17.7, 16.5 (d, $J_{C\text{-}P}$ = 4.9 Hz), 16.4 (d, $J_{C\text{-}P}$ = 4.8 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 25.09, 26.66; IR (film) υ_{max}: 3399, 2981, 2931, 2866, 1574, 1510, 1483, 1444, 1386, 1330, 1238, 1163, 1097, 1047, 1023, 966, 793, 765, 685 cm^{-1}; HRMS (ESI): m/z 493.16276 ([M + Na]$^+$, $C_{21}H_{32}N_2NaO_6P_2^+$ calcd. 493.1628).

*Tetraethyl (5,6-Dimethyl-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3l**, New Compound).* Yellow oil; 147 mg, 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.63 (d, J = 4.0 Hz, 1H), 8.21 (d, J = 8.6 Hz, 1H), 7.34 (dd, J = 8.6, 4.1 Hz, 1H), 6.64 (d, J = 6.7 Hz, 1H), 4.35−4.41 (m, 1H), 4.16−4.28 (m, 4H), 3.74−4.00 (m, 5H), 2.68−2.74 (m, 1H), 2.48 (s, 3H), 2.47 (s, 3H), 1.98−2.22 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H),

dx.doi.org/10.1021/jo501842p | J. Org. Chem. 2015, 80, 1192−1199

1.21 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 145.9, 137.8 (dd apparent t, $J_{C\text{-}P}$ = 6.4 Hz), 136.4 (d, $J_{C\text{-}P}$ = 3.1 Hz), 133.7 (d, $J_{C\text{-}P}$ = 4.0 Hz), 132.0, 126.9 (d, $J_{C\text{-}P}$ = 2.4 Hz), 121.1, 117.6 (d, $J_{C\text{-}P}$ = 2.7 Hz), 108.4 (d, $J_{C\text{-}P}$ = 6.6 Hz), 63.0 (d, $J_{C\text{-}P}$ = 6.8 Hz), 62.7 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.6 (d, $J_{C\text{-}P}$ = 6.9 Hz), 61.9 (d, $J_{C\text{-}P}$ = 7.3 Hz), 45.4 (dd, $J_{C\text{-}P}$ = 156.3, 1.3 Hz), 33.3 (dd, $J_{C\text{-}P}$ = 141.1, 14.6 Hz), 22.8 (dd apparent t, $J_{C\text{-}P}$ = 4.7 Hz), 16.6, 16.53 (d, $J_{C\text{-}P}$ = 5.4 Hz, overlap), 16.51 (d, $J_{C\text{-}P}$ = 5.4 Hz, overlap), 16.4 (d, $J_{C\text{-}P}$ = 5.5 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.9 Hz), 14.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ = 26.47, 25.62; IR (film) υ_{max}: 3395, 2982, 2931, 2905, 2869, 1572, 1510, 1474, 1443, 1392, 1367, 1311, 1294, 1251, 1165, 1096, 1022, 964, 792, 686 cm^{-1}; HRMS (ESI): m/z 507.1785 ($[M + Na]^+$, $C_{22}H_{34}N_2NaO_6P_2^+$ calcd. 507.1784).

*Tetraethyl (6-Bromo-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3m**, New Compound).* Yellow oil; 152 mg, 57% yield. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.70 (dd, J = 4.1, 1.3 Hz, 1H), 8.33 (dd, J = 8.5, 1.2 Hz, 1H), 7.61 (d, J = 1.4 Hz, 1H), 7.43 (dd, J = 8.4, 4.2 Hz, 1H), 6.59 (d, J = 5.0 Hz, 1H), 4.17−4.30 (m, 5H), 3.97−4.09 (m, 4H), 3.42 (dt, J = 24.1, 4.4 Hz, 1H), 2.59−2.70 (m, 1H), 2.12−2.31 (m, 1H), 1.37 (t, J = 7.1 Hz, 3H, overlap), 1.33 (t, J = 7.0 Hz, 3H, overlap), 1.27 (t, J = 7.0 Hz, 3H, overlap), 1.24 (t, J = 7.0 Hz, 3H, overlap); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 147.7, 140.2 (dd, $J_{C\text{-}P}$ = 10.2, 6.7 Hz), 138.2 (d, $J_{C\text{-}P}$ = 2.4 Hz), 135.1, 132.4 (d, $J_{C\text{-}P}$ = 3.3 Hz), 126.8 (d, $J_{C\text{-}P}$ = 2.1 Hz), 122.4, 109.6 (d, $J_{C\text{-}P}$ = 7.1 Hz), 105.7 (d, $J_{C\text{-}P}$ = 3.1 Hz), 63.0 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.8 (d, $J_{C\text{-}P}$ = 7.1 Hz), 62.6 (d, $J_{C\text{-}P}$ = 7.3 Hz), 45.4 (d, $J_{C\text{-}P}$ = 159.2 Hz), 34.6 (dd, $J_{C\text{-}P}$ = 142.7, 14.2 Hz), 22.1 (dd apparent t, $J_{C\text{-}P}$ = 5.0 Hz), 16.53 (d, $J_{C\text{-}P}$ = 5.2 Hz, overlap), 16.50 (d, $J_{C\text{-}P}$ = 5.4 Hz, overlap), 16.42 (d, $J_{C\text{-}P}$ = 5.1 Hz, overlap), 16.37 (d, $J_{C\text{-}P}$ = 5.3 Hz, overlap); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 26.08, 24.44; IR (film) υ_{max}: 3396, 2981, 2932, 2907, 2868, 1608, 1511, 1471, 1390, 1368, 1317, 1259, 1162, 1096, 1023, 967, 793, 762, 670, 561, 529 cm^{-1}; HRMS (ESI): m/z 557.0585 ($[M + Na]^+$, $C_{20}H_{29}BrN_2NaO_6P_2^+$ calcd. 557.0576).

*Tetraethyl (6-(Dimethylamino)-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3n**, New Compound).* Yellow oil; 132 mg, 53% yield. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.68 (dd, J = 4.1, 1.6 Hz, 1H), 8.42 (dd, J = 8.5, 1.6 Hz, 1H), 7.33 (dd, J = 8.4, 4.2 Hz, 1H), 7.05 (d, J = 1.2 Hz, 1H), 6.27 (d, J = 4.3 Hz, 1H), 4.16−4.26 (m, 5H), 3.88−4.04 (m, 4H), 3.89−3.48 (m, 1H), 2.74 (s, 6H), 2.62−2.69 (m, 1H), 2.15−2.37 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H, overlap), 1.32 (t, J = 7.1 Hz, 3H, overlap), 1.26 (t, J = 7.1 Hz, 3H), 1.16 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 147.5, 139.4 (d, $J_{C\text{-}P}$ = 2.8 Hz), 138.7 (d, $J_{C\text{-}P}$ = 2.5 Hz), 136.7 (dd, $J_{C\text{-}P}$ = 10.9, 7.5 Hz), 132.3, 124.1 (d, $J_{C\text{-}P}$ = 1.8 Hz), 120.8, 118.2 (d, $J_{C\text{-}P}$ = 3.3 Hz), 108.4 (d, $J_{C\text{-}P}$ = 7.4 Hz), 63.0 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.73 (d, $J_{C\text{-}P}$ = 6.8 Hz), 62.70 (d, $J_{C\text{-}P}$ = 7.2 Hz), 62.3 (d, $J_{C\text{-}P}$ = 7.3 Hz), 45.8, 45.6 (d, $J_{C\text{-}P}$ = 159.9 Hz), 35.1 (dd, $J_{C\text{-}P}$ = 141.7, 14.1 Hz), 22.8 (dd apparent t, $J_{C\text{-}P}$ = 5.1 Hz), 16.7 (d, $J_{C\text{-}P}$ = 4.9 Hz), 16.6 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.5 (d, $J_{C\text{-}P}$ = 5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 26.77, 25.08; IR (film) υ_{max}: 3400, 2980, 2935, 2908, 2864, 2826, 2781, 1613, 1577, 1510, 1482, 1451, 1386, 1369, 1342, 1292, 1260, 1162, 1096, 1024, 967, 876, 797, 766, 683 cm^{-1}; HRMS (ESI): m/z 522.1888 ($[M + Na]^+$, $C_{22}H_{35}N_3NaO_6P_2^+$ calcd. 522.1893).

*Tetraethyl (5,6-Dimethoxy-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3o**, New Compound).* Yellow oil; 198 mg, 77% yield. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.59 (dd, J = 4.2, 1.6 Hz, 1H), 8.24 (dd, J = 8.5, 1.6 Hz, 1H), 7.32 (dd, J = 8.4, 4.2 Hz, 1H), 6.38 (d, J = 6.0 Hz, 1H), 4.32−4.39 (m, 1H), 4.15−4.28 (m, 4H), 4.06 (s, 3H), 3.84−4.05 (m, 5H), 3.83 (s, 3H), 2.64−2.80 (m, 1H), 1.97−2.17 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 148.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 145.9, 137.1 (dd, $J_{C\text{-}P}$ = 8.6, 6.1 Hz), 134.6 (d, $J_{C\text{-}P}$ = 2.7 Hz), 134.3 (d, $J_{C\text{-}P}$ = 2.9 Hz), 129.3, 123.7 (d, $J_{C\text{-}P}$ = 1.9 Hz), 121.3, 104.1 (d, $J_{C\text{-}P}$ = 7.5 Hz), 62.8 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.7 (d, $J_{C\text{-}P}$ = 7.1 Hz), 62.3 (d, $J_{C\text{-}P}$ = 7.1 Hz), 62.0 (d, $J_{C\text{-}P}$ = 7.2 Hz), 61.0, 60.7, 45.3 (d, $J_{C\text{-}P}$ = 157.2 Hz), 30.1 (dd, $J_{C\text{-}P}$ = 142.6, 14.5 Hz), 22.3 (dd apparent t, $J_{C\text{-}P}$ = 4.4 Hz), 16.5 (d, $J_{C\text{-}P}$ = 5.5 Hz), 16.32 (d, $J_{C\text{-}P}$ = 5.8 Hz, overlap), 16.29 (d, $J_{C\text{-}P}$ = 5.6 Hz, overlap); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 26.58, 25.50; IR (film) υ_{max}: 3042, 2982, 2935, 2907, 2875, 2834, 1610, 1574, 1511, 1399, 1373, 1347, 1312, 1293, 1240, 1164, 1104, 1049, 1023, 964, 866, 794, 701 cm^{-1}; HRMS (ESI): m/z 539.1677 ($[M + Na]^+$, $C_{22}H_{34}N_2NaO_8P_2^+$ calcd. 539.1683).

*Tetraethyl (6-Phenyl-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3p**, New Compound).* Yellow oil; 236 mg, 89% yield. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.71 (d, J = 4.0 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 7.38−7.45 (m, 4H), 7.30−7.38 (m, 2H), 7.29 (dd, J = 8.4, 3.9 Hz, 1H), 6.64 (d, J = 5.0 Hz, 1H), 4.35 (ddd, J = 11.6, 8.2, 3.3 Hz, 1H), 4.20−4.30 (m, 4H), 3.95−4.08 (m, 4H), 3.51 (dt, J = 24.1, 4.6 Hz, 1H), 2.64−2.75 (m, 1H), 2.19−2.39 (m, 1H), 1.39 (t, J = 7.1 Hz, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 147.1, 139.7, 139.6 (dd, $J_{C\text{-}P}$ = 10.3, 6.7 Hz), 137.5 (d, $J_{C\text{-}P}$ = 2.0 Hz), 133.8, 130.0, 129.9 (d, $J_{C\text{-}P}$ = 3.3 Hz), 128.3, 126.7, 126.0 (d, $J_{C\text{-}P}$ = 1.9 Hz), 121.3, 108.3 (d, $J_{C\text{-}P}$ = 7.1 Hz), 62.9 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.6 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.5 (d, $J_{C\text{-}P}$ = 7.2 Hz), 62.2 (d, $J_{C\text{-}P}$ = 7.2 Hz), 45.4 (d, $J_{C\text{-}P}$ = 159.3 Hz), 34.8 (dd, $J_{C\text{-}P}$ = 141.8, 14.4 Hz), 22.2 (dd apparent t, $J_{C\text{-}P}$ = 5.0 Hz), 16.5 (d, $J_{C\text{-}P}$ = 4.3 Hz,), 16.4 (d, $J_{C\text{-}P}$ = 4.8 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 26.60, 24.86; IR (film) υ_{max}: 3396, 3057, 3024, 2981, 2931, 2906, 2867, 1599, 1572, 1510, 1478, 1445, 1392, 1369, 1336, 1313, 1259, 1163, 1096, 1048, 1023, 966, 796, 766, 705, 687 cm^{-1}; HRMS (ESI): m/z 555.1778 ($[M + Na]^+$, $C_{26}H_{34}N_2NaO_6P_2^+$ calcd. 555.1784).

*(7-Methyl-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis-(diphenylphosphine oxide) (**3q**, New Compound).* Pale yellow solid; 275 mg, 92% yield. mp: 219−221 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.39 (d, J = 4.6 Hz, 1H), 7.86−7.95 (m, 4H), 7.76−7.81 (m, 2H), 7.63−7.67 (m, 2H), 7.43−7.56 (m, 8H), 7.36−7.41 (m, 4H), 67.08 (d, J = 4.3 Hz, 1H), 6.75 (d, J = 8.7 Hz, 1H), 6.60 (s, 1H), 6.36 (d, J = 8.6 Hz, 1H), 5.02−5.07 (m, 1H), 3.98 (br s, 1H), 2.48−2.55 (m, 1H, overlap), 2.50 (s, 3H, overlap), 2.19−2.36 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 146.8, 143.6, 141.5 (dd, $J_{C\text{-}P}$ = 7.4, 5.4 Hz), 137.3 (d, $J_{C\text{-}P}$ = 2.0 Hz), 132.2 (d, $J_{C\text{-}P}$ = 2.6 Hz), 132.0 (d, $J_{C\text{-}P}$ = 2.4 Hz), 131.9 (d, $J_{C\text{-}P}$ = 95.8 Hz, overlap), 131.81 (d, $J_{C\text{-}P}$ = 2.2 Hz, overlap), 131.76 (d, $J_{C\text{-}P}$ = 9.1 Hz, overlap), 131.6 (d, $J_{C\text{-}P}$ = 8.7 Hz, overlap), 131.4 (d, $J_{C\text{-}P}$ = 8.5 Hz), 131.3 (d, $J_{C\text{-}P}$ = 8.3 Hz), 131.2 (d, $J_{C\text{-}P}$ = 95.3 Hz), 130.2 (d, $J_{C\text{-}P}$ = 99.1 Hz), 129.5 (d, $J_{C\text{-}P}$ = 96.9 Hz), 128.81 (d, $J_{C\text{-}P}$ = 11.6 Hz), 128.79 (d, $J_{C\text{-}P}$ = 11.2 Hz), 128.6 (d, $J_{C\text{-}P}$ = 11.5 Hz), 128.4 (d, $J_{C\text{-}P}$ = 11.3 Hz), 128.2 (d, $J_{C\text{-}P}$ = 2.8 Hz), 127.5 (d, $J_{C\text{-}P}$ = 1.5 Hz), 121.1, 109.3 (d, $J_{C\text{-}P}$ = 2.0 Hz), 107.8 (d, $J_{C\text{-}P}$ = 5.8 Hz), 47.3 (d, $J_{C\text{-}P}$ = 80.7 Hz), 38.0 (dd, $J_{C\text{-}P}$ = 68.3, 11.1 Hz), 21.6 (br s), 18.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ = 31.36, 30.51; IR (film) υ_{max}: 3380, 3054, 2963, 2925, 2855, 1724, 1672, 1613, 1591, 1567, 1521, 1479, 1437, 1410, 1378, 1341, 1315, 1262, 1189, 1117, 1025, 963, 800, 726, 699 cm^{-1}; HRMS (ESI): m/z 621.1832 ($[M + Na]^+$, $C_{37}H_{32}N_2NaO_2P_2^+$ calcd. 621.1831).

*(5,6-Dimethoxy-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(diphenylphosphine oxide) (**3r**, New Compound).* Yellow solid; 154 mg, 48% yield. mp: 212−215 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.49 (dd, J = 4.1, 1.5 Hz, 1H), 8.14 (dd, J = 8.4, 1.5 Hz, 1H), 7.95−8.04 (m, 4H), 7.85−7.90 (m, 2H), 7.48−7.58 (m, 7H), 7.36−7.45 (m, 4H), 7.26−7.32 (m, 2H), 7.13−7.18 (m, 2H), 6.32 (d, J = 4.8 Hz, 1H), 5.45 (dt, J = 12.2, 3.5 Hz, 1H), 4.19−4.25 (m, 1H), 3.49 (s, 3H), 3.41 (s, 3H), 2.45−2.54 (m, 1H), 2.03−2.22 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 146.9 (d, $J_{C\text{-}P}$ = 3.4 Hz), 145.9, 137.8 (dd, $J_{C\text{-}P}$ = 6.4, 4.9 Hz), 134.5 (d, $J_{C\text{-}P}$ = 2.5 Hz), 133.6 (d, $J_{C\text{-}P}$ = 2.0 Hz), 132.8 (d, $J_{C\text{-}P}$ = 99.0 Hz), 132.2 (d, $J_{C\text{-}P}$ = 2.5 Hz), 131.91 (d, $J_{C\text{-}P}$ = 3.3 Hz, overlap), 131.88 (d, $J_{C\text{-}P}$ = 3.4 Hz), 131.85 (d, $J_{C\text{-}P}$ = 9.0 Hz, overlap), 131.7 (d, $J_{C\text{-}P}$ = 8.3 Hz), 131.6 (d, $J_{C\text{-}P}$ = 9.3 Hz), 131.5 (d, $J_{C\text{-}P}$ = 8.7 Hz), 131.1 (d, $J_{C\text{-}P}$ = 91.9 Hz), 131.0 (d, $J_{C\text{-}P}$ = 2.4 Hz), 130.6 (d, $J_{C\text{-}P}$ = 96.2 Hz), 129.9 (d, $J_{C\text{-}P}$ = 96.6 Hz), 129.0, 128.8 (d, $J_{C\text{-}P}$ = 11.4 Hz), 128.7 (d, $J_{C\text{-}P}$ = 10.9 Hz, overlap), 128.6 (d, $J_{C\text{-}P}$ = 11.2 Hz, overlap), 127.6 (d, $J_{C\text{-}P}$ = 11.8 Hz), 123.6 (d, $J_{C\text{-}P}$ = 2.0 Hz), 121.2, 103.7 (d, $J_{C\text{-}P}$ = 6.0 Hz), 61.1, 59.4, 46.8 (d, $J_{C\text{-}P}$ = 78.7 Hz), 33.8 (dd, $J_{C\text{-}P}$ = 68.6, 10.8 Hz), 21.8 (br s); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 31.23, 33.38; IR (film) υ_{max}: 3384, 3054, 2926, 2854, 1676, 1609, 1591, 1572, 1510, 1475, 1437, 1399, 1376, 136, 1313, 1262, 1189, 1118, 1071, 1041, 993, 959, 924, 861, 810, 791, 749, 723, 711, 696 cm^{-1}; HRMS (ESI): m/z 667.1887 ($[M + Na]^+$, $C_{38}H_{34}N_2NaO_4P_2^+$ calcd. 667.1886).

dx.doi.org/10.1021/jo501842p | J. Org. Chem. 2015, 80, 1192−1199

*(6-(Dimethylamino)-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(diphenylphosphine oxide) (**3s**, New Compound).* Yellow solid; 298 mg, 95% yield. mp: 206.3−207.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.50 (dd, J = 4.1, 1.4 Hz, 1H), 8.25 (dd, J = 8.5, 1.5 Hz, 1H), 7.85−7.96 (m, 4H), 7.74−7.83 (m, 2H), 7.62−7.70 (m, 2H), 7.31−7.50 (m, 12H), 7.21 (dd, J = 8.4, 4.2 Hz, 1H), 6.19 (d, J = 3.4 Hz, 1H), 5.92 (br s, 1H), 5.05−5.20 (m, 1H), 3.83−3.95 (m, 1H), 2.43−2.55 (m, 1H), 2.21−2.41 (m, 1H), 2.26 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 146.9, 138.4 (d, $J_{C\text{-}P}$ = 1.9 Hz), 138.1 (d, $J_{C\text{-}P}$ = 2.1 Hz), 137.4 (dd, $J_{C\text{-}P}$ = 8.5, 5.5 Hz), 132.1 (d, $J_{C\text{-}P}$ = 96.4 Hz), 131.9 (d, $J_{C\text{-}P}$ = 1.8 Hz), 131.7 (d, $J_{C\text{-}P}$ = 1.9 Hz), 131.5, 131.5 (d, $J_{C\text{-}P}$ = 9.0 Hz), 131.4 (d, $J_{C\text{-}P}$ = 8.5 Hz), 131.12 (d, $J_{C\text{-}P}$ = 8.8 Hz), 131.11 (d, $J_{C\text{-}P}$ = 97.0 Hz), 131.0 (d, $J_{C\text{-}P}$ = 8.2 Hz), 130.2 (d, $J_{C\text{-}P}$ = 96.7 Hz), 129.5 (d, $J_{C\text{-}P}$ = 96.7 Hz), 128.6 (d, $J_{C\text{-}P}$ = 10.9 Hz), 128.5 (d, $J_{C\text{-}P}$ = 11.5 Hz), 128.4 (d, $J_{C\text{-}P}$ = 11.2 Hz), 128.3 (d, $J_{C\text{-}P}$ = 10.9 Hz), 123.5 (d, $J_{C\text{-}P}$ = 1.4 Hz), 120.3, 117.4 (br s), 107.1 (d, $J_{C\text{-}P}$ = 6.1 Hz), 47.1 (d, $J_{C\text{-}P}$ = 81.4 Hz), 44.9, 37.9 (dd, $J_{C\text{-}P}$ = 68.0, 11.4 Hz), 21.8 (br s); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 31.25, 30.40; IR (film) υ_{max}: 33384, 3054, 2976, 2936, 2860, 2826, 2781, 1611, 1590, 1575, 1509, 1482, 1452, 1437, 1382, 1343, 1313, 1292, 1263, 1191, 1150, 1117, 1064, 1030, 998, 913, 878, 817, 794, 724, 706, 670 cm^{-1}; HRMS (ESI): m/z 650.2107 ([M + Na]$^+$, $C_{38}H_{35}N_3NaO_2P_2^+$ calcd. 650.2097).

*Tetraethyl (6-(4-(Trifluoromethyl)phenyl)-1,2,3,4-tetrahydro-1,10-phenanthroline-2,4-diyl)bis(phosphonate) (**3t**, New Compound).* Yellow oil; 48 mg, 16% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.73 (dd, J = 4.0, 1.6 Hz, 1H), 8.11 (dd, J = 8.6, 1.5 Hz, 1H), 7.69 (d, J = 8.1 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 1.6 Hz, 1H), 7.32 (dd, J = 8.3, 3.8 Hz, 1H), 6.71 (d, J = 5.1 Hz, 1H), 4.21−4.37 (m, 5H), 3.97−4.07 (m, 4H), 3.47−3.55 (m, 1H), 2.67−2.74 (m, 1H), 2.19−2.38 (m, 1H), 1.39 (t, J = 7.1 Hz, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 147.4, 143.6, 140.3 (dd, $J_{C\text{-}P}$ = 10.0, 6.7 Hz), 137.5 (d, $J_{C\text{-}P}$ = 2.3 Hz), 133.3, 130.3, 130.2, 128.8 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 125.7 (d, $J_{C\text{-}P}$ = 2.3 Hz, overlap), 125.3 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 124.9 (d, $J_{C\text{-}P}$ = 2.9 Hz), 124.3 (q, $^1J_{C\text{-}F}$ = 272.1 Hz, overlap), 121.6, 108.3 (d, $J_{C\text{-}P}$ = 7.3 Hz), 63.0 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.7 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.6 (d, $J_{C\text{-}P}$ = 7.4 Hz), 62.2 (d, $J_{C\text{-}P}$ = 7.4 Hz), 45.5 (d, $J_{C\text{-}P}$ = 159.4 Hz), 34.8 (dd, $J_{C\text{-}P}$ = 142.1, 14.3 Hz), 22.2 (dd apparent t, $J_{C\text{-}P}$ = 5.2 Hz), 16.6 (d, $J_{C\text{-}P}$ = 5.8 Hz,), 16.5 (d, $J_{C\text{-}P}$ = 5.8 Hz), 16.4 (d, $J_{C\text{-}P}$ = 5.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ = 26.42, 24.62; IR (film) υ_{max}: 3394, 2982, 2931, 2905, 2869, 1615, 1598, 1571, 1511, 1484, 1444, 1414, 1392, 1369, 1325, 1243, 1164, 1123, 1066, 1049, 1023, 966, 846, 798, 690 cm^{-1}; HRMS (ESI): m/z 623.1650 ([M + Na]$^+$, $C_{27}H_{33}F_3N_2NaO_6P_2^+$ calcd. 623.1658).

■ ASSOCIATED CONTENT

Supporting Information

Copies of compound NMR spectra, crystallographic data (CIF file) of **3f**, experimental procedures, and results from mechanism experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: gaoxingchem@xmu.edu.cn (Y.G.).
*E-mail: xpengxiang@xmu.edu.cn (P.X.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Chinese National Natural Science Foundation (No. 21202135), the Natural Science Foundation of Fujian Province of China (No. 2013J05031), NFFTBS (No. J1210014), PCSIRT, and the National Basic Research Program of China (2012CB821600).

■ REFERENCES

(1) For selected reviews, see: (a) Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317. (b) Smith, N. D.; Mancuso, J.; Lautens, M. *Chem. Rev.* **2000**, *100*, 3257. (c) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (d) Chemler, S. R.; Fuller, P. H. *Chem. Soc. Rev.* **2007**, *36*, 1153. (e) Müller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795. (f) Jerphagnon, T.; Pizzuti, M. G.; Minnaard, A. J.; Fering, B. L. *Chem. Soc. Rev.* **2009**, *38*, 1039. (g) Kobayashi, S.; Mori, Y.; Fossey, J. S.; Salter, M. M. *Chem. Rev.* **2011**, *111*, 2626. (h) Zhao, D. P.; Wang, R. *Chem. Soc. Rev.* **2012**, *41*, 2095. (i) Zeng, X. *Chem. Rev.* **2013**, *113*, 6864. (j) Muñoz, M. P. *Chem. Soc. Rev.* **2014**, *43*, 3164.

(2) (a) Moonen, K.; Laureyn, I.; Stevens, C. V. *Chem. Rev.* **2004**, *104*, 6177. (b) Claeys, D. D.; Moonen, K.; Roman, B. I.; Nemykin, V. N.; Zhdankin, V. V.; Waroquier, M.; Speybroeck, V. V.; Stevens, C. V. *J. Org. Chem.* **2008**, *73*, 7921. (c) Piotrowska, D. G.; Balzarini, J.; Głowacka, I. E. *Eur. J. Med. Chem.* **2012**, *47*, 501. (d) Evitt, A. S.; Cox, R. J. *Mol. BioSyst.* **2011**, *7*, 1564.

(3) (a) Redmore, D. U.S. Patent 3,673,196, 1972. *Chem. Abstr.* **1972**, *77*, 88653p. (b) Redmore, D. U.S. Patent 3,775,057, 1973. *Chem. Abstr.* **1974**, *80*, 147521. (c) Redmore, D. U.S. Patent 3,786,055, 1974. *Chem. Abstr.* **1974**, *80*, 96154. (d) Redmore, D. U.S. Patent 3,810,907, 1974. *Chem. Abstr.* **1974**, *81*, 37646. (e) Redmore, D. U.S. Patent 3,888,627, 1975. *Chem. Abstr.* **1975**, *83*, 97570k.

(4) (a) Protopopova, G. V.; Reidalova, L. I.; Pavlenko, A. F.; Sologub, L. S.; Kukhar, V. P.; Petrenko, V. S. *Fiziol. Akt. Veshchestva* **1980**, *12*, 16. (b) Kukhar, V. P.; Cherepenko, T. I.; Pavlenko, A. F. *Dokl. Akad. Nauk Ukr. SSR, Ser. B: Geol., Khim. Biol. Nauki* **1982**, *12*, 60. (c) Akiba, K.; Tsuzuki, K. Jpn. Kokai Tokkyo Koho 61221102, 1986. (d) Malhotra, S. K.; Evoy, I. L. U.S. Patent 4,606,757, 1986.

(5) (a) Desos, P.; Lepagnol, J. M.; Morain, P.; Lestage, P.; Cordi, A. A. *J. Med. Chem.* **1996**, *39*, 197. (b) Cordi, A. A.; Desos, P.; Ruano, E.; Al-Badri, H.; Fugier, C.; Chapman, A. G.; Meldrum, B. S.; Thomas, J.-Y.; Roger, A.; Lestage, P. *Il Farmaco* **2002**, *57*, 787.

(6) (a) Kosolapoff, G. M.; Roy, C. H. *J. Org. Chem.* **1961**, *26*, 1895. (b) Griffin, C. E.; Peller, R. P.; Peters, J. A. *J. Org. Chem.* **1965**, *30*, 91. (c) Seyferth, D.; Paetsch, J. *J. Org. Chem.* **1969**, *34*, 1483. (d) Redmore, D. *Chem. Rev.* **1971**, *71*, 315. (e) Van der Jeught, S.; Stevens, C. V. *Chem. Rev.* **2009**, *109*, 2672 and references therein. (f) Pan, X.-Q.; Zou, J.-P.; Zhang, G.-L.; Zhang, W. *Chem. Commun.* **2010**, *46*, 1721. (g) Arshad, N.; Hashim, J.; Kappe, C. O. *J. Org. Chem.* **2008**, *73*, 4755. (h) Sun, W.-B.; Ji, Y.-F.; Pan, X.-Q.; Zhou, S.-F.; Zou, J.-P.; Zhang, W.; Asekun, O. *Synthesis* **2013**, *45*, 1529.

(7) (a) Suezawa, H.; Hirota, M.; Shibata, Y.; Takeuchi, I.; Hamada, Y. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2362. (b) Shibata, Y.; Takeuchi, I.; Hamada, Y. *Yakugaku Zasshi* **1987**, *107*, 945. (c) Takeuchi, I.; Hamada, Y.; Hatano, K.; Kurono, Y.; Yashiro, T. *Chem. Pharm. Bull.* **1990**, *38*, 1504.

(8) Takeuchi, I.; Shibata, Y.; Hamada, Y. *Heterocycles* **1985**, *23*, 1635.

(9) (a) Takeuchi, I.; Shibata, Y.; Hamada, Y.; Kido, M. *Heterocycles* **1986**, *24*, 647. (b) Takeuchi, I.; Hamada, Y.; Taira, Z. *Heterocycles* **1991**, *32*, 261.

(10) Mitrofanov, A.; Lemeune, A. B.; Stern, C.; Guilard, R.; Gulyukina, N.; Beletskaya, I. *Synthesis* **2012**, *44*, 3805.

(11) De Blieck, A.; Catak, S.; Debrouwer, W.; Drabowicz, J.; Hemelsoet, K.; Verstraelen, T.; Waroquier, M.; Van Speybroeck, V.; Stevens, C. V. *Eur. J. Org. Chem.* **2013**, 1058.

(12) Zain, R.; Stawinski, J. *J. Chem. Soc., Perkin Trans. 2* **1996**, 795.

(13) Afarinkia, K.; Rees, C. W.; Cadogan, J. I. G. *Tetrahedron* **1990**, *46*, 7175.

(14) De Blieck, A.; Masschelein, K. G. R.; Dhaene, F.; Rozycka-Sokolowska, E.; Marciniak, B.; Drabowiczc, J.; Stevens, C. V. *Chem. Commun.* **2010**, *46*, 258.

(15) Selected recent publications: (a) Mucha, A.; Kafarski, P.; Berlicki, Ł. *J. Med. Chem.* **2011**, *54*, 5955. (b) Naydenova, E. D.; Todorov, P. T.; Troev, K. D. *Amino Acids* **2010**, *38*, 23. (c) Sienczyk, M.; Oleksyszyn, J. *Curr. Med. Chem.* **2009**, *16*, 1673. (d) Wang, Q.; Zhu, M.; Zhu, R.; Lu, L.; Yuan, C.; Xing, S.; Fu, X.; Mei, Y.; Hang, Q. *Eur. J. Med. Chem.* **2012**, *49*, 354. (e) Huang, X.-C.; Wang, M.; Pan, Y.-

M.; Tian, X.-Y.; Wang, H.-S.; Zhang, Y. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 5283.

dx.doi.org/10.1021/jo501842p | *J. Org. Chem.* 2015, 80, 1192−1199