DOI: 10.1002/ejoc.200900698

Phosphonylation of 2-Amino- and 2-Amido-3-bromopyridines and 2-Amino-3-chloroquinoxalines with Triethyl Phosphite

M. Shaker S. Adam,[a] Markus K. Kindermann,[a] Martin Köckerling,[b] and Joachim W. Heinicke*[a]

Keywords: Cross-coupling / Palladium / Nitrogen heterocycles / Phosphorus / Phosphonylation

The Tavs reaction of 2-amino- and 2-acylamido-3-bromopyridines **1** and **2** with triethyl phosphite in the presence of palladium acetate or chloride allows the synthesis of 2-amino- and 2-acylamidopyridine-3-phosphonates **3** and **4**. A second ring nitrogen atom causes strong activation and leads to excellent yields in the phosphonylation of 2-amino-3-chloroquinoxalines. 2,3-Dichloroquinoxaline does not need a catalyst and undergoes double phosphonylation with sodium diethyl phosphite under Michaelis–Becker conditions. The results show an activating influence of pyridine nitrogen (–M) and deactivating influence of the amino group (+M). The reactivity of **1** and **2** in the Tavs coupling is compared with that of the 3-NH-2-bromopyridine position isomers and 2-bromoanilines and discussed in terms of the opposite effects of pyridine and amino(amido) nitrogen and different position of the N atoms towards the reaction site. The advantage of the Tavs reaction is the easy optimization because neither auxiliary ligands are required nor a base to trap the halide or a solvent. Triethyl phosphite itself acts as ligand and forms $Pd^0\{P(OEt)_3\}_n$ in the initial phase of the reaction. The structures of the products and the expected intramolecular N–H···O=P hydrogen bridging bonds were proven by solution NMR and by X-ray crystal structure analysis of single crystalline **3c**.

Introduction

Phosphonic acid derivatives are of broad interest particularly with regard to the large number of biologically active compounds containing such P–O functional groups.[1] The access to phosphonylated azaheterocycles and their importance in synthetic, agrochemical and medicinal chemistry has very recently been reviewed.[2] Whereas aliphatic representatives are easily available by alkylation of di- or trialkyl phosphite, well known as Michaelis–Becker or Arbuzov reactions,[3] the direct arylation of phosphites requires either activation by strongly electron-withdrawing groups such as in dinitroarenes or pyridine *N*-oxides,[4] or activation by UV light, known for aryl iodides.[5] Another route to these materials is transition metal catalysis, introduced by Tavs,[6] using trialkyl phosphite, and by Hirao et al.,[7] using dialkyl phosphite in the presence of an auxiliary ligand and a base in a suitable solvent, respectively. Tavs reactions usually need higher reaction temperatures. Therefore, to avoid thermal decomposition or competing side reactions, in the last years P–C cross coupling reactions using dialkyl phosphite were preferred. Despite donor atoms tend to block the catalyst metal, under suitable conditions also some heteroaryl phosphonates became accessible.[8–12] Additional NH-functional groups in the heteroarylhalides increase, however, the probability to deactivate the catalyst, and to the best of our knowledge only a very recent paper describes the Hirao-type coupling of a limited variety of NH-functional bromopyridines, 2-bromo-5-amino- and several amino-3-bromopyridines. Thorough optimization experiments with variation of the ligand (Pd/ligand ratio usually 10:30 mol-%), base, solvent and reaction time (24–72 h) led to very good yield with 2-amino-3-bromo-4-methylpyridine whereas the yields in the coupling of the closely related 4-amino-3-bromopyridine remained zero or low, even after long reaction time.[12] This shows that the position of the substituents in NH-functionally substituted heteroaryl halides plays a crucial role in transition metal catalysis or its blockage by coordination of heteroatom(s) and that even small changes may require new time consuming optimizations.

The Tavs procedure is more easy to perform, does neither need auxiliary ligands (triethyl phosphite itself acts as ligand[13]) nor a base or solvent, and for thermally sufficiently stable aromatic compounds this reaction is thus an advantageous alternative. Optimization is reduced to screening for suitable transition metal precursors. For application to NH-functionally substituted aryl or heteroaryl halides the transition metal must tolerate the heteroatoms,

[a] Institut für Biochemie, Ernst-Moritz-Arndt-Universität Greifswald,
Felix-Hausdorff-Str. 4, 17489 Greifswald, Germany
Fax: +49-3834-864377
E-mail: heinicke@uni-greifswald.de
[b] Anorganische Chemie-Festkörperchemie, Universität Rostock, Albert-Einstein-Str. 3a, 18059 Rostock, Germany

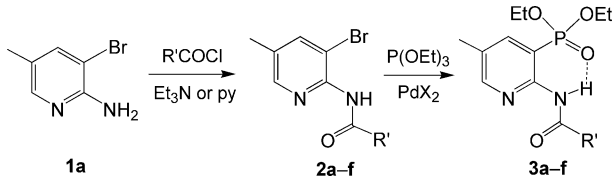
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.200900698.

also its position relative to the reaction centre must be taken into account. We used the Tavs reaction to synthesize *o*-amino(amido)benzenephosphonates as starting materials for benzo-fused P=C–N heterocycles[14–16] and recently demonstrated the applicability also to 3-amino- and 3-amido-2-phosphonopyridines, likewise used as building blocks for heterocycles.[17,18] Whereas *N*-secondary *o*-anilido phosphonates were obtained in high yields from triethyl phosphite and *o*-bromoanilides in the presence of anhydrous nickel bromide,[15] the cross coupling with *N*-basic *o*-bromoanilines and 3-amino- or 3-amido-2-bromopyridines requires palladium catalysts that are more tolerant towards other functional groups.[16] For the 3-NH-functional 2-bromopyridines the yields were only low to moderate, although for this position the C–halogen bond should be activated by the adjacent pyridine N-atom.[18] In the isomers with bromine in 3- and the amino or amido group in 2-position the C–Br bond will not be activated by the pyridine nitrogen, but the ring N-atom is more remote to the catalyst metal and catalyst blockage less probable. This prompted us to explore if this makes these compounds comparable to 2-bromoanilides or -anilines, allows the use of Ni catalysts for the coupling of *N*-acyl-bromopyridines or leads to improved yields with Pd catalysts. To additionally get evidence whether the electron-withdrawing power of pyridine-type nitrogen (σ^2-N) atoms has indeed an impact on the Tavs coupling or not, to open a route to the still unknown 2-aminoquinoxaline-3-phosphonates, and to more generally show if the Tavs protocol is suitable for the phosphonylation of NH-functionally substituted N-heteroaryl halides, we included 2-amino-3-chloroquinoxalines into this investigation.

2. Results and Discussion

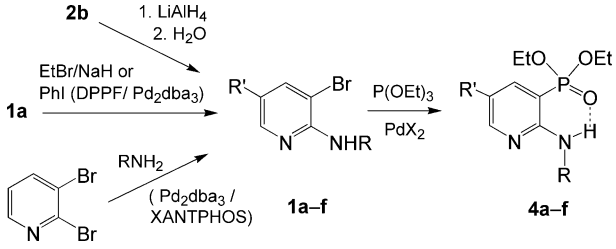
2.1. Synthesis of 2-Amino- and 2-Amidopyridine-3-phosphonates

The 2-amino-3-bromopyridine **1a** and various 2-acylamido-3-bromopyridines **2a**–**f**, obtained from **1a** and the respective acyl chlorides, were used in this study. Attempts aiming at cross coupling of various 2-acylamido-3-bromopyridines **2** with triethyl phosphite in the presence of anhydrous $NiBr_2$ failed, even for conditions with high temperatures and long reaction time (200 or 225 °C/15 to 60 min). The coupling requires the presence of palladium acetate or palladium chloride (8–12 mol-%) under harsh conditions (heating for 10 min at 170 °C bath temperature). The acylamidopyridine-3-phosphonates **3a**–**f** (Scheme 1) are then obtained in moderate yields, highest for the pivaloyl compound **3a** with the bulky +I *tert*-butyl group (NMR scale 70%, preparative scale 40%) and for the π-excess heteroaryl derivatives **3b** and **3c**, clearly lower for the benzamides **3d** and **3e**, and lowest for the naphthoylamido-pyridinephosphonate **3f**. Prolonged heating of **2a** with $P(OEt)_3/PdCl_2$ (10 mol-%) also resulted in lower yields. After 10 min at 170 °C, 70% of **3a** was detected (by ^{1}H NMR integration) in the crude product, after further 10 min at 180 °C only 30–40%, and after 40 min all **3a** was decomposed. The ^{31}P NMR spectrum after 10 min reaction time displayed signals for **3a**, $(EtO)_2PHO$ and $(EtO)_3PO$. The signal for the latter is increasing with the reaction time. After heating for longer times further signals were observed in the phosphate region, indicating P–C bond cleavage in connection with formation of highly viscous condensation products.



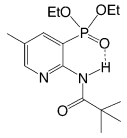
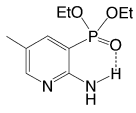
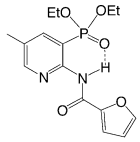
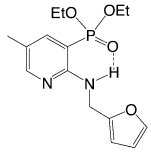
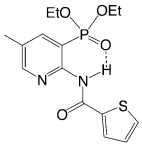
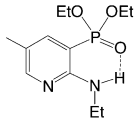
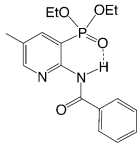
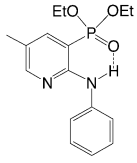
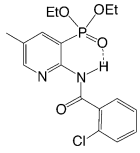
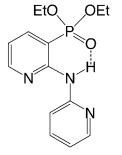
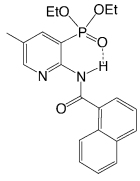
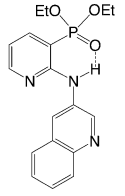
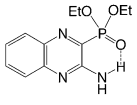
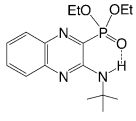
Scheme 1. Synthesis of 2-acylamidopyridine-3-phosphonates **3a**–**f** (**a** R = *t*Bu, **b** R = 2-furyl, **c** R = 2-thienyl, **d** R = Ph, **e** R = 4-ClC_6H_4, **f** R = 1-naphthyl, X = OAc or Cl).

The primary amino-bromopyridine **1a** is more susceptible to side reactions than the acylamides **2** and provides the 2-aminopyridine-3-phosphonate **4a** under the above conditions only in low yield (19%). Prolonged heating of **1a** with $P(OEt)_3/PdCl_2$ (10 mol-%) did not lead to improved formation of **4a** but to yellowish and finally brown (after 35–40 min) condensation products with high viscosity and low content of **4a**. To access **4a**, the Hirao coupling is clearly more suitable.[12] Because the yields in the Pd-catalyzed Tavs coupling of *N*-secondary *o*-bromoanilines improved strongly with bulkier *N*-substituents,[16] some *N*-alkyl- and *N*-aryl-2-amino-3-bromopyridines **1b**–**f** were prepared and subjected to this P–C coupling protocol (Scheme 2). The *N*-(phenylamino)pyridine-3-phosphonate **4d** was obtained in good and the primary *N*-alkyl derivatives **4b** and **4c** in moderate yields, similar to comparably *N*-substituted 2-anilinophosphonates.[16] As shown for the anilinophosphonates, the outcome can further be improved by more bulky *N*-alkyl groups. An additional nitrogen atom in the *N*-substituent, however, lowers the yields as demonstrated for the *N*-(heteroarylamino)pyridinephosphonates **4e** and **4f** (Table 1).



Scheme 2. Synthesis of 2-aminopyridine-3-phosphonates **4a**–**f** (**a** R = H, R′ = Me; **b** R = CH_2-2′-furyl, R′ = Me; **c** R = Et, R′ = Me; **d** R = Ph, R′ = Me; **e** R = 2-pyridyl, R′ = H; **f** R = 3-quinolyl, R′ = H; X = OAc or Cl).

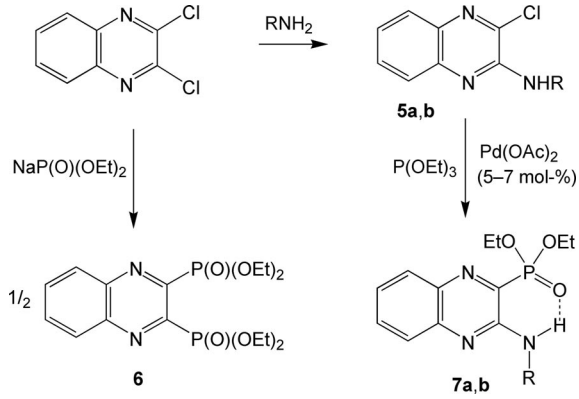
Table 1. Pd-catalyzed phosphonylation of 2-amino- or 2-amido-substituted 3-bromopyridines and 3-chloroquinoxalines with $P(OEt)_3$.[a]

		% Yield (mol-% Pd)			% Yield (mol-% Pd)
3a		40 (12) 70[b]	**4a**		19 (10)
3b		42 (10)	**4b**		45 (10)
3c		40 (8)	**4c**		44 (10)
3d		32 (12)	**4d**		60 (8)
3e		36 (12)	**4e**		36 (10)
3f		21 (8)	**4f**		21 (8)
7a		89 (5.5)	**7b**		75 (7)

[a] Conditions: 1.2 equiv. of $P(OEt)_3$ were used; heating usually 10 min at 170 °C, in the case of **7a** 2.5 h/180 °C, **7b** 1 h/160 °C; yields refer to isolated products. [b] NMR yield at optimal reaction time.

2.2. Synthesis of Quinoxaline-2,3-diphosphonates and 2-Aminoquinoxaline-3-phosphonates

Due to its strong electron deficiency, 2,3-dichloroquinoxaline is more reactive towards nucleophiles than bromo- and in particular chloropyridines. This allows for phosphonylation without a transition metal catalyst. Heating with sodium diethyl phosphite leads to a double Michaelis–Becker reaction with formation of quinoxaline-2,3-diphosphonate **6**. Selective mono-phosphonylation could not be achieved by an equimolar ratio of the reactants. In this case unconverted dichloroquinoxaline was recovered, showing that monophosphonylation causes increased reactivity of the remaining C–Cl bond. The amino groups in 2-amino-3-chloroquinoxaline **5a**[19] and 2-(*tert*-butylamino)-3-chloroquinoxaline **5b**[20] accomplish the contrary. Attempts to couple the 2-amino-3-chloroquinoxalines **5a** and **5b** simply by heating with sodium diethyl phosphite (Michealis–Becker protocol) or with triethyl phosphite (Arbuzov protocol) failed, even in the presence of anhydrous $NiCl_2$ or $NiBr_2$ (5–100 mol-%) under forced conditions (120–225 °C up to 20 min). Furthermore, heating with diethyl phosphite in the presence of excess base (Et_3N or iPr_2NH or NaO*t*Bu) and catalytic amounts of $Pd(OAc)_2$ in toluene (Hirao protocol) or *N*-methylpyrrolidone (180–225 °C) did not lead to phosphonylation. However, heating of **5a** or **5b** with triethyl phosphite in the presence of palladium acetate as catalyst provided the 2-aminoquinoxaline-3-phosphonates **7a** and **7b** in excellent yields (Scheme 3).



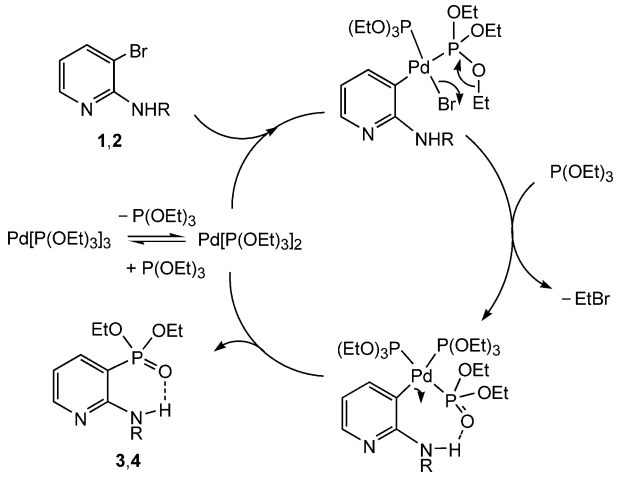
Scheme 3. Synthesis of **6** and substituted 2-aminoquinoxaline-3-phosphonates **7a**,**b** (**a** R = H, **b** R = *t*Bu).

2.3. Remarks on Mechanistic Aspects

The easy reaction of 2,3-dichloroquinoxaline with amines and sodium diethyl phosphite is due to the promotion of nucleophilic substitution by electron deficiency. Replacement of the first chlorine by a phosphono group causes enhanced activation, replacement of chlorine by the electron-donating amino group decreases the reactivity, so that a catalyst becomes necessary, like as for the 2-amino-3-bromopyridines. The much higher yield in the coupling of **5a** compared to **1a** reflects the activation of the C–halogen bond by the electron withdrawing effect of σ^2-N atoms, although the diminished nucleophilic reactivity of the amino group certainly also contributes to the excellent coupling results by lower tendency to side reactions. In **1a** the –M effect of the pyridine nitrogen on the 3-position is low and the reactivity rather controlled by the +M effect of the 2-amino group. That the reactivity of **1** and **2** in the Tavs coupling is comparable with that of the position isomeric 3-amino- and 3-amido-2-bromopyridines may be attributed to the contrary effects of adjacent pyridine and amino/

amido nitrogen atoms (–M vs. +M effect by *o* and *o′* position) and the proximity of both N-atoms to the reaction site in the latter.

A proposal for a possible mechanism for the Pd-catalyzed Tavs coupling of amino- and amido pyridine bromides with triethyl phosphite, apart from a distinct initiation similar to that for P–C coupling with diethyl phosphite,[8,21,22] is depicted in Scheme 4.



Scheme 4. Proposed mechanism for the Pd-catalyzed aryl phosphonylation with $P(OEt)_3$.

Because the behavior of $Pd(OAc)_2$ and $PdCl_2$ in the Tavs coupling was similar but for the Hirao-type coupling different,[22] a NMR experiment was performed to shed light on the reason. We observed that $PdCl_2$ on heating with triethyl phosphite is reduced to give a $[Pd^0\{P(OEt)_3\}_n]$ species, similarly as reported for $NiCl_2$[23] or for $Pd(OAc)_2$ with phosphanes.[24] Evidence is provided by ^{31}P NMR spectra (in $CDCl_3$ at 25 °C) of the crude product mixture formed by refluxing excess triethyl phosphite with $PdCl_2$ (10 min). Broadened signals for a dynamic system of the $Pd(P(OEt)_3)_4$ complex[25] and $P(OEt)_3$ ($\delta^{31}P$ 156.8 and 136.4 ppm) with a small downfield phosphorus coordination chemical shift ($\Delta\delta$ = 20.4 ppm) were observed along with signals for $(EtO)_2PHO$ and a smaller amount of $(EtO)_3PO$. The amount of the Pd^0 complex did not significantly increase if heating was prolonged (to 20 min). The ^{31}P coordination chemical shift is similar to the known value for $Pd^0(P(OMe)_3)_4/P(OMe)_3$ ($\Delta\delta$ = 21 ppm[26]) whereas $PdCl_2(P(OEt)_3)_2$ displays an upfield shift (δ = 92.0, $\Delta\delta$ = –46 ppm[27]). On addition of **1a** or **2a** the Pd^0 complex is no longer detectable by ^{31}P NMR spectroscopy. Rapid insertion of Pd^0 into the C–Br bond, the typical oxidative addition step in Pd-catalyzed cross couplings,[8] is assumed to form an intermediate complex $[pyPd^{II}\{P(OEt)_3\}_2Br]$. Subsequent elimination of EtBr (evaporates from the mixture) converts the triethyl phosphite to a diethyl phosphonate ligand (cf. Arbuzov reactions[2]) and generates intermediates $[pyPd^{II}\{PO(OEt)_2\}L_2]$ as discussed for the Hirao coupling.[8,21,22] These undergo reductive elimination to afford the product with regeneration of Pd^0, here stabilized by triethyl phosphite as ligand (Scheme 4). $[RC_6H_4Pd^{II}\{PO(OR')_2\}(bipy)]$ species, related to the assumed second intermediate, have recently been reported and were shown to eliminate arylphosphonates.[21] $(EtO)_2PHO$ and $(EtO)_3PO$ are formed in connection with the reduction of $PdCl_2$ to the initial Pd^0 catalyst.

2.4. Structural Aspects

Evidence for the structures of **1**–**7** is given by conclusive NMR and mass spectroscopic data, for **3c** additionally by crystal structure analysis. The characteristic ^{31}P resonances of **3a**–**f** and **4a**–**f** appear only marginally below those of 2-acylanilido-[15] and 2-anilinophosphonates[16] (δ = 16.5–20.4 vs. 18.3–22.6 ppm) and indicate thus close electronic similarity. The isomeric 3-acylamido- and 3-aminopyridine-2-phosphonates (δ = 11.3–12.3; 14.5 ppm)[18] absorb at markedly higher field, halfway to 2-aminoquinoxaline-3-phosphonates **7a**,**b**, which by further electron release resonate in

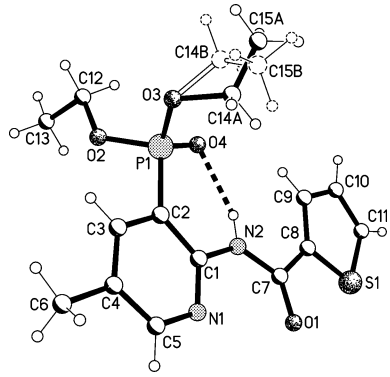


Figure 1. Molecular structure of **3c** in the crystal with one disordered ethyl group (78:22%). Selected bond lengths (Å) and angles (°): C2–P1 1.790(2), P1–O4 1.468(1), P1–O2 1.559(1), P1–O3 1.566(2), C1–N1 1.330(2), C1–N2 1.398(2), C5–N1 1.343(2), N2–C7 1.362(2), C1–C2 1.413(2), C2–C3 1.392(2); C3–C2–P1 118.5(1), C1–C2–P1 123.9(1), C2–C1–N2 118.4(1), N1–C1–N2 118.9(1), O4–P1–O2 115.56(9), O4–P1–O3 114.1(1), O2–P1–O3 102.2(1), O4–P1–C2 113.46(7), O2–P1–C2 103.05(7), O3–P1–C2 107.22(8); N2···O 42.743(2).

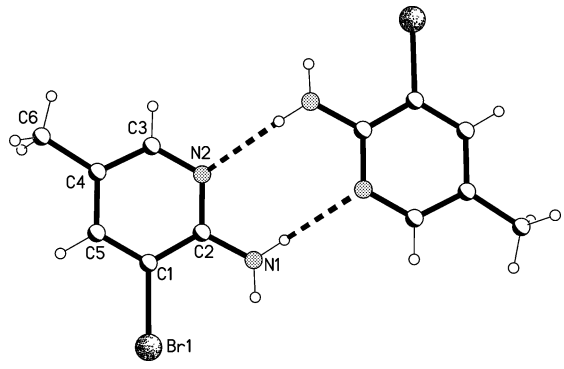


Figure 2. Molecular structure of **1a** in the crystal, showing the formation of hydrogen bridged dimers. Selected bond lengths (Å) and angles (°): C1–Br1 1.903(2), C2–N2 1.349(2), C2–N1 1.361(2), C3–N2 1.339(2), C1–C2 1.405(2), C1–C5 1.369(3); C5–C1–Br1 120.4(1), C2–C1–Br1 119.2(1), C1–C2–N1 122.9(2), N1–C2–N2 117.4(2).

the range of δ = 9.4–9.8 ppm. The electronic effects are also reflected in the ^{13}C chemical shifts, which are strongly influenced by changes of the π-electron density. The most characteristic feature in the solution ^1H NMR spectra of **3** and **4** compared to **1** and **2** is the large downfield shift of the NH signals ($\Delta\delta$ = 1.9–2.8 ppm). This indicates strong intramolecular hydrogen bonds to the phosphono group, confirmed by single-crystal X-ray structure analysis of **3c** (Figure 1). The π-systems of the amido group and pyridine ring are nearly coplanar. The small interplanar angle (3.1°) allows stabilization by extended delocalization. In the absence of the phosphono group 2-aminopyridines prefer intermolecular N–H···N hydrogen bonds between the amino group and the pyridine nitrogen atom, forming pairs of molecules, as seen in the structure of **1a** (Figure 2). Both compounds, **3c** and **1a**, crystallize monoclinic in the space group $P2_1/n$. All bond lengths and angles are observed within the expected ranges.

Conclusions

The basic pyridine nitrogen in **2** prevents nickel-catalyzed Tavs phosphonylation, which is highly efficient for the electronically related *o*-bromoanilides (see comparison of the phosphorus resonance of the products). Phosphonylation of 2-amino or 2-acylamido-3-bromopyridines **1** and **2** with triethyl phosphite can, however, be achieved in the presence of palladium acetate or chloride by short heating at high temperature (170 °C). *N*-Alkyl, *N*-aryl or *N*-acyl groups improve the yield, suitable substituents strongly. The coupling results are comparable to those of 3-amino/3-amido-2-bromo-position isomers despite in **1** and **2** the reaction site, the 3-C–Br bond, lacks activation by the –M effect of the pyridine nitrogen. That the reactivity of the two isomeric *o*-amino-bromopyridines is levelled out may be attributed to compensation of the –M-activating effect (in 2- and 4-position) by the deactivating effect of the 3-amino group (+M in 2- and 4-position) in the 3-NH-2-Br isomer and the proximity of both nitrogen atoms to the reaction site at C-2. The activation of the phosphonylation by the –M effect of σ^2-nitrogen was shown for dichloroquinoxaline, which couples even without a transition metal catalyst, and for 2-amino-3-chloroquinoxaline which gives high yields using the Tavs protocol with palladium catalysts more tolerant towards functional groups. In conclusion, the above results outline that amino or amido substituted electron-deficient N-heteroaryl bromides with sufficient activation by one or better more σ^2N atoms are able to undergo Pd-catalyzed phosphonylation simply by heating with triethyl phosphite in the presence of a Pd^{II} salt which at about 170 °C forms $Pd^0\{P(OEt)_3\}_n$ as the active catalysts.

Experimental Section

General: Reactions with moisture- or air-sensitive compounds were conducted in dried and deoxygenated solvents under an argon atmosphere using Schlenk techniques. 2-Amino-3-bromo-5-methylpyridine (**1a**), 2,3-dibromopyridine, triethyl phosphite and catalyst reagents were used as received from commercial suppliers. **1c** and **1d** were prepared from **1a** by Pd-catalyzed *N*-alkylation[28] with ethyl bromide or *N*-arylation with iodobenzene.[29] **1e** was synthesized by Pd-catalyzed monoarylation of 2,3-dibromopyridine with 2-aminopyridine.[30] The acylation of **1a** to **2a**–**f** was carried out in analogy to the syntheses of the respective 2-amido-3-bromo isomers.[31] NMR spectra were measured at 25 °C on a multinuclear FT-NMR spectrometer Bruker ARX300 or AVANCE300 at 300.1 (^1H), 75.5 (^{13}C), and 121.5 (^{31}P) MHz. The ^1H, ^{13}C and ^{31}P chemical shifts δ are given in ppm relative to Me_4Si and H_3PO_4 (85%), respectively, as external standards. The assignments made correspond to position numbers in the pyridine or quinoxaline ring and in the N-substituents (denoted by additional ′ or *i*, *o*, *m*, *p* for phenyl). Coupling constants refer to J_{HH} in ^1H and J_{PC} in ^{13}C NMR unless denoted otherwise. Splitting pattern for larger and smaller coupling constant are given in the same order as the *J* values. τ (in compound **6**) denotes a three or five line X signal (^{13}C) coupling with two chemically equivalent phosphorus nuclei (ABX type by different $^{12}C/^{13}C$ surrounding of the ^{31}P nuclei), $|J+J'|$ the distance of line 1 to 3 or 2 to 4. Mass spectra were measured on a single-focusing sector-field mass spectrometer AMD40, high-resolution mass spectra on a double-focussing sector field mass spectrometer MAT 95 (Fa. Finnigan) with EI (70 eV) or ESI. PFK were used as references. Elemental analyses were carried out with a CHNS-932 analyzer from LECO using standard conditions. IR spectra were recorded as KBr pellets, or using capillaries with nujol on a Nicolet® Magna550.

3-Bromo-2-[(furan-2-ylmethyl)amino]-5-methylpyridine (1b): A solution of **2b** (see below; 1.0 g, 3.56 mmol) in diethyl ether (30 mL) was added dropwise at 0 °C to $LiAlH_4$ tablets (0.41 g, 10.80 mmol) stirred in diethyl ether (30 mL). Stirring was continued for 2 d. Then degassed water was added dropwise at 5–10 °C until the evolution of hydrogen ceased. Solids were filtered off and washed with diethyl ether. The filtrate was dried by Na_2SO_4, the solvent was removed in vacuo, and the remaining pale yellow viscous liquid was purified by column chromatography using silica gel and ethyl acetate/*n*-hexane (10:90%) to give 0.64 g (67%) of a white powder, m.p. 48 °C. ^1H NMR ($CDCl_3$): δ = 2.18 (s, 3 H, 5-Me), 4.48 (d, ^3J = 3.3 Hz, 2 H, NCH_2), 4.80 (very br. s, 1 H, NH), 6.22 (dd, ^3J = 3.2, ^4J = 0.7 Hz, 1 H, 3′-H), 6.31 (dd, ^3J = 3.2, ^4J = 1.9 Hz, 1 H, 4′-H), 6.40 (d, ^3J = 8.4 Hz, 1 H, 4-H), 7.27 (dd, ^3J = 8.4, ^4J = 2.0 Hz, 1 H, 4-H), 7.35 (dd, ^3J = 3.2, ^4J = 0.7 Hz, 1 H, 5′-H), 7.93 (s, 1 H, 6-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 17.39 (5-Me), 39.63 (NCH_2), 106.81, 107.09, 110.32, 122.23 (CH-4′, C_q-3, C_q-5), 138.76 (C_q-4), 141.89 (CH-5′), 147.07 (CH-6), 152.72 (C_q-2′), 156.28 (C_q-2) ppm. Mass calcd. for $C_{11}H_{11}BrN_2O$: 266.01, 268.00 (100, 97 rel.%). MS (EI 70 eV, 140 °C): *m*/*z* (%) = 268 (5) [M^+], 266 (7) [M^+], 188 (32), 159 (44), 81 (100). $C_{11}H_{11}BrN_2O$ (267.12): calcd. C 49.46, H 4.15, N 10.49; found C 49.24, H 4.36, N 10.26.

3-Bromo-2-(ethylamino)-5-methylpyridine (1c): Was prepared in analogy to (3-bromopyridin-2-yl)ethylamine[28] from **1a** (4.0 g, 21.4 mmol), added to a suspension of NaH (0.62 g, 25.7 mmol) in THF (20 mL) at –20 °C and heated at 40 °C for 30 min, by reaction with ethyl bromide (2.4 mL, 3.51 g, 32.2 mmol) (room temperature, 2 h 50 °C) and extraction with CH_2Cl_2; yield 4.31 g (94%) of **1c**. ^1H NMR ($CDCl_3$: δ = 1.25 (t, ^3J = 7.2 Hz, 3 H, CH_3), 2.14 (s, 3 H, 5-Me), 3.45 (qd, ^3J = 7.2, $^3J_{NH}$ = 5.5, 2 H, CH_2), 4.78 (br. s, 1 H, NH), 7.43 (d, ^4J = 1.9 Hz, 1 H, 4-H), 7.87 (br. d, $^4J \approx$ 2 Hz, 1 H, 6-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 14.00 (Me), 16.79 (Me-5), 36.53 (NCH_2), 105.09 (C_q-3), 122.00 (C_q-5), 140.11 (CH-4), 146.13 (CH-6), 152.72 (C_q-2) ppm. Mass calcd. for $C_8H_{11}BrN_2$: 214.01, 216.01 (100, 97 rel.%). MS (EI 70 eV, 20 °C): *m*/*z* (%) =

217 (4) [M + 1$^+$], 216 (38) [M$^+$], 215 (13), 214 (42) [M$^+$], 201 (97), 199 (100), 92 (43), 44 (89). $C_8H_{11}BrN_2$ (215.09): calcd. C 44.67, H 5.15, N 13.05; found C 44.25, H 5.32, N 13.24.

(3-Bromo-5-methylpyridin-2-yl)aniline (1d): This compound was prepared in analogy to (3-bromopyridine-2-yl)aniline[29] from a mixture of **1a** (4.2 g, 22.5 mmol), iodobenzene (3.09 mL, 27.0 mmol), *t*BuONa (2.99 g, 31.2 mmol), $Pd_2(dba)_3$ [dba = dibenzylideneacetone] (1.06 g, 1.16 mmol) and DPPF [1,1′-bis(diphenylphosphanyl)ferrocene] (1.25 g, 2.26 mmol) in toluene (50 mL) at 100 °C for 20 h. After cooling, the reaction mixture was diluted with Et_2O and filtered through a Celite pad. The solvent was removed in vacuo, and the product was purified by column chromatography using silica gel (25% ethyl acetate/75% *n*-hexane) to give 3.80 g (64%) of **1d** as pale yellow oil. ^{1}H NMR ($CDCl_3$): δ = 2.23 (s, 3 H, 5-Me), 6.64 (br. s, 1 H, NH), 7.02 (tm, 1 H, *p*-H), 7.26–7.36 (m, 5 H, *m*-H, *o*-H, 4-H), 8.02 (br., 1 H, 6-H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 17.50 (Me-5), 108.24 (C_q-3), 119.76 (2 CH-*o*), 122.38 (CH-*p*), 124.09 (C_q-5), 129.25 (2 CH-*m*), 138.75 (CH-4), 140.80 (C_q-*i*), 147.62 (CH-6), 153.76 (C_q-2) ppm. Mass calcd. for $C_{12}H_{11}BrN_2$: 262.01, 264.01 (100, 97 rel.%). MS (EI, 200 °C): *m*/*z* (%) = 265 (5) [M + 1$^+$], 264 (49) [M$^+$], 263 (100) [M – 1$^+$ and M + 1$^+$ (^{79}Br)], 262 (53) [M$^+$], 261 (91) [M – 1$^+$], 182 (20), 181 (17), 77 (25), 51 (17). $C_{12}H_{11}BrN_2$ (263.13): calcd. C 54.77, H 4.21, N 10.25; found C 54.63, H 4.53, N 10.53.

3-[(3-Bromopyridin-2-yl)amino]quinoline (1f): $Pd_2(dba)_3$ (0.29 g, 0.32 mmol, 2 mol-%) was mixed with XANTPHOS (0.41 g, 0.71 mmol, 4.4 mol-%) in DME (5 mL) for 15 min at room temperature. After the change of the colour of the solution red to yellow, a solution of 2,3-dibromopyridine (3.8 g, 16.0 mmol), 3-aminoquinoline (2.78 g, 19.3 mmol) and Cs_2CO_3 (20.9 g, 64.2 mmol) in DME (50 mL) was added. The reaction mixture was refluxed for 2 h. After cooling the solvent was removed in vacuo, and the product was extracted with $CHCl_3$ and purified by column chromatography using silica gel (35% ethyl acetate/65% *n*-hexane) to yield 3.5 g (73%) of white crystals of **1f**. ^{1}H NMR ($CDCl_3$): δ = 6.75 (dd, ^3J = 7.8, 4.8 Hz, 1 H, 5-H), 7.25 (br., 1 H, NH, superimposed by solvent), 7.52 (td, ^3J = 8.1, 6.9, ^4J = 1.3 Hz, 1 H, 6′-H), 7.59 (td, ^3J = 8.4, 6.9, ^4J = 1.6 Hz, 1 H, 7′-H), 7.81 (dd, ^3J = 7.8, ^4J = 1.6 Hz, 1 H, 4-H), 7.81 (d superimposed, ^3J = 8 Hz, 1 H, 5′-H), 8.05 (br. d, ^3J = 8.3 Hz, 1 H, 8′-H), 8.25 (dd, ^3J = 4.8, ^4J = 1.6 Hz, 1 H, 6-H), 8.83, 8.90 (2d, ^4J = 2.4 Hz, 2 H, 2′-H, 4′-H) ppm. Mass calcd. for $C_{14}H_{10}BrN_3$: 299.01, 301.00 (100, 97 rel.%). MS (EI, 345 °C): *m*/*z* (%) = 301 (34) [M$^+$], 300 (74) [M – 1$^+$], 299 (39) [M$^+$], 298 (57) [M – 1$^+$], 188 (41), 159 (57), 81 (100), 57 (98), 55 (54), 43 (72). $C_{14}H_{10}BrN_3$ (300.15): calcd. C 56.02, H 3.36, N 14.00; found C 55.83, H 3.58, N 14.35.

General Procedure for 2a–f: cf. ref.[31]; the acyl chloride was added dropwise to a solution of **1a** and pyridine or triethylamine in THF at –10 °C. The reaction mixture was stirred at –10 °C for 1 h and at room temperature overnight, was washed several times with water, and the product was extracted by ethyl acetate. The product solution was dried with solid $MgSO_4$. Ethyl acetate was removed in vacuo, and the residue was purified by column chromatography using silica gel (20–30% ethyl acetate and 80–70% *n*-hexane).

***N*-(3-Bromo-5-methylpyridin-2-yl)pivaloylamide (2a):** Reaction of pivaloyl chloride (3.21 mL, 25.7 mmol) with **1a** (4.0 g, 21.4 mmol) and triethylamine (4.61 mL, 32.1 mmol) in THF (20 mL) provided 4.80 g (83%) of **2a**, m.p. 156 °C. ^{1}H NMR ($CDCl_3$): δ = 1.36 (s, 9 H, CMe_3), 2.31 (s, 3 H, 5-CH_3), 7.72 (d, ^4J = 1.8 Hz, 1 H, 4-H), 7.90 (very br. s, 1 H, NH), 8.25 (d, ^4J = 1.8 Hz, 1 H, 6-H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 17.46 (Me-5), 27.51 (C*Me*$_3$), 40.02 (*C*Me$_3$), 112.95 (C_q-3), 131.70 (C_q-5), 141.63 (CH-4), 146.25 (C_q-2), 147.66 (CH-6), 176.02 (CO) ppm. MS (EI 70 eV, 300 °C): *m*/*z* (%) = 271 (3.5), 269 (4) [M – 1$^+$], 228 (4), 226 (4), 190 (88) [M – Br$^+$], 187 (43), 185 (48), 57 (100). $C_{11}H_{15}BrN_2O$ (271.15): calcd. C 48.72, H 5.58, N 10.33; found C 48.79, H 5.72, N 9.92.

***N*-(3-Bromo-5-methylpyridin-2-yl)-2-furoylamide (2b):** Reaction of 2-furoyl chloride (2.43 mL, 24.1 mmol) with **1a** (4.5 g, 24.1 mmol) and pyridine (24 mL) gave 4.8 g (71%) of **2b**, m.p. 93 °C. ^{1}H NMR ($CDCl_3$): δ = 2.33 (s, 3 H, 5-Me), 6.57 (d, ^3J = 3.5, 1.7 Hz, 1 H, 4′-H), 7.31 (d, ^3J = 3.5, ^4J = 0.7 Hz, 1 H, 3′-H), 7.55 (br. d, ^3J = 1.6, ^4J = 0.6 Hz, 1 H, 5′-H), 7.76 (d, ^4J = 1.3 Hz, 1 H, 4-H), 8.29 (br. d, ^4J = 1.1 Hz, 1 H, 6-H), 8.75 (very br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 298 K): δ = 17.42 (s, 5-Me), 112.17 (3-C_q), 112.59 (4′-CH), 116.09 (3′-CH), 131.77 (5-C_q), 141.82 (4-CH), 144.60 (5′-CH), 145.65 (2′-C_q), 147.42 (2-C_q), 147.49 (6-CH), 155.19 (C_q, CO) ppm. MS (EI 70 eV, 345 °C): *m*/*z* (%) = 282 (1) [M$^+$], 280 (1) [M$^+$], 254 (54), 252 (55), 228 (11), 226 (13), 201 (8) [M – Br$^+$], 95 (100), 51 (9). $C_{11}H_9BrN_2O_2$ (281.11): calcd. C 47.00, H 3.23, N 9.97; found C 47.31, H 3.65, N 9.81.

***N*-(3-Bromo-5-methylpyridin-2-yl)-2-thenoylamide (2c):** Reaction of 2-thiophenylacetyl chloride (2.80 mL, 25.7 mmol) with **1a** (4.8 g, 25.7 mmol) and pyridine (24 mL) gave 5.3 g (70%) of **2c**, m.p. 115 °C. ^{1}H NMR ($CDCl_3$): δ = 2.33 (s, 3 H, 5-Me), 7.14 (d, ^3J = 5.0, 3.7 Hz, 1 H, 4′-H), 7.57 (d, ^3J = 5.0, ^4J = 1.1 Hz, 1 H, 3′-H), 7.70 (dd, ^3J = 3.7, ^4J = 1.1 Hz, 1 H, 5′-H), 7.76 (d, ^4J = 2.0, ^4J = 0.6 Hz, 1 H, 4-H), 8.26 (br. s, 1 H, 6-H), 8.39 (very br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 17.51 (s, 5-Me), 112.94 (3-C_q), 127.88 (4′-CH), 129.44, 131.48 (5′-CH, 3′-CH), 132.08 (5-C_q), 138.59 (2′-C_q), 141.94 (4-CH), 146.05 (2-C_q), 147.64 (br., 6-CH), 159.33 (C_q, CO) ppm. MS (EI 70 eV, 345 °C): *m*/*z* (%) = 298 (2), 296 (2) [M$^+$], 270 (2.5), 268 (2.5), 218 (5), 217 (40) [M – Br$^+$], 111 (5), 110 (100), 45 (25), 44 (26). $C_{11}H_9BrN_2OS$ (297.17): calcd. C 44.46, H 3.05, N 9.43; found C 43.93, H 2.90, N 9.09.

***N*-(3-Bromo-5-methylpyridin-2-yl)benzamide (2d):** Reaction of benzoyl chloride (2.82 mL, 24.1 mmol) with **1a** (4.5 g, 24.1 mmol) and pyridine (24 mL) provided 5.2 g (84%) of **2d**, m.p. 135 °C. ^{1}H NMR ($CDCl_3$): δ = 2.35 (s, 3 H, 5-Me), 7.46–7.60 (m, 3 H, *m*-CH, *p*-CH), 7.78 (d, ^4J = 1.2 Hz, 1 H, 4-H), 7.96 (dm, ΣJ = 9.6 Hz, 2 H, *o*-CH), 8.30 (br. s, 1 H, 6-H), 8.43 (very br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 298 K): δ = 17.52 (s, 5-Me), 112.85 (3-C_q), 127.50, 128.83 (2 *o*-CH, 2 *m*-CH), 132.00 (*i*-C_q), 132.27 (*p*-CH), 134.26 (5-C_q), 141.90 (4-CH), 146.36 (2-C_q), 147.69 (6-CH), 165.10 (C_q, CO) ppm. MS (EI 70 eV, 250 °C): *m*/*z* (%) = 292 (4) [M$^+$], 290 (4) [M$^+$], 291 (2), 289 (2), 264 (6), 263 (16), 262 (6), 261 (16), 211 (46) [M – Br$^+$], 106 (8), 105 (100), 77 (60), 51 (14). $C_{13}H_{11}BrN_2O$ (291.14): calcd. C 53.63, H 3.81, N 9.62; found C 53.28, H 4.19, N 9.42.

***N*-(3-Bromo-5-methylpyridin-2-yl)-2-chlorobenzamide (2e):** Reaction of 2-chlorobenzoyl chloride (4.15 mL, 32.7 mmol) with **1a** (6.0 g, 32.1 mmol) and pyridine (34 mL) provided 6.1 g (58%) colourless solid **2e**, m.p. 54–59 °C, slightly contaminated by the *N*-bis(chlorobenzoylation) product **2e′**. **2e** ^{1}H NMR ($CDCl_3$ 7.25): δ = 2.33 (s, 3 H, 5-Me), 7.24–7.26 (m, 1 H, aryl-H), 7.35–7.47 (m, 2 H, aryl-H), 7.72–7.84 (m, 2 H, aryl-H), 8.26 (d, ^4J = 1.6 Hz, 1 H, 6-H), 8.48 (br., 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 17.68 (5-Me), 119.77 (C_q-3), 127.25, 130.33, 130.79 (very br.), 131.87 (CH), 132.26 (C_q-2′), 134.77 (C_q-5), 135.59 (C_q-1), 141.90 (br) (CH-4), 145.9 (very br., C_q), 147.6 (very br.) (CH-6), 168.46 (C_q, CO) ppm. Mass calcd. for $C_{13}H_{10}BrClN_2O$: 323.97, 325.96 (100, 97 rel.%). MS (EI 70 eV, 130 °C): *m*/*z* (%) = 328 (0.6), 326 (2.6) [M$^+$], 324 (2) [M$^+$], 310 (2.7), 308 (2), 292 (1.6), 290 (1.4), 139 (100) [$ClC_6H_4CO^+$]. (impurity by **2e′**: ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 17.55

(5-Me), 126.48, 129.23, 131.67, 142.76, 148.62 (CH) ppm, C_q signals at noise level. MS: *m*/*z* = 430, 428 [**2c**′ – Cl^+]).

(3-Bromo-5-methylpyridin-2-yl)-1-naphthoylamide (2f): Reaction of 1-naphthoyl chloride (3.29 mL, 21.4 mmol) with **1a** (4.0 g, 21.4 mmol) and pyridine (24 mL) provided 4.9 g (67%) of **2f**, m.p. 128 °C. ^{1}H NMR ($CDCl_3$): δ = 2.04 (s, 3 H, 5-CH_3), 7.52–7.64 (m, 3 H, naph), 7.91 (dd, ^3J = 7.1, ^4J = 1.1 Hz, 1 H, naph), 7.93–7.98 (m, 1 H, naph), 8.05 (d, ^3J = 8.6 Hz, 1 H, naph), 8.07 (d, J = 1 Hz, 1 H, 4-H), 8.33 (d, ^4J = 1.1 Hz, 1 H, 6-H), 8.42–8.49 (m, 1 H, naph) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 17.49 (Me-5), 113.89 (C_q-3), 125.87 (CH), 126.47 (CH), 127.08 (CH), 127.57 (CH), 128.15 (CH), 129.47 (CH), 131.60 (C_q-5), 132.24 (CH), 135.25 (C_q, naph), 144.14 (CH-4), 147.74 (CH-6), 148.95 (C_q-2), 150.82, 170.57, 171.39 (2 C_q and CO) ppm. MS (EI 70 eV, 150 °C): *m*/*z* (%) = 342 (7) [M^+], 341 (2), 340 (7) [M^+], 314 (8), 312 (9), 156 (15), 155 (100), 77 (12). $C_{17}H_{13}BrN_2O$ (341.20): calcd. C 59.84, H 3.84, N 8.21; found C 59.64, H 3.86, N 7.80.

General Procedure for Diethyl 2-Acylamido- and 2-Amino-3-pyridinephosphonates 3 and 4: A mixture of solid **1** or **2** and palladium acetate or chloride was placed into a distillation apparatus and heated at 170 °C. Then triethyl phosphite was added slowly, and heating was continued for a total reaction time of 10 min unless indicated otherwise. The resulting product was purified by column chromatography on silica gel using ethyl acetate/*n*-hexane.

Diethyl [5-Methyl-2-(pivaloylamino)pyridin-3-yl]phosphonate (3a): Reaction of **2a** (4.8 g, 17.7 mmol) with $P(OEt)_3$ (3.7 mL, 21.3 mmol, 1.2 equiv.) in the presence of $Pd(OAc)_2$ (0.47 g, 2.09 mmol, 12 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (85:15%) or by distillation at 10^{-6} mbar/100–105 °C (bath temperature) gave 2.32 g (40%) of **3a** as pale yellow oil. ^{1}H NMR ($CDCl_3$): δ = 1.34 (s, 9 H, CMe_3), 1.34 (t, ^3J = 7.0 Hz, 6 H, CH_3), 2.33 (s, 3 H, 5-Me), 4.06 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 8.2 Hz, 2 H_A, OCH_2), 4.14 (m, ^2J = 12.0, ^3J = 7.1, $^3J_{PH}$ = 14.6 Hz, 2 H_B, OCH_2), 7.73 (dd, $^3J_{PH}$ = 14.6, ^4J = 2.3 Hz, 1 H, 4-H), 8.50 (d, ^4J = 2.3, $^5J_{PH}$ = 1.5 Hz, 1 H, 6-H), 10.13 (br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 16.27 (d, ^3J = 6.4 Hz, CH_3), 17.73 (s, 5-Me), 27.40 (C*Me*$_3$), 40.28 (*C*Me_3), 62.93 (d, ^2J = 5.6 Hz, OCH_2), 110.88 (d, ^1J = 182.8 Hz, C_q-3), 128.08 (d, ^3J = 10.3 Hz, C_q-5), 142.12 (d, ^2J = 5.5 Hz, CH-4), 151.77 (d, ^2J = 9.5 Hz, C_q-2), 153.11 (s, CH-6), 176.42 (s, CO) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 17.70 ppm. MS (EI 70 eV, 150 °C): *m*/*z* (%) = 328 (8) [M^+], 272 (13), 271 (100) [M – CMe_3^+], 243 (23), 215 (51), 163 (32), 107 (25), 57 (26). $C_{15}H_{25}N_2O_4P$ (328.34): calcd. C 54.57, H 7.67, N 8.53; found C 54.31, H 7.74, N 8.41.

Screening Test: 2a (1.2 g, 4.4 mmol) was heated with $P(OEt)_3$ (0.95 mL, 5.5 mmol, 1.2 equiv.) in the presence of $PdCl_2$ (80 mg, 10 mol-%). After 10 min at 170 °C the crude yield of **3a** was about 70% based on ^{1}H NMR integration of NH and aryl CH-4 signals. The ^{31}P NMR signal intensity ratio (not quantitatively) was 48:25:27% for **3a**: $(EtO)_2PHO$/$(EtO)_3PO$ for large signals, others were small. Heating further 10 min at 180 °C led to a drop of the ^{31}P signal of **3a** by ca. 50% relative to the signal of $(EtO)_2PHO$ in favor of the signal for $(EtO)_3PO$ and to new ^{31}P NMR signals in the phosphate region (δ = 0.7, 1.5, 3.6 ppm), indicating P–C bond cleavage. Also the yield by ^{1}H NMR integration became lower. This trend continued on further heating; after 40 min almost all **3a** was decomposed.

Diethyl [2-(2-Furoylamino)-5-methylpyridin-3-yl]phosphonate (3b): Reaction of **2b** (5.4 g, 19.2 mmol) with $P(OEt)_3$ (4.0 mL, 23.1 mmol, 1.2 equiv.) in the presence of $Pd(OAc)_2$ (0.43 g, 1.92 mmol, 10 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (60:40%) gave 2.73 g (42%) of white solid **3b**, m.p. 109 °C. ^{1}H NMR ($CDCl_3$): δ = 1.35 (t, ^3J = 7.1, Hz, 6 H, CH_3), 2.35 (s, 3 H, 5-Me), 4.11 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 8.1 Hz, 2 H_A, OCH_2), 4.22 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 14.2 Hz, 2 H_B, OCH_2), 6.54 (dd, ^3J = 3.5, 1.7 Hz, 1 H, 4′-H), 7.30 (dd, ^3J = 3.6, ^4J = 0.6 Hz, 1 H, 3′-H), 7.59 (dd, ^3J = 1.7, ^4J = 0.7 Hz, 1 H, 5′-H), 7.78 (ddd, $^3J_{PH}$ = 14.8, ^4J = 2.5, ^4J = 0.5 Hz, 1 H, 4-H), 8.54 (d, ^4J = 2.5, ^5J = 1.3 Hz, 1 H, 6-H), 10.98 (br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 16.24 (d, ^3J = 6.6 Hz, CH_3), 17.78 (5-Me), 63.07 (d, ^2J = 5.4 Hz, OCH_2), 110.79 (d, $^1J_{PC}$ = 182.4 Hz, C_q-3), 112.26 (CH-4′), 115.74 (CH-3′), 128.37 (d, ^3J = 10.0 Hz, C_q-5), 142.26 (d, ^2J = 5.4 Hz, CH-4), 145.06 (CH-5′), 148.06 (C_q-2′), 151.26 (d, ^2J = 9.4 Hz, C_q-2), 153.25 (CH-6), 155.34 (CO) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 17.37 ppm. MS (EI 70 eV, 345 °C): *m*/*z* (%) = 338 (8) [M^+], 311 (15), 310 (100), 284 (18), 282 (18), 254 (30), 236 (21), 95 (69). $C_{15}H_{19}N_2O_5P$ (338.30): calcd. C 53.26, H 5.66, N 8.28; found C 52.93, H 5.87, N 8.15.

Diethyl [5-Methyl-2-(2-thenoylamino)pyridin-3-yl]phosphonate (3c): Reaction of **2c** (5.0 g, 16.8 mmol) with $P(OEt)_3$ (3.5 mL, 20.18 mmol, 1.2 equiv.) in the presence of $Pd(OAc)_2$ (0.45 g, 2.0 mmol, 8.4 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (65:35%) gave 2.4 g (40%) of pale yellow solid **3c**, m.p. 94 °C. Single crystals suitable for crystal structure determination were grown by slow evaporation of a $CHCl_3$ solution (crystal data in Table 2, selected bond lengths and angles in Figure 1). ^{1}H NMR ($CDCl_3$): δ = 1.35 (t, ^3J = 7.1, Hz, 6 H, CH_3), 2.35 (s, 3 H, 5-Me), 4.12 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 8.0 Hz, 2 H_A, OCH_2), 4.21 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 14.8 Hz, 2 H_B, OCH_2), 7.12 (dd, ^3J = 5.0, 3.8 Hz, 1 H, 4′-H), 7.56 (dd, ^3J = 5.0, ^4J = 1.0 Hz, 1 H, 3′-H), 7.72 (dd, $^3J_{PH}$ = 14.7, ^4J = 2.4 Hz, 1 H, 4-H), 7.85 (dd, ^3J = 3.8, ^4J = 1.0 Hz, 1 H, 5′-H), 8.53 (unresolved dd, 1 H, 6-H), 11.20 (br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 16.26 (d, ^3J = 6.5 Hz, CH_3), 17.78 (5-Me), 63.11 (d, ^2J = 5.6 Hz, OCH_2), 109.92 (d, $^1J_{PC}$ = 181.7 Hz, C_q-3), 127.91 (CH-4′), 128.08 (d, ^3J = 10.0 Hz, C_q-5), 128.90 (CH-3′), 131.57 (CH-5′), 140.35 (C_q-2′), 141.99 (d, ^2J = 5.1 Hz, CH-4), 151.72 (d, ^2J = 9.8 Hz, C_q-2), 153.42 (CH-6), 158.93 (CO) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 18.09 ppm. MS (EI 70 eV, 345 °C): *m*/*z* (%) = 354 (16) [M^+], 323 (13), 246 (15), 186 (15), 110 (100), 95 (28). $C_{15}H_{19}N_2O_4PS$ (354.36): calcd. C 50.84, H 5.40, N 7.91; found C 50.71, H 5.72, N 7.62.

Diethyl (2-Benzoylamino-5-methylpyridin-3-yl)phosphonate (3d): Reaction of **2d** (4.5 g, 15.5 mmol) with $P(OEt)_3$ (3.3 mL, 19.0 mmol, 1.2 equiv.) in the presence of $Pd(OAc)_2$ (0.43 g, 1.92 mmol, 12 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (65:35%) gave 1.7 g (32%) of pale yellow solid **3d**, m.p. 86 °C. ^{1}H NMR ($CDCl_3$): δ = 1.34 (t, ^3J = 7.1 Hz, 6 H, CH_3), 2.36 (s, 3 H, 5-Me), 4.10 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 8.1 Hz, 2 H_A, OCH_2), 4.20 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 14.8 Hz, 2 H_B, OCH_2), 7.46–7.57 (m, 3 H, *m*- and *p*-H), 7.75 (dd, $^3J_{PH}$ = 14.6, ^4J = 2.4 Hz, 1 H, 4-H), 8.11 (td, ^3J = 7.7–8.2, ^4J = 1.4–1.9 Hz, 2 H, *o*-H), 8.57 (d, ^4J = 2.4, $^5J_{PH}$ = 1.4 Hz, 1 H, 6-H), 11.14 (br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 16.26 (d, ^3J = 6.6 Hz, CH_3), 17.81 (5-Me), 62.83 (d, ^2J = 5.4 Hz, OCH_2), 110.52 (d, $^1J_{PC}$ = 183.0 Hz, C_q-3), 127.63 (2 CH-*o* or CH-*m*), 128.24 (d, ^3J = 10.5 Hz, C_q-5), 128.73 (2 CH-*o* or CH-*m*), 131.99 (CH-*p*), 134.59 (C_q-*i*), 142.04 (d, ^2J = 5.3 Hz, CH-4), 151.93 (d, ^2J = 9.2 Hz, C_q-2), 153.38 (CH-6), 164.41 (CO) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 17.89 ppm. MS (EI 70 eV, 345 °C): *m*/*z* (%) = 349 (3) [M + 1^+], 348 (27) [M^+], 347 (14), 320 (22), 319 (100), 291 (13), 240 (11), 211 (11), 105 (95), 77 (72). $C_{17}H_{21}N_2O_4P$ (348.33): calcd. C 58.62, H 6.08, N 8.04; found C 58.68, H 6.28, N 7.87.

Diethyl [2-(2-Chlorobenzoylamino)-5-methylpyridin-3-yl]phosphonate (3e): Reaction of **2e** (5.69 g, 17.5 mmol) with $P(OEt)_3$ (3.61 mL,

21.0 mmol, 1.2 equiv.) in the presence of $Pd(OAc)_2$ (0.37 g, 2.10 mmol, 12 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (65:35%) gave 2.4 g (36%) of pale yellow solid **3e**, m.p. 109 °C. ^{1}H NMR ($CDCl_3$): δ = 1.32 (t, ^3J = 7.1 Hz, 6 H, CH_3), 2.36 (s, 3 H, 5-Me), 4.11 (m, ^2J = 10.1, ^3J = 7.0, $^3J_{PH}$ = 8.2 Hz, 2 H_A, OCH_2), 4.20 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 14.3 Hz, 2 H_B, OCH_2), 7.31–7.46 (m, 3 H, 3′-, 4′- and 5′-H), 7.66 (dd, ^3J = 6.7, ^4J = 2.6, ^4J = 1.4 Hz, 1 H, 6′-H), 7.78 (dd, $^3J_{PH}$ = 14.7, ^4J = 2.6 Hz, 1 H, 4-H), 8.52 (unresolved dd, 1 H, 6-H), 10.55 (br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 16.24 (d, ^3J = 6.5 Hz, CH_3), 17.79 (5-Me), 63.04 (d, ^2J = 5.4 Hz, OCH_2), 111.02 (d, $^1J_{PC}$ = 182.6 Hz, C_q-3), 127.06 (CH-5′), 128.77 (d, ^3J = 10.0 Hz, C_q-5), 129.19 (CH-6′), 130.38 (CH-3′), 131.03 (C_q-2′), 131.99 (CH-4′), 136.11 (C_q-*i*), 142.25 (d, ^2J = 5.4 Hz, CH-4), 151.15 (d, ^2J = 9.4 Hz, C_q-2), 153.19 (d, ^4J = 0.9 Hz, CH-6), 164.57 (CO) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 16.57 ppm. MS (EI 70 eV, 140 °C): *m*/*z* (%) = 383 (2.4), 354 (18), 349 (21), 348 (100) [M^+], 319 (23), 292 (23), 139 (41), 111 (29). HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{20}ClN_2O_4P$ 382.09, [M + H^+]: 383.09217; found 383.09220.

Diethyl [5-Methyl-2-(1-naphthoylamino)pyridin-3-yl]phosphonate (3f): Reaction of **2f** (5.0 g, 14.65 mmol) with $P(OEt)_3$ (3.15 mL, 18.2 mmol, 1.2 equiv.) in the presence of $Pd(OAc)_2$ (0.39 g, 1.74 mmol, 8.4 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (55:45%) gave 1.2 g (21%) of pale yellow solid **3f**, m.p. 110 °C. ^{1}H NMR ($CDCl_3$): δ = 1.30 (t, ^3J = 7.1 Hz, 6 H, CH_3), 2.38 (s, 3 H, 5-Me), 4.10 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 8.1 Hz, 2 H_A, OCH_2), 4.18 (m, ^2J = 10.1, ^3J = 7.2, $^3J_{PH}$ = 15.1 Hz, 2 H_B, OCH_2), 7.49–7.60 (m, 3 H, aryl-H), 7.81 (dd, $^3J_{PH}$ = 14.7, ^4J = 2.0 Hz, 1 H, 4-H), 7.86–8.01 (m, 3 H, aryl-H), 8.61 (unresolved dd, 1 H, 6-H), 8.64 (dd, ^3J = 7.4, ^4J = 1.8 Hz, 1 H, 8′-H), 10.66 (br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 16.19 (d, ^3J = 6.6 Hz, CH_3), 17.79 (s, 5-Me), 63.00 (d, ^2J = 5.4 Hz, OCH_2), 111.20 (d, $^1J_{PC}$ = 182.7 Hz, C_q-3), 124.77 (CH), 125.40 (CH), 125.81 (CH), 126.38 (CH), 127.12 (CH), 128.25 (CH), 128.62 (d, ^3J = 10.6 Hz, C_q-5), 130.52 (C_q), 131.41 (CH), 133.84 (C_q), 133.91 (C_q), 142.30 (d, ^2J = 5.4 Hz, CH-4), 151.57 (d, ^2J = 9.6 Hz, C_q-2), 153.26 (CH-6), 166.68 (CO) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 17.27 ppm. MS (EI 70 eV, 345 °C): *m*/*z* (%) = 398 (18) [M^+], 370 (14), 369 (42), 171 (61), 155 (84), 148 (71), 127 (100), 91 (80), 84 (43), 72 (51), 57 (84). HRMS (ESI): *m*/*z* calcd. for $C_{21}H_{23}N_2O_4P$ 398.14, [M + H^+]: 399.14681; found 399.14682.

Diethyl (2-Amino-5-methylpyridin-3-yl)phosphonate (4a): Reaction of **1a** (5.0 g, 26.7 mmol) with $P(OEt)_3$ (5.5 mL, 31.7 mmol) in the presence of $Pd(OAc)_2$ (0.60 g, 2.67 mmol, 10 mol-%) and distillation at 10^{-6} mbar/120–123 °C (bath temperature) provided the product contaminated by **4c** in 80:20 mol-% ratio (based on ^{1}H NMR integration). Column chromatography with ethyl acetate/*n*-hexane (75:25%) gave 1.2 g (19%) of pure white solid **4a**, m.p. 69–71 °C. ^{1}H NMR ($CDCl_3$): δ = 1.34 (t, ^3J = 7.0 Hz, 6 H, CH_3), 2.20 (d, ^5J = 0.5 Hz, 3 H, 5-Me), 4.05 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 8.1 Hz, 2 H_A, OCH_2), 4.16 (m, ^2J = 10.2, ^3J = 7.1, $^3J_{PH}$ = 14.4 Hz, 2 H_B, OCH_2), 5.65 (br. s, 2 H, NH), 7.57 (dd, $^3J_{PH}$ = 15.1, ^4J = 2.3 Hz, 1 H, 4-H), 8.04 (dd, ^4J = 2.3, $^5J_{PH}$ = 1.9 Hz, 1 H, 6-H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 16.21 (d, ^3J = 6.4 Hz, CH_3), 17.16 (5-Me), 62.23 (d, ^2J = 5.2 Hz, OCH_2), 103.37 (d, $^1J_{PC}$ = 185.8 Hz, C_q-3), 121.74 (d, ^3J = 10.6 Hz, C_q-5), 142.77 (d, ^2J = 6.3 Hz, CH-4), 153.09 (CH-6), 158.29 (d, ^2J = 10.5 Hz, C_q-2) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 19.70 ppm. MS (EI 70 eV, 100 °C): *m*/*z* (%) = 245 (7), 244 (68) [M^+], 216 (12), 188 (18), 171 (22), 135 (19), 107 (100), 80 (14), 53 (16). $C_{10}H_{17}N_2O_3P$ (244.23): calcd. C 49.18, H 7.02, N 11.47; found C 49.50, H 6.90, N 11.40.

Screening Test: 1a (1.0 g, 5.3 mmol) was heated with $P(OEt)_3$ (1.1 mL, 1.2 equiv.) in the presence of $PdCl_2$ (94 mg, 10 mol-%). After 10 min at 170 °C the crude yield of **4a** was about 14% based on ^{1}H NMR integration of NH and aryl CH-4 signals. The ^{31}P NMR signal intensity ratio (not quantitatively) was 31:42:27% for **4a**: $(EtO)_2PHO$/$(EtO)_3PO$ for large signals except of unreacted $P(OEt)_3$, and other small signals. Heating for further 10 min at 180 °C led to a drop of the ^{31}P signal of **4a** relative to those of $(EtO)_2PHO$ and $(EtO)_3PO$ (rel. intensity 12:37:31%), and to stronger signals for $EtP(O)(OEt)_2$ and an unknown with δ = 3.2 ppm (5 and 15% rel. intensity). Proton signal integration gave similar yield as after 10 min whereas longer heating led to a decrease.

Diethyl {2-[(Furan-2-ylmethyl)amino]-5-methylpyridin-3-yl}phosphonate (4b): Triethyl phosphite (0.31 mL, 1.80 mmol) was added to a mixture of solid **1b** (0.40 g, 1.50 mmol) and palladium acetate (34 mg, 0.15 mmol, 10 mol-%) at 180 °C in a distillation apparatus, and heating was continued for 15–20 min. The product was purified by column chromatography on silica gel using ethyl acetate/*n*-hexane (30:70%) yielding 0.22 g (45%) of yellow oil. ^{1}H NMR ($CDCl_3$): δ = 1.24 (t, ^3J = 7.1, Hz, 6 H, CH_3), 2.12 (s, 3 H, 5-Me), 4.00 (m, 4 H, OCH_2), 4.59 (d, ^3J = 5.5 Hz, 2 H, NCH_2), 6.15 (d, ^3J = 2.7 Hz, 1 H, 3′-H), 6.23 (dd, ^3J = 3.2, ^3J = 1.8 Hz, 1 H, 4′-H), 6.92 (br. s, NH), 7.27 (dd, ^3J = 1.8, ^4J = 0.8 Hz, 1 H, 5′-H), 7.49 (dd, $^3J_{PH}$ = 15.4, ^4J = 2.3 Hz, 1 H, 4-H), 8.05 (t, ^4J = 2.2, $^5J_{PH}$ = 2.0 Hz, 1 H, 6-H) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 19.02 ppm. MS (EI 70 eV, 100 °C): *m*/*z* (%) = 325 (100) [M^+]. HRMS (EI): *m*/*z* calcd. for $C_{15}H_{21}N_2O_4P$ 324.13, [M + H^+]: 325.13117; found 325.13123.

Diethyl (2-Ethylamino-5-methylpyridin-3-yl)phosphonate (4c): Reaction of **1c** (4.81 g, 22.4 mmol) with triethyl phosphite (5.39 mL, 26.8 mmol, 1.2 equiv.) in the presence of $PdCl_2$ (0.40 g, 2.24 mmol, 10 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (10:90%) gave 2.68 g (44%) of **4c** as pale yellow oil. ^{1}H NMR ($CDCl_3$): δ = 1.24 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.34 (t, ^3J = 7.1 Hz, 6 H, CH_3), 2.17 (s, 3 H, 5-Me), 3.44 (qd, ^3J = 7.2, 5.3 Hz, 2 H, CH_2), 4.05 (m, ^2J = 10.1, $^3J_{PH}$ = 8.0, ^3J = 7.1 Hz, 2 H_A, OCH_2), 4.14 (m, $^3J_{PH}$ = 14.6, ^2J = 10.1, ^3J = 7.1 Hz, 2 H_B, OCH_2), 6.65 (br. s, 1 H, NH), 7.51 (dd, $^3J_{PH}$ = 15.6, ^4J = 2.3 Hz, 1 H, 4-H), 8.09 (br. d, ^4J = 2.0 Hz, 1 H, 6-H) ppm. ^{13}C{H} NMR ($CDCl_3$): δ = 14.67 (s, CH_3), 16.10 (d, ^3J = 6.5 Hz, CH_3), 16.99 (s, 5-Me), 35.93 (s, NCH_2), 62.05 (d, ^2J = 5.1 Hz, OCH_2), 102.92 (d, $^1J_{PC}$ = 184.9 Hz, C_q-3), 119.43 (d, ^3J = 11.0 Hz, C_q-5), 142.65 (d, ^2J = 6.3 Hz, CH-4), 152.74 (d, ^4J = 1.0 Hz, CH-6), 157.72 (d, ^2J = 11.1 Hz, C_q-2) ppm. ^{31}P{H} NMR ($CDCl_3$): δ = 20.43 ppm. MS (EI 70 eV, 25 °C): *m*/*z* (%) = 274 (10), 273 (64) [M^+], 259 (14), 258 (100), 229 (41), 202 (46), 183 (38), 93 (27). HRMS (ESI): *m*/*z* calcd. for $C_{12}H_{21}N_2O_3P$: 272.13, [M + H]$^+$: 273.13625; found 273.13625.

Diethyl [5-Methyl-2-(phenylamino)pyridin-3-yl]phosphonate (4d): Reaction of **1d** (8.60 g, 32.7 mmol) with $P(OEt)_3$ (6.80 mL, 39.2 mmol) in the presence of $Pd(OAc)_2$ (0.88 g, 3.92 mmol, 8.3 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (10:90%) gave 6.3 g (60%) of white solid **4d**, m.p. 60 °C. ^{1}H NMR ($CDCl_3$): δ = 1.35 (td, ^3J = 7.1, $^4J_{PH}$ = 0.5 Hz, 6 H, CH_3), 2.23 (d, $^5J_{PH}$ = 0.5 Hz, 3 H, 5-Me), 4.08 (m, ^2J = 10.2, ^3J = 7.0, $^3J_{PH}$ = 8.2 Hz, 2 H_A, OCH_2), 4.19 (m, ^2J = 10.1, ^3J = 7.1, $^3J_{PH}$ = 14.2 Hz, 2 H_B, OCH_2), 6.98 (tt, ^3J = 7.4, ^4J = 1.1 Hz, 1 H, *p*-H), 7.30 (tm, ^3J = 8.5, 7.4 Hz, 2 H, *m*-H), 7.62 (dd, $^3J_{PH}$ = 15.5, ^4J = 2.3 Hz, 1 H, 4-H), 7.62–7.67 (superimposed dd, ^3J = 8.5, ^4J = 1.1 Hz, 2 H, *o*-H), 8.20 (d, ^4J = 2.2, $^5J_{PH}$ = 2 Hz, 1 H, 6-H), 9.20 (br. s, 1 H, NH) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 16.19 (d, ^3J = 6.6 Hz, CH_3), 17.28 (5-Me), 62.49 (d, ^2J = 5.1 Hz, OCH_2), 105.17 (d, $^1J_{PC}$ = 182.7 Hz, C_q-3), 119.65 (2 CH-*o*), 121.87 (CH-*p*), 122.40 (d, ^3J = 10.5 Hz, C_q-5), 128.66 (2 CH-*m*), 140.35 (C_q-*i*),

142.64 (d, ^2J = 6.4 Hz, CH-4), 152.32 (CH-6), 155.21 (d, ^2J = 9.7 Hz, C_q-2) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 19.70 ppm. IR (KBr): $\tilde{\nu}$ = 3429–3308 (very br.) (H_2O, NH), 1240 (very strong, P=O) cm^{-1}. MS (EI 70 eV, 270 °C): *m*/*z* (%) = 321 (10), 320 (100) [M^+], 319 (84), 291 (18), 263 (19), 245 (68), 183 (26), 131 (10), 77 (28). $C_{16}H_{21}N_2O_3P$ (320.32): calcd. C 59.99, H 6.61, N 8.75; found C 60.13, H 6.80, N 8.61.

Diethyl [2-(Pyridin-2-ylamino)pyridin-3-yl]phosphonate (4e): Reaction of **1e** (0.61 g, 2.44 mmol) with triethyl phosphite (0.43 mL, 2.48 mmol) in the presence of $Pd(OAc)_2$ (55 mg, 0.245 mmol, 10 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (25:75%) gave 0.27 g (36%) **4e** as pale yellow oil. ^1H NMR ($CDCl_3$): δ = 1.28 (t, ^3J = 7.1 Hz, 6 H, CH_3), 4.06 (m, ^2J = 10.1, $^3J_{PH}$ = 8.5, ^3J = 7.1 Hz, 2 H_A, OCH_2), 4.16 (m, $^3J_{PH}$ = 14.3, ^2J = 10.2, ^3J = 7.1 Hz, 2 H_B, OCH_2), 6.79 (ddd, ^3J = 7.5, 4.9, $^4J_{PH}$ = 2.2 Hz, 1 H, 5-H), 6.83 (ddd, ^3J = 7.2, 4.9, ^4J = 1.0 Hz, 1 H, 5′-H), 7.58 (ddd, ^3J = 8.6, 7.2, ^4J = 1.9 Hz, 1 H, 4′-H), 7.85 (ddd, $^3J_{PH}$ = 15.2, ^3J = 7.5, ^4J = 2.0 Hz, 1 H, 4-H), 8.24 (ddd, ^3J = 4.9, ^4J = 1.9, $^5J_{PH}$ = 0.7 Hz, 1 H, 6′-H), 8.32 (br. d, ^3J = 8.6 Hz, $^4J \approx {}^5J$, small, 1 H, 3′-H), 8.35 (dt, ^3J = 4.9, ^4J = 2.0, $^5J_{PH} \approx$ 2.5 Hz, 1 H, 6-H), 9.71 (br. s, 1 H, NH) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 16.26 (d, ^3J = 6.3 Hz, CH_3), 62.73 (d, ^2J = 5.2 Hz, OCH_2), 107.46 (d, $^1J_{PC}$ = 183.1 Hz, C_q-3), 113.14 (CH-3′), 114.69 (d, ^3J = 10.5 Hz, CH-5), 117.51 (CH-5′), 137.58 (CH-4′), 142.82 (d, ^2J = 5.9 Hz, CH-4), 148.22 (CH-6′), 151.98 (CH-6), 153.21 (C_q-2′), 155.62 (d, ^2J = 9.6 Hz, C_q-2) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 18.12 ppm. MS (EI 70 eV, 345 °C): *m*/*z* (%) = 308 (0.6), 307 (8) [M^+], 234 (10), 199 (13), 171 (100), 78 (10). HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{18}N_3O_3P$: 307.10, [M + H]$^+$: 308.11600; found 308.11585.

Diethyl [2-(Quinolin-3-ylamino)pyridin-3-yl]phosphonate (4f): Reaction of **1f** (5.50 g, 18.3 mmol) with triethyl phosphite (3.79 mL, 21.9 mmol) in the presence of $Pd(OAc)_2$ (0.49 g, 2.18 mmol, 8.4 mol-%) and purification by column chromatography with ethyl acetate/*n*-hexane (30:70%) gave 1.38 g (21%) yellow solid **4f**, m.p. 94 °C. ^1H NMR ($CDCl_3$): δ = 1.30 (t, ^3J = 7.1 Hz, 6 H, CH_3), 4.04 (m, ^2J = 10.1, $^3J_{PH}$ = 8.1, ^3J = 7.1 Hz, 2 H_A, OCH_2), 4.12 (m, $^3J_{PH}$ = 14.2, ^2J = 10.2, ^3J = 7.1 Hz, 2 H_B, OCH_2), 6.78 (ddd, ^3J = 7.5, 4.9, $^4J_{PH}$ = 2.2 Hz, 1 H, 5-H), 7.42 (td, ^3J = 7.8, 7.1, ^4J = 1.3 Hz, 1 H, 6′-H), 7.48 (td, ^3J = 8.3, 7.1, ^4J = 1.5 Hz, 1 H, 7′-H), 7.72 (dd, ^3J = 7.8, ^4J = 1.4 Hz, 1 H, 5′-H), 7.76 (ddd, $^3J_{PH}$ = 15.2, ^3J = 7.5, ^4J = 2.0 Hz, 1 H, 4-H), 7.96 (d, ^3J = 8.3 Hz, 1 H, 8′-H), 8.38 (dt, ^3J = 4.9, ^4J = 2.0, $^5J_{PH}$ = 2.4 Hz, 1 H, 6-H), 8.78 (d, ^4J = 2.5 Hz, 1 H, 4′-H), 8.88 (d, ^4J = 2.6 Hz, 1 H, 2′-H), 9.85 (br. s, 1 H, NH) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 16.28 (d, ^3J = 6.5 Hz, CH_3), 62.83 (d, ^2J = 5.4 Hz, OCH_2), 106.36 (d, $^1J_{PC}$ = 183.3 Hz, C_q-3), 114.48 (d, ^3J = 10.3 Hz, CH-5), 121.81 (CH-4′), 126.74 (CH-5′), 127.00 (CH-7′), 127.34 (CH-6′), 128.64 (C_q-4a′), 128.87 (CH-8′), 133.85 (C_q-3a′), 142.31 (d, ^2J = 5.4 Hz, CH-4), 144.09 (C_q-8a′), 145.79 (CH-2′), 152.35 (CH-6), 156.85 (d, ^2J = 10.6 Hz, C_q-2) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 19.02 ppm. MS (EI 70 eV, 345 °C): *m*/*z* (%) = 359 (23), 358 (100) [M + 1$^+$], 357 (95) [M^+], 329 (38), 300 (42), 282 (81), 221 (20), 220 (55), 219 (24), 149 (20). HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{20}N_3O_3P$ 357.13, [M + H]: 358.13146; found 358.13150.

Quinoxaline Derivatives 5–7: 2,3-Dichloroquinoxaline,[32] 3-chloroquinoxalin-2-amine (**5a**)[19] and *N*-(3-bromoquinoxalin-2-yl)-*tert*-butylamine (**5b**)[20] were synthesized according to known procedures, **5a** slightly modified, using a reaction temperature of 80 °C instead of 140 °C, yield 67%, m.p. 137–139 °C. NMR spectroscopic data of **5a** (not given in ref.[19]) and corrected NMR spectroscopic data of **5b** are presented.

3-Chloroquinoxalin-2-amine (5a): ^1H NMR ($CDCl_3$): δ = 5.53 (br. s, 2 H, NH_2), 7.47 (td, ^3J = 8.3, 6.8, ^4J = 1.7 Hz, 1 H, 6-H), 7.63 (td, ^3J = 8.3, 6.8, ^4J = 1.4 Hz, 1 H, 7-H), 7.69 (dd br, ^3J = 8.3, ^4J = 1.5, ^5J = 0.5 Hz, 1 H, 8-H), 7.86 (ddd, ^3J = 8.2, ^4J = 1.3, ^5J = 0.5 Hz, 1 H, 5-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 125.41 (CH-6), 126.06 (CH-8), 128.10 (CH-5), 130.63 (CH-7), 137.05, 137.33 (C_q-4a, C_q-3), 140.31 (C_q-8a), 148.71 (C_q-2) ppm. MS (EI 70 eV, 165 °C): *m*/*z* (%) = 181 (30) [M^+(^{37}Cl)], 179 (100) [M^+(^{35}Cl)], 144 (84), 117 (23), 102 (8), 90 (26), 44 (81).

***N*-(3-Bromoquinoxalin-2-yl)-*tert*-butylamine (5b):** ^1H NMR ($CDCl_3$): δ = 1.57 (s, 9 H, CMe_3), 5.49 (br. s, 1 H, NH), 7.36 (td, ^3J = 8.3, 7.0, ^4J = 1.5 Hz, 1 H, 6-H), 7.55 (td, ^3J = 8.4, 7.0, ^4J = 1.5 Hz, 1 H, 7-H), 7.70 (ddd, ^3J = 8.3, ^4J = 1.3, ^5J = 0.3 Hz, 1 H, 8-H), 7.76 (ddd, ^3J = 8.4, ^4J = 1.3, ^5J = 0.3 Hz, 1 H, 5-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 29.0 (CMe_3), 52.9 (CMe_3), 125.7 (CH-6), 127.2 (CH-8), 129.0 (CH-5), 130.7 (CH-7), 137.4, 139.1 (C_q-4a, C_q-3), 142.2 (C_q-8a), 148.3 (C_q-2) ppm.

Diethyl (3-Aminoquinoxalin-2-yl)phosphonate (7a): Triethyl phosphite (1.86 mL, 10.7 mmol) was added to a mixture of solid **5a** (1.3 g, 7.24 mmol) and $Pd(OAc)_2$ (90 mg, 0.40 mmol, 5.5 mol-%). The reaction mixture was refluxed for almost 2.5 h at 180 °C. The resulting crude product was distilled at 160 °C (bath)/10^{-6} mbar to give 1.81 g (89%) yellow solid **7a**, m.p. 57 °C. ^1H NMR ($CDCl_3$): δ = 1.39 (dd, ^3J = 6.9, ^4J = 0.6 Hz, 6 H, CH_3), 4.28 (m, 4 H, OCH_2), 6.54 (br. s, 2 H, NH), 7.43 (td, ^3J = 8.3, 6.0, ^4J = 2.4 Hz, 1 H, 7-H), 7.61–7.70 (m, 2 H, 5-H, 6-H), 7.97 (dp, ^3J = 8.2, ^4J = 1.4, $^5J \approx {}^5J_{PH}$ = 0.7 Hz, 1 H, 8-H) ppm. $^{13}C\{H\}$ NMR ($CDCl_3$): δ = 16.20 (d, ^3J = 6.3 Hz, CH_3), 63.91 (d, ^2J = 6.0 Hz, OCH_2), 125.18 (s, CH-7), 125.73 (d, ^5J = 2.5 Hz, CH-5), 129.83 (d, ^4J = 1.2 Hz, CH-8), 132.48 (s, CH-6), 136.59 (d, ^1J = 218.1 Hz, C_q-2), 137.33 (d, ^3J = 19.8 Hz, C_q-8a), 142.46 (d, ^4J = 2.3 Hz, C_q-4a), 153.59 (d, ^2J = 28.2 Hz, C_q-3) ppm. $^{31}P\{H\}$ NMR ($CDCl_3$): δ = 9.37 ppm. IR (KBr): $\tilde{\nu}$ = 1231 (P=O), 1030 (C–O) cm^{-1}. MS (EI 70 eV, 300 °C): *m*/*z* (%) = 282 (5) [M^+], 281 (55), 280 (1), 237 (21), 208 (33), 145 (90). $C_{12}H_{16}N_3O_3P$ (281.25): calcd. C 51.25, H 5.73, N 14.94; found C 51.12, H 5.90, N 14.45.

Diethyl [3-(*tert*-Butylamino)quinoxalin-2-yl]phosphonate (7b): Triethyl phosphite (1.86 mL, 10.7 mmol) was added to a mixture of solid **5b** (1.30 g, 5.52 mmol) and palladium acetate (90 mg, 0.4 mmol, 7.2 mol-%). The reaction mixture was refluxed for almost 1 h at 160 °C (bath). Then the resulting crude product was distilled at 65–75 °C/10^{-6} mbar to give 1.40 g (75%) yellow oily **7b**. ^1H (with and without coupling to ^{31}P) and CH-COSY NMR ($CDCl_3$): δ = 1.37 (dd, ^3J = 7.1, $^4J_{PH}$ = 0.4 Hz, 6 H, CH_3), 1.56 (s, 9 H, CMe_3), 4.23 (m, ^2J = 10.1, $^3J_{PH}$ = 8.0, ^3J = 7.0 Hz, 2 H, OCH_A), 4.30 (m, ^2J = 10.1, $^3J_{PH}$ = 7.9, ^3J = 7.1 Hz, 2 H, OCH_B), 7.31 (td, ^3J = 8.3, 6.7, ^4J = 1.6 Hz, 1 H, 7-H), 7.57 (tdd, ^3J = 8.2, 6.7, ^4J = 1.4, J_{PH} = 0.4 Hz, 1 H, 6-H), 7.64 (ddd, ^3J = 8.4, ^4J = 1.6, ^5J = 0.6 Hz, 1 H, 5-H), 7.74 (br. s, 1 H, NH), 7.86 (dp, ^3J = 8.3, ^4J = 1.4, ^5J = 0.6, $^5J_{PH}$ = 0.7 Hz, 1 H, 8-H) ppm. $^{13}C\{H\}$ NMR and CH COSY NMR ($CDCl_3$): δ = 16.21 (d, ^3J = 6.3 Hz, CH_3), 28.47 (s, CMe_3), 51.79 (s, CMe_3), 63.83 (d, ^2J = 6.2 Hz, OCH_2), 123.97 (s, CH-7), 126.57 (d, ^5J = 2.6 Hz, CH-5), 129.61 (d, ^4J = 1.4 Hz, CH-8), 131.74 (s, CH-6), 135.80 (d, ^3J = 19.8 Hz, C_q-8a), 137.61 (d, ^1J = 213.6 Hz, C_q-2), 142.74 (d, ^4J = 2.3 Hz, C_q-4a), 152.87 (d, ^2J = 27.6 Hz, C_q-3) ppm. $^{31}P\{H\}$ NMR ($CDCl_3$): δ = 9.82 ppm. IR (KBr): $\tilde{\nu}$ = 1230 (m, P=O), 1052 cm^{-1}. MS (EI 70 eV, 65 °C): *m*/*z* (%) = 338 (1) [M^+], 337 (20), 323 (15), 322 (100), 294 (8), 248 (17), 184 (87), 145 (41). $C_{16}H_{24}N_3O_3P$ (337.35): calcd. C 56.96, H 7.17, N 12.46; found C 56.82, H 7.26, N 12.84.

Diethyl Quinoxaline-2,3-diphosphonate (6): Under argon, sodium pellets (1.0 g, 43.5 mmol) were added with stirring to a solution of diethyl phosphite (6.03 mL, 46.8 mmol) in dry diethyl ether (50 mL) at room temperature. Hydrogen slowly evolved. After the

Table 2. Crystal and structure refinement data of **1a** and **3c**.

	1a	**3c**
Empirical formula	$C_6H_7BrN_2$	$C_{15}H_{19}N_2O_4PS$
Formula weight	187.05	354.35
Temperature	293(2) K	293(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/n$
Unit cell dimensions	a = 6.199(3) Å	a = 10.7353(2) Å
	b = 10.582(4) Å	b = 9.6415(2) Å
	c = 11.218(4) Å	c = 16.7093(4) Å
	β = 102.68(2)°	β = 92.084(1)°
Volume	717.9(5) Å^3	1728.34(6) Å^3
Z	4	4
Density (calculated)	1.731 g/cm^3	1.362 g/cm^3
Absorption coefficient	5.634 mm^{-1}	0.300 mm^{-1}
F(000)	368	744
Crystal size	0.58 × 0.32 × 0.32 mm	0.43 × 0.35 × 0.32 mm
θ range data collection	3.47–36.07°	2.22–36.33°
Index ranges	$-9 \le h \le 10$,	$-15 \le h \le 17$
	$-17 \le k \le 17$	$-14 \le k \le 16$
	$-18 \le l \le 18$	$-20 \le l \le 27$
Reflections collected	17363	27227
Independent reflections	3378 [R(int) = 0.0304]	8355 [R(int) = 0.0245]
Absorption correction	multiscan (SADABS)	multiscan (SADABS)
Refinement method	full-matrix least-squares on F^2	full-matrix least-squares on F^2
Data/restraints/parameters	3378/0/82	8355/0/228
Goodness-of-fit on F[a]	1.005	1.105
Final R indices, [$I > 2\sigma(I)$][a]	$R1$ = 0.0341, $wR2$ = 0.0808	$R1$ = 0.0622, $wR2$ = 0.1943
Extinction coefficient	–	0.009(3)
Largest diff. peak and hole	0.410 and –0.491 e Å^{-3}	0.661 and –0.530 e Å^{-3}

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$.

sodium was fully consumed (several hours) a solution of 2,3-dichloroquinoxaline (2.2 g, 11.05 mmol) in diethyl ether (50 mL) was added slowly (over 1 h), and then the mixture was stirred for 2 d at room temperature. The white precipitate was removed by filtration, and then the solvent was evaporated in vacuo. The crude product was washed with water, extracted with chloroform and the extract dried by $MgSO_4$. The solvent was removed in vacuo and the residue heated under high vacuum at 180 °C (bath) for almost 1 h to remove the excess amount of $HP(O)(OEt)_2$ yielding 3.20 g (73%) of spectroscopically pure **6**, m.p. 67–70 °C. ^{1}H NMR ($CDCl_3$): δ = 1.46 (d, ^3J = 7.1 Hz, 12 H, CH_3), 4.37–4.50 (m, 8 H, OCH_2), 7.92 ($m_{AA'BB'}$, 2 H, 6- and 7-H), 8.22 ($m_{AA'BB'}$, 2 H, 5- and 8-H) ppm. ^{13}C{H} NMR ($CDCl_3$): δ = 16.33 (τ, $|^3J + {}^6J|$ = 5.9 Hz, CH_3), 63.95 (τ,$|^2J \approx {}^5J|$ = 5 Hz, OCH_2), 129.85 (s, CH-6, CH-7), 132.39 (s, CH-5, CH-8), 140.70 (τ_{ABX}, 5 lines, $|^3J + {}^4J|$ = 17.0 Hz, C_q-4a and –8a), 150.00 (dd, ^1J = 226.3, ^2J = 29.8 Hz, C_q-2, C_q-3) ppm. ^{31}P{H} NMR ($CDCl_3$): δ = 7.38 ppm; small impurity by an unknown compound containing three P atoms: δ = 1.86, 4.07, 17.32 (A, B, C); J_{PP}(AB) = 1.6–1.9, J_{PP}(AC) = 16.2, J_{PP}(BC) = 13.6 Hz. IR (KBr): $\tilde{\nu}$ = (PO) = 1263 cm^{-1}. MS (EI 70 eV, 250 °C): m/z (%) = 403 (3) [M$^+$], 402 (14), 358 (5), 266 (31), 222 (26), 193 (41), 130 (100), 102 (42). $C_{16}H_{24}N_2O_6P_2$ (402.32): calcd. C 47.77, H 6.01, N 6.96; found C 47.51, H 6.37, N 6.83.

Crystal Structure Analysis: Crystals were glued on the tip of thin glass fibers. X-ray intensity data were collected at room temperature using a Bruker–Nonius Apex X8-diffractometer equipped with a CCD-detector. Graphite monochromated Mo-K_α radiation (λ = 0.71073 Å) was employed. First unit cell dimensions were obtained from the reflections, which were taken from a total of 36 frames, measured in three different crystal directions. Data collection and reduction including corrections for Lorentz and polarization effects were done using Bruker–Nonius Software.[33] The structure was solved via Direct Methods and refined by full-matrix least-square methods on F^2 using the SHELX-97 program package.[34] All atoms (except hydrogen) were treated anisotropically. Crystal data, data collection and refinement parameters are given in Table 2. One ethyl group of **3c** is disordered on two locations (solid and open lines in Figure 1) with little change in the bond lengths [O3–C14A 1.45(5) and O3–C14B 1.43(1) Å]. The C14A–C15A part is occupied by 78% and the C14B, C15B part by the remaining 22%.

For selected bond lengths and angles of **1a** and **3c** see Figures 1 and 2.

CCDC-706484 (for **1a**) and -706483 (for **3c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see also the footnote on the first page of this article): ^{1}H and/or ^{13}C NMR spectra of the compounds **2e**, **3e**, **3f**, **4b**, **4c**, **4e**, and **4f** (Figures S1–S9).

Acknowledgments

Financial support from the Deutsche Forschungsgemeinschaft (DFG) and a fellowship (to M. S. S. A.) from the Deutsche Akademische Auslandsdienst (DAAD) is gratefully acknowledged. We thank B. Niaz for detecting the formation of $[Pd^0\{P(OEt)_3\}_4]$, B. Witt and W. Heiden for measuring numerous NMR and mass spectra, Dr. H. Frauendorf and G. Sommer-Udvarnoki (Georg-August-Universität Göttingen, Institut für Organische und Biomolekulare Chemie) for HRMS measurements.

[1] a) P. Savignac, B. Iorga, *Modern Phosphonate Chemistry*, CRC Press, **2003**; b) *Aminophosphonic and Aminophosphinic Acids* (Eds.: V. P. Kuhkar, H. R. Hudson), Wiley, Chichester, **2000**.

[2] a) S. Van der Jeught, C. V. Stevens, *Chem. Rev.* **2009**, *109*, 2672–2702; b) K. Moonen, I. Laureyn, C. V. Stevens, *Chem. Rev.* **2004**, *104*, 6177–6216.

[3] a) D. E. C. Corbridge, *Phosphorus 2000: Chemistry, Biochemistry and Technology*, Elsevier, Amsterdam, **2000**, chapter 6, pp. 297–454; b) K. H. Worms, M. Schmidt-Dunker, *Organic Phosphorus Compounds* (Eds.: G. M. Kosolapoff, L. Maier), Wiley, New York, **1976**; c) K. Sasse, *Methoden der organischen Chemie* (Ed.: E. Müller), Thieme, Stuttgart, **1963**.

[4] a) L. Achremowicz, *Synthesis* **1975**, 653–654; b) T. Kato, N. Katagiri, A. Wagai, *Chem. Pharm. Bull.* **1981**, *29*, 1069–1075; c) A. A. Russell, R. L. Meline, E. N. Duesler, R. T. Paine, *Inorg. Chim. Acta* **1995**, *231*, 1–5; d) D. Redmore, *J. Org. Chem.* **1970**, *35*, 4114–4117.

[5] a) A. Boumekouez, E. About-Jaudet, N. C. P. Savignac, *J. Organomet. Chem.* **1992**, *440*, 297–301; b) J. F. Bunnett, X. Creary, *J. Org. Chem.* **1974**, *39*, 3612–3614.

[6] P. Tavs, *Chem. Ber.* **1970**, *103*, 2428–2436.

[7] a) T. Hirao, T. Masunaga, Y. Yamada, Y. Ohshiro, T. Agawa, *Bull. Chem. Soc. Jpn.* **1982**, *55*, 909–913; b) T. Hirao, T. Masunaga, Y. Ohshiro, T. Agawa, *Synthesis* **1981**, 56–57.

[8] J. F. Hartwig, in: *Handbook of Organopalladium Chemistry for Organic Synthesis*, vol. 1 (Eds.: E.-I. Negishi, A. de Meijere), Wiley Interscience, New York, **2002**, pp. 1051–1096.

[9] a) D. Gelman, L. Jiang, S. L. Buchwald, *Org. Lett.* **2003**, *5*, 2315–2318; b) A. Osuka, N. Ohmasa, Y. Yoshida, H. Suzuki, *Synthesis* **1983**, 69–71.

[10] a) K. Bravo-Altamirano, Z. Huang, J.-L. Montchamp, *Tetrahedron* **2005**, *61*, 6315–6329; b) Y. Belabassi, S. Alzghari, J.-L. Montchamp, *J. Organomet. Chem.* **2008**, *693*, 3171–3178.

[11] a) L. J. Gooßen, M. K. Dezfuli, *Synlett* **2005**, *3*, 445–448; b) J. Park, P. Ho Lee, *Bull. Korean Chem. Soc.* **1997**, *18*, 1130–1132.

[12] A. Bessmertnykh, C. M. Douaihy, S. Muniappan, R. Guilard, *Synthesis* **2008**, 1575–1579.

[13] T. M. Balthazor, J. A. Miles, B. R. Stults, *J. Org. Chem.* **1978**, *43*, 4538–4540.

[14] R. K. Bansal, J. Heinicke, *Chem. Rev.* **2001**, *101*, 3549–3578.

[15] a) R. K. Bansal, N. Gupta, J. Heinicke, G. N. Nikonov, F. Saguitova, D. C. Sharma, *Synthesis* **1999**, 264–269; b) J. Heinicke, N. Gupta, A. Surana, N. Peulecke, B. Witt, K. Steinhauser, R. K. Bansal, P. G. Jones, *Tetrahedron* **2001**, *57*, 9963–9972.

[16] a) B. R. Aluri, Ph. D. Thesis, Greifswald, **2008**; b) B. R. Aluri, M. K. Kindermann, P. G. Jones, I. Dix, J. Heinicke, *Inorg. Chem.* **2008**, *47*, 6900–6912.

[17] M. S. S. Adam, Ph. D. Thesis, Greifswald, **2008**.

[18] M. S. S. Adam, O. Kühl, M. K. Kindermann, J. Heinicke, P. G. Jones, *Tetrahedron* **2008**, *64*, 7960–7967.

[19] W. Deuschel, G. Riedel (Badische Anilin- & Soda-Fabrik A.-G.), **1962**, DE 1135471 (30. Aug. 1962, appl. 19. June 1960).

[20] O. Kühl, P. Lönnecke, J. Heinicke, *New J. Chem.* **2002**, *29*, 771–777.

[21] M. C. Kohler, R. A. Stockland Jr., N. P. Rath, *Organometallics* **2006**, *25*, 5746–5756.

[22] M. Kaleck, J. Stawinski, *Organometallics* **2007**, *26*, 5840–5847.

[23] T. M. Balthazor, R. C. Grabiak, *J. Org. Chem.* **1980**, *45*, 5425–5426.

[24] a) C. Amatore, A. Jutand, A. Thuilliez, *Organometallics* **2001**, *20*, 3241–3249; b) C. Amatore, E. Carre, A. Jutand, M. A. M'Barki, *Organometallics* **1995**, *14*, 1818–1826.

[25] a) M. Meier, F. Basolo, R. G. Pearson, *Inorg. Chem.* **1969**, *8*, 795–801; b) M. Meier, F. Basolo, *Inorg. Synth.* **1990**, *28*, 104–107.

[26] C. Crocker, R. J. Goodfellow, *J. Chem. Res. (S)* **1979**, 378–379.

[27] A. G. Troitskaya, G. A. Levshina, T. V. Zykova, L. F. Gogolyukhina, *Zh. Obshch. Khim.* **1976**, *46*, 1235–1237.

[28] I.-C. Grig-Alexa, A.-L. Finaru, L. Ivan, P. Caubère, G. Guillaumet, *Synthesis* **2006**, 619–628.

[29] T. Iwaki, A. Yasuhara, T. Sakamoto, *J. Chem. Soc. Perkin Trans. 1* **1999**, 1505–1510.

[30] K. T. J. Loones, B. U. W. Maes, C. Meyers, J. Deruytter, *J. Org. Chem.* **2006**, *71*, 260–264.

[31] E. Garnier, S. Blanchard, I. Rodriguez, C. Jarry, J. Leger, P. Caubere, G. Guillaumet, *Synthesis* **2003**, *13*, 2033–2040.

[32] C. A. Obafemi, W. Pfleiderer, *Helv. Chim. Acta* **1994**, *77*, 1549–1556.

[33] *SADABS*, Bruker AXS Inc., Madison, WI (USA), **2003**.

[34] *SHELXS-97* and *SHELXL-97*, programs for the solution and refinement of crystal structures: G. M. Sheldrick, University of Göttingen, Germany, **1997**.

Received: June 22, 2009
Published Online: August 10, 2009

