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Diversity-Oriented Synthesis toward Aryl- and Phosphoryl-Functionalized Imidazo[1,2-*a*]pyridines

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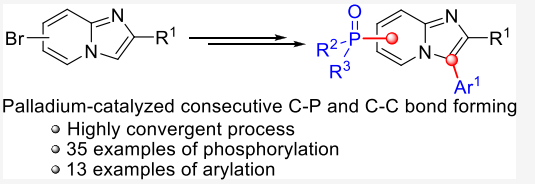
ABSTRACT: We report herein an efficient synthesis of diversely polysubstituted imidazo[1,2-*a*]pyridines, a family of aza-heterocycles endowed with numerous biological properties, through a sequence involving two consecutive palladium-catalyzed cross-coupling reactions. First, we demonstrated that a Hirao coupling occurred straightforwardly in high yields at positions 3, 5, and 6 of imidazopyridine derivatives, giving access to a wide variety of substituted phosphonates, phosphinates, and phosphine oxides. In a second step, direct CH-arylation of phosphorylimidazopyridines with aryl halides was found to be effective and fully selective, leading to 3-aryl-substituted imidazopyridines in moderate to high yields depending on steric hindrance.



INTRODUCTION

Diversity-oriented synthesis (DOS) is an affordable methodology to explore the chemical space for the identification of new and potentially biologically active molecules.[1] In spite of the emergence of biologics, small molecules still carry promising novelties for medicinal applications. To meet such demands in molecular diversity, DOS is probably one of the best approaches to keep the doors open for fast hit and lead discovery.[2] The term "diversity" is somewhat subjective. Nevertheless, there is a consensus around the structural modifications of skeletal, appendages, functional groups, and stereochemistry.[3] These principal structural features already identified can be used in a build, couple, and pair approach when complex polycyclic molecules, i.e., natural product like compounds, are targeted.[4] Consequently, DOS methodology has allowed the efficient construction of many chemical libraries feeding the field of drug discovery.

Imidazo[1,2-*a*]pyridines[5] are a family of aza-heterocycles offering peculiar interest in medicinal chemistry (Figure 1). The imidazo[1,2-*a*]pyridine heterocyclic core is naturally occurring, and several commercial drugs are already on the market. For instance, alpidem and zolpidem are widely used in the treatment of anxiety and insomnia.[6] Minodronate is a representative member of a larger family of nitrogen-based bisphosphonates (third generation bisphosphonate) for the treatment of osteoporosis.[7] More recently, GlaxoSmithKline developed a potent noncompetitive CXCR4 receptor antagonist, namely GSK812397, that proved to be efficient for the treatment of HIV infection,[8] while trisubstituted-imidazopyridines revealed targeting of the Snake Venom Phospholipase A2.[9] Zolimidine is a gastroprotective drug used for the treatment of peptic ulcer and gastroesophageal reflux.[10]

Owing to their broad biological importance, it is therefore not surprising that the synthetic community has spearheaded many efforts toward the synthesis and functionalization of

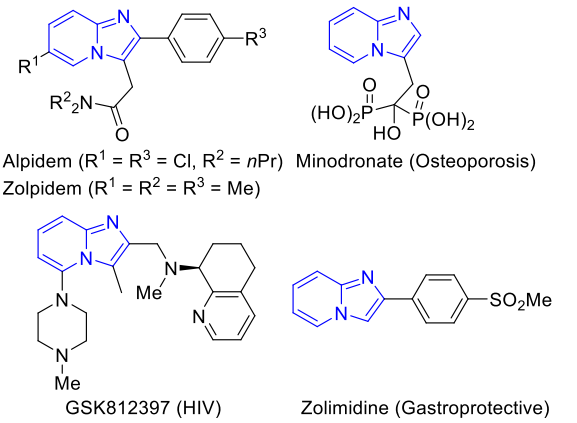


Figure 1. Representative marketed and bioactive imidazo[1,2-*a*]pyridines.

imidazo[1,2-*a*]pyridine derivatives. Another interesting feature of these heterocyclic scaffolds can be associated with their multifaceted chemical behavior.[11] Imparted by their structure and their reactivity, imidazo[1,2-*a*]pyridine cores are perfectly adequate motifs allowing the introduction of molecular adornments using transition-metal-catalyzed reactions. These features make them particularly attractive for DOS approaches (Figure 2).[12] When designing new libraries, labeled fragments for NMR-based screening may greatly facilitate hit or lead

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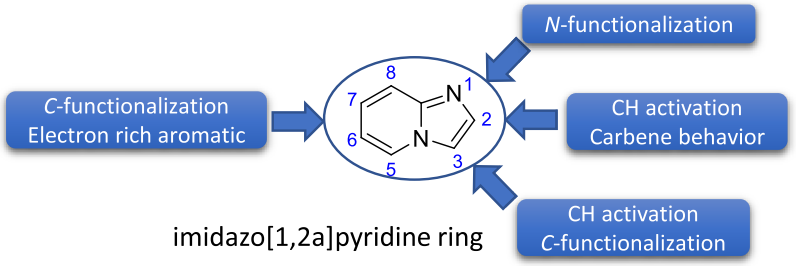


Figure 2. Imidazo[1,2-*a*]pyridines as scaffold for DOS.

optimizations.[13] As a result, ^{31}P NMR screening of compounds that incorporated a phosphorus atom proved to be a highly valuable approach for medicinal chemists.[14]

In our previous studies on the synthesis of bioactive and neutral phosphorus-based molecules, we designed two families of compounds with potent biological activities as anticancer drugs[15] or as neuroactive agents.[16] Continuing our research program aimed at the synthesis of biologically relevant molecules, we investigated a diversity-oriented synthesis of aryl- and phosphoryl-decorated imidazo[1,2-*a*]pyridines as a central core.

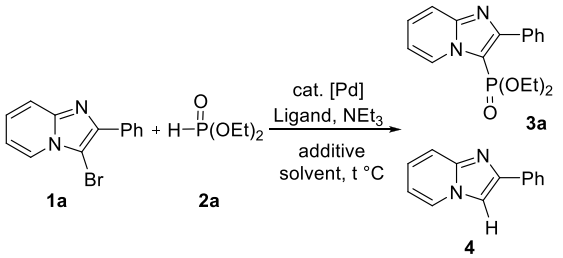
RESULTS AND DISCUSSION

Palladium-catalyzed cross-coupling reactions are exceptionally powerful and reliable synthetic methods to build C−C or C-heteroatom bonds.[17] Searching for highly convergent syntheses, we have designed a sequential approach allowing the consecutive formation of both P−C and C−C bond, linking easily independent subunits to differently substituted imidazo-[1,2-*a*]pyridines. First, the sequence involves the P−C(sp^2) bond formation through Hirao-coupling[18] reaction, and second, it involves a highly regioselective and then a direct C−H arylation of imidazopyridines.

Easily available 3-bromo-2-phenylimidazo[1,2-*a*]pyridine **1a**[19,20] and diethyl phosphite as phosphorylating agent were chosen for preliminary optimization of the Hirao coupling reactions. Palladium acetate and xantphos were used as the catalytic system along with triethylamine as a base. This system proved to be efficient when nitrogen-based heterocycles were the substrates of the reaction.[21] The solvent and the temperature of the reaction failed to give the expected phosphonate, and only the reduced imidazopyridine **4** was formed and isolated almost quantitatively (Table 1, entries 1 and 2). Similarly, changing the palladium source by palladium dichloride bis(triphenylphosphine) did not improve the reaction outcome (entry 3). Gratefully, the use of tris-(dibenzylideneacetone)dipalladium(0) and xantphos furnished the diethyl imidazopyridylphosphonate **3a** in 60% yield along with 20% of the debrominated secondary product **4** (entry 4). Reducing the reaction time from 21 to 4 h significantly improved the yield of the targeted phosphonate **3a** up to 72%, suggesting that the phosphonate product is prone to degradation over the course of the reaction. From the results depicted in Table 1, it is also clear that the outcome of this Hirao coupling is highly ligand dependent. Indeed, only the reduced imidazopyridine **4** was formed when the reaction was performed with other bidentate ligands such as dppf, dppp or SPhos (Table1, entries 6 to 8).

Under the optimal operating conditions, 3-bromo-2-phenylimidazo[1,2-*a*]pyridine **1a** was subsequently reacted

Table 1. Optimization of the Reaction Conditions for Hirao Coupling[a]



entry	cat. [Pd]	ligand	conditions	yield (%) of **3a**/**4**
1	$Pd(OAc)_2$	Xantphos	KOAc[b], THF, reflux, 36 h	0/75
2	$Pd(OAc)_2$	Xantphos	KOAc[b], THF, μW, 90 °C, 10 min	0/100[c]
3	$PdCl_2(PPh_3)_2$		PhMe, 110 °C, 24 h	0/100[c]
4	Pd_2dba_3	Xantphos	PhMe, 110 °C, 21 h	60/20
5[d]	Pd_2dba_3	Xantphos	PhMe, 110 °C, 4 h	72/17
6	Pd_2dba_3	dppf	PhMe, 110 °C, 46 h	0/11 (53)[d]
7	Pd_2dba_3	dppp	PhMe, 110 °C, 4 d	0/100[c]
8	Pd_2dba_3	SPhos	PhMe, 110 °C, 4 d	0/100[c]

[a]Reaction conditions: **1a** (0.366 mmol), **2a** (0.366 mmol, 1 equiv), [Pd] (10 mol %), ligand (20 mol %), and NEt_3 (0.732 mmol, 2 equiv) in 3.6 mL of solvent; the reactions were stopped after the total consumption of reagent **1a**, determined by TLC. [b]10 mol % of KOAc was added. [c]Indicated by TLC. [d]Reaction conditions with 1.1 equiv of **1a**.

with various phosphites and secondary phosphine oxides **2a**−**f**. As can be seen in Scheme 1, the reaction appeared to be poorly general, and it turns out that the nature of the substituents at the phosphorus atom has a dramatic influence on the reaction. Only diethyl phosphonate derivative **3a** and diphenylphosphine oxide **3b** were isolated in 72% and 27% yield, respectively, whereas the unwanted reduced products were observed in all the other reactions. Phosphorylation of imidazopyridines at position 3 using Hirao coupling also appeared to be poorly efficient, and the reduction of the bromide derivative was the main reaction. It should be noted that such a reduction process mediated by *H*-phosphoryl derivatives was already observed for aryl halides.[22] Moreover and to the best of our knowledge, only two papers dealing with the phosphorylation at position 3 of imidazopyridines were reported in the literature. Singh et al. disclosed a Mn^{III}-mediated regioselective method for the direct C−H phosphonation of imidazo[1,2-*a*]pyridines in good to moderate yields,[23] while Marugan et al. showed that highly reactive and electrophilic diphenyliodophosphine smoothly reacted with imidazo[1,2-*a*]pyridine and 2-methylimidazo[1,2-*a*]-

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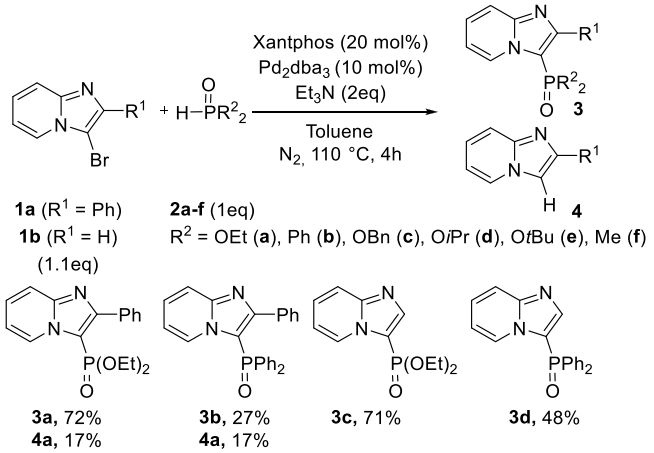
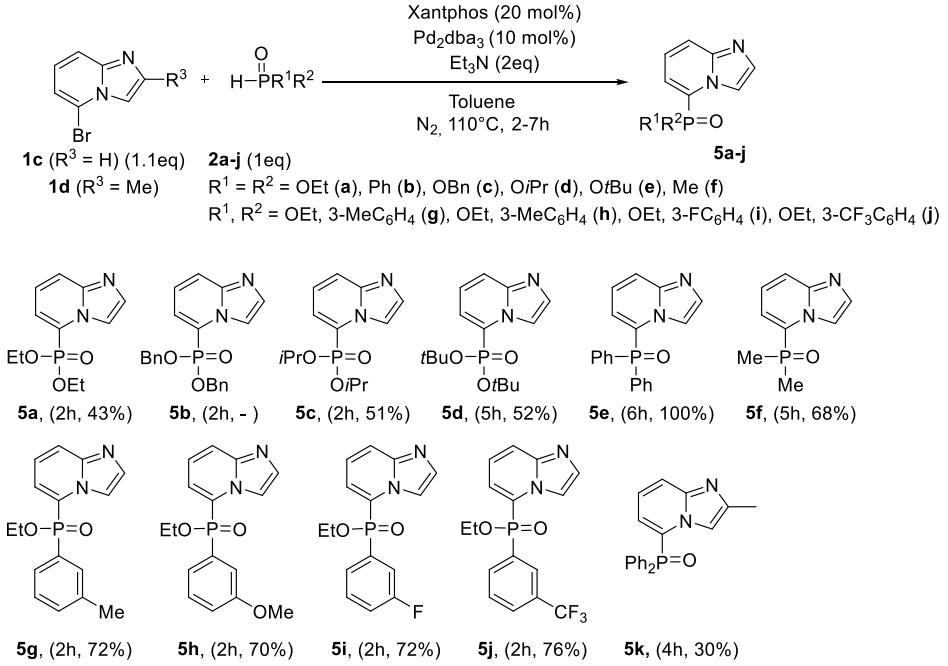
Scheme 1. Phosphorylation at Position 3 of Imidazopyridines 1a and 1b



pyridine leading to the corresponding 3-(diphenylphosphino)-imidazo[1,2-*a*]pyridines in moderate yields.[24] Since the best results were obtained with diethyl phosphite **2a** and diphenylphosphine oxide **2b**, we used them for the phosphorylation of the 3-bromoimidazo[1,2-*a*]pyridine **1b**. The corresponding diethyl phosphonate **3c** was obtained in 71% yield and the diphenylphosphine oxide derivative **3d** in 48% yield.

By contrast, 5-bromoimidazo[1,2-*a*]pyridines **1c** and **1d** proved to be suitable partners in such coupling reactions as outlined in Scheme 2. Using the previously developed conditions, 5-bromoimidazo[1,2-*a*]pyridine **1c** (R^3 = H) was reacted with various dialkyl phosphites **2**. The resulting phosphonates **5a−d** were obtained in moderate yields (43−52%). It is worth noting that even the sterically hindered di-*tert*-butyl phosphite gave the expected phosphonate in 52% yield. However, the reaction failed when using dibenzyl phosphite as no phosphonate derivative **5b** was observed. This result may be attributed to the high instability of the dibenzyl moiety under such conditions leading to the cleavage of the benzyl as previously reported by Virieux et al.[25] As outlined in Scheme 2, secondary phosphine oxides reacted smoothly, affording the tertiary phosphine oxides **5e−f** in 68% to quantitative yields. When the reactions were conducted with aryl *H*-phosphinates **2g−j**, the corresponding cross-coupling products **5g−j** were isolated in yields ranging from 70 to 76%. Our studies also revealed that the electronic nature of the substituents on aryl *H*-phosphinates had only a small influence on the yield of the reaction. Both electron-donating and -withdrawing groups were well tolerated. Finally, a coupling reaction was attempted on 2-methylimidazopyridine **1d**. The resulting phosphine oxide **5k** was isolated in a disappointing 30% yield, contrasting with the expected good result based on the in situ monitoring of the reaction by ^{31}P NMR which highlighted a complete and clean conversion of the starting material. To the best of our knowledge, only one paper described the phosphorylation of related heterocycles at position 5 in low to moderate yields.[26] Moreover, the reaction has a relatively narrow substrate scope and required the presence of a cyano group at position 8 for the direct nucleophilic aromatic substitution of the bromide. Consequently, the above-described Hirao coupling reaction clearly appeared as an efficient approach for the direct introduction of a phosphorus-based functional group at position 5 of imidazopyridines. For example, our method was successfully applied for the gram-scale synthesis of compound **5e** without

Scheme 2. Scope of the Palladium Coupling Reactions of 5-Bromoimidazopyridine 1c[a] and 1d[b]



[a]Reaction conditions: under nitrogen atmosphere, **1c** (0.508 mmol, 1.1 equiv), **2a−j** (0.462 mmol, 1 equiv), [Pd] (10 mol %), ligand (20 mol %), and NEt_3 (0.924 mmol, 2 equiv) in 4.6 mL of dry toluene; the reactions were stopped after the total consumption of reagent **1c**, determined by TLC. [b]Reaction conditions: under nitrogen atmosphere, **1d** (1.10 mmol, 1.1 equiv), **2e** (1.00 mmol, 1 equiv), [Pd] (10 mol %), ligand (20 mol %) and NEt_3 (2.0 mmol, 2 equiv) in 25 mL of dry toluene; the reaction was stopped after the total consumption of reagent **1c**, determined by TLC.

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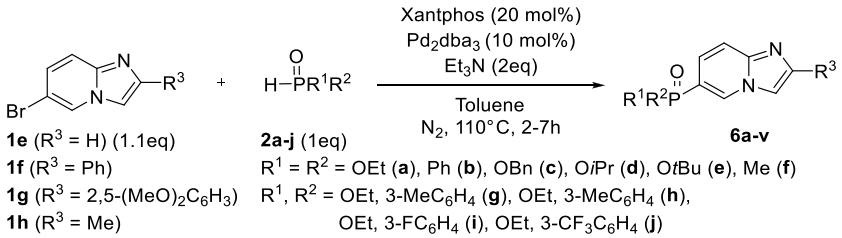
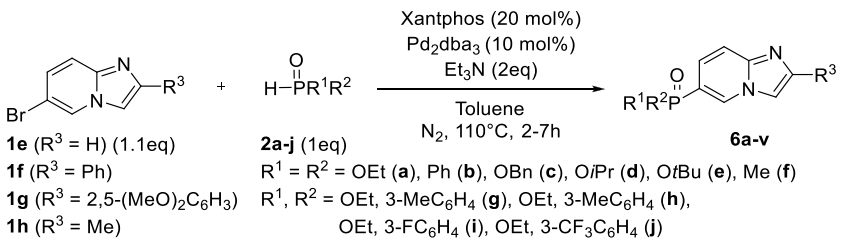
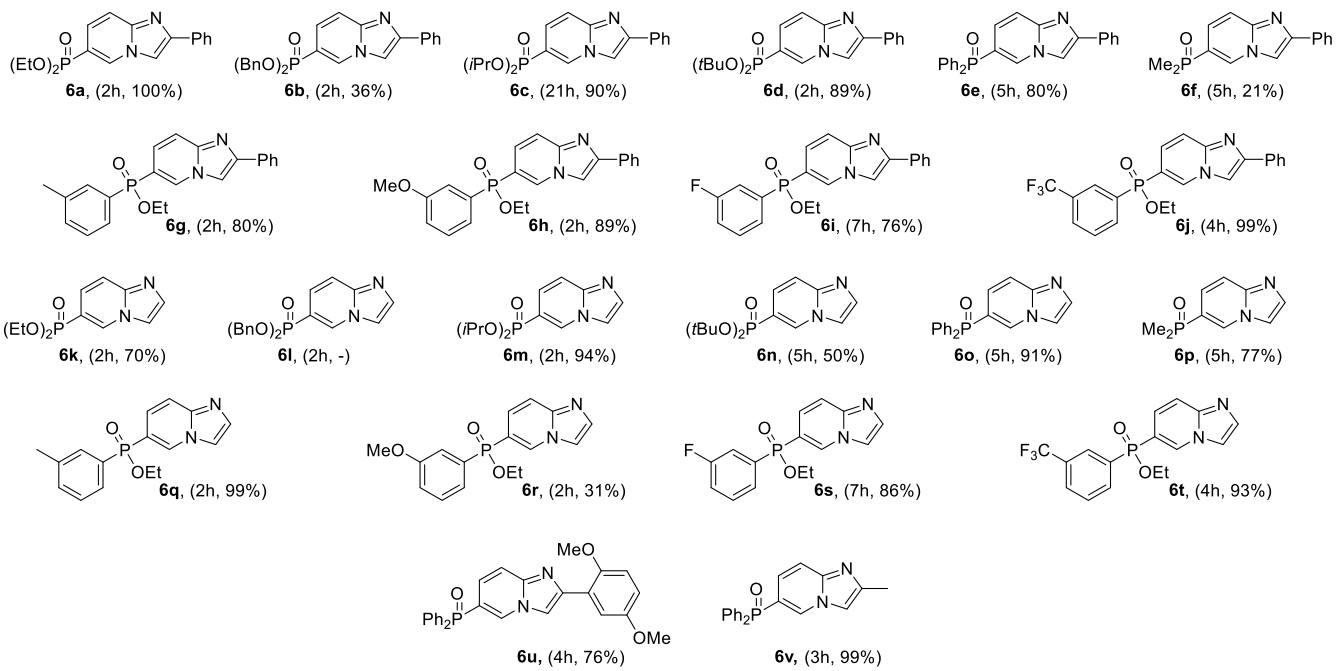
Scheme 3. Scope of the Palladium Coupling Reactions of 6-Bromoimidazopyridines 1e−h[a,b]







[a]Reaction conditions: under nitrogen atmosphere, **1e−f** (0.403−0.508 mmol, 1.1equiv), **2a−j** (0.366−0.462 mmol, 1 equiv), [Pd] (10 mol %), ligand (20 mol %) and NEt_3 (2 equiv) in dry toluene (c = 1 M); the reactions were stopped after the total consumption of reagent **1e,f**, determined by TLC. [b]Reaction conditions: under nitrogen atmosphere, **1g−h** (1.10 mmol, 1.1equiv), **2e** (1.00, 1 equiv), [Pd] (10 mol %), ligand (20 mol %), and NEt_3 (2 equiv) in dry toluene (c = 1 M), the reactions were stopped after the total consumption of reagent **1g,h**, determined by TLC.

erosion of the chemical yield, thus demonstrating the practicality and the usefulness of the herein reported protocol.

Having validated the Hirao coupling reaction for 5-bromoimidazo[1,2-*a*]pyridine derivatives **1c,d**, we next examined the reaction of 6-bromoimidazo[1,2-*a*]pyridines **1e−h**, and the results of these experiments are reported in Scheme 3. It turned out that under the optimized conditions imidazopyridine derivatives **1e−h** were also suitable substrates for this palladium-catalyzed coupling process, irrespective of the substitution patterns. As mentioned before, when dibenzyl phosphite was used as the coupling partner, only a low yield (36%) of the phosphonate **6b** was obtained, while no reaction occurs with the imidazopyridine **1e**. Nonetheless, we were gratified to find that for all other substrates the reactions proceeded smoothly giving the expected phosphonate, phosphine oxide, and phosphinate products **6a−v** in generally high to quantitative yields, regardless of the nature of the substituent at position 2. A noticeable exception was the reaction between the dimethylphosphine oxide **2f** and the imidazopyridine **1f** that furnished the corresponding derivative **6f** in nonreproducible 21% yield. Here again, the robustness of the Hirao protocol for the direct introduction of phosphorus-based functional group at position 6 of imidazopyridines was demonstrated by the gram-scale synthesis of several phosphoryl imidazopyridines (**6a**, **6f**, **6k**, **6o**, **6p**).

3-Aryl-substituted imidazo[1,2-*a*]pyridines attracted substantial interest in the design of new potent drugs. They revealed nanomolar bioactivities acting as potent γ-secretase modulators or antitumor agents.[27] Having phosphorus-functionalized imidazopyridines in hand, we decided to take advantage of the inherent reactivity of such nitrogen-based heterocycles, and more specifically, we turned our attention to

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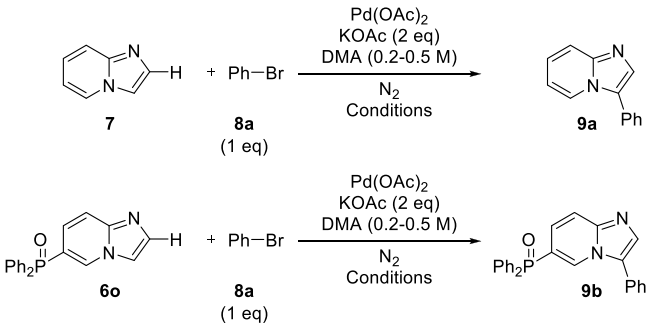
the direct C−H bond activation at position 3. Several papers validated this approach. For instance, the Doucet group reported the selective direct 3-CH-arylation of imidazo[1,2-*a*]pyridines with aryl bromides through a phosphine-free palladium-catalyzed reaction.[28] Various other catalytic systems were subsequently developed for the coupling of aryl halides including supported catalysts on magnetically recyclable nanoparticles,[29] coupling reactions in PEG-medium,[30] or in water.[31]

Therefore, we first optimized the reaction on model substrates, using either imidazopyridine **7** or diphenylphosphine oxide derivative **6o** and bromobenzene **8a** arylating reagent, to explore the difference in reactivity induced by the presence of a phosphoryl group starting from the conditions developed by Doucet.[28] As illustrated in Table 2, 3-

Table 2. Optimization of the Reaction Conditions for Direct C−H Bond Activation at Position 3



entry	substrate	$Pd(OAc)_2$ (mol %)	conditions	yield (%)
1	**7**	2.5 mol %	140 °C, 4 h	100
2	**7**	2.5 mol %	170 °C, 30 min	100
3	**7**	2.5 mol %	MW, 150 °C, 30 min	100
4	**6o**	2.5 mol %	MW 150 °C, 30 min	86
5	**6o**	2.5 mol %	MW 170 °C, 30 min	89
6	**6o**	10 mol %	MW, 170 °C, 30 min	96

phenylimidazo[1,2-*a*]pyridine **9a** was obtained quantitatively after 4 h of heating at 140 °C using 2.5 mol % of palladium acetate as catalyst in the presence of potassium acetate as a base (Table 2, entry 1). Increasing the temperature from 140 to 170 °C undergoes rapid product formation in only 30 min while maintaining 100% yield. Similar high results were obtained using microwave activation at 150 °C, also giving compound **9a** in quantitative yield after 30 min (Table 2, entries 2 and 3). We then moved to imidazo[1,2-*a*]pyridin-6-yldiphenylphosphine oxide **6o**. The first trial was conducted using 2.5 mol % of palladium acetate under microwave activation. After 30 min at 150 °C, the 3-phenylimidazopyridine **9b** was isolated in 86% (Table 2, entry 4). Increasing the temperature to 170 °C while keeping the ratio of palladium unchanged increased the yield to 89% (Table 2, entry 5). The best conditions were observed with heating at 170 °C under microwave activation using 10 mol % of palladium acetate. The imidazopyridine **9a** was then isolated in 96% yield after purification by silica gel chromatography (Table 2, entry 6). To shorten the reaction time, it was necessary to increase the amount of palladium acetate from 2.5 to 10 mol % while maintaining temperature to 170 °C. Fortunately, phosphine oxide **9b** was stable enough and no degradation was observed.

With these conditions in hand, the scope of the CH-coupling reaction was explored as illustrated in Scheme 4. To assess the influence of substituents on the course of the reaction, i.e., at position 2 and 5 or 6, imidazopyridine **7** (R^1 = R^2 = H) was reacted with either bromobenzene or *ortho*-sterically hindered aryl bromides, leading to CH-coupling products **9a−g**. Steric hindrance carried by the aromatic halide has a strong influence on the reaction. All the resulting coupling products **9c−g** showed significantly lower yields compared to imidazopyridine **9a** (Scheme 4, compare **9a** vs **9c-g**). No coupling reaction (**9f**) was observed when 1-bromo-2-methylnaphthalene was used as substrate of the reaction. Introducing a phenyl substituent at position 2 of the imidazopyridine (R^1 = H, R^2 = Ph) resulted in even more difficult coupling reactions. Only the 2,3-diphenyl- and 2-phenyl-3-naphthylimidazopyridines **9h** and **9i** were isolated in 59% and 80% yields, respectively, meaning that steric strains were too important to form derivatives **9j** and **9k** from 2-bromotoluene and 2-bromoanisole. Having the vision of the limits for this CH-coupling, we next attempted to generate the phosphine oxides **9b** and **9l−o** from imidazopyridine **6o** (R^1 = $Ph_2P(O)$, R^2 = H) and **6p** (R^1 = $Me_2P(O)$, R^2 = H). Similarly, to the naked imidazopyridine **7**, the reactions were successful for phenyl and 1-naphthyl bromides, and the resulting products **9b** and **9l−o** were obtained in yields ranging from 58% to 75%. Noticeably, the reaction carried out with 2-bromoanisole failed to give the corresponding anisyl derivative **9m**, probably due to steric reasons as mentioned before. For comparison, the unsubstituted analogue **9e** was only obtained in low yield (21%). Then the last series was formed from imidazopyridine **6e** (R^1 = $Ph_2P(O)$, R^2 = Ph), resulting in the formation of the desired coupling products **9p−s** with disparate success. Indeed, 2-phenylimidazopyridine **9p** and naphthyl derivative **9q** were obtained in 100% and 50% yields, respectively, while the reaction completely failed to provide either imidazopyridine derivative **9r** or **9s**.

In contrast with all the synthesized 2-arylimidazopyridines **9**, it can be noticed that imidazopyridine **9q** is the unique compound that exhibits diastereotopic atoms. Due to the complex proton NMR, this effect was only and clearly visible in ^{13}C NMR. All of the carbons of the diphenylphosphinyl group presented different chemical shifts. The magnitude of diastereotopic splitting appears small, with $\Delta\delta$ ranging from 0.01 to 0.13 ppm, and it mainly depends on that how far the stereogenic element from the considered diastereotopic atoms. These splittings are consistent with axial chirality. Compounds **9i**, **9l**, and even **9o** may also exhibit reduced rotation due to steric hindrance, but there is no eligible atom to observe such phenomena by NMR.

CONCLUSIONS

In conclusion, imidazo[1,2-*a*]pyridines are an exceptional and versatile platform for medicinal chemistry. These aza-heterocycles have played important roles in many FDA-approved drugs leading to various medicinally active series of molecules. In this context, we have developed a general and affordable approach to introduce diversity in dedicated positions. First, we demonstrated that Hirao coupling occurred straightforwardly in high yields at positions 3, 5, and 6 of various imidazopyridines leading to a wide range of substituted phosphonates, phosphinates, and phosphine oxides. For position 3, the coupling was impeded by the concurrent reduction of the 3-bromoimidazopyridine. If such a reaction was already observed, the reduced products were obtained sometimes almost quantitatively. In a second step, using a

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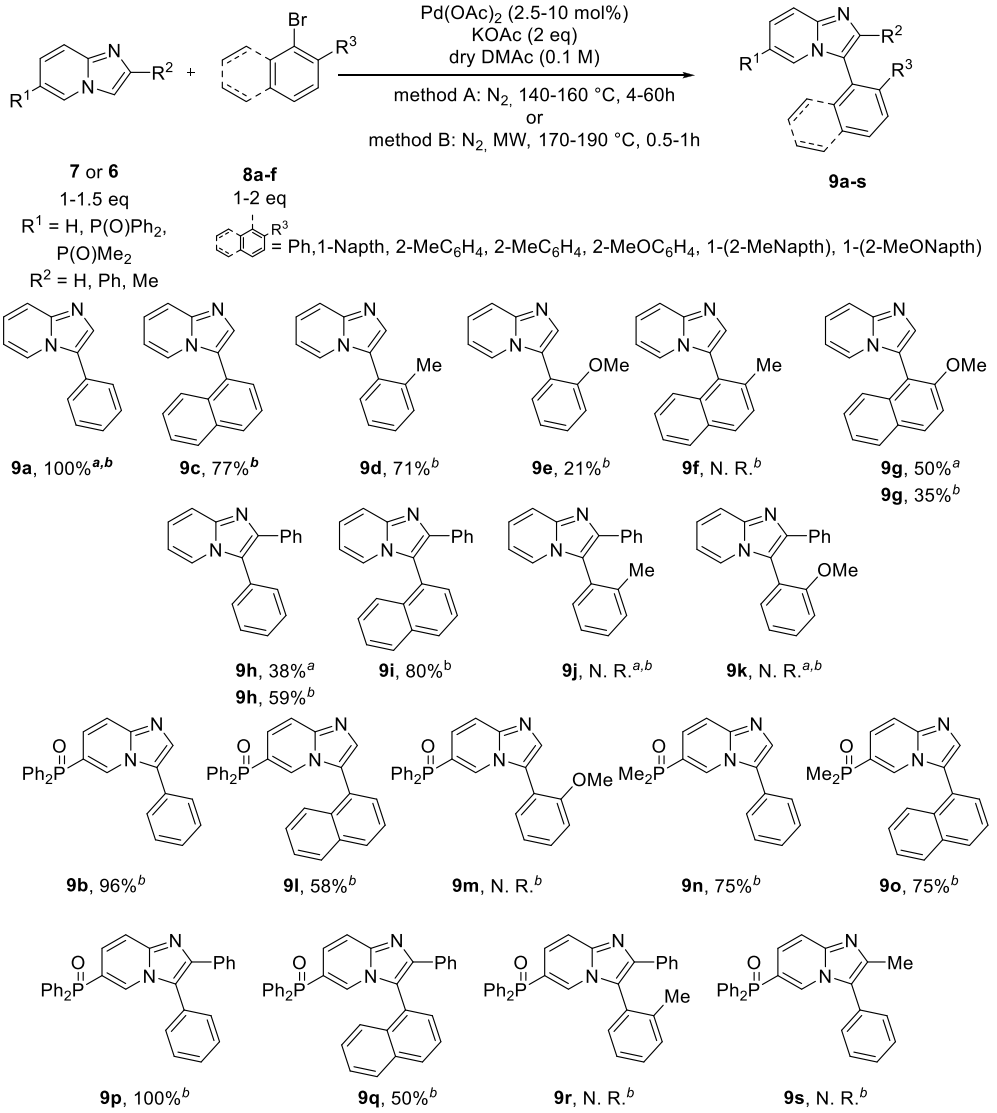
Scheme 4. Direct C−H Palladium-Coupling Reactions of Imidazopyridines with Aryl Bromides 9a−s[a]



[a]The reactions were stopped after the total consumption of reagent **7** or **6o**. Method A was carried out under thermal conditions. Method B was carried out under microwave heating. [b]NR = no reaction.

simple palladium catalytic system, direct CH coupling of phosphorylimidazopyridines with aryl halides was found to be effective and fully selective leading to several 3-aryl-substituted imidazopyridines in moderate to high yields. Although this CH-activation is highly selective, steric hindrance is a critical parameter and only some combinations of reactants were effective.

EXPERIMENTAL SECTION

Measurements. All experiments were carried out under nitrogen atmosphere. All commercially available materials were used as received without further purification. Imidazopyridines **7** and **1a−h** were, respectively, obtained from known procedures by reaction of 2-aminopyridine, 2-amino-5-bromopyridine, and 2-amino-6-bromopyridine with chloroacetaldehyde, chloroacetophenone, or chloroacetone.[19] Bromination at position 3 was accomplished using *N*-bromosuccinimide.[20] Microwave reactions were performed using CEM Discover apparatus using 10 and 35 mL sealed reactors for respectively small- and large-scale synthesis. Reactions were performed by maintaining the temperature to the set point. ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR spectra were measured on a Bruker Avance 400 (^{1}H: 400 MHz, ^{13}C: 100.61 MHz, ^{31}P: 161.97 MHz). Chemical shifts are reported in delta (δ) units, part per million (ppm) downfield from tetramethylsilane (TMS) relative to the residual deuterated solvent peaks. Coupling constants are reported in hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal. High-resolution mass spectroscopic (HRMS) analyses were measured on a Xevo G2 Q TOF spectrometer using the electrospray method by the Laboratoire de Mesures Physiques of the University of Montpellier.

Typical Procedure for the Preparation of 3-Phosphoryl-2-phenylimidazo[1,2-a]pyridines ***3a,b.*** Under nitrogen atmosphere, a mixture of 3-bromo-2-phenylimidazo[1,2-*a*]pyridine **1a** (110 mg, 0.403 mmol), phosphorus derivatives (**2a−f**) (0.366 mmol), Pd_2dba_3 (34 mg, 0.037 mmol), xantphos (42 mg, 0.073 mmol), and triethylamine (102 μL, 0.732 mmol) in dry toluene (3.6 mL) was stirred at reflux. After completion of the reaction indicated by TLC, the mixture was cooled to room temperature, filtered on Celite, and washed with ethyl acetate (20 mL), and the filtrate was concentrated under vacuum. The crude residue was then purified by flash chromatography (silica gel, cyclohexane/ethyl acetate (80/20 to 50/50)) to give the desired products (**3a,b**).

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*Diethyl (2-phenylimidazo[1,2-a]pyridin-3-yl)phosphonate (**3a**):* orange oil, (87 mg, yield = 72%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (dt, J_{HH} = 7.0, 1.2 Hz, 1H), 7.90−7.82 (m, 2H), 7.72 (ddt, J = 9.0, 1.8, 1.1 Hz, 1H), 7.48−7.35 (m, 4H), 6.95 (td, J = 6.9, 1.3 Hz, 1H), 4.18−4.04 (m, 2H), 3.91 (ddq, J = 10.0, 8.0, 7.1 Hz, 2H), 1.13 (td, J = 7.1, 0.7 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.2 (d, J = 17.6 Hz, C), 148.3 (d, J = 14.4 Hz, C), 133.8 (s, C), 129.9 (s, CH), 129.0 (s, CH), 128.6 (s, CH), 128.0 (s, CH), 127.6 (s, CH), 117.5 (s, CH), 113.6 (s, CH), 107.4 (d, J = 226.9 Hz, PC), 62.6 (d, J = 5.0 Hz, CH_2), 16.0 (d, J = 7.3 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 8.17; HR-MS (m/z) [M + H]$^+$ calcd for $C_{17}H_{20}N_2O_3P$ = 331.1212, found = 331.1215.

*Diphenyl (2-phenylimidazo[1,2-a]pyridin-3-yl)phosphine oxide (**3b**):* yellow oil, (39 mg, yield = 27%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (dt, J = 7.0, 1.2 Hz, 1H), 7.71 (dq, J = 9.0, 1.2 Hz, 1H), 7.56−7.50 (m, 4H), 7.42−7.30 (m, 3H), 7.29−7.20 (m, 4H), 7.13−7.07 (m, 2H), 7.02−6.99 (m, 1H), 6.96−6.88 (m, 2H), 6.77 (td, J = 6.9, 1.3 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.7 (d, J = 13.2 Hz, C), 148.1 (d, J = 10.2 Hz, C), 133.7 (s, C), 132.2 (d, J = 2.9 Hz, CH), 131.8 (d, J = 10.4 Hz, CH), 131.4 (d, J = 111.9 Hz, PC), 129.5 (d, J = 0.7 Hz, CH), 128.6 (d, J = 12.8 Hz, CH), 128.4 (d, J = 0.7 Hz, CH), 127.7 (s, CH), 127.7 (s, CH), 127.4 (s, CH), 117.5 (s, CH), 113.4 (s, CH), 110.6 (d, J = 123.1 Hz, PC); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 18.83; HR-MS (m/z) [M + H]$^+$ calcd for $C_{25}H_{20}N_2OP$ = 395.1308, found = 395.1327.

*Typical Procedure for the Preparation of 3-Phosphorylimidazo-[1,2-a]pyridines **3c,d**.* Under nitrogen atmosphere, a mixture of 3-bromoimidazo[1,2-*a*]pyridine **1b** (217 mg, 1.10 mmol), phosphorus derivatives (**2a, 2b**) (1.00 mmol), Pd_2dba_3 (92 mg, 0.1 mmol), xantphos (116 mg, 0.2 mmol), and triethylamine (280 μL, 2.00 mmol) in dry toluene (10 mL) was stirred at reflux. After completion of the reaction indicated by TLC, the mixture was cooled to room temperature, filtered on Celite, and washed with ethyl acetate (50 mL), and the filtrate was concentrated under vacuum. The crude residue was purified by flash chromatography (silica gel, cyclohexane/ethyl acetate (80/20 to 50/50)) to give the desired product (**3c,d**).

*Diethyl imidazo[1,2-a]pyridin-3-ylphosphonate (**3c**):* yellow oil (180 mg, yield = 71%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (bd, J = 6.9 Hz, 1H), 8.02 (s, 1H), 7.64 (ddt, J = 9.1, 2.2, 1.2 Hz, 1H), 7.29 (ddd, J = 9.1, 6.8, 1.3 Hz, 1H), 6.89 (td, J = 6.9, 1.2 Hz, 1H), 4.18−4.07 (m, 2H), 4.07−3.97 (m, 2H), 1.24 (td, J = 7.1, 0.6 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.0 (d, J = 13.5 Hz, C), 143.7 (d, J = 18.8 Hz, CH), 127.2 (s, CH), 127.1 (s, CH), 117.9 (d, J = 0.8 Hz, CH), 113.8 (s, CH), 111.7 (d, J = 229.1 Hz, PC), 62.7 (d, J = 5.2 Hz, CH_3), 16.2 (d, J = 6.8 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 7.05; HR-MS (m/z) [M + H]$^+$ calcd for $C_{11}H_{16}N_2O_3P$ = 255.0893, found = 255.0901.

*Imidazo[1,2-a]pyridin-3-yldiphenylphosphine oxide (**3d**):* yellow oil (153 mg, yield = 48%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (dt, J = 6.9, 1.4 Hz, 1H), 7.74−7.61 (m, 5H), 7.59−7.49 (m, 2H), 7.49−7.40 (m, 4H), 7.38 (s, 1H), 7.32−7.22 (m, 1H), 6.77 (tt, J = 6.8, 1.7 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.7 (d, J = 9.5 Hz, C), 143.9 (d, J = 15.5 Hz, CH), 132.6 (d, J = 2.9 Hz, CH), 131.7 (d, J = 10.6 Hz, CH), 131.1 (d, J = 111.9 Hz, PC), 128.9 (d, J = 12.8 Hz, CH), 127.5 (s, CH), 127.4 (s, CH), 118.0 (s, CH), 115.5 (d, J = 125.0 Hz, PC), 113.7 (s, CH); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 16.87; HR-MS (m/z) [M + H]$^+$ calcd for $C_{19}H_{16}N_2OP$ = 319.0995, found = 319.1007.

*Typical Procedure for the Preparation of 5-Phosphorylimidazo-[1,2-a]pyridines **5a−k**.* Under nitrogen atmosphere, a mixture of 5-bromoimidazo[1,2-*a*]pyridine **1c** (100 mg, 0.508 mmol), phosphorus derivatives (**2a−j**) (0.462 mmol), Pd_2dba_3 (42 mg, 0.046 mmol), xantphos (53 mg, 0.092 mmol), and triethylamine (129 μL, 0.924 mmol) in dry toluene (4.6 mL) was stirred at reflux. After completion of the reaction indicated by TLC, the mixture was cooled to room temperature, filtered on Celite, washed with ethyl acetate (20 mL), and concentrated under vacuum. The crude residue was then purified by flash chromatography (silica gel, dichloromethane/(dichloromethane/MeOH 10%) (90/10 to 70/30)) to give the desired product (**5a−j**).

*Diethyl imidazo[1,2-a]pyridin-5-ylphosphonate (**5a**):* orange oil (50 mg, yield = 43%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 1.3, 0.8 Hz, 1H), 7.77 (ddt, J = 9.1, 2.2, 1.0 Hz, 1H), 7.67 (d, J = 1.3 Hz, 1H), 7.50 (ddd, J = 11.6, 6.9, 1.2 Hz, 1H), 7.17 (ddd, J = 9.1, 6.9, 3.6 Hz, 1H), 4.20 (ddq, J = 10.2, 8.2, 7.1 Hz, 2H), 4.07 (ddq, J = 10.2, 8.5, 7.1 Hz, 2H), 1.27 (td, J = 7.1, 0.6 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.2 (d, J = 5.9 Hz, C), 134.2 (s, CH), 126.2 (d, J = 207.5 Hz, PC), 122.6 (d, J = 13.5 Hz, CH), 122.2 (d, J = 15.2 Hz, CH), 122.1 (s, CH), 63.3 (d, J = 5.3 Hz, CH_2), 16.2 (d, J = 6.3 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 7.71; HR-MS (m/z) [M + H]$^+$ calcd for $C_{11}H_{16}N_2O_3P$ = 255.0899, found = 255.0905.

*Diisopropyl imidazo[1,2-a]pyridin-5-ylphosphonate (**5c**):* orange oil (66 mg, yield = 51%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, J = 1.3, 0.8 Hz, 1H), 7.74 (ddt, J = 9.0, 2.1, 1.0 Hz, 1H), 7.65 (d, J = 1.3 Hz, 1H), 7.50 (ddd, J = 11.6, 6.9, 1.3 Hz, 1H), 7.16 (ddd, J = 9.1, 6.9, 3.5 Hz, 1H), 4.69 (dhept, J = 7.8, 6.2 Hz, 2H), 1.35 (d, J = 6.2 Hz, 6H), 1.10 (d, J = 6.2 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.2 (d, J = 5.9 Hz, C), 134.0 (CH), 127. Five (d, J = 207.3 Hz, PC), 122.7 (d, J = 13.5 Hz, CH), 121.8 (d, J = 12.7 Hz, CH), 121.8 (d, J = 3.0 Hz, CH), 114.2 (CH), 72.6 (d, J = 5.4 Hz, CH_2), 24.1 (d, J = 4.1 Hz, CH_3), 23.5 (d, J = 4.9 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 5.07; HR-MS (m/z) [M + H]$^+$ calcd for $C_{13}H_{20}N_2O_3P$ = 283.1212, found = 283.1218.

*Di-tert-butyl imidazo[1,2-a]pyridin-5-ylphosphonate (**5d**):* orange oil (75 mg, yield = 52%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, J = 1.3, 0.8 Hz, 1H), 7.70 (ddt, J = 9.0, 2.1, 1.0 Hz, 1H), 7.65 (d, J = 1.3 Hz, 1H), 7.47 (ddd, J = 11.9, 6.9, 1.3 Hz, 1H), 7.15 (ddd, J = 9.0, 6.9, 3.6 Hz, 1H), 1.40 (s, 18H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.3 (d, J = 5.8 Hz, C), 133.7 (S, CH), 131.0 (d, J = 211.4 Hz, PC), 123.0 (d, J = 13.9 Hz, CH), 121.0 (d, J = 3.1 Hz, CH), 120. Five (d, J = 13.6 Hz, CH), 114.1 (S, CH), 84.7 (d, J = 7.6 Hz, OC), 30.2 (d, J = 4.1 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ −2.32; HR-MS (m/z) [M + H]$^+$ calcd for $C_{15}H_{24}N_2O_3P$ = 311.1519, found = 311.1528.

*Imidazo[1,2-a]pyridin-5-yldiphenylphosphine oxide (**5e**):* pale brown solid (1.47 g, yield = 100% for 1.00 g of 5-bromoimidazo-[1,2-*a*]pyridine, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (t, J = 1.1 Hz, 1H), 7.80 (dddd, J = 9.1, 2.1, 1.2, 0.8 Hz, 1H), 7.76−7.67 (m, 4H), 7.67−7.60 (m, 3H), 7.57−7.48 (m, 4H), 7.10 (ddd, J = 9.3, 6.9, 2.5 Hz, 1H), 6.65 (ddd, J = 10.7, 6.9, 1.2 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.2 (d, J = 3.4 Hz, C), 134.5, (s, CH), 133.2 (d, J = 2.9 Hz, CH), 132.1 (d, J = 10.3 Hz, CH), 130.4 (d, J = 109.4 Hz, PC), 129.2 (d, J = 12.7 Hz, CH), 129.1 (d, J = 109.3 Hz, PC), 122.4 (d, J = 11.1 Hz, CH), 121.8 (d, J = 2.4 Hz, CH), 121.7 (d, J = 12.6 Hz, CH), 114.6 (s, CH); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 25.17; HR-MS (m/z) [M + H]$^+$ calcd for $C_{19}H_{16}N_2OP$ = 319.0995, found = 319.1006.

*Imidazo[1,2-a]pyridin-5-yldimethylphosphine oxide (**5f**):* brown solid (666 mg, yield = 68% for 1.00 g of 5-bromoimidazo[1,2-*a*]pyridine, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (t, J = 1.0 Hz, 1H), 7.80 (ddt, J = 8.9, 1.9, 1.0 Hz, 1H), 7.76 (d, J = 1.3 Hz, 1H), 7.21 (ddd, J = 9.1, 6.9, 2.5 Hz, 1H), 7.14 (ddd, J = 9.9, 6.9, 1.2 Hz, 1H), 1.94 (d, J = 13.3 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.4 (d, J = 3.4 Hz, C), 134.7 (s, CH), 131.8 (d, J = 101.8 Hz, PC), 122.8 (d, J = 10.4 Hz, CH), 121.6 (d, J = 2.4 Hz, CH), 117.7 (d, J = 11.6 Hz, CH), 113. Five (s, CH), 16.3 (d, J = 74.2 Hz, PCH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 31.02; MS (ESI+) m/z = [M + H]$^+$ calcd for $C_9H_{12}N_2OP$ = 195.0682, found = 195.0688.

*Ethyl imidazo[1,2-a]pyridin-5-yl(m-tolyl)phosphinate (**5g**):* brown oil, (100 mg, yield = 72%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (t, J = 1.0 Hz, 1H), 7.70 (ddt, J = 9.1, 2.0, 1.0 Hz, 1H), 7.59−7.49 (m, 3H), 7.43 (ddd, J = 10.0, 6.9, 1.2 Hz, 1H), 7.29−7.21 (m, 2H), 7.14 (ddd, J = 9.4, 6.9,

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2.7 Hz, 1H), 4.19 (ddq, J = 10.1, 8.1, 7.1 Hz, 1H), 4.07 (ddq, J = 10.0, 7.8, 7.0 Hz, 1H), 2.25 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.2 (d, J = 1.6 Hz, C), 138.7 (d, J = 13.5 Hz, C), 134.9 (s, CH), 133.4 (d, J = 3.0 Hz, CH), 131.9 (d, J = 17.3 Hz, CH), 131.9 (d, J = 10.4 Hz, CH), 130.5 (d, J = 142.5 Hz), 128.7 (d, J = 14.2 Hz, CH), 128.5 (d, J = 10.0 Hz, CH), 124.4 (d, J = 9.1 Hz, CH), 118.0 (d, J = 12.5 Hz, CH), 116.6 (d, J = 142.0 Hz, PC), 113.4 (s, CH), 61.5 (d, J = 5.9 Hz, CH_2), 21.3 (d, J = 0.9 Hz, CH_3), 16.5 (d, J = 6.5 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.63; MS (ESI+) m/z = $[M + H]^+$ calcd for $C_{16}H_{18}N_2O_2P$ = 301.1106, found = 301.1114.

*Ethyl imidazo[1,2-a]pyridin-5-yl(3-methoxyphenyl)phosphinate (**5h**):* orange oil (102 mg, yield = 70%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, J = 1.3, 0.7 Hz, 1H), 7.72 (dddd, J = 9.1, 2.0, 1.2, 0.8 Hz, 1H), 7.58 (d, J = 1.3 Hz, 1H), 7.44 (ddd, J = 10.1, 6.9, 1.2 Hz, 1H), 7.33−7.27 (m, 3H), 7.16 (ddd, J = 9.0, 6.9, 2.8 Hz, 1H), 7.03−7.00 (m, 1H), 4.22 (ddq, J = 10.1, 8.0, 7.1 Hz, 1H), 4.11 (ddq, J = 10.1, 7.9, 7.0 Hz, 1H), 3.72 (s, 3H), 1.33 (td, J = 7.1, 0.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.7 (d, J = 17.5 Hz, C), 145.2 (d, J = 4.4 Hz, C), 134.2 (s, CH), 130.2 (d, J = 16.5 Hz, CH), 129.1 (d, J = 145.1 Hz, PC), 129.0 (d, J = 146.9 Hz, PC), 123.6 (d, J = 10.5 Hz, CH), 122.7 (d, J = 11.2 Hz, CH), 121.8 (d, J = 2.7 Hz, CH), 121.4 (d, J = 11.0 Hz, CH), 119.1 (d, J = 3.0 Hz, CH), 116.5 (d, J = 12.1 Hz, CH), 113.5 (s, CH), 62.4 (d, J = 5.9 Hz, CH_2), 55.4 (s, OCH_3), 16.3 (d, J = 6.4 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 22.26; HR-MS (m/z) $[M + H]^+$ calcd for $C_{16}H_{18}N_2O_3P$ = 317.1055, found = 317.1065.

*Ethyl (3-fluorophenyl)(imidazo[1,2-a]pyridin-5-yl)phosphinate (**5i**):* brown oil (99 mg, yield = 72%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, J = 1.3, 0.7 Hz, 1H), 7.74 (dddd, J = 9.1, 2.0, 1.2, 0.8 Hz, 1H), 7.59 (d, J = 1.3 Hz, 1H), 7.53 (ddt, J = 12.8, 7.6, 1.2 Hz, 1H), 7.48 (ddd, J = 9.9, 6.8, 1.2 Hz, 1H), 7.50−7.43 (m, 1H), 7.38 (ddddd, J = 8.1, 7.5, 5.1, 4.6, 0.4 Hz, 1H), 7.21−7.14 (m, 2H), 4.24 (ddq, J = 10.1, 8.0, 7.1 Hz, 1H), 4.12 (ddq, J = 10.1, 8.0, 7.0 Hz, 1H), 1.34 (td, J = 7.0, 0.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.5 (dd, J = 251.1, 19.7 Hz, CF), 145.1 (s, C), 134.4 (s, CH), 131.4 (dd, J = 145.9, 5.9 Hz, PC), 131.02 (dd, J = 16.3, 7.5 Hz, CH), 128.4 (d, J = 148.5 Hz, PC), 127.2 (dd, J = 10.3, 3.3 Hz, CH), 122.6 (d, J = 11.2 Hz, CH), 122.1 (d, J = 2.7 Hz, CH), 121.7 (d, J = 10.8 Hz, CH), 120.5 (dd, J = 21.1, 2.9 Hz, CH), 118.28 (dd, J = 22.6, 11.4 Hz, CH), 113.35 (s, CH), 62.70 (d, J = 5.9 Hz, CH_2), 16.29 (d, J = 6.3 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 20.34 (d, J = 7.4 Hz); MS (ESI+) m/z = $[M + H]^+$ calcd for $C_{15}H_{15}FN_2O_2P$ = 305.0855, found = 305.0866.

*Ethyl imidazo[1,2-a]pyridin-5-yl(3-(trifluoromethyl)phenyl)-phosphinate (**5j**):* brown oil (125 mg, yield = 76%, cyclohexane/ethyl acetate (80/20 to 50/50)); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 13.1 Hz, 1H), 8.02 (s, 1H), 7.92 (dd, J = 12.8, 7.7 Hz, 1H), 7.79−7.72 (m, 2H), 7.60 (d, J = 1.3 Hz, 1H), 7.54 (td, J = 7.8, 3.4 Hz, 1H), 7.50 (ddd, J = 10.1, 6.9, 1.2 Hz, 1H), 7.19 (ddd, J = 9.0, 6.9, 2.9 Hz, 1H), 4.27 (ddq, J = 10.1, 8.1, 7.1 Hz, 1H), 4.16 (ddq, J = 10.1, 8.1, 7.0 Hz, 1H), 1.36 (td, J = 7.1, 0.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.2 (d, J = 4.1 Hz, C), 134.7 (dq, J = 10.9, 1.3 Hz, CH), 134.55 (s, CH), 131.5 (qd, J = 33.0, 14.2 Hz, C), 130.51 (d, J = 146.6 Hz, PC), 129.88 (qd, J = 3.4, 3.4 Hz, CH), 129.60 (d, J = 13.8 Hz, CH), 128.25 (dq, J = 11.5, 3.8 Hz, CH), 128.14 (d, J = 148.9 Hz, PC), 127.4 (qd, J = 272.9, 2.2 Hz, CF_3), 122.67 (d, J = 11.3 Hz, CH), 122.30 (d, J = 2.7 Hz, CH), 121.90 (d, J = 11.0 Hz, CH), 113.27 (s, CH), 62.94 (d, J = 5.9 Hz, CH_2), 16.30 (d, J = 6.3 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 20.13; MS (ESI+) m/z = $[M + H]^+$ calcd for $C_{16}H_{15}F_3N_2O_2P$ = 355.0823, found = 355.0829.

*Typical Procedure for the Preparation of 6-Phosphoryl-2-phenylimidazo[1,2-a]pyridines **6a−j**.* Under nitrogen atmosphere, a mixture of 6-bromo-2-phenylimidazo[1,2-*a*]pyridine **1f** (110 mg, 0.403 mmol), P−H derivatives (**2a−j**) (0.366 mmol), Pd_2dba_3 (34 mg, 0.037 mmol), xantphos (42 mg, 0.073 mmol), and triethylamine (102 μL, 0.732 mmol) in dry toluene (3.6 mL) was stirred at reflux. After completion of the reaction indicated by TLC, the mixture was cooled to room temperature, filtered on Celite, and washed with ethyl acetate (20 mL), and the filtrate was concentrated under vacuum. The crude residue was then purified by flash chromatography (silica gel, cyclohexane/ethyl acetate 50/50) to give the desired products (**6a−j**).

*Diethyl (2-phenylimidazo[1,2-a]pyridin-6-yl)phosphonate (**6a**):* orange oil (142 mg, yield = 100%, cyclohexane/ethyl acetate 50/50). Large-scale synthesis was accomplished starting from imidazopyridine **1f** (1.1 g, 3.66 mmol), diethyl phosphite **2a** (429 μL, 3.33 mmol), Pd_2dba_3 (305 mg, 0.33 mmol), xantphos (385 mg, 0.667 mmol), and triethylamine (928 μL, 6.67 mmol) in dry toluene (35 mL) affording 1.11 g of **6a** (yield = 100%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (ddd, J = 11.2, 1.5, 1.0 Hz, 1H), 7.99−7.94 (m, 2H), 7.93 (d, J = 0.7 Hz, 1H), 7.72 (ddt, J = 9.2, J = 3.4, J = 0.9 Hz, 1H), 7.48−7.42 (m, 2H), 7.39−7.32 (m, 2H), 4.27−4.06 (m, 4H), 1.35 (td, J = 7.1, 0.6 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.1 (s, C), 145.5 (d, J = 1.5 Hz, C), 132.8 (s, C), 131.9 (d, J = 19.8 Hz, CH), 129.0 (s, CH), 128.8 (s, CH), 126.4 (s, CH), 125.3 (d, J = 7.2 Hz, CH), 117.7 (d, J = 13.9 Hz, CH), 113.74 (d, J = 198.0 Hz, PC), 108.9 (s, CH), 62.8 (d, J = 5.4 Hz, CH_2), 16.5 (d, J = 6.4 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 16.28; HR-MS (m/z) $[M + H]^+$ calcd for $C_{17}H_{20}N_2O_3P$ = 331.1212, found = 331.1216.

*Dibenzyl (2-phenylimidazo[1,2-a]pyridin-6-yl)phosphonate (**6b**):* yellow solid (59 mg, yield = 36%, cyclohexane/ethyl acetate 50/50); ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, J = 11.4, 1.5, 1.0 Hz, 1H), 7.97−7.94 (m, 2H), 7.85 (d, J = 0.6 Hz, 1H), 7.60 (ddt, J = 9.3, 3.6 Hz, 0.9 Hz, 1H), 7.48−7.42 (m, 2H), 7.40−7.27 (m, 2H), 5.15 (dd, J = 11.7, 8.6 Hz, 1H), 5.10 (dd, J = 11.7, 8.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.5 (s, C), 145.7 (d, J = 1.6 Hz, C), 135.8 (d, J = 6.5 Hz, C), 133.2 (s, C), 132.0 (d, J = 20.2 Hz, CH), 129.0 (s, CH), 128.8 (s, CH), 128.8 (s, CH), 128.7 (s, CH), 128.3 (s, CH), 126.4 (s, CH), 124.8 (d, J = 7.6 Hz, CH), 117.7 (d, J = 14.3 Hz, CH), 113.1 (d, J = 200.6 Hz, PC), 108.9 (s, CH), 68.3 (d, J = 5.3 Hz, CH_2); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 17.49; HR-MS (m/z) $[M + H]^+$ calcd for $C_{27}H_{24}N_2O_3P$ = 455.1525, found = 455.1526.

*Diisopropyl (2-phenylimidazo[1,2-a]pyridin-6-yl)phosphonate (**6c**):* brown solid (118 mg, yield = 90%, cyclohexane/ethyl acetate 50/50); ^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (ddd, J = 11.2, 1.5, J = 1.0 Hz, 1H), 7.99−7.93 (m, 2H), 7.91 (d, J = 0.7 Hz, 1H), 7.66 (ddt, J = 9.2, J = 3.4, J = 0.9 Hz, 1H), 7.49−7.42 (m, 2H), 7.39−7.30 (m, 2H), 4.73 (dhept, J = 8.0, 6.2 Hz, 2H), 1.41 (d, J = 6.2 Hz, 6H), 1.26 (d, J = 6.2 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.4 (s, C), 145.7 (d, J = 1.6 Hz, C), 133.2 (s, C), 131.7 (d, J = 19.9 Hz, CH), 129.0 (s, CH), 128.6 (s, CH), 126.3 (s, CH), 125.2 (d, J = 7.3 Hz, CH), 117.7 (d, J = 13.8 Hz, CH), 114.8 (d, J = 198.5 Hz, PC), 108.9 (s, CH), 71.6 (d, J = 5.5 Hz, CH), 24.2 (d, J = 4.0 Hz, CH_3), 24.0 (d, J = 4.9 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 14.17; HR-MS (m/z) $[M + H]^+$ calcd for $C_{19}H_{24}N_2O_3P$ = 359.1525, found = 359.1528.

*Di-tert-butyl (2-phenylimidazo[1,2-a]pyridin-6-yl)phosphonate (**6d**):* orange oil (135 mg, yield = 89%, cyclohexane/ethyl acetate 50/50); ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (ddd, J = 11.4, 1.5, 1.0 Hz, 1H), 7.97−7.94 (m, 2H), 7.90 (d, J = 0.7 Hz, 1H), 7.63 (ddt, J = 9.2, 3.3, 0.9 Hz, 1H), 7.47−7.42 (m, 2H), 7.37−7.30 (m, 2H), 1.50 (d, J = 0.4 Hz, 18H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.1 (s, C), 145.7 (d, J = 1.5 Hz, C), 133.4 (s, C), 130.9 (d, J = 20.7 Hz, CH), 128.9 (s, CH), 128.4 (s, CH), 126.3 (s, CH), 125.7 (d, J = 6.6 Hz, CH), 118.7 (d, J = 203.2 Hz, PC), 117.3 (d, J = 13.8 Hz, CH), 108.9 (s, CH), 83.5 (d, J = 7.7 Hz, C), 30.6 (d, J = 4.1 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 7.10; HR-MS (m/z) $[M + H]^+$ calcd for $C_{21}H_{28}N_2O_3P$ = 387.1838, found = 387.1834.

*Diphenyl (2-phenylimidazo[1,2-a]pyridin-6-yl)phosphine oxide (**6e**):* yellow powder (115 mg, yield = 80%, cyclohexane/ethyl acetate 50/50). Large-scale synthesis was accomplished starting from imidazopyridine **1f** (2.00 g, 7.32 mmol), diphenylphosphine oxide **2b** (673 mg, 6.67 mmol), Pd_2dba_3 (606 mg, 0.667 mmol), xantphos (772 mg, 1.33 mmol), and triethylamine (1.90 mL, 13.3 mmol) in dry toluene (50 mL) affording 2.44 g of **6e** (yield = 93%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (ddd, J = 9.9, 1.6 Hz, 1.0 Hz, 1H), 7.97−7.92 (m, 2H), 7.90 (d, J = 0.7 Hz, 1H), 7.76−7.70 (m, 4H), 7.65 (ddt, J = 9.3, 2.6, 0.9 Hz, 1H), 7.63−7.58 (m, 2H), 7.54−7.49 (m, 4H), 7.47−7.42 (m, 2H), 7.37−7.33 (m, 1H), 7.16 (td, J = 9.0, 1.6 Hz, 1H);

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$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.6 (s, C), 145.5 (d, J = 1.4 Hz, C), 133.2 (s, C), 132.7 (d, J = 2.8 Hz, CH), 132.1 (d, J = 10.2 Hz, CH), 131.8 (d, J = 15.8 Hz, CH), 131.7 (d, J = 107.3 Hz, PC), 129.0 (d, J = 12,4 Hz, CH), 129.0 (s, CH), 128.6 (s, CH), 126.4 (s, CH), 125.2 (d, J = 9.3 Hz, CH), 117.6 (d, J = 11.8 Hz, CH), 117.3 (d, J = 108.2 Hz, PC), 109.1 (s, CH); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 26.84; HR-MS (m/z) $[M + H]^+$ calcd for $C_{25}H_{20}N_2OP$ = 395.1313, found = 395.1317.

*Dimethyl (2-phenylimidazo[1,2-a]pyridin-6-yl)phosphine oxide (**6f**):* green powder (25 mg, yield = 21%, cyclohexane/ethyl acetate 50/50); ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (dt, J = 9.9, 1.3 Hz, 1H), 7.97−7.91 (m, 3H), 7.66 (dd, J = 9.5, 2.4 Hz, 1H), 7.45−7.38 (m, 2H), 7.36−7.30 (m, 1H), 7.11 (td, J = 9.0, 1.5 Hz, 1H), 1.76 (d, J = 13.2 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.3 (s, C), 145.4 (d, J = 1.3 Hz, C), 133.1 (s, C), 130.5 (d, J = 14.3 Hz, CH), 128.9 (s, CH), 128.5 (s, CH), 126.3 (s, CH), 122.9 (d, J = 10.5 Hz, CH), 118.9 (d, J = 102.2 Hz, PC), 117.9 (d, J = 11.7 Hz, CH), 109.2 (s, CH), 18.2(d, J = 73.0 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 33.82; HR-MS (m/z) nd.

*Ethyl (2-phenylimidazo[1,2-a]pyridin-6-yl)(m-tolyl)phosphinate (**6g**):* orange solid (111 mg, yield = 80%, cyclohexane/ethyl acetate 50/50); ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (dt, J = 10.0, 1.3 Hz, 1H), 7.97−7.93 (m, 2H), 7.92 (d, J = 0.5 Hz, 1H), 7.71−7.59 (m, 3H), 7.47−7.41 (m, 2H), 7.39−7.32 (m, 3H), 7.29 (td, J = 9.2, J = 1.5 Hz, 1H), 4.27−4.07 (m, 2H), 2.39 (d, J = 0.7 Hz, 3H), 1.41 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147.5 (s, C), 145.6 (d, J = 1.4 Hz, C), 138. Nine (d, J = 13.5 Hz, C), 133.6 (d, J = 3.0 Hz, CH), 133.2 (s, C), 132.1 (d, J = 10.3 Hz, CH), 131.7 (d, J = 17.4 Hz, CH), 130.6 (d, J = 142.6 Hz, PC), 128.9 (s, CH), 128.8 (d, J = 14.2 Hz, CH), 128.6 (d, J = 10.1 Hz, CH), 128.6 (s, CH), 126.3 (s, CH), 124.9 (d, J = 9.0 Hz, CH), 117.8 (d, J = 12.6 Hz, CH), 116.7 (d, J = 142.0 Hz, PC), 109.0 (s, CH), 61.7 (d, J = 5.8 Hz, CH_2), 21.5 (s, CH_3), 16.7 (d, J = 6.7 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 29.22; HR-MS (m/z) $[M + H]^+$ calcd for $C_{22}H_{22}N_2O_2P$ = 377.1419, found = 377.1422.

*Ethyl (3-methoxyphenyl)(2-phenylimidazo[1,2-a]pyridin-6-yl)-phosphinate (**6h**):* orange oil (128 mg, yield = 89%, cyclohexane/ethyl acetate 50/50); ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (ddd, J = 10.1, 1.5, 1.0 Hz, 1H), 7.97−7.93 (m, 2H), 7.92 (d, J = 0.7 Hz, 1H), 7.64 (ddt, J = 9.2, 3.1, 0.9 Hz, 1H), 7.47−7.32 (m, 6H), 7.29 (td, J = 9.3, 1.5 Hz, 1H), 7.11−7.06 (m, 1H), 4.23−4.09 (m, 2H), 3.84 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.8 (d, J = 16.9 Hz, C), 147.5, 145.6 (d, J = 1.5 Hz, C), 133.2 (s, C), 132.1 (d, J = 142.0 Hz, PC), 131.7 (d, J = 17.5 Hz, CH), 130.3 (d, J = 15.9 Hz, CH), 129.0 (s, CH), 128.6 (s, CH), 126.3 (s, CH), 124.8 (d, J = 9.0 Hz, CH), 123.7 (d, J = 9.9 Hz, CH), 118.8 (d, J = 2.9 Hz, CH), 117.8 (d, J = 12.6 Hz, CH), 116.5 (d, J = 143.2 Hz, PC), 116.5 (d, J = 11.5 Hz, CH), 109.0 (s, CH), 61. Eight (d, J = 5.8 Hz, CH_2), 55.6 (s, OCH_3), 16.7 (d, J = 6.6 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 28.84; HR-MS (m/z) $[M + H]^+$ calcd for $C_{22}H_{22}N_2O_3P$ = 393.1368, found = 393.1372.

*Ethyl (3-fluorophenyl)(2-phenylimidazo[1,2-a]pyridin-6-yl)-phosphinate (**6i**):* brown oil (106 mg, yield = 76%, cyclohexane/ethyl acetate 50/50); ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (ddd, J = 10.1, 1.5, 1.0 Hz, 1H), 7.97−7.94 (m, 2H), 7.93 (d, J = 0.7 Hz, 1H), 7.68−7.59 (m, 2H), 7.56 (dddd, J = 13.6, 8.4, 2.7, 1.2 Hz, 1H), 7.51−7.42 (m, 3H), 7.38−7.33 (m, 1H), 7.29−7.22 (m, 3H), 4.25−4.10 (m, 2H), 1.42 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.7 (dd, J = 250.5, 19.1 Hz, C), 147.7 (s, C), 145.6 (d, J = 1.5 Hz, C), 133.6 (dd, J = 142.9, 5.8 Hz, PC), 133.1 (s, C), 131.9 (d, J = 17.5 Hz, CH), 131.0 (dd, J = 15.8, 7.4 Hz, CH), 129.0 (s, CH), 128.7 (s, CH), 127.3 (dd, J = 9.8, 3.3 Hz, CH), 126.4 (s, CH), 124.5 (d, J = 9.1 Hz, CH), 120.0 (dd, J = 21.2, 2.8 Hz, CH), 118.5 (dd, J = 22.4, 10.8 Hz, CH), 118.0 (d, J = 12.7 Hz, CH), 115.9 (d, J = 144.3 Hz, PC), 109.1 (s, CH), 62.0 (d, J = 5.8 Hz, CH_2), 16.6 (d, J = 6.5 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 27.16 (d, J = 7.2 Hz); HR-MS (m/z) $[M + H]^+$ calcd for $C_{21}H_{19}FN_2O_2P$ = 381.1168, found = 381.1170.

*Ethyl (2-phenylimidazo[1,2-a]pyridin-6-yl)(3-(trifluoromethyl)-phenyl)phosphinate (**6j**):* orange oil (156 mg, yield = 99%, cyclohexane/ethyl acetate 50/50); ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (ddd, J = 10.2, 1.5, 1.0 Hz, 1H), 8.13 (dddt, J = 12.7, 2.1, 1.4, 0.7 Hz, 1H), 8.07−7.98 (m, 1H), 7.98−7.93 (m, 3H), 7.82 (ddtd, J = 7.9, 1.9, 1.2, 0.6 Hz, 1H), 7.70−7.60 (m, 2H), 7.49−7.41 (m, 2H), 7.40−7.33 (m, 1H), 7.25 (td, J = 9.3, 1.5 Hz, 1H), 4.30−4.11 (m, 2H), 1.43 (td, J = 7.1, 0.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 147. Eight (s, C), 145.6 (d, J = 1.5 Hz, C), 134.8 (d, J = 10.1 Hz, CH), 133.1 (s, C), 132.7 (d, J = 143.8 Hz, PC), 132.1 (d, J = 17.5 Hz, CH), 131.5 (dd, J = 33.1, 13.9 Hz, C), 129.6 (d, J = 13.3 Hz, CH), 129.4 (quint, J = 3.3, 3.3 Hz, CH), 129.0 (s, CH), 128.7 (s, CH), 128.4 (dq, J = 11.0, 3.6 Hz, CH), 126.4 (s, CH), 124.3 (d, J = 9.1 Hz, CH), 118.1 (d, J = 12.7 Hz, CH), 115.5 (d, J = 144.5 Hz, PC), 109.1 (s, CH), 62.2 (d, J = 5.9 Hz, CH_3), 16.7 (d, J = 6.5 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 26.91 (q, J = 1.0 Hz); HR-MS (m/z) $[M + H]^+$ calcd for $C_{22}H_{19}F_3N_2O_2P$ = 431.1136, found = 431.1137.

*Typical Procedure for the Preparation of 6-Phosphorylimidazo-[1,2-a]pyridines **6k−t**.* Under nitrogen atmosphere, a mixture of 6-bromoimidazo[1,2-*a*]pyridine (**1e**) (100 mg, 0.508 mmol), phosphorus derivatives (**2a−j**) (0.462 mmol), Pd_2dba_3 (42 mg, 0.046 mmol), xantphos (53 mg, 0.092 mmol), and triethylamine (129 μL, 0.924 mmol) in dry toluene (4.6 mL) was stirred at reflux. After completion of the reaction indicated by TLC, the mixture was cooled to room temperature, filtered on Celite, and washed with ethyl acetate (20 mL), and the filtrate was concentrated under vacuum. The crude residue was then purified by flash chromatography (silica gel, dichloromethane/(dichloromethane/MeOH 10%) (90/10 to 70/30)) to give the desired products **(6k-t).**

*Diethyl imidazo[1,2-a]pyridin-6-ylphosphonate (**6k**):* brown oil (82 mg, yield = 70%, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)). Large-scale synthesis was accomplished starting from imidazopyridine **1e** (1.00 g, 5.08 mmol), diethyl phosphite **2a** (595 μL, 4.62 mmol), Pd_2dba_3 (211 mg, 0.231 mmol), xantphos (267 mg, 0.462 mmol), and triethylamine (1.30 mL, 9.24 mmol) in dry toluene (50 mL) affording 1.19 g of **6k** (yield = 100%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (ddd, J = 11.3, 1.5, 1.0 Hz, 1H), 7.63−7.54 (m, 3H), 7.24 (ddd, J = 10.1, 9.2, J = 1.5 Hz, 1H), 4.16−3.96 (m, 4H), 1.25 (td, J = 7.1, 0.6 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.3 (s, CH), 134.9 (s, CH), 132.1 (d, J = 19.7 Hz, CH), 124.4 (d, J = 7.6 Hz, CH), 118.0 (d, J = 14.0 Hz, CH), 113.3 (s, CH), 113.2 (d, J = 198.3 Hz, PC), 62.5 (d, J = 5.4 Hz, CH_2), 16.3 (d, J = 6.5 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 16.44; HR-MS (m/z) $[M + H]^+$ calcd for $C_{11}H_{16}N_2O_3P$ = 255.0899, found = 255.0904.

*Diisopropyl imidazo[1,2-a]pyridin-6-ylphosphonate (**6m**):* brown oil (122 mg, yield = 94%, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)); ^1H NMR (400 MHz, DMSO-d_6) δ 9.04 (dt, J = 11.3, 1.3 Hz, 1H), 8.13 (s, 1H), 7.69−7.66 (m, 2H), 7.27 (td, J = 9.6, 1.6 Hz, 1H), 4.59 (dhept, J = 8.0 Hz, 6.1 Hz, 2H), 1.29 (d, J = 6.2 Hz, 6H), 1.17 (d, J = 6.2 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 144.3 (s, C), 134.3 (s, CH), 132.7 (d, J = 20.5 Hz, CH), 124.2 (d, J = 7.9 Hz, CH), 117.2 (d, J = 14.0 Hz, CH), 114.4 (s, CH), 113.6 (d, J = 196.9 Hz, C), 70.6 (d, J = 5.5 Hz, CH), 23.7 (d, J = 4.0 Hz, CH_3), 23.5 (d, J = 4.9 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, DMSO-d_6) δ 14.38; HR-MS (m/z) $[M + H]^+$ calcd for $C_{13}H_{20}N_2O_3P$ = 283.1212, found = 283.1218.

*Di-tert-butyl imidazo[1,2-a]pyridin-6-ylphosphonate (**6n**):* brown oil (75 mg, yield = 50%, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)); ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, J = 11.5 Hz, 1H), 7.66 (s, 1H), 7.64−7.58 (m, 2H), 7.31 (td, J = 10.4, 1.5 Hz, 1H), 1.47 (s, 18H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.4 (s, C), 134.7 (s, CH), 131.1 (d, J = 20.7 Hz, CH), 125.4 (d, J = 6.6 Hz, CH), 118.4 (d, J = 202.6 Hz, PC), 117.7 (d, J = 13.8 Hz, CH), 113.3 (s, CH), 83.4 (d, J = 7.8 Hz, C), 30.5 (d, J = 4.1 Hz, CH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 7.05; HR-MS (m/z) $[M + H]^+$ calcd for $C_{15}H_{24}N_2O_3P$ = 311.1519, found = 311.1526

*Imidazo[1,2-a]pyridin-6-yldiphenylphosphine oxide (**6o**):* Large-scale synthesis was accomplished starting from imidazopyridine **1e** (500 mg, 2.54 mmol), diphenylphosphine oxide **2b** (467 mg, 2.31 mmol), Pd_2dba_3 (212 mg, 0.231 mmol), xantphos (267 mg, 0.462 mmol), and triethylamine (0.644 mL, 4.62 mmol) in dry toluene (25

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mL) affording an orange powder (667 mg, yield = 91%, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (ddd, J = 10.0, 1.6, 1.0 Hz, 1H), 7.75−7.67 (m, 5H), 7.67−7.62 (m, 2H), 7.62−7.56 (m, 2H), 7.53−7.47 (m, 4H), 7.15 (ddd, J = 9.4, 8.7, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.3 (d, J = 1.4 Hz, C), 135.3 (s, CH), 132.7 (d, J = 2.8 Hz, CH), 132.2 (s, CH), 132.1 (d, J = 10.2 Hz, CH), 131.7 (s, J = 12.4 Hz, PC), 129.0 (d, J = 12.4 Hz, CH), 124.9 (d, J = 9.4 Hz, CH), 118.1 (d, J = 11.8 Hz, CH), 117.4 (d, J = 107.9 Hz, PC), 113.6 (s, CH); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 26.74; MS (ESI+) m/z = [M + H] $^{+}$ calcd for $C_{19}H_{16}N_2OP$ = 319.1000, found = 319.1006.

*Imidazo[1,2-a]pyridin-6-yldimethylphosphine oxide (**6p**):* brown powder (360 mg, yield = 77% for 500 mg of 6-bromoimidazo[1,2-*a*]pyridine, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (ddd, J = 9.9, 1.6, 1.0 Hz, 1H), 7.75−7.62 (m, 3H), 7.10 (ddd, J = 9.3, 8.7, 1.6 Hz, 1H), 1.77 (d, J = 13.2 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145. Two (d, J = 1.1 Hz, C), 135.2 (s, CH), 130.9 (d, J = 13.9 Hz, CH), 122.4 (d, J = 10.6 Hz, CH), 118.8 (d, J = 101.7 Hz, PC), 118. Six (d, J = 11.6 Hz, CH), 113.6 (s, CH), 18.2 (d, J = 73.1 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 32.88; MS (ESI+) m/z = [M + H]$^{+}$ calcd for $C_9H_{12}N_2OP$ = 195.0687, found = 195.0690.

*Ethyl imidazo[1,2-a]pyridin-6-yl(m-tolyl)phosphinate (**6q**):* orange oil (138 mg, yield = 99%, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (dt, J = 10.1, 1.3 Hz, 1H), 7.63−7.50 (m, 5H), 7.33−7.24 (m, 2H), 7.22 (td, J = 9.2, 1.5 Hz, 1H), 4.16−3.97 (m, 2H), 2.29 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.1 (d, J = 1.2 Hz, C), 138.6 (d, J = 13.5 Hz, C), 134.8 (s, CH), 133.4 (d, J = 3.0 Hz, CH), 131.9 (d, J = 17.1 Hz, CH), 131.8 (d, J = 10.5 Hz, CH), 130.4 (d, J = 142.5 Hz, PC), 128.6 (d, J = 14.2 Hz, CH), 128.4 (d, J = 10.1 Hz, CH), 124.3 (d, J = 9.0 Hz, CH), 117.9 (d, J = 12.5 Hz, CH), 116.5 (d, J = 142.0 Hz, PC), 113.4 (s, CH), 61.4 (d, J = 5.8 Hz, CH_2), 21.3 (s, CH_3), 16.4 (d, J = 6.5 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 29.16; MS (ESI+) m/z = [M + H]$^{+}$ calcd for $C_{16}H_{18}N_2O_2P$ = 301.1106, found = 301.1117

*Ethyl imidazo[1,2-a]pyridin-6-yl(3-methoxyphenyl)phosphinate (**6r**):* green oil (45 mg, yield = 31%, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (ddd, J = 10.2, 1.5, 1.0 Hz, 1H), 7.67−7.60 (m, 2H), 7.60 (ddt, J = 9.2, 3.0, 0.9 Hz, 1H), 7.39−7.29 (m, 3H), 7.25 (td, J = 9.2, 1.5 Hz, 1H), 7.07−6.99 (m, 1H), 4.16−4.06 (m, 2H), 3.78 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.7 (d, J = 16.9 Hz, C), 145.2 (s, C), 135.0 (s, CH), 131.9 (d, J = 142.0 Hz, PC), 131.9 (d, J = 17.5 Hz, CH), 130.1 (d, J = 15.9 Hz, CH), 124.4 (d, J = 9.0 Hz, CH), 123.6 (d, J = 9.9 Hz, CH), 118.7 (d, J = 2.9 Hz, CH), 118.1 (d, J = 12.5 Hz, CH), 116.5 (d, J = 143.1 Hz, PC), 116.4 (d, J = 11.5 Hz, CH), 113.4 (s, CH), 61.7 (d, J = 5.8 Hz, CH_2), 55.5 (s, CH_3), 16.5 (d, J = 6.6 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 28.78; HR-MS (m/z) [M + H]$^{+}$ calcd for $C_{16}H_{18}N_2O_3P$ = 317.1055, found = 317.1063

*Ethyl (3-fluorophenyl)(imidazo[1,2-a]pyridin-6-yl)phosphinate (**6s**):* green oil (118 mg, yield = 86%, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (ddd, J = 10.2, 1.6, 1.0 Hz, 1H), 7.63 (bs, 2H), 7.60−7.51 (m, 2H), 7.51−7.43 (m, 1H), 7.50−7.43 (m, 1H), 7.19 (td, J = 9.2, 1.5 Hz, 1H), 7.19−7.12 (m, 1H), 4.17−3.99 (m, 2H), 1.33 (td, J = 7.0, 0.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.5 (dd, J = 250.5, 19.0 Hz, C), 145.1 (s, C), 135.1 (s, CH), 133.4 (dd, J = 142.7, 5.8 Hz, PC), 132.2 (d, J = 17.4 Hz, CH), 130.8 (dd, J = 15.8, 7.4 Hz, CH), 127.1 (dd, J = 9.7, 3.3 Hz, CH), 124.0 (d, J = 9.2 Hz, CH), 119.7 (dd, J = 21.1, 2.8 Hz, CH), 118.2 (dd, J = 22.3, 10.9 Hz, CH), 118.2 (d, J = 12.7 Hz, CH), 115.7 (d, J = 144.3 Hz, PC), 113.5 (s, CH), 61.8 (d, J = 5.9 Hz, CH_2), 16.4 (d, J = 6.5 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 27.09 (d, J = 7.1 Hz); MS (ESI +) m/z = [M + H]$^{+}$ calcd for $C_{15}H_{15}FN_2O_2P$ = 305.0855, found = 305.0862.

*Ethyl imidazo[1,2-a]pyridin-6-yl(3-(trifluoromethyl)phenyl)-phosphinate (**6t**):* green oil (153 mg, yield = 93%, dichloromethane/(dichloromethane 90/MeOH 10) (90/10 to 70/30)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (dt, J = 10.2, 1.3 Hz, 1H), 8.04 (d, J = 12.6 Hz, 1H), 7.93 (dd, J = 12.2, 7.6 Hz, 1H), 7.74−7.60 (m, 3H), 7.60−7.51 (m, 2H), 7.18 (td, J = 9.3, 1.6 Hz, 1H), 4.19−4.00 (m, 2H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.1 (d, J = 1.4 Hz, C), z135.1 (s, CH), 134.6 (dq, J = 10.2, 1.3 Hz, CH), 132.5 (d, J = 143.5 Hz, PC), 132.4 (d, J = 17.5 Hz, CH), 131.2 (qd, J = 33.0, 13.9 Hz, C), 129.4 (d, J = 13.2 Hz, CH), 129.2 (qd, J = 3.5, 2.7 Hz, CH), 128.1 (dq, J = 11.3, 3.8 Hz, CH), 123.8 (d, J = 9.3 Hz, CH), 123.4 (qd, J = 272.8, 2.1 Hz, CF_3), 118.3 (d, J = 12.7 Hz, CH), 115.4 (d, J = 144.5 Hz, PC), 113.6 (s, CH), 62.0 (d, J = 5.9 Hz, CH_2), 16.4 (d, J = 6.4 Hz, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 26.86 (q, J = 1.0 Hz); HR-MS (m/z) [M + H]$^{+}$ calcd for $C_{16}H_{15}F_3N_2O_2P$ = 355.0823, found = 355.0835.

*Typical Procedure for the Phosphorylation of 5-Bromo- and 6-Bromoimidazo[1,2-a]pyridine Derivatives **1d,g,h**.* Under nitrogen atmosphere, a mixture of bromoimidazo[1,2-*a*]pyridine derivatives (**1d,g,h**) (1.10 mmol), diphenylphosphine oxide (1.00 mmol), Pd_2dba_3 (92 mg, 0.1 mmol), xantphos (116 mg, 0.2 mmol), and triethylamine (280 μL, 2.00 mmol) in dry toluene (10 mL) was stirred at reflux. After completion of the reaction indicated by TLC, the mixture was cooled to room temperature, filtered on Celite, washed with ethyl acetate (50 mL), and concentrated under vacuum. The crude residue was then purified by flash chromatography (silica gel, ethyl acetate 100%) to give the desired product (**5k**, **6u**, **6v**).

*(2-Methylimidazo[1,2-a]pyridin-5-yl)diphenylphosphine oxide (**5k**):* beige powder (214 mg, yield = 30%, ethyl acetate 100%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (bs, 1H), 7.73−7.65 (m, 5H), 7.65−7.59 (m, 2H), 7.55−7.45 (m, 4H), 7.03 (ddd, J = 9.0, 7.0, 2.5 Hz, 1H), 6.55 (ddd, J = 10.6, 7.0, 1.2 Hz, 1H), 2.36 (d, J = 0.9 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.7 (d, J = 3.6 Hz, C), 144.5 (s, C), 133.1 (d, J = 2.9 Hz, CH), 132.1 (d, J = 10.3 Hz, CH), 129.3 (d, J = 109.9 Hz, PC), 129.2 (d, J = 109.3 Hz, PC), 129.2 (d, J = 12.7 Hz, CH), 121.9 (d, J = 11.1 Hz, CH), 121.1 (d, J = 12.9 Hz, CH), 120.5 (d, J = 2.4 Hz, CH), 111.8 (s, CH), 14.5 (s, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 25.46; HR-MS (m/z) [M + H]$^{+}$ calcd for $C_{20}H_{18}N_2OP$ = 333.1151, found = 333.1168.

*(2-(2,5-Dimethoxyphenyl)imidazo[1,2-a]pyridin-6-yl)-diphenylphosphine oxide (**6u**):* yellow powder (344 mg, yield = 76%, ethyl acetate 100%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (ddd, J = 10.0, 1.6, 1.0 Hz, 1H), 8.24 (d, J = 0.8 Hz, 1H), 7.95 (d, J = 3.0 Hz, 1H), 7.77−7.68 (m, 4H), 7.63 (ddt, J = 9.3, 2.6, 0.9 Hz, 1H), 7.61−7.56 (m, 2H), 7.55−7.47 (m, 4H), 7.17 (td, J = 9.1, 1.6 Hz, 1H), 6.93 (d, J = 8.9 Hz, 1H), 6.87 (dd, J = 8.9, 3.1 Hz, 1H), 3.92 (s, 3H), 3.87 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.1 (s, C), 151.5 (s, C), 144.2 (d, J = 1.4 Hz, C), 142.8 (s, C), 132.6 (d, J = 2.8 Hz, CH), 132.1 (d, J = 10.2 Hz, CH), 131.8 (d, J = 16.5 Hz, CH), 131.7 (d, J = 107.1 Hz, PC), 128.9 (d, J = 12.4 Hz, CH), 125.0 (d, J = 9.1 Hz, CH), 122.5 (s, C), 117.3 (d, J = 11.8 Hz, CH), 116.9 (d, J = 108.9 Hz, PC), 115.5 (s, CH), 113.6 (s, CH), 113.3 (s, CH), 112.4 (s, CH), 56.1 (s, 2 OCH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 26.99; HR-MS (m/z) [M + H]$^{+}$ calcd for $C_{27}H_{24}N_2O_3P$ = 455.1519, found 455.1534.

*(2-Methylimidazo[1,2-a]pyridin-6-yl)diphenylphosphine oxide (**6v**):* brown powder (710 mg, yield = 99%, ethyl acetate 100%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (ddd, J = 10.0, 1.6 Hz, 1.0 Hz, 1H), 7.74−7.66 (m, 4H), 7.62−7.55 (m, 2H), 7.55−7.46 (m, 5H), 7.39−7.36 (m, 1H), 7.09 (td, J = 9.0, 1.6 Hz, 1H), 2.46 (d, J = 0.9 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.2 (s, C), 144.8 (d, J = 1.3 Hz, C), 132.6 (d, J = 2.8 Hz, CH), 132.0 (d, J = 10.2 Hz, CH), 131.6 (d, J = 155.8 Hz, PC), 131.3 (d, J = 16.0 Hz, CH), 128.9 (d, J = 12.4 Hz, CH), 124.6 (d, J = 9.5 Hz, CH), 116.8 (d, J = 11.9 Hz, CH), 116.4 (d, J = 109.0 Hz, PC), 110.6 (s, CH), 14.4 (s, CH_3); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 26.99; HR-MS (m/z) [M + H]$^{+}$ calcd for $C_{20}H_{18}N_2OP$ = 333.1151, found = 333.1164.

Typical Procedure for the Arylation of Imidazo[1,2-a]pyridine Derivatives. **Method A.** In a Schlenk flask under nitrogen atmosphere, a mixture of imidazo[1,2-*a*]pyridine derivative **7** or **6** (100−500 mg, 1−1.5 equiv), aryl bromide derivatives **8a−f** (1 equiv), KOAc (2 equiv), and $Pd(OAc)_2$ (2.5−10 mol %) in dry DMAc (0.1 M) was stirred at 140 or 160 °C. After completion of the reaction

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indicated by TLC or ^{31}P NMR, the mixture was cooled to room temperature. Water was added, and the solution was extracted three times with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under vacuum. The crude residue was purified by flash chromatography. **Method B.** A mixture of imidazo[1,2-*a*]pyridine derivative **7** or **6** (100−500 mg, 1−1.5 equiv), aryl bromide derivatives **8a−f** (1 equiv), KOAc (2 equiv), $Pd(OAc)_2$ (2.5−10 mol %), and dry DMAc (0.1 M) was introduced in a microwave 35-ML sealed tube equipped with a magnetic stirrer. The tube was saturated with a nitrogen atmosphere and stirred at room temperature for 5 min, then the tube was subjected to MW heating at 170 or 190 °C for 30 min or 1 h. The temperature of the reaction rose gradually in less than 1 min to the set point. After a return to room temperature, water was added, and the solution was extracted three times with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under vacuum. The crude residue was then purified by flash chromatography.

*3-Phenylimidazo[1,2-a]pyridine (**9a**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (50/50): brown oil (method A: 631 mg, yield = Q for 500 mg of imidazo[1,2-*a*]pyridine; method B: 323 mg, yield = Q for 250 mg of imidazo[1,2-*a*]pyridine). Known compound:[28] ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (dt, J = 7.0, 1.2 Hz, 1H), 7.70 (bs, 1H), 7.68 (dt, J = 9.1, 1.2 Hz, 1H), 7.59−7.48 (m, 4H), 7.45−7.38 (m, 1H), 7.20 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.80 (td, J = 6.8, 1.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 146.2 (s, C), 132.6 (s, CH), 129.4 (s, C), 129.4 (s, CH), 128.3 (s, CH), 128.2 (s, CH), 125.9 (s, C), 124.4 (s, CH), 123.5 (s, CH), 118.4 (s, CH), 112.7 (s, CH).

*3-(Naphthalen-1-yl)imidazo[1,2-a]pyridine (**9c**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (50/50): brown oil (method B: 1.44 g, yield = 77% for 1.00 g of imidazo[1,2-*a*]pyridine). Known compound:[28] ^1H NMR (400 MHz, $CDCl_3$) δ 8.01−7.93 (m, 2H), 7.80 (bs, 1H) 7.43 (ddd, J = 8.5, 6.6, 1.3 Hz, 1H), 7.71 (dt, J = 6.9, 1.2 Hz, 1H), 7.62−7.56 (m, 2H), 7.56−7.48 (m, 2H), 7.43 (ddd, J = 8.5, 6.6, 1.3 Hz, 1H), 7.24 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.72 (td, J = 6.8, 1.2 Hz, 1H).

*3-(o-tolyl)imidazo[1,2-a]pyridine (**9d**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (50/50): brown solid (method B: 114 mg, yield = 71% for 100 mg of imidazo[1,2-*a*]pyridine). Known compound:[28] ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (dt, J = 6.9, 1.2 Hz, 1H), 7.63 (dt, J = 9.1, 1.2 Hz, 1H), 7.56 (bs, 1H), 7.36−7.20 (m, 4H), 7.12 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.69 (td, J = 6.8, 1.2 Hz, 1H), 2.09 (s, 3H).

*3-(2-Methoxyphenyl)imidazo[1,2-a]pyridine (**9e**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (80/20 to 50/50): brown solid (method B: 52 mg, yield = 21% for 200 mg of imidazo[1,2-*a*]pyridine). Known compound:[28] ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (dt, J = 6.9, 1.1, 1H), 7.68−7.64 (m, 2H), 7.47−7.38 (m, 2H), 7.18 (ddd, J = 9.1, 6.7, 1.3, 1H), 7.10−7.02 (m, 2H), 6.75 (td, J = 6.8, 1.2, 1H), 3.79 (s, 3H).

*3-(2-Methoxynaphthalen-1-yl)imidazo[1,2-a]pyridine (**9g**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (50/50 to 0/100): brown solid (method A: 579 mg, yield = 50% for 748 mg of imidazo[1,2-*a*]pyridine; method B: 41 mg, yield = 35% for 75 mg of imidazo[1,2-*a*]pyridine). Known compound:[28] ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, J = 9.2, 0.7 Hz, 1H), 7.89−7.84 (m, 1H), 7.80−7.74 (m, 2H), 7.61−7.54 (m, 2H), 7.45−7.35 (m, 3H), 7.23 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.72 (td, J = 6.8, 1.2 Hz, 1H), 3.84 (s, 3H).

*2,3-Diphenylimidazo[1,2-a]pyridine (**9h**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (90/10 to 50/50): brown oil (method A: 70 mg, yield = 38% for 200 mg of 2-phenylimidazo[1,2-*a*]pyridine; method B: 109 mg, yield = 59% for 200 mg of 2-phenylimidazo[1,2-*a*]pyridine). Known compound:[28] ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (dt, J = 7.0, 1.2 Hz, 1H), 7.71−7.64 (m, 3H), 7.56−7.43 (m, 5H), 7.31−7.26 (m, 2H), 7.26−7.22 (m, 1H), 7.20 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.73 (td, J = 6.8, 1.2 Hz, 1H).

*3-(naphthalen-1-yl)-2-phenylimidazo[1,2-a]pyridine (**9i**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (80/20 to 50/50): brown oil (method B: 120 mg, yield = 80% for 150 mg of imidazo[1,2-*a*]pyridine). Known compound:[28] ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.0, 1.5 Hz, 1H), 8.00 (dt, J = 8.4, 1.1 Hz, 1H), 7.78 (dt, J = 9.1, 1.1 Hz, 1H), 7.64−7.52 (m, 5H), 7.42 (dt, J = 6.9, 1.2 Hz, 1H), 7.41−7.37 (m, 2H), 7.23 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 7.20−7.15 (m, 3H), 6.64 (td, J = 6.8, 1.2 Hz, 1H).

*Diphenyl(3-phenylimidazo[1,2-a]pyridin-6-yl)phosphine Oxide (**9b**).* The crude residue was purified by flash chromatography eluted with dichloromethane/MeOH 10% (90/10 to 50/50): yellow oil (method B: 158 mg, yield = 96% for 200 mg of imidazo[1,2-*a*]pyridin-6-yldiphenylphosphine oxide); ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (ddd, J = 10.3, 1.6, 1.0 Hz, 1H), 7.77 (s, 1H), 7.73−7.66 (m, 5H), 7.62−7.55 (m, 2H), 7.53−7.44 (m, 8H), 7.43−7.37 (m, 1H), 7.17 (ddd, J = 9.3, 8.7, 1.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.9 (d, J = 2.6 Hz, C), 133.9 (s, CH), 132.6 (d, J = 2.8 Hz, CH), 132.1 (d, J = 10.1 Hz, CH), 131.8 (d, J = 107.1 Hz, PC), 129.9 (d, J = 16.3 Hz, CH), 129.5 (s, CH), 128.9, (d, J = 12.4 Hz, CH), 128.8 (s, CH), 128.3 (s, C), 128.2 (s, CH), 124.7 (d, J = 9.7 Hz, CH), 118.4 (d, J = 11.8 Hz, CH), 117.6 (d, J = 107.9 Hz, PC); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 27.15; HR-MS (m/z) $[M + H]^+$ calcd for $C_{25}H_{20}N_2OP$ = 395.1313, found = 395.1315.

*(3-(Naphthalen-1-yl)imidazo[1,2-a]pyridin-6-yl)-diphenylphosphine Oxide (**9l**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (50/50 to 0/100): yellow oil (method B: 94 mg, yield = 58% for 100 mg of imidazo[1,2-*a*]pyridin-6-yldiphenylphosphine oxide); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (ddd, J = 10.2, 1.5, 1.0 Hz, 1H), 7.95−7.89 (m, 2H), 7.85 (s, 1H), 7.75 (ddd, J = 9.3, 2.5, 1.0 Hz, 1H), 7.61−7.43 (m, 10H), 7.41−7.33 (m, 5H), 7.24 (ddd, J = 9.3, 8.8, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.7 (d, J = 1.7 Hz, C), 135.4 (s, CH), 134.1 (s, C), 132.5 (d, J = 2.8 Hz, CH), 132.0 (d, J = 10.1 Hz (s, CH)), 131.9 (s, C), 131.5 (d, J = 106.8 Hz, PC), 130.3 (d, J = 17.2 Hz, CH), 130.1 (s, CH), 129.2 (s, CH), 129.0 (s, CH), 128.8 (d, J = 12.4 Hz, CH), 127.2 (s, CH), 126.6 (s, CH), 125.7 (s, CH), 125.2 (s, C), 125.0 (s, C), 124.9 (d, J = 9.3 Hz, CH), 124.8 (s, CH), 118.3 (d, J = 11.7 Hz, CH), 117.5 (d, J = 108.1 Hz, PC). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 27.14; HR-MS (m/z) $[M + H]^+$ calcd for $C_{29}H_{22}N_2OP$ = 445.1464, found = 445.1482.

*Dimethyl(3-phenylimidazo[1,2-a]pyridin-6-yl)phosphine Oxide (**9n**).* The crude residue was purified by flash chromatography eluted with dichloromethane/MeOH 10% (90/10 to 50/50): yellow oil (method B: 70 mg, yield = 75% for 100 mg of imidazo[1,2-*a*]pyridin-6-yldimethylphosphine oxide); ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, J = 10.1 Hz, 1H), 7.74−7.66 (m, 2H), 7.54−7.43 (m, 4H), 7.42−7.34 (m, 1H), 7.09 (td, J = 8.9, 1.5 Hz, 1H), 1.72 (d, J = 13.2 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.7 (s, C), 133.7 (s, CH), 129.5 (s, CH), 128.8 (s, CH), 128.3 (d, J = 13.6 Hz (s, CH), 127.7 (d, J = 109.7 Hz, PC), 127.1 (s, CH), 122.2 (d, J = 10.8 Hz, CH), 118.9 (d, J = 101.5 Hz, PC), 118.8 (d, J = 11.8 Hz, CH), 18.1 (d, J = 73.0 Hz, PCH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 33.04; HR-MS (m/z) $[M + H]^+$ calcd for $C_{15}H_{16}N_2OP$ = 271.1000, found = 271.1006.

*Dimethyl(3-(naphthalen-1-yl)imidazo[1,2-a]pyridin-6-yl)-phosphine Oxide (**9o**).* The crude residue was purified by flash chromatography eluted with dichloromethane/MeOH 10% (90/10 to 50/50): brown oil (method B: 82 mg, yield = 75% for 100 mg of imidazo[1,2-*a*]pyridin-6-yldimethylphosphine oxide); ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (ddd, J = 10.0, 1.6, 1.0 Hz, 1H), 8.00−7.94 (m, 1H), 7.94−7.89 (m, 1H), 7.83 (s, 1H), 7.79 (ddd, J = 9.2, 2.7, 1.0 Hz, 1H), 7.57 (s, 1H), 7.56 (d, J = 1.6 Hz, 1H), 7.53−7.46 (m, 2H), 7.40 (ddd, J = 8.6, 6.6, 1.3 Hz, 1H), 7.19 (td, J = 9.0, 1.6 Hz, 1H), 1.66 (d, J = 13.1 Hz, 6H, 2 CH_3); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.5 (d, J = 0.9 Hz, C), 135.2 (s, CH), 134.0 (s, C), 132.2 (s, C), 130.2 (s, CH), 129.2 (s, CH), 128.8 (s, CH), 128.5 (d, J = 15.0 Hz, CH), 127.2 (s, CH), 126.6 (s, CH), 125.6 (s, CH), 125.1 (s, C), 124.8 (d, PC one transition is missing), 124.7 (s, CH), 122.6 (d, J = 10.5 Hz, CH), 119.0 (d, J = 101.7 Hz, PC), 118.6 (d, J = 11.6 Hz, CH), 18.05 (d, J =

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73.0 Hz, PCH_3); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 33.11; HR-MS (m/z) $[M + H]^+$ calcd for $C_{19}H_{18}N_2OP$ = 321.1151, found = 321.1166.

*(2,3-Diphenylimidazo[1,2-a]pyridin-6-yl)diphenylphosphine Oxide (**9p**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (50/50 to 0/100): yellow oil (method B: 159 mg, yield = 100% for 200 mg of diphenyl(2-phenylimidazo[1,2-*a*]pyridin-6-yl)phosphine oxide); ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (ddd, J = 10.2, 1.6, 1.0 Hz, 1H), 7.76−7.66 (m, 7H), 7.64−7.56 (m, 2H), 7.55−7.46 (m, 7H), 7.44−7.39 (m, 2H), 7.36−7.28 (m, 3H), 7.18 (td, J = 9.0, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.6 (d, J = 1.5 Hz, C), 143.9 (s, C), 133.6 (s, C), 132.6 (d, J = 2.8 Hz, CH), 132.1 (d, J = 10.1 Hz, CH), 131.8 (d, J = 125.2 Hz, PC), 129.9 (s, CH), 129.8 (d, J = 16.8 Hz, CH), 129.4 (s, CH), 128.9 (d, J = 12.4 Hz, CH), 128.8 (s, C),128.5 (s, CH), 128.3 (s, CH), 128.1 (s, CH), 125.3 (d, J = 9.6 Hz, CH), 122.3 (s, CH), 117.5 (d, J = 11.8 Hz, CH), 117.1 (d, J = 108.4 Hz, C); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 27.12; HR-MS (m/z) $[M + H]^+$ calcd for $C_{31}H_{24}N_2OP$ = 471.1621, found = 471.1630.

*3-(Naphthalen-1-yl)-2-phenylimidazo[1,2-a]pyridin-6-yl)-diphenylphosphine Oxide (**9q**).* The crude residue was purified by flash chromatography eluted with cyclohexane/ethyl acetate (50/50 to 0/100): yellow oil, (method B: 66 mg, yield = 50% for 100 mg of diphenyl(2-phenylimidazo[1,2-*a*]pyridin-6-yl)phosphine oxide); ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.8, 1.4 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.84−7.77 (m, 2H), 7.66−7.55 (m, 8H), 7.55−7.49 (m, 3H), 7.44−7.35 (m, 5H), 7.34−7.30 (m, 1H), 7.28 (td, J = 9.0, 1.5 Hz, 1H), 7.24−7.19 (m, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.9 (d, J = 1.5 Hz, C), 144.7 (s, C), 134.2 (s, C), 133.4 (s, C), 132.4 (d, J = 2.8 Hz, CH), 132.4 (d, J = 2.8 Hz, CH), 132.1 (s, C), 131.9 (d, J = 10.1 Hz, CH), 131.9 (d, J = 10.1 Hz, CH), 131.5 (d, J = 107.1 Hz, PC), 131.3 (d, J = 107.1 Hz, PC), 130.5 (s, CH), 130.4 (s, CH), 130.1 (d, J = 17.1 Hz, CH), 129.0 (s, CH), 128.7 (d, J = 12.4 Hz, CH), 128.7 (d, J = 12.4 Hz, CH), 128.5 (s, CH), 128.0 (s, CH), 127.7 (s, CH), 127.4 (s, CH), 126.7 (s, CH), 126.1 (s, CH), 126.0 (s, C), 125.5 (d, J = 9.4 Hz, CH), 124.7 (s, CH), 120.3 (s, C), 117.5 (d, J = 11.7 Hz, CH), 117.3 (d, J = 108.5 Hz, PC); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 27.11; HR-MS (m/z) $[M + H]^+$ calcd for $C_{35}H_{26}N_2OP$ = 521.1777, found = 521.1796.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02059.

HR-ESI-MS and ^1H, ^{13}C, ^{31}P spectra for described compounds. (PDF)

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Notes

The authors declare no competing financial interest.

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