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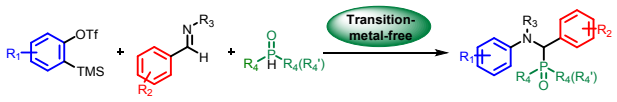
Synthesis of α-aminophosphonates via phosphonylation of an aryne–imine adduct

Taehyun Lim and Byeong Moon Kim *

Department of Chemistry, College of Natural Sciences, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul 08826, Republic of Korea

Supporting Information Placeholder



ABSTRACT: Multicomponent phosphonylation is accomplished upon the reaction of an imine with an aryne generated in situ in the presence of a dialkyl phosphite. This transition-metal-free protocol shows a broad substrate scope, providing a variety of α-aminophosphonates in moderate to good yields. A plausible mechanism for the reaction is proposed based on a deuterium exchange experiment.

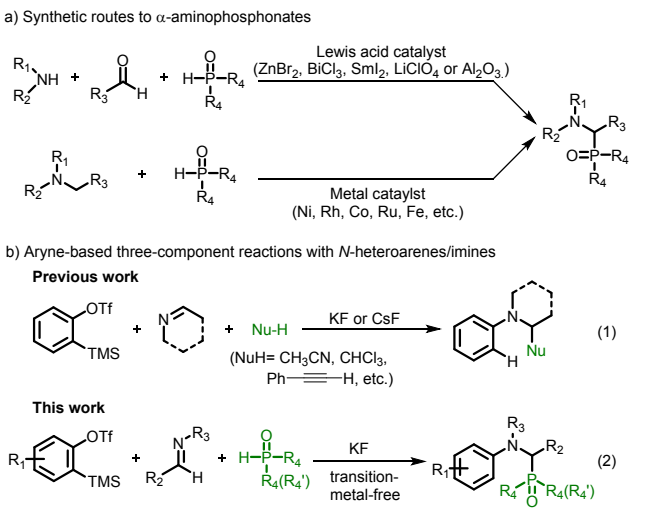
Organophosphorus compounds are becoming increasingly important in many applications, such as agricultural and medicinal chemistry.[1] In particular, α-aminophosphonic acids and α-aminophosphonates are expected to possess a diverse range of biological activities because they are structurally analogous to many enzyme inhibitors[2] and antitumor[3] and antibiotic agents.[4]

Several methods have been developed toward the synthesis of α-aminophosphonates. General reaction protocols employing a conventional nucleophilic addition reaction between a phosphonate and imine (Pudovik reaction)[5] and the Kabachnik– Fields reaction,[6] which involves a three-component reaction consisting of an amine, carbonyl compound, and H-phosphonate, have been previously reported.

In addition, the reaction of an imine generated from an aldehyde and an amine or an amino acid derivative with an H-phosphonate in the presence of a Lewis acid catalyst such as $ZnBr_2$,[7] $BiCl_3$,[8] SmI_2,[9] $LiClO_4$[10] and Al_2O_3 (with microwave irradiation)[11] or a transition metal catalyst containing [Ni],[12] [Rh],[13] [Co],[14] [Ru],[15] [Fe],[16] or others[17] has recently attracted considerable attention. However, many of these methods require harsh reaction conditions or stoichiometric amounts of toxic metal reagents, which are expensive and sensitive to moisture and/or air (Scheme 1a).

To overcome the drawbacks of these existing methods and expand the substrate scope in the classical imine-phosphite reaction, we envisioned the use of arynes as a new type of substrate. Arynes have been successfully used toward the construction of several useful synthetic intermediates and the total synthesis of natural products in the absence of transition metal catalysts.[18] Generally, arynes play a major role in the construction of σ-insertion compounds.[19] Notably, arynes can serve as an electrophile toward diverse nitrogen nucleophiles and their resulting aryl anions capture various electrophiles.[20] Especially, Cheng and Tian groups reported that the zwitterion species generated from *N*-heteroarenes/imines with arynes can abstract a proton from protic nucleophiles (Scheme 1b, eq 1).[21]

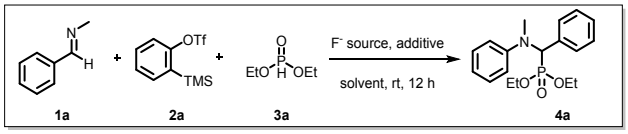
Scheme 1. Synthetic strategies for α-aminophosphonates



Inspired by these works, we have developed a one-pot multicomponent phosphonylation reaction of an aryne, imine, and dialkyl phosphite toward the synthesis of a variety of α-aminophosphonates (Scheme 1b, eq 2). This method provides an efficient and mild procedure applicable to various substrates, which removes the need for transition-metal-based catalysis.

For our initial reaction optimization study, we used imine **1a**, a commercially available benzyne precursor, 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2a**), and diethyl phosphite (**3a**) as model substrates (Table 1).

Table 1. Optimization of the Reaction Conditions[a]



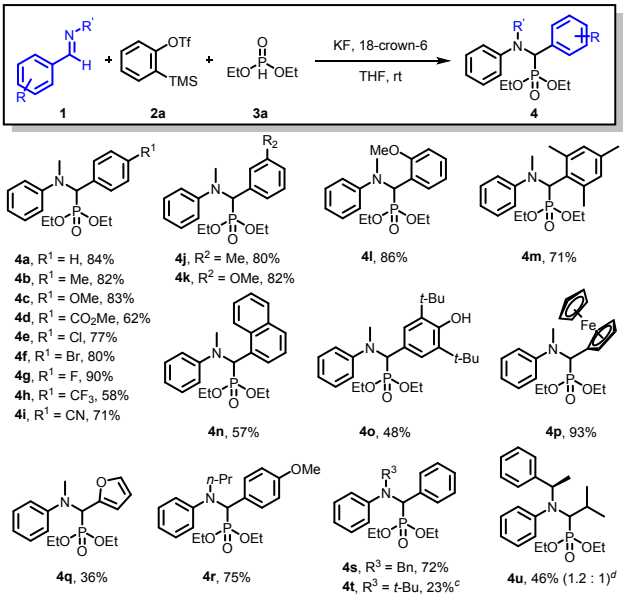
entry	F⁻ source (equiv)	additive (equiv)	3a (equiv)	solvent (M)	yield (%)[b]
1	CsF (3.0)	-	2.0	CH_3CN (0.15)	trace
2	KF (3.0)	-	2.0	THF (0.15)	0
3	TBAF (3.0)	-	2.0	THF (0.15)	0
4	TBAT (3.0)	-	2.0	THF (0.15)	15
5	TBAF (3.0)	18-crown-6 (3.0)	2.0	THF (0.15)	0
6	TBAT (3.0)	18-crown-6 (3.0)	2.0	THF (0.15)	21
7	CsF (3.0)	18-crown-6 (3.0)	2.0	THF (0.15)	23
8	KF (3.0)	18-crown-6 (3.0)	2.0	THF (0.15)	58
9[c]	KF (3.0)	18-crown-6 (3.0)	2.0	THF (0.15)	44
10	KF (3.0)	18-crown-6 (3.0)	2.0	THF (0.6)	70
11	KF (3.0)	18-crown-6 (3.0)	3.0	THF (0.6)	74
12	KF (3.0)	18-crown-6 (3.0)	3.0	THF (1.0)	77
13	KF (3.0)	18-crown-6 (3.0)	5.0	THF (1.0)	82
14	KF (3.0)	18-crown-6 (3.0)	5.0	neat	78
15	KF (2.0)	18-crown-6 (2.0)	5.0	THF (1.0)	84

[a]Reaction conditions: **1a** (0.15 mmol), **2a** (0.23 mmol), **3a**, fluoride source, additive, solvent, rt, 12 h. [b]Yield of the isolated product. [c]The reaction was carried out at 0 °C.

Several commonly used fluoride sources were screened under various conditions. In the reaction employing cesium fluoride, trace amount of **4a** was detected in the absence of an additive (entry 1). The use of other common fluoride sources including tetrabutylammonium-fluoride (TBAF), or potassium fluoride did not provide the desired product (entries 2 and 3). Use of tetrabutylammonium difluorotriphenylsilicate (TBAT) could promote this phosphonylation reaction to give 15% yield of the desired product (entry 4). Even with the use of 18-crown-6 as an additive with TBAF, the desired product was not obtained (entry 5). On the other hand, use of the fluoride source such as TBAT, cesium fluoride or potassium fluoride in the presence of 18-crown-6 provided the desired product **4a** in 21, 23 and 58% yield, respectively (entries 6, 7 and 8). In addition, there was an observable temperature effect as a lower yield (44%) of **4a** was detected when the reaction was carried out at 0 °C (entry 9). The results obtained upon varying the reaction concentration indicate that increasing the concentration improved the yield of the desired product (entry 8 and entries 10–13). Therefore, we carried out the reaction under solvent-free conditions, which proceeded to give **4a**, albeit in a slightly decreased yield, presumably due to the poor solubility of the reagents (entry 14). Finally, performing the reaction using KF/18-crown-6 (2.0 equiv) and 5.0 equiv of diethyl phosphite resulted in the formation of **4a** in 84% yield (Table 1, entry 15).

Under the optimized reaction conditions, we then explored the scope of the imine substrate. As illustrated in Scheme 2, the three-component phosphonylation of **2a** and diethyl phosphite (**3a**) with a variety of aromatic *N*-alkylimines gave their corresponding products (**4a**–**4u**) in moderate to good yields except for a few cases. A series of *para*-substituted aromatic *N*-alkyl imines, including those with electron-donating or withdrawing substituents, were examined under the optimized reaction conditions. The reactions of aromatic *N*-methylimines bearing electron-donating substituents at the *para*-position proceeded smoothly to give their corresponding products (**4b** and **4c**) in high yield. Electron-withdrawing groups such as halogen, trifluoromethyl, and nitrile were well tolerated in the reaction and the reactions of the substrates gave **4e**–**4i** in 58–90% yield. Furthermore, the reactions of aromatic *N*-methylimines bearing electron-donating substituents at the *meta*- or *ortho*-position of the aryl group proceeded to provide their corresponding products (**4k** and **4l**) in good yields. The reactions using bulky imines also afforded **4m** and **4n** in 71 and 57% yield, respectively. Notably, the reaction of 2,6-di-*tert*-butyl-4-((methylimino)methyl)phenol furnished in 48% yield the desired phosphorylation product **4o**, which is a known matrix metalloproteinase inhibitor.[22] In the case of heteroaryl substituted imines, the reaction using *N*-methyl-1-(furan-2-yl)methanimine gave **4q** in 36% yield, whereas *N*-methyl-1-(pyridin-2-yl)methanimine did not give the desired product under the standard reaction conditions.

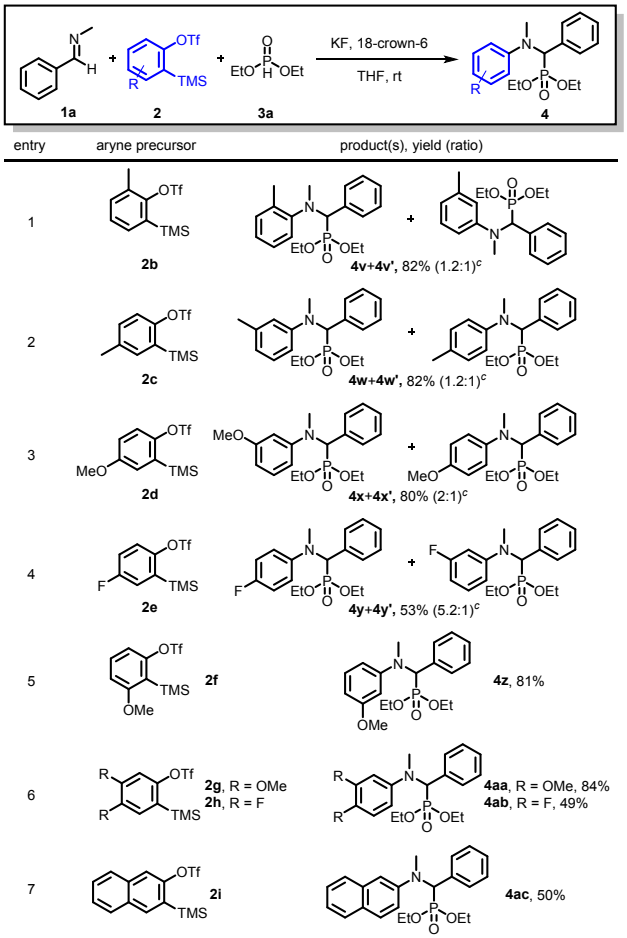
Scheme 2. Scope of the Imine Substrates Used in the Reaction[a,b]



[a]Reaction conditions: **1** (0.15 mmol), **2a** (0.23 mmol), **3a** (0.75 mmol), KF (0.30 mmol), 18-crown-6 (0.30 mmol), THF (1.0 M), rt, 12 h. [b]Yield of isolated product. [c]The reaction was carried out at 50 °C. [d]Determined using ^{1}H NMR analysis of the reaction mixture.

Next, the reactions of other *N*-alkyl-substituted aromatic and alkyl imines were studied. *N*-propyl- and *N*-benzyl-1-phenylmethanimines gave phosphonylation products **4r** and **4s** in 76 and 72%, respectively. However, the reaction of bulky *N*-*t*-butyl-1-phenylmethanimine was sluggish. The desired product **4t** was obtained in 23% yield, even upon heating at 50 °C. The reaction of (*S,E*)-2-methyl-*N*-(1-phenylethyl)propan-1-imine, an imine derived from an aliphatic aldehyde containing a stereocenter, also furnished the desired product (**4u**) in moderate yield (46%) as a 1.2:1 mixture of diastereoisomers.

Table 2. Scope of the Substituted Arynes Used in the Reaction[a,b]

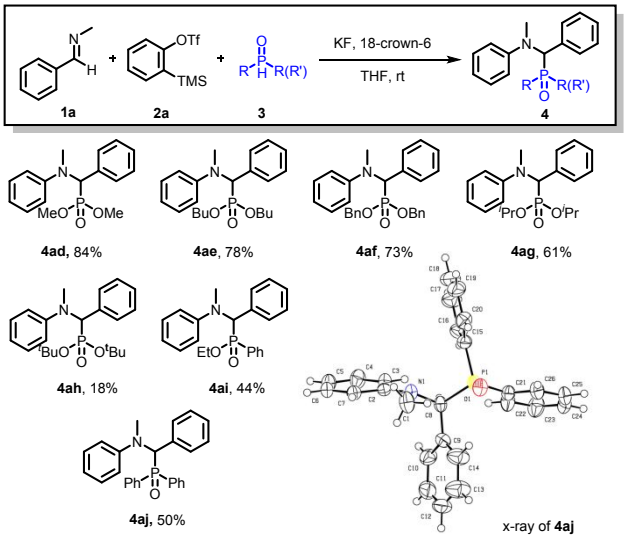


[a]Reaction conditions: **1a** (0.15 mmol), **2** (0.23 mmol), **3a** (0.75 mmol), KF (0.30 mmol), 18-crown-6 (0.30 mmol), THF (1.0 M), rt, 12 h. [b]Yield of the isolated product. [c]Determined using ^{1}H or ^{31}P NMR spectroscopy.

With these results in hand, we examined the scope of this reaction using a variety of substituted arynes. Various disubstituted aryne precursors were assessed in terms of the yield and regioselectivity for the α-aminophosphonate formed (Table 2). When unsymmetrical 3-methyl- and 4-methylbenzyne were generated from **2b** and **2c**, respectively, an inseparable 1.2:1 mixture of their regioisomers was obtained. The reaction with 4-methoxybenzyne **2d** proceeded smoothly, giving **4x** and **4x'** in 2:1 ratio and 80% yield, while higher regioselectivity (5.2:1) was observed in the reaction of 4-fluorobenzyne **2e**, with decreased yield of 53%. Notably, 3-methoxybenzyne generated from **2f** afforded **4z** as the sole product in 81% yield upon the reaction with imine **1a** and phosphonate **3a**. These results could be attributed to the different degrees of aryne distortions as predicted by Houk, effecting the observed regioselectivity.[23] In the case of 4,5-disubstituted dimethoxy- and 4,5-difluoroarynes (**2g** and **2h**), their corresponding phosphonylation products (**4aa** and **4ab)** were also formed in 84 and 49% yield, respectively. In addition, the reaction carried out using symmetrical naphthalyne afforded **4ac** in 50% yield.

Finally, we examined various phosphites under the optimized reaction conditions. The reactions carried out using dimethyl and dibutyl phosphite gave **4ad** and **4ae** in 84 and 78% yield, respectively. Furthermore, dibenzyl and diisopropyl phosphites also provided α-aminophosphates **4af** and **4ag** in 73 and 61% yield, respectively. However, the reaction of di-*tert*-butyl phosphite with benzyne precursor **2a** gave the desired product (**4ah**) in only 18% yield under the same conditions. In addition, the reaction of ethyl phosphinate under the optimized conditions gave a 1:1 diastereomeric mixture of phosphonylation product **4ai** in 44% yield. In the reaction using diphenylphosphine oxide as an alternative phosphine source, we obtained the desired product **4ag** in 50% yield. The structure of **4aj** was confirmed by single-crystal X-ray analysis[24]

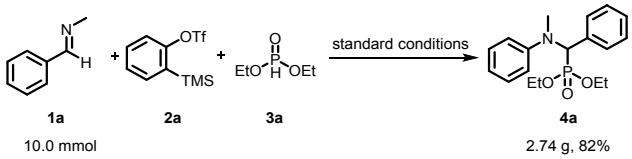
Scheme 3. Scope of the Phosphites Used in the Reaction and a Crystal Structure of 4aj[a,b]



[a]Reaction conditions: **1a** (0.15 mmol), **2a** (0.23 mmol), **3** (0.75 mmol), KF (0.30 mmol), 18-crown-6 (0.30 mmol), THF (1.0 M), rt, 12 h. [b]Yield of the isolated product.

To highlight the utility of this synthetic approach, we investigated the gram-scale synthesis starting from *N*-methylimine **1a** (10.0 mmol), benzyne precursor **2a** and diethyl phosphite **3a**. The reaction afforded 2.74g of **4a** in 82% isolated yield under the optimized reaction conditions (Scheme 4). This is the first preparation of compound **4a** without the use of transition-metal reagents.

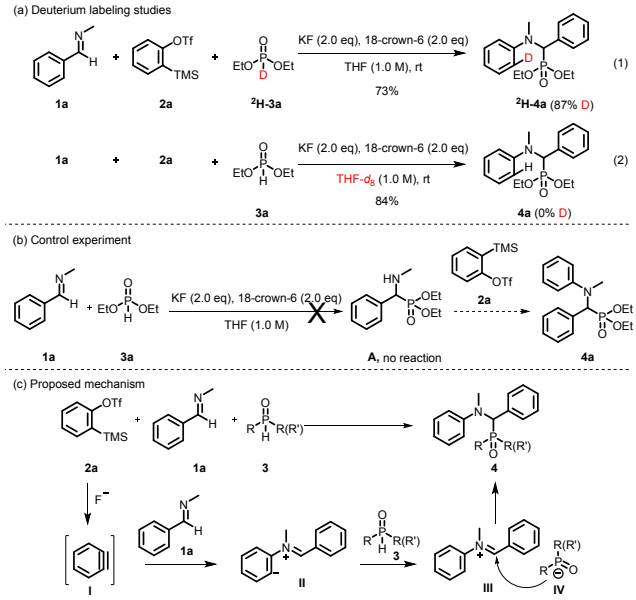
Scheme 4. Scale-up Experiment



We subsequently investigated the mechanism of the three-component phosphonylation reaction, as shown in Scheme 5. Treating *N*-methyl imine **1a** with aryne precursor **2a** in the presence of deuterated diethyl phosphite (**^{2}H-3a**) under the optimized reaction conditions resulted in the formation of the α-aminophosphonate product with 87% deuterium incorporation at the 2-position of the benzene ring (Scheme 5a,

eq 1). Subsequently, when we performed the reaction using **1a** and **2a** in the presence of **3a** in THF-d_8. The reaction afforded **4a** with no incorporation of deuterium at the 2-position (Scheme 5a, eq 2). This demonstrates that the deprotonated phosphite **IV** undergoes nucleophilic addition to iminium intermediate **III** to furnish α-aminophosphonate **4a**. To understand the mechanism of multicomponent reaction, a control experiment was carried out (Scheme 5b). When the reaction of **1a** and **3a** was performed in the absence of **2a** under the standard conditions, the reaction did not produce the desired product **A**, leaving **1a** unchanged. This result indicates that the reaction proceeds through a three-component reaction involving an aryne, which is an essential component in this reaction system.

Scheme 5. Mechanistic Study



Based upon these observations, a plausible reaction mechanism was proposed (Scheme 5c). Iminium zwitterion **II**, which is generated via nucleophilic addition of imine **1a** to aryne **I**, abstracts a proton from dialkyl phosphite **3** leading to the formation of phosphite anion **IV**. Phosphite anion **IV** adds to the iminium carbon in **III**, which results in the formation of the desired α-aminophosphonate product (**4a**).

In conclusion, we have developed a one-pot multicomponent phosponylation reaction consisting of an aryne, imine, and dialkyl phosphite as an efficient synthetic method for the construction of α-aminophosphonates. This method does not require the use of transition-metal-based catalysts. The reaction of a wide range of imines, arynes, and phosphites can efficiently be carried out under the optimized conditions.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, all reactions were carried out using standard Schlenk techniques. THF was purified from distillation over sodium/benzophenone and was transferred under argon. 18-crown-6 was recrystallized from CH_3CN and KF was vacuum-dried at 110 °C. Thin layer chromatography (TLC) was performed using Merck silica gel 60 F_{254} and spots were visualized under 254 nm UV light and/or stained by ceric ammonium molybdate solutions. Column chromatography was performed on silica gel (Merck 9385 Kiesel gel 60) using hexane/ethyl acetate as an eluent. ^{1}H, ^{19}F{^{1}H}, ^{31}P{^{1}H} and ^{13}C{^{1}H} NMR spectra were recorded on an Agilent 400–MR DD2 (^{1}H, 400 MHz; ^{19}F{^{1}H}, 376 MHz; ^{31}P{^{1}H}, 162 MHz; ^{13}C{^{1}H}, 101 MHz) or ^{13}C{^{1}H} NMR spectra was recorded on a Varian/Oxford As-500 (^{13}C{^{1}H}, 126 MHz) spectrophotometer. Chemical shift values were recorded as parts per million (δ) relative to tetramethylsilane as an internal standard and coupling constants in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. GC analyses were carried out with a 7980A GC system from Agilent Technologies, equipped with an HP-5 column. High–resolution mass spectra were obtained on a JEOL JMS–700 gas chromatography–mass spectrometer using double focusing mass spectrometer (magnetic sector and electrostatic sector) via electron impact (EI) mode or fast atom bombardment (FAB) mode.

General Procedure for the Multicomponent Reaction of Imines, Aryne Precursors, and Dialkyl Phosphites. A flame-dried Schlenk tube containing KF (17.4 mg, 0.300 mmol) and 18-crown-6 (79.4 mg, 0.300 mmol) was evacuated and purged with nitrogen gas for three times. To the flask were then added imine (**1**) (1.00 equiv, 0.150 mmol), aryne precursor (**2**) (0.230 mmol), dialkyl phosphite (**3**) (0.750 mmol) and THF (0.15 mL) via syringes. The reaction mixture was allowed to stir at rt for 12 h. The reaction mixture was treated with water (15 mL), and the resulting mixture was extracted with ethyl acetate (15 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by silica gel flash chromatography (hexane/ethyl acetate as an eluent).

A Large Scale Synthesis of 4a. A flame-dried Schlenk tube containing KF (1.16 g, 20.0 mmol) and 18-crown-6 (5.28 g, 20.0 mmol) was evacuated and purged with nitrogen gas three times. To the flask were then added *N*-methylimine **1a** (1.24 mL, 10.0 mmol), aryne precursor **2a** (3.64 mL, 15.0 mmol), diethyl phosphite **3a** (6.44 mL, 50.0 mmol) and THF (10.0 mL) via syringes. The reaction mixture was allowed to stir at rt for 12 h. The reaction mixture was treated with water (100 mL), and the resulting mixture was extracted with ethyl acetate (100 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by silica gel flash chromatography (hexane/ethyl acetate as an eluent) to give 2.74 g of **4a** in 82% yield.

Deuterium Labeling Experiment in Presence of Deuterium Substituted Diethyl Phosphite. A flame-dried Schlenk tube containing KF (17.4 mg, 0.300 mmol) and 18-crown-6 (79.4 mg, 0.300 mmol) was evacuated and purged with nitrogen gas three times. To the flask were then added *N*-methylimine **1a** (0.150 mmol), aryne precursor **2a** (0.230 mmol), deuterium substituted diethyl phosphite (**^{2}H-3a**) (104 μL, 0.750 mmol) and THF (0.15 mL) via syringes. The reaction mixture was allowed to stir at rt for 12 h. The reaction mixture was treated with water (15 mL), and the resulting mixture was extracted with ethyl acetate (15 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by silica gel flash chromatography (hexane/ethyl acetate as an eluent).

Deuterium Labeling Experiment with THF-d_8. A flame-dried Schlenk tube containing KF (17.4 mg, 0.300 mmol) and 18-crown-6 (79.4 mg, 0.300 mmol) was evacuated and purged with nitrogen gas three times. To the flask were then added *N*-methylimine **1a** (0.150 mmol), aryne precursor **2a**

(0.230 mmol), diethyl phosphite **3a** (97.0 μL, 0.750 mmol) and THF-d_8 (0.15 mL) via syringes. The reaction mixture was allowed to stir at rt for 12 h. The reaction mixture was treated with water (15 mL), and the resulting mixture was extracted with ethyl acetate (15 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by silica gel flash chromatography (hexane/ethyl acetate as an eluent).

*Diethyl ((methyl(phenyl)amino)(phenyl)methyl)phosphonate **(4a)***. Pale yellow oil (42.0 mg, 84%); R_f = 0.23 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.3 Hz, 2H), 7.34 – 7.22 (m, 5H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.78 (t, *J* = 7.3 Hz, 1H), 5.33 (d, *J* = 24.8 Hz, 1H), 4.20 – 3.97 (m, 4H), 2.95 (s, 3H), 1.20 (q, *J* = 6.9 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 150.3 (d, *J* = 7.3 Hz), 134.6 (d, *J* = 7.1 Hz), 129.3, 129.0 (d, *J* = 8.3 Hz), 128.6, 128.0, 118.1, 113.9, 63.1 (d, *J* = 7.1 Hz), 62.5, 62.2 (d, *J* = 7.2 Hz), 61.2, 34.9, 16.6 (d, *J* = 5.6 Hz), 16.4 (d, *J* = 5.7 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 21.9. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{24}NO_3P$ 333.1494; found 333.1497.

*Diethyl ((methyl(phenyl)amino)(p-tolyl)methyl)phosphonate **(4b)***. Pale yellow oil (42.7 mg, 82%); R_f = 0.25 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.9 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.78 (t, *J* = 7.3 Hz, 1H), 5.29 (d, *J* = 24.6 Hz, 1H), 4.24 – 3.95 (m, 4H), 2.93 (s, 3H), 2.32 (s, 3H), 1.25 – 1.17 (m, *J* = 7.1, 4.7 Hz, 6H).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 150.3 (d, *J* = 7.4 Hz), 137.6, 131.3 (d, *J* = 7.2 Hz), 129.1, 128.8 (d, *J* = 8.6 Hz), 117.9, 113.9, 63.0 (d, *J* = 7.1 Hz), 62.1 (d, *J* = 6.9 Hz), 60.9 (d, *J* = 3.1 Hz), 34.6, 21.1, 16.5 (d, *J* = 5.6 Hz), 16.3 (d, *J* = 5.5 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 22.2. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_3P$ 347.1650; found 347.1653.

*Diethyl ((4-methoxyphenyl)(methyl(phenyl)amino)methyl)-phosphonate **(4c)***. Pale yellow oil (45.2 mg, 83%); R_f = 0.28 (ethyl acetate/n-hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.6 Hz, 2H), 7.26 – 7.23 (m, 2H), 6.86 (dd, *J* = 15.4, 8.5 Hz, 4H), 6.79 (t, *J* = 7.2 Hz, 1H), 5.26 (d, *J* = 24.6 Hz, 1H), 4.24 – 3.95 (m, 4H), 3.79 (s, 3H), 2.92 (s, 3H), 1.21 (q, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.2, 150.3 (d), 130.2 (d, *J* = 8.8 Hz), 129.1, 126.3 (d), 118.0, 114.0, 113.8, 63.0 (d), 62.0 (d, *J* = 19.8 Hz), 60.6 (d), 55.2, 34.5, 16.5, 16.3. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 22.1. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_4P$ 363.1599; found 363.1600.

*Methyl 4-((diethoxyphosphoryl)(methyl(phenyl)amino)-methyl)benzoate **(4d)***. Pale yellow oil (36.4 mg, 62%); R_f = 0.14 (ethyl acetate/n-hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 2H), 6.87 (d, *J* = 8.1 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 1H), 5.35 (d, *J* = 25.4 Hz, 1H), 4.23 – 3.99 (m, 4H), 3.91 (s, 1H), 2.97 (s, 3H), 1.26 – 1.17 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.7, 149.9 (d, *J* = 7.2 Hz), 139.8 (d, *J* = 7.0 Hz), 129.7 (d, *J* = 7.2 Hz), 129.2, 128.6 (d, *J* = 7.9 Hz), 118.3, 113.9, 63.3 (d), 62.3 (d), 60.9 (d), 52.1 (d, *J* = 2.9 Hz), 34.9, 16.6 (d, *J* = 5.9 Hz), 16.4 (d, *J* = 4.5 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 21.2. HRMS (EI) m/z: $[M]^+$ calcd for $C_{20}H_{26}NO_5P$ 391.1549; found 391.1549.

*Diethyl ((4-chlorophenyl)(methyl(phenyl)amino)methyl)-phosphonate **(4e)***. Pale yellow oil (42.5 mg, 77%); R_f = 0.31 (ethyl acetate/n-hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.30 – 7.20 (m,4H), 6.85 (d, *J* = 8.2 Hz, 2H), 6.79 (t, *J* = 7.3 Hz, 1H), 5.25 (d, *J* = 25.0 Hz, 1H), 4.24 – 3.87 (m, 4H), 2.91 (s, 3H), 1.25 – 1.15 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 150.2 (d, *J* = 7.1 Hz), 134.0, 133.2 (d, *J* = 7.4 Hz), 130.3 (d, *J* = 8.3 Hz), 129.4, 128.8, 118.5, 114.2, 63.3 (d, *J* = 6.9 Hz), 62.3 (dd, *J* = 27.8, 4.9 Hz), 60.9 (d, *J* = 2.6 Hz), 34.9, 16.6 (d, *J* = 5.4 Hz), 16.5 (d, *J* = 4.8 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 21.4. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{23}ClNO_3P$ 367.1104; found 367.1105.

*Diethyl ((4-bromophenyl)(methyl(phenyl)amino)-methyl)phosphonate **(4f)***. Pale yellow oil (49.5 mg, 80%); R_f = 0.29 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.25 (t, *J* = 7.9 Hz, 2H), 6.86 (d, *J* = 8.2 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 1H), 5.25 (d, *J* = 25.0 Hz, 1H), 4.26 – 3.95 (m, 4H), 2.93 (s, 3H), 1.25 – 1.19 (m, *J* = 7.0, 3.5 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.1 (d, *J* = 7.4 Hz), 133.7 (d, *J* = 7.4 Hz), 131.8, 130.6 (d, *J* = 8.2 Hz), 129.4, 122.2, 118.5, 114.1, 63.4 (d, *J* = 7.1 Hz), 62.4 (d, *J* = 8.9 Hz), 60.7 (d, *J* = 3.9 Hz), 34.8, 16.6 (d, *J* = 4.9 Hz), 16.5 (d, *J* = 5.9 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 21.3. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{23}BrNO_3P$ 411.0599; found 411.0595.

*Diethyl ((4-fluorophenyl)(methyl(phenyl)amino)-methyl)phosphonate **(4g)***. Pale yellow oil (47.4 mg, 90%); R_f = 0.29 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 8.5, 5.6 Hz, 2H), 7.26 (t, 2H), 7.01 (t, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 5.28 (d, *J* = 24.8 Hz, 1H), 4.22 – 3.97 (m, 4H), 2.93 (s, 3H), 1.21 (q, *J* = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.7 (d), 161.3, 150.2 (d, *J* = 7.4 Hz), 130.7 (t, *J* = 8.3 Hz), 129.4, 118.4, 115.5 (d, *J* = 21.4 Hz), 114.1, 63.3 (d, *J* = 7.1 Hz), 62.2 (d, *J* = 12.4 Hz), 60.5 (d, *J* = 3.7 Hz), 34.7, 16.6 (d, *J* = 5.4 Hz), 16.4 (d, *J* = 5.7 Hz). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -114.2. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 21.7. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{23}FNO_3P$ 351.1400; found 351.1398.

*Diethyl ((methyl(phenyl)amino)(4-(trifluoromethyl)phenyl)-methyl)phosphonate **(4h)***. Pale yellow oil (34.9 mg, 58%); R_f = 0.25 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.27 (t, *J* = 7.7 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.82 (t, *J* = 7.2 Hz, 1H), 5.35 (d, *J* = 25.4 Hz, 1H), 4.27 – 3.97 (m, 4H), 2.97 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.0 (d, *J* = 7.1 Hz), 139.0, 129.4, 129.1 (d, *J* = 7.9 Hz), 125.6 (d), 125.6 (d), 118.6, 114.0, 63.5 (d, *J* = 7.2 Hz), 62.4 (d, *J* = 7.1 Hz), 60.9, 35.0, 16.6 (d), 16.5 (d). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -62.7. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 21.1. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{23}F_3NO_3P$ 401.1368; found 401.1365.

*Diethyl ((4-cyanophenyl)(methyl(phenyl)amino)methyl)-phosphonate **(4i)***. Pale yellow oil (38.2 mg, 71%); R_f = 0.32 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 3H), 7.26 (t, 3H), 6.85 (d, *J* = 8.3 Hz, 3H), 5.33 (d, *J* = 25.6 Hz, 1H), 4.20 – 3.99 (m, 4H), 2.96 (s, 3H), 1.23 (t, *J* = 6.9 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.9 (d, *J* = 6.9 Hz), 140.5 (d, *J* = 7.4 Hz), 132.5, 129.5, 129.4 (d, *J* = 7.7 Hz), 118.9, 118.7, 114.1, 112.0, 63.6 (d, *J* = 7.3 Hz), 62.6 (d, *J* = 10.7 Hz), 61.1 (d, *J* = 3.2 Hz), 35.1, 16.6 (d, *J* = 5.5 Hz), 16.5 (d, *J* = 5.3 Hz).^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 20.6. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{23}N_2O_3P$ 358.1446; found 358.1447.

*Diethyl ((methyl(phenyl)amino)(m-tolyl)methyl)phosphonate **(4j)***. Pale yellow oil (41.7 mg, 80%); R_f = 0.29 (ethyl acetate/n-hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 2H), 7.20 – 7.11 (m, 3H),7.02 (d, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 8.1

Hz, 2H), 6.71 (t, *J* = 7.1 Hz, 1H), 5.22 (d, *J* = 24.7 Hz, 1H), 4.17 – 3.83 (m, 4H), 2.89 (s, 3H), 2.21 (s, 3H), 1.19 – 1.08 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.3 (d, *J* = 7.1 Hz), 138.2, 134.5 (d, *J* = 7.1 Hz), 129.5 (d, *J* = 8.7 Hz), 129.3, 128.8, 128.4, 126.0 (d, *J* = 8.2 Hz), 118.0, 113.8, 63.1 (d, *J* = 7.1 Hz), 62.4 (dd, *J* = 25.0, 5.5 Hz), 60.9 (d, *J* = 3.8 Hz), 34.9, 21.6, 16.6 (d, *J* = 5.4 Hz), 16.4 (d, *J* = 5.6 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_3P$ 347.1650; found 347.1647.

Diethyl ((3-methoxyphenyl)(methyl(phenyl)amino)-methyl)phosphonate (***4k***). Pale yellow oil (44.7 mg, 82%); R_f = 0.28 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, *J* = 7.9, 3.0 Hz, 3H), 7.12 – 7.05 (m, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.83 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.78 (t, *J* = 7.2 Hz, 1H), 5.29 (d, *J* = 25.0 Hz, 1H), 4.25 – 3.95 (m, 4H), 3.77 (s, 3H), 2.97 (s, 3H), 1.27 – 1.19 (m, *J* = 15.1, 8.0 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.7, 150.3 (d, *J* = 7.2 Hz), 136.1 (d, *J* = 7.2 Hz), 129.6, 129.3, 121.2 (d, *J* = 8.1 Hz), 118.1, 114.5 (d, *J* = 8.5 Hz), 113.9, 113.4, 63.2 (d, *J* = 7.0 Hz), 62.5 (dd, *J* = 30.8, 5.4 Hz), 61.0 (d, *J* = 3.7 Hz), 55.3 (d, *J* = 2.6 Hz), 34.9, 16.6 (d, *J* = 4.3 Hz), 16.4 (d, *J* = 5.6 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 21.9. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_4P$ 363.1599; found 363.1601.

Diethyl ((2-methoxyphenyl)(methyl(phenyl)amino)-methyl)phosphonate (***4l***). Pale yellow oil (47.0 mg, 86%); R_f = 0.32 (ethyl acetate/n-hexane, 1:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.6 Hz, 1H), 7.29 – 7.18 (m, *J* = 16.0, 8.5, 4.3 Hz, 3H), 6.95 (t, *J* = 8.2 Hz, 3H), 6.81 (d, *J* = 8.2 Hz, 1H), 6.73 (t, *J* = 7.2 Hz, 1H), 5.72 (d, *J* = 22.9 Hz, 1H), 4.22 – 3.86 (m, 4H), 3.52 (s, 3H), 2.87 (s, 3H), 1.21 – 1.10 (m, *J* =16.9, 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.0 (d, *J* = 12.2 Hz), 150.8 (d, *J* = 6.5 Hz), 131.2 (d, *J* = 4.1 Hz), 129.5, 128.8, 122.9 (d, *J* = 10.0 Hz), 120.3, 117.7, 114.3, 110.8, 63.0 (d, *J* = 7.0 Hz), 62.2 (d, *J* = 7.5 Hz), 55.8 (d, *J* = 3.4 Hz), 55.5 (d, *J* = 2.0 Hz), 54.2 (d, *J* = 3.3 Hz), 34.4, 29.8, 16.6 (d, *J* = 5.4 Hz), 16.4 (d, *J* = 5.5 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_4P$ 363.1599; found 363.1596.

Diethyl (mesityl(methyl(phenyl)amino)methyl)phosphonate (***4m***). Pale yellow oil (40.0 mg, 71%); R_f = 0.23 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (t, *J* = 7.3 Hz, 2H), 6.82 (s, 2H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 8.1 Hz, 2H), 5.27 (d, *J* = 28.7 Hz, 1H), 4.17 – 4.02 (m, 2H), 3.86 – 3.74 (m, 1H), 3.46 – 3.38 (m, 1H), 3.36 (s, 3H), 2.51 (s, 6H), 2.22 (s, 3H), 1.31 (t, *J* = 6.8 Hz, 3H), 1.12 – 1.04 (m, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.4 (d, *J* = 12.6 Hz), 137.1 (d, *J* = 3.1 Hz), 129.5, 129.0, 117.7, 113.7, 63.4 (d, *J* = 6.9 Hz), 61.9 (d, *J* = 7.7 Hz), 61.0, 59.5, 38.2 (d, *J* =5.2 Hz), 21.5, 20.9, 16.5 (t, *J* = 5.6 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.6. HRMS (EI) m/z: $[M]^+$ calcd for $C_{21}H_{30}NO_3P$ 375.1963; found 375.1966.

Diethyl ((methyl(phenyl)amino)(naphthalen-1-yl)methyl)-phosphonate (***4n***). Pale yellow oil (32.8 mg, 57%); R_f = 0.33 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.2 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.25 (t, *J* = 4.2 Hz, 1H), 7.00 (d, *J* = 8.3 Hz, 2H), 6.83 (t, *J* = 7.3 Hz, 1H), 5.92 (d, *J* = 21.6 Hz, 1H), 4.27 – 3.93 (m, 4H), 2.79 (s, 3H), 1.24 – 1.15 (m, *J* = 11.7, 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.8 (d, *J* = 4.5 Hz), 134.1 (d, *J* = 1.9 Hz), 132.6 (d, *J* = 14.7 Hz), 130.8 (d, *J* = 10.1 Hz), 129.5, 129.1, 129.0, 128.8 (d, *J* = 4.8 Hz), 126.7, 125.8, 125.1, 123.8, 117.9, 113.6 (d, *J* = 1.4 Hz), 62.7 (dd, *J* = 113.7, 7.2 Hz), 58.6, 56.9, 34.1, 16.7 (d, *J* = 5.4 Hz), 16.5 (d, *J* = 5.6 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.6. HRMS (EI) m/z: $[M]^+$ calcd for $C_{22}H_{26}NO_3P$ 383.1650; found 383.1652.

Diethyl ((3,5-di-tert-butyl-4-hydroxyphenyl)(methyl-(phenyl)amino)methyl)phosphonate (***4o***). *Orange oil (33.2 mg, 48%);* R_f = 0.23 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 2H), 7.26 – 7.22 (m, *J* = 7.5 Hz, 2H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 5.25 (d, *J* = 24.6 Hz, 1H), 5.18 (s, 1H), 4.13 – 3.93 (m, 4H), 2.93 (s, 3H), 1.39 (s, 18H), 1.19 (q, *J* = 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 153.5 (d, *J* = 0.9 Hz), 150.7 (d, *J* = 7.0 Hz), 137.3 (d, *J* = 0.9 Hz), 135.8, 129.2, 125.7 (d, *J* = 8.6 Hz), 124.9 (d, *J* = 7.4 Hz), 117.9, 116.6 (d, *J* = 4.6 Hz), 114.2, 62.9 (d, *J* = 7.0 Hz), 62.7, 62.2 (d, *J* = 7.3 Hz), 61.1, 34.5, 30.4, 30.2, 16.7 (d, *J* = 5.4 Hz), 16.5 (d, *J* = 5.6 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 23.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{26}H_{40}NO_4P$ 461.2695; found 461.2694.

Diethyl (ferrocenylethyl(methyl(phenyl)amino)methyl)-phosphonate (***4p***). Orange oil (59.6 mg, 93%); R_f = 0.23 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.79 (t, *J* = 7.2 Hz, 1H), 5.23 (d, *J* = 22.4 Hz, 1H), 4.53 (s, 1H), 4.19 – 4.07 (m, 10H), 4.01 – 3.90 (m, 1H), 2.80 (s, 3H), 2.04 (s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 1H), 1.19 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.2 (d, *J* = 5.9 Hz), 129.3, 117.8, 113.6, 69.6, 69.3, 68.2, 67.5, 63.2 (d, *J* = 7.1 Hz), 61.8 (d, *J* = 7.6 Hz), 58.9 (d, *J* = 3.7 Hz), 57.3 (d, *J* = 3.9 Hz), 34.5, 16.7 (d, *J* = 4.9 Hz), 16.6 (d, *J* = 5.8 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 21.9. HRMS (EI) m/z: $[M]^+$ calcd for $C_{22}H_{28}FeNO_3P$ 441.1156; found 441.1157.

Diethyl (furan-2-yl(methyl(phenyl)amino)methyl)-phosphonate (***4q***). Pale yellow oil (17.5 mg, 36%); R_f = 0.20 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 1.7 Hz, 1H), 7.29 – 7.24 (m, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 1H), 6.63 – 6.60 (m, 1H), 6.37 – 6.34 (m, *J* = 3.2, 1.9 Hz, 1H), 5.30 (d, *J* = 24.6 Hz, 1H), 4.24 – 3.98 (m, 4H), 2.93 (s, 3H), 1.26 – 1.20 (m, *J* = 7.1, 2.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 150.5 (d, *J* = 6.5 Hz), 148.3 (d), 143.0 (d), 129.5, 118.8, 114.6 (d), 111.1 (d, *J* = 3.2 Hz), 110.7, 63.6 (d, *J* = 6.9 Hz), 62.9 (d, *J* = 7.2 Hz), 56.6 (d, *J* = 166.0 Hz), 34.8, 16.8 (d, *J* = 5.7 Hz), 16.7 (d, *J* = 5.7 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 19.6. HRMS (EI) m/z: $[M]^+$ calcd for $C_{16}H_{22}NO_4P$ 323.1286; found 323.1287.

Diethyl ((4-methoxyphenyl)(phenyl(propyl)amino)methyl)-phosphonate (***4r***). Pale yellow oil (44.0 mg, 75%); R_f = 0.29 (ethyl acetate/n-hexane, 1:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.7 Hz, 2H), 7.26 – 7.18 (m, *J* = 8.6, 7.4 Hz, 2H), 6.85 (dd, *J* = 21.3, 8.4 Hz, 4H), 6.76 (t, *J* = 7.2 Hz, 1H), 5.18 (d, *J* = 23.8 Hz, 1H), 4.21 – 3.91 (m, 4H), 3.77 (s, 3H), 3.44 – 3.34 (m, 1H), 3.19 – 3.10 (m, 1H), 1.59 – 1.48 (m, 1H), 1.18 (dd, *J* = 15.4, 7.1 Hz, 6H), 0.75 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.3, 148.8 (d, *J* = 6.3 Hz), 130.8 (d, *J* = 9.3 Hz), 129.2, 127.1 (d, *J* = 8.3 Hz), 118.2, 115.7, 113.8, 62.9 (d, *J* = 7.1 Hz), 62.6, 62.1 (d, *J* = 7.3 Hz), 61.0, 55.3, 48.7, 20.4 (d, *J* = 1.3 Hz), 16.6 (d, *J* = 5.7 Hz), 16.5 (d, *J* = 5.6 Hz), 11.4. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.4. HRMS (EI) m/z: $[M]^+$ calcd for $C_{21}H_{30}NO_4P$ 391.1912; found 391.1915.

Diethyl ((benzyl(phenyl)amino)(phenyl)methyl)phosphonate (***4s***). Pale yellow oil (44.2 mg, 72%); R_f = 0.21 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.1 Hz, 2H), 7.35 – 7.26 (m, 3H), 7.19 – 7.05 (m, *J* = 4.2 Hz, 7H), 6.88

(d, J = 8.2 Hz, 2H), 6.74 (t, J = 7.3 Hz, 1H), 5.45 (d, J = 24.5 Hz, 1H), 4.91 (d, J = 16.9 Hz, 1H), 4.61 (d, J = 16.9 Hz, 1H), 4.16 – 3.85 (m, 4H), 1.18 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 148.7 (d, J = 6.2 Hz), 138.9, 134.9 (d, J = 7.1 Hz), 129.7 (d, J = 8.6 Hz), 129.0, 128.6, 128.2, 128.1, 127.0, 126.3, 118.8, 116.3, 63.5, 62.6 (d, J = 8.5 Hz), 62.0, 51.6, 16.5 (d), 16.4 (d, J = 5.6 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.3. HRMS (EI) m/z: $[M]^+$ calcd for $C_{24}H_{28}NO_3P$ 409.1807; found 409.1809.

Diethyl ((tert-butyl(phenyl)amino)(phenyl)methyl)-phosphonate ***(4t)***. Pale yellow oil (13.0 mg, 23%); R_f = 0.32 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.09 (m, 8H), 7.01 – 6.94 (m, 2H), 4.88 (d, J = 25.8 Hz, 1H), 4.24 – 4.13 (m, 2H), 3.84 – 3.47 (m, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.20 (s, 9H), 0.93 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 144.8, 137.1, 135.0 (d, J = 2.0 Hz), 131.9 (d, J = 9.0 Hz), 127.6, 127.6, 127.2, 126.2, 62.1, 60.2 (d, J = 166.6 Hz), 57.8 (d, J = 9.2 Hz), 30.6, 16.7 (d), 16.2 (d). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 23.4. HRMS (EI) m/z: $[M]^+$ calcd for $C_{21}H_{30}NO_3P$ 375.1963; found 375.1966.

Diethyl (2-methyl-1-(phenyl((R)-1-phenylethyl)-amino)propyl)phosphonate ***(4u)***. Pale yellow oil (26.9 mg, 46%); R_f = 0.24 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.4 Hz, 2H), 7.34 – 7.18 (m, J = 23.3, 15.9, 7.9 Hz, 7H), 6.92 (t, J = 7.2 Hz, 1H), 5.13 (qd, J = 6.8, 2.8 Hz, 1H), 4.03 – 3.76 (m, 4H), 3.19 (dd, J = 17.5, 10.3 Hz, 1H), 2.30 – 2.17 (m, 1H), 1.39 (d, J = 6.8 Hz, 3H), 1.13 (q, J = 7.1 Hz, 6H), 0.98 (d, J = 7.8 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.5, 143.1, 128.5, 128.4, 128.1, 127.0, 118.1, 117.2, 62.9, 61.9 (d, J = 7.3 Hz), 61.5, 60.8 (d, J = 7.8 Hz), 58.0, 29.1 (d, J = 8.6 Hz), 21.2, 20.9 (d, J = 13.4 Hz), 18.3, 16.3 (t, J = 6.5 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 29.1. HRMS (EI) m/z: $[M]^+$ calcd for $C_{22}H_{32}NO_3P$ 389.2120; found 389.2117.

Diethyl ((methyl(o-tolyl)amino)(phenyl)methyl)phosphonate ***(4v)*** *and diethyl ((methyl(m-tolyl)amino)(phenyl)methyl)-phosphonate* ***(4v')***. Pale yellow oil (42.7 mg, 82%); R_f = 0.24 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.1 Hz, 2H), 7.36 – 7.31 (m, 2H), 7.27 – 7.15 (m, 6H), 7.11 – 7.05 (m, 2H), 6.94 – 6.86 (m, 2H), 6.70 (d, 1H), 6.65 – 6.60 (m, J = 6.4 Hz, 2H), 6.54 (d, J = 7.4 Hz, 1H), 5.25 (d, J = 24.9 Hz, 1H), 4.39 (d, J = 22.8 Hz, 1H), 4.15 – 3.89 (m, 6H), 3.88 – 3.77 (m, 1H), 3.62 – 3.55 (m, 1H), 2.86 (s, 3H), 2.83 (s, 3H), 2.33 (s, 3H), 2.25 (s, 3H), 1.26 – 1.08 (m, 9H), 0.95 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 151.1 (d, J = 11.9 Hz), 150.4 (d, J = 7.4 Hz), 139.0, 134.6 (d, J = 7.4 Hz), 133.5, 133.3 (d), 131.2, 130.4, 130.3, 129.1, 128.9 (d, J = 8.4 Hz), 128.6, 128.1, 127.9 (d, J = 3.3 Hz), 126.0, 123.9, 123.3, 119.1, 114.7, 111.2, 66.4 (d), 64.9 (d), 63.2 (d), 62.7 (d), 62.5 (d, J = 7.1 Hz), 61.1 (d), 38.7, 34.9, 22.0, 18.5, 16.6 (d), 16.5 (d), 16.4 (d), 16.3 (d). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 23.3, 22.1. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_3P$ 347.1650; found 347.1651.

Diethyl ((methyl(m-tolyl)amino)(phenyl)methyl)phosphonate ***(4w)*** *and diethyl ((methyl(p-tolyl)amino)(phenyl)methyl)-phosphonate* ***(4w')***. Pale yellow oil (42.7 mg, 82%). R_f = 0.21 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (t, J = 7.7 Hz, 4H), 7.35 – 7.27 (m, 6H), 7.17 – 7.10 (m, 1H), 7.06 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.6 Hz, 2H), 6.70 (d, J = 6.7 Hz, 2H), 6.62 (d, J = 7.4 Hz, 1H), 5.29 (t, J = 25.2 Hz, 2H), 4.24 – 3.96 (m, 8H), 2.94 (s, 3H), 2.91 (s, 3H), 2.32 (s, 3H), 2.27 (s, 3H), 1.26 – 1.17 (m, 12H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.4 (d, J = 7.4 Hz), 148.3 (d, J = 8.0 Hz), 139.0, 134.7, 134.6, 134.5 (d, J = 7.6 Hz), 129.8, 129.1 (d, J = 7.9 Hz), 129.0, 128.9, 128.6, 128.5, 127.9, 127.5, 119.1, 114.7, 114.4, 111.2, 63.3 (d, J = 3.7 Hz), 63.2 (d, J = 2.7 Hz), 62.7 (d, J = 3.9 Hz), 62.2, 61.7 (d, J = 3.7 Hz), 61.1 (d, J = 3.7 Hz), 34.9 (d, J = 3.8 Hz), 22.0, 20.40, 16.6 (d, J = 3.0 Hz), 16.4 (d, J = 5.1 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.1, 22.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_3P$ 347.1650; found 347.1647.

Diethyl (((3-methoxyphenyl)(methyl)amino)(phenyl)methyl)-phosphonate ***(4x)*** *and diethyl (((4-methoxyphenyl)-(methyl)amino)(phenyl)methyl)phosphonate* ***(4x')***. Pale yellow oil (43.6 mg, 80%); R_f = 0.31 (ethyl acetate/n-hexane, 1:2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 7.3 Hz, 2H), 7.45 (d, J = 7.0 Hz, 4H), 7.35 – 7.28 (m, J = 12.7, 6.2 Hz, 9H), 7.16 (t, J = 8.2 Hz, 1H), 6.84 (s, 8H), 6.51 (d, J = 8.1 Hz, 1H), 6.41 (s, 1H), 6.36 (d, J = 8.1 Hz, 1H), 5.31 (d, J = 24.9 Hz, 1H), 5.14 (d, J = 24.6 Hz, 2H), 4.26 – 3.93 (m, 12H), 3.78 (s, 3H), 3.76 (s, 6H), 2.95 (s, 3H), 2.86 (s, 6H), 1.26 – 1.16 (m, J = 26.8, 12.9, 6.9 Hz, 18H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 160.8, 152.8, 151.7 (d, J = 7.3 Hz), 145.2 (d, J = 8.9 Hz), 134.6, 134.1 (d, J = 7.5 Hz), 130.0, 129.2 (d, J = 8.8 Hz), 128.9 (d, J = 8.3 Hz), 128.6, 128.5, 128.0 (d, J = 3.2 Hz), 116.5 (d, J = 0.8 Hz), 114.7, 106.9, 102.8, 100.6, 64.5, 63.3 (d, J = 7.4 Hz), 62.6 – 62.1 (m), 61.1, 55.8, 55.3, 35.2, 35.1, 29.8, 16.7 (d, J = 5.8 Hz), 16.4 (d, J = 5.7 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.2, 21.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_4P$ 363.1599; found 363.1595.

Diethyl (((4-fluorophenyl)(methyl)amino)(phenyl)methyl)-phosphonate ***(4y)*** *and diethyl (((3-fluorophenyl)(methyl)-amino)(phenyl)methyl)phosphonate* ***(4y')***. Pale yellow oil (27.9 mg, 53%); R_f = 0.35 (ethyl acetate/n-hexane, 1:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, J = 14.3, 6.8 Hz, 12.2H), 7.41 – 7.28 (m, 19.1H), 7.17 (dd, J = 15.5, 8.0 Hz, 1H), 6.95 (t, J = 8.7 Hz, 9.7H), 6.86 – 6.77 (m, J = 9.1, 4.4 Hz, 10.6H), 6.63 (d, J = 8.6 Hz, 1H), 6.55 (d, J = 12.5 Hz, 1H), 6.47 (t, J = 8.1 Hz, 1H), 5.26 (d, J = 24.7 Hz, 1H), 5.16 (d, J = 24.7 Hz, 5.2H), 4.31 – 3.87 (m, 24.4H), 2.96 (s, 3H), 2.90 (s, 15.6H), 1.29 – 1.14 (m, J = 20.7, 7.1 Hz, 37.7H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 157.3, 155.4, 147.2 (d, J = 6.3 Hz), 134.1 (d, J = 7.2 Hz), 130.4, 129.2 – 128.5 (m), 128.2 (d, J = 8.4 Hz), 115.9 – 115.5 (m), 104.4, 77.4, 77.2, 76.9, 64.0, 63.2 (d, J = 7.1 Hz), 62.7, 62.6 – 62.1 (m), 60.9, 35.3, 35.1, 16.7 (d, J = 5.7 Hz), 16.5 (d, J = 5.7 Hz). $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -112.3, -127.0. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 21.8, 21.4. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{23}FNO_3P$ 351.1400; found 351.1396.

Diethyl (((3-methoxyphenyl)(methyl)amino)(phenyl)methyl)-phosphonate ***(4z)***. Pale yellow oil (44.2 mg, 81%); R_f = 0.24 (ethyl acetate/n-hexane, 1:2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 7.0 Hz, 2H), 7.36 – 7.25 (m, J = 8.0, 2.6 Hz, 3H), 7.16 (t, J = 8.2 Hz, 1H), 6.51 (dd, J = 8.3, 2.3 Hz, 1H), 6.42 (t, J = 2.2 Hz, 1H), 6.36 (dd, J = 8.1, 2.1 Hz, 1H), 5.31 (d, J = 24.9 Hz, 1H), 4.23 – 3.96 (m, 4H), 3.78 (s, 3H), 2.95 (s, 3H), 1.25 – 1.18 (m, J = 13.1, 7.0 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.8, 151.7 (d, J = 7.4 Hz), 134.6 (d, J = 7.0 Hz), 130.0, 128.9 (d, J = 8.3 Hz), 128.6, 128.0, 106.9, 102.8, 100.6, 63.2 (d, J = 7.1 Hz), 62.4 (d, J = 24.9, 5.6 Hz), 61.0 (d, J = 3.7 Hz), 55.3 (d, J = 2.6 Hz), 35.1, 16.6 (d, J = 4.6 Hz), 16.4 (d, J = 5.7 Hz).$^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 21.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{26}NO_4P$ 363.1599; found 363.1599.

Diethyl (((3,4-dimethoxyphenyl)(methyl)amino)(phenyl)-methyl)phosphonate ***(4aa)***. Pale yellow oil (49.6 mg, 84%); R_f

= 0.36 (ethyl acetate/n-hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.43 (m, 2H), 7.35 – 7.28 (m, 3H), 6.78 (d, *J* = 8.7 Hz, 1H), 6.52 (d, *J* = 2.7 Hz, 1H), 6.38 (dd, *J* = 8.7, 2.8 Hz, 1H), 5.14 (d, *J* = 24.6 Hz, 1H), 4.26 – 3.94 (m, 4H), 3.85 (s, 3H), 3.83 (s, 3H), 2.88 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.7, 145.8 (d, *J* = 8.8 Hz), 142.4, 134.1 (d, *J* = 7.4 Hz), 129.1 (d, *J* = 8.7 Hz), 128.5, 128.0 (d, *J* = 0.6 Hz), 112.6, 106.7, 100.9, 64.7 (d, *J* = 3.9 Hz), 63.2 (d, *J* = 9.6, 5.5 Hz), 62.3 (d, *J* = 7.1 Hz), 56.5 (d, *J* = 2.7 Hz), 55.9 (d, *J* = 2.8 Hz), 35.4, 16.7 (d, *J* = 5.7 Hz), 16.4 (d, *J* = 5.8 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 22.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{20}H_{28}NO_5P$ 393.1705; found 393.1709.

Diethyl (((3,4-difluorophenyl)(methyl)amino)(phenyl)-methyl)phosphonate ***(4ab)***. Pale yellow oil (27.1 mg, 49%); R_f = 0.21 (ethyl acetate/n-hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 6.8 Hz, 2H), 7.37 – 7.30 (m, 3H), 7.02 (q, *J* = 19.1, 9.2 Hz, 1H), 6.70 – 6.61 (m, *J* = 13.6, 6.7, 3.1 Hz, 1H), 6.57 – 6.50 (m, 1H), 5.13 (d, *J* = 24.7 Hz, 1H), 4.27 – 3.94 (m, 4H), 2.91 (s, 3H), 1.28 – 1.15 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 151.7 (d, *J* = 13.2 Hz), 149.8 (d, *J* = 13.2 Hz), 147.6 (td, *J* = 7.9, 1.9 Hz), 144.4 (d, *J* = 12.8 Hz), 142.5 (d, *J* = 13.0 Hz), 134.0 (d, *J* = 6.7 Hz), 128.9 (d, *J* = 8.4 Hz), 128.7, 128.3 (d, *J* = 0.7 Hz), 117.4 (dd, *J* = 17.7, 1.8 Hz), 109.3, 103.2 (dd, *J* = 21.1, 1.2 Hz), 63.3, 62.9 (dd, *J* = 89.2, 7.2 Hz), 62.0, 35.3, 16.6 (d, *J* = 5.5 Hz), 16.4 (d, *J* = 5.7 Hz). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -136.6, -152.0. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 21.4. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{22}F_2NO_3P$ 369.1305; found 369.1306.

Diethyl ((methyl(naphthalen-2-yl)amino)(phenyl)methyl)-phosphonate ***(4ac)***. Pale yellow oil (28.8 mg, 50%); R_f = 0.22 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.69 (m, *J* = 12.6, 8.6 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.35 – 7.29 (m, 4H), 7.28 – 7.23 (m, 2H), 7.04 (d, *J* = 2.3 Hz, 1H), 5.46 (d, *J* = 24.6 Hz, 1H), 4.29 – 3.96 (m, 4H), 3.03 (s, 3H), 1.25 – 1.18 (m, *J* = 7.1, 3.3 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.2 (d, *J* = 7.6 Hz), 134.9, 134.3 (d, *J* = 7.4 Hz), 129.2, 129.0 (d, *J* = 8.6 Hz), 128.6, 128.1, 127.6 (d, *J* = 18.8 Hz), 126.5 (d, *J* = 6.3 Hz), 122.9, 117.2, 108.7, 63.2 (d, *J* = 27.6 Hz), 62.4 (d, *J* = 7.3 Hz), 61.5 (d, *J* = 3.5 Hz), 35.1, 16.7 (d, *J* = 4.4 Hz), 16.5 (d, *J* = 4.9 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 21.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{22}H_{26}NO_3P$ 383.1650; found 383.1654.

Dimethyl ((methyl(phenyl)amino)(phenyl)methyl)-phosphonate ***(4ad)***. Pale yellow oil (38.5 mg, 84%); R_f = 0.22 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 6.8 Hz, 2H), 7.35 – 7.22 (m, 5H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 5.34 (d, *J* = 24.6 Hz, 1H), 3.74 (d, *J* = 10.4 Hz, 3H), 3.67 (d, *J* = 10.7 Hz, 3H), 2.92 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.2 (d, *J* = 7.5 Hz), 134.2 (d, *J* = 7.2 Hz), 129.4, 128.9 (d, *J* = 8.6 Hz), 128.7, 128.2, 118.4, 114.1, 61.8 (d, *J* = 160.8, 3.7 Hz), 53.9 (d, *J* = 6.9 Hz), 52.8 (d, *J* = 7.3 Hz), 34.8. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 24.2. HRMS (EI) m/z: $[M]^+$ calcd for $C_{16}H_{20}NO_3P$ 305.1181; found 305.1182.

Dibutyl ((methyl(phenyl)amino)(phenyl)methyl)phosphonate ***(4ae)***. Pale yellow oil (45.6 mg, 78%); R_f = 0.28 (ethyl acetate/n-hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.0 Hz, 2H), 7.30 (t, *J* = 7.8 Hz, 3H), 7.25 – 7.21 (m, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.78 (t, *J* = 7.3 Hz, 1H), 5.33 (d, *J* = 25.0 Hz, 1H), 4.14 – 3.88 (m, 4H), 2.96 (s, 3H), 1.55 – 1.47 (m, *J* = 13.0, 6.5 Hz, 4H), 1.37 – 1.20 (m, *J* = 14.9, 12.4, 7.5 Hz, 4H), 0.84 (td, *J* = 7.4, 1.6 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.2 (d, *J* = 7.3 Hz), 134.7 (d, *J* = 7.1 Hz), 129.2, 128.9 (d, *J* = 8.3 Hz), 128.5, 127.9, 118.0, 113.8, 66.3 (d, *J* = 79.9, 7.4 Hz), 65.6 (d, *J* = 6.0 Hz), 62.5, 60.9, 34.9, 32.7 (d, *J* = 5.6 Hz), 32.5 (d, *J* = 6.2 Hz), 18.8, 18.7 (d, *J* = 4.6 Hz), 13.6. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 22.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{22}H_{32}NO_3P$ 389.2120; found 389.2121.

Dibenzyl ((methyl(phenyl)amino)(phenyl)methyl)-phosphonate ***(4af)***. Pale yellow oil (50.1 mg, 73%); R_f = 0.36 (ethyl acetate/n-hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.47 (m, 2H), 7.34 – 7.14 (m, 15H), 6.86 (d, *J* = 8.3 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 5.40 (d, *J* = 24.8 Hz, 1H), 5.12 – 4.89 (m, 4H), 2.96 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.2 (d, *J* = 7.2 Hz), 136.4 (d, *J* = 5.9 Hz), 136.1 (d, *J* = 6.0 Hz), 134.3 (d, *J* = 7.5 Hz), 129.3, 129.1, 129.0, 128.7, 128.6, 128.5, 128.4 (d, *J* = 4.5 Hz), 128.2, 128.1, 127.1, 118.3, 114.1, 68.1 (d), 63.0 (d, *J* = 3.7 Hz), 61.4 (d, *J* = 3.6 Hz), 35.0. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 22.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{28}H_{28}NO_3P$ 457.1807; found 457.1809.

Diisopropyl ((methyl(phenyl)amino)(phenyl)methyl)-phosphonate ***(4ag)***. Pale yellow oil (33.1 mg, 61%); R_f = 0.33 (ethyl acetate/n-hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.3 Hz, 2H), 7.35 – 7.19 (m, 5H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 5.27 (d, *J* = 25.9 Hz, 1H), 4.83 – 4.55 (m, 2H), 2.99 (s, 3H), 1.30 (dd, 6H), 1.06 (dd, *J* = 15.9, 6.2 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.4 (d, *J* = 8.0 Hz), 134.9 (d, *J* = 7.2 Hz), 129.2, 129.0 (d, *J* = 8.1 Hz), 128.5, 127.9 (d, *J* = 1.0 Hz), 117.9, 114.0, 71.5 (d, *J* = 90.9, 7.6 Hz), 62.9 (d, *J* = 3.8 Hz), 61.3 (d, *J* = 3.8 Hz), 34.9, 24.5 (d, *J* = 30.2 Hz), 23.7. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 20.2. HRMS (EI) m/z: $[M]^+$ calcd for $C_{20}H_{28}NO_3P$ 361.1807; found 361.1807.

Di-tert-butyl ((methyl(phenyl)amino)(phenyl)methyl)-phosphonate ***(4ah)***. Pale yellow oil (10.5 mg, 18%); R_f = 0.32 (ethyl acetate/n-hexane, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.8 Hz, 2H), 7.32 – 7.18 (m, *J* = 16.1, 11.6, 7.0 Hz, 6H), 6.83 (d, *J* = 7.3 Hz, 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 5.16 (d, *J* = 27.1 Hz, 1H), 3.01 (s, 3H), 1.38 (d, *J* = 6.8 Hz, 19H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.6 (d, *J* = 8.0 Hz), 136.1 (d, *J* = 6.0 Hz), 129.2, 128.7 (d, *J* = 7.3 Hz), 128.3, 127.4 (d, *J* = 1.5 Hz), 117.4, 113.5 (d, *J* = 1.1 Hz), 83.5 (d, *J* = 76.8, 10.1 Hz), 65.1, 63.4, 35.0, 30.5 (d, *J* = 3.8 Hz). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 13.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{22}H_{32}NO_3P$ 389.2120; found 389.2121.

Ethyl ((methyl(phenyl)amino)(phenyl)methyl)(phenyl)phosphinate ***(4ai)*** Pale beige solid (24.1 mg, 44%); R_f = 0.20 (ethyl acetate/n-hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 1H), 7.77 – 7.68 (m, 1H), 7.57 (d, *J* = 7.3 Hz, 1H), 7.50 – 7.29 (m, 6H), 7.23 – 7.16 (m, 2H), 7.05 (t, *J* = 7.9 Hz, 1H), 6.81 – 6.61 (m, 2H), 6.50 (d, *J* = 8.2 Hz, 1H), 5.36 (d, *J* = 18.2 Hz, 1H), 4.16 – 3.88 (m, 2H), 3.02 (d, *J* = 44.1 Hz, 3H), 1.26 – 1.19 (m, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 150.5 (d, *J* = 6.1 Hz), 150.1 (d, *J* = 7.8 Hz), 134.8 (d, *J* = 2.7 Hz), 134.4 (d, *J* = 7.4 Hz), 132.4, 132.4 (d, *J* = 1.2 Hz), 132.4, 132.2, 132.1 (d, *J* = 3.0 Hz), 132.0, 129.5, 129.4 (d, *J* = 1.0 Hz), 129.3, 129.1, 129.0, 128.6, 128.5, 128.6, 128.5, 128.4, 128.0 (d, *J* = 7.7 Hz), 118.0 (d, *J* = 6.0 Hz), 113.9 (d, *J* = 5.5 Hz), 65.2 (d, *J* = 3.6 Hz), 64.4 (d, *J* = 3.5 Hz), 64.3 (d, *J* = 3.5 Hz), 63.5 (d, *J* = 3.9 Hz), 61.6, 61.3 (d, *J* = 6.9 Hz), 35.5, 35.0, 16.8 (d, *J* = 5.7 Hz), 16.6

(d, J = 5.3 Hz). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 38.1, 38.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{22}H_{24}NO_2P$ 365.1545; found 365.1543.

*((Methyl(phenyl)amino)(phenyl)methyl)diphenylphosphine-oxide (**4aj**)*. White solid (29.8 mg, 50%); R_f = 0.28 (ethyl acetate/n-hexane, 1:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.74 (m, 2H), 7.65 – 7.56 (m, J = 10.2, 7.9 Hz, 2H), 7.50 – 7.28 (m, 8H), 7.22 – 7.17 (m, 3H), 7.14 (t, 2H), 6.71 (t, J = 7.3 Hz, 1H), 6.61 (d, J = 8.2 Hz, 2H), 5.57 (d, J = 11.4 Hz, 1H), 3.20 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 150.1 (d, J = 7.1 Hz), 134.6 (d, J = 2.5 Hz), 133.0 (d, J = 2.4 Hz), 132.0 (d, J = 2.6 Hz), 131.9 (d, J = 2.7 Hz), 131.5, 131.4, 131.3, 129.7 (d, J = 6.0 Hz), 129.2, 128.7 (d, J = 10.4 Hz), 128.6 (d, J = 10.4 Hz), 128.5, 128.0 (d, J = 1.2 Hz), 117.9, 113.5, 64.3 (d, J = 77.8 Hz), 36.1 (d, J = 2.3 Hz). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 31.1. HRMS (EI) m/z: $[M]^+$ calcd for $C_{26}H_{24}NOP$ 397.1596; found 397.1592.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Crystal structure data for **4aj** (file type, i.e., CIF)

Single-crystal data for **4aj**, ^1H NMR spectra of mechanistic studies and ^1H, $^{13}C\{^{1}H\}$, $^{19}F\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR spectra of compounds (file type, i.e., PDF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: kimbm@snu.ac.kr.

ORCID

B. Moon Kim: 0000-0001-6924-268X

Notes

Any additional relevant notes should be placed here.

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(24) For more X-ray crystal structure information of **4aj** (CCDC: 2024059), see the Supporting Information. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.