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An Approach to Nonsymmetric Bis(tertiary phosphine oxides) Comprising Heterocyclic Fragments via the Pd-Catalyzed Phosphorylation

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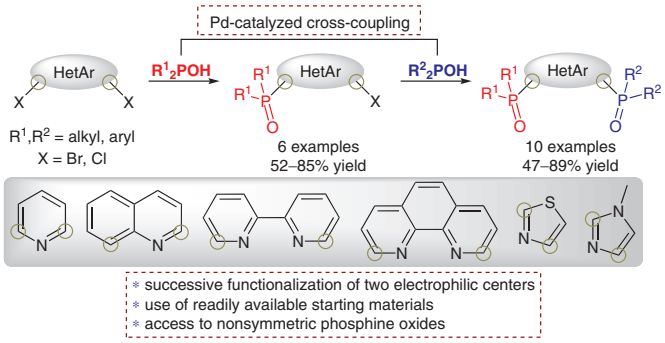

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Abstract Nonsymmetric tertiary phosphine oxides with different five- and six-membered heterocyclic fragments such as pyridine, 2,2′-bipyridine, 1,10-phenantroline, quinoline, imidazole, and thiazole were synthesized in good yields via the successive introduction of phosphine oxide groups into the initial dihalogenated heterocycles by means of Pd-catalyzed phosphorylation reaction. The synthesis of pyridine-type compounds is hindered by competing double coupling, while for five-membered heterocycles the principal difficulty is the dehalogenation. Both side processes were successfully suppressed by the use of an excess of a dihalide (which can be easily recovered during the product purification step), proper phosphine ligand for palladium, and nonpolar solvent such as toluene.

Key words cross-coupling, phosphorylation, nonsymmetric phosphine oxide, palladium, heterocycles, dehalogenation

Tertiary phosphine oxides (TPOs) have a number of applications;[1–5] one of the most interesting and promising is their use as ligands for different metals, especially from *f*-block.[6,7] Such complexes possess potentially valuable photophysical properties[8–12] and upon the complexation the extractive separation of actinide and lanthanide ions mixtures can be achieved as a part of the spent nuclear fuel reprocessing cycle.[13–15] Due to the high complexity of biphasic multicomponent extraction systems, it is often difficult to establish the structure–property relationships, therefore the search for a compound with valuable properties usually proceeds in a form of screening through a library of similar substances. In the framework of our ongoing research in the field of the *f*-elements chemistry,[16–18] the access to a number of structurally diverse heterocycle-based phosphine oxides is needed, and it was found that palladium-catalyzed phosphorylation is the method of choice for the synthesis of such compounds from secondary phosphine oxides (SPOs) and halogenated heterocycles.[19,20] In our previous studies, (hetero)aromatic (di)halides were subjected to the double coupling with two equivalents of the same SPO. However, selective monophosphorylation of a molecule bearing two identical sites (for example, substitution of one chlorine atom in 2,6-dichloropyridine) remains essentially unexplored. Thus, the purposes of the present study are (1) to investigate possible approaches to the monophosphorylation of heterocyclic dihalides with the formation of monohalophosphine oxides, which can be used for further functionalization by means of cross-coupling or related chemistry and (2) to synthesize a series of heterocyclic bis(phosphine oxides) by the successive introduction of two different SPOs into Pd-catalyzed phosphorylation.

A number of nitrogen heterocycles such as 2,6-dichloropyridine (**$PyCl_2$**), 6,6′-dichloro-2,2′-bipyridine (**$BipyCl_2$**), 2,9-dichloro-1,10-phenanthroline (**$PhenCl_2$**), 8-bromo-2-chloroquinoline (**QuinBrCl**), 2,4-dibromothiazole (**$ThzBr_2$**), and 2,4-dibromo-1-methyl-1*H*-imidazole (**$ImBr_2$**) were selected as electrophilic reaction partners. The work was started from the cross-coupling between equimolar amounts of Ph_2POH and **QuinBrCl** (Scheme 1) because of the presence in dihalide's structure of two different halogen atoms which may have different reactivity in cross-coupling process. During the first stage compound **1** was successfully synthesized (resonance shift in ^{31}P NMR spectrum is about 20 ppm, in the characteristic range for tertiary phosphine oxide group near the nitrogen atom in heterocycle). Thus, the chlorine atom which is located in *ortho* position of pyridine ring reacts faster than the bromine. The possibility of the S_NAr mechanism operation as the plausible explanation was ruled out by the uncatalyzed reaction results. The subsequent cross-coupling of **1** with *n*-Oct_2POH resulted in the formation of the quinoline-based nonsymmetric tertiary phosphine oxide **2** in good yield.

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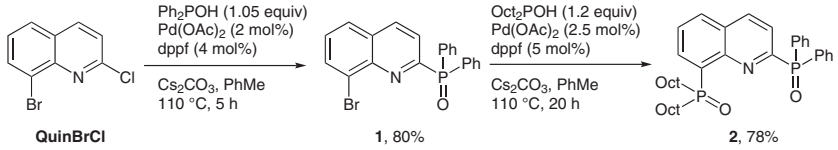
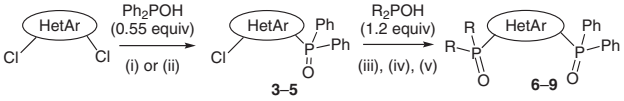


Scheme 1 Synthesis of mono- and bis(phosphorylated) quinoline derivatives

The attempts to introduce one Ph_2PO group into other pyridine heterocycles (**$PyCl_2$**, **$BipyCl_2$**, **$PhenCl_2$**) using equimolar ratio of the coupling partners led to the mixtures consisting mainly of mono and bis(phosphorylated) derivatives of these heterocycles (Supporting Information (SI): Table S1, No. 1, 2, 4, 7). These results are the evidence that some acceleration of the second phosphorylation occurs after the installation of the first phosphine oxide group. The decrease of the reaction temperature (SI: Table S1, No. 1, 2) as well as the increase of a catalyst loading (SI: Table S1, No. 5, 6) had only insignificant influence on the outcome in all cases. To solve the problem of the bis(phosphine oxides) formation the amount of Ph_2POH was reduced twice relative to dichloroheterocycles keeping all other conditions unchanged. The approach worked well in the cases of **$PyCl_2$** and **$BipyCl_2$** (double phosphorylation byproducts were not observed in ^{31}P NMR of reaction mixtures) in contrast to **$PhenCl_2$** (product/byproduct ratio was about 1:1). Additional optimization of phosphine ligand (SI: Table S1, No. 9–12) revealed that DPEPhos was more effective ligand for the synthesis of **5**. Thus, the compounds **3–5** were successfully synthesized in good yields (Table 1); it should be noted that the excess of a dichloroheterocycle can be readily recovered during the chromatographic purification of a target phosphine oxide that makes their further utilization possible. For obtaining the nonsymmetric tertiary phosphine oxides **6–10** the compounds **3–5** were introduced in the cross-coupling reaction with several SPOs. n-Oct_2POH reacted slower than $(3,5\text{-}Me_2Ph)_2POH$ therefore the reaction with the former was conducted for 20 h (instead of 7 h for the latter) and with increased amount of the catalyst. It is interesting to note that the reaction with $(4\text{-}CF_3Ph)_2POH$ (with the formation of **10**) was carried out in toluene since only decomposition of the SPO was found in DMF, which is consistent with our previous observations.[20] Moreover, using toluene as a solvent, $Py[(4\text{-}CF_3Ph)_2P(O)]_2$ (**10A**) was successfully obtained (see the SI) in high yield (which was shown to be impossible in DMF).[20] The reasons for such a behavior are currently under investigation.

Unlike to pyridine-type heterocycles reactions of **$ThzBr_2$** and **$ImBr_2$** with Ph_2POH led not only to desired products and bis(phosphorylated) compounds but also to byproducts resulted from debromination (SI: Tables S2, S4). In the absence of a catalyst the debromination was the main reaction pathway (SI: S2, No. 9; S4, No. 12–14). The best results for the synthesis of **11** were achieved (Table 2) by the use of substoichiometric amount of Ph_2POH: with 0.6 equiv (relative to **$ThzBr_2$**) the reaction produced only unreacted **$ThzBr_2$** and **11** without monobromothiazole. In the case of imidazole, any amount of SPO led to monobromoimidazole formation, so to maximize the yield of **12** 0.8 equiv (relative to **$ImBr_2$**) was used. For both heterocycles the phosphorylation reaction showed strong dependence upon the phosphine ligand employed and the best outcome was obtained with dppf. It should be noted that unreacted dihalides can be recovered easily during the purification of products. It is also noteworthy that not only the SPO concentration and the phosphine ligand, but the solvent plays a role (SI: S4, No. 6, 7) in the debromination process as well. When comparing the outcomes of reactions in DMF and PhMe one can see that the debromination predominates over cross-coupling in the former solvent. There are two mechanistic possibilities: DMF can act as debrominating agent by itself[21–23] or it can accelerate the SPO-mediated debromination owing to its high polarity, since the charged intermediates were proposed for related transformations.[24]

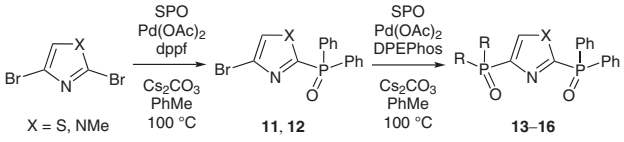
Table 1 Synthesis of Mono- and Bis(phosphorylated) Derivatives of Pyridine, Bipyridine, and Phenanthroline



Compound	HetAr	R	Yield (%)[a]	Conditions[b]
3	Py	–	81[c]	(i)
4	Bipy	–	85[c]	(i)
5	Phen	–	71[c]	(ii)
6	Py	*m*-xylyl	89	(iii)
7	Py	*n*-Oct	78	(iv)
8	Bipy	*n*-Oct	85	(iv)
9	Phen	*n*-Oct	47	(iv)
10	Py	4-CF_3Ph	75	(v)

[a] Reactions were carried out at 110 °C at 0.3–3 mmol scale, all yields are isolated.
[b] Conditions (i): $Pd(OAc)_2$ (1 mol%), dppf (2 mol%), K_2CO_3, DMF, 7 h. Conditions: (ii) $Pd(OAc)_2$ (2 mol%), DPEPhos (4 mol%), K_2CO_3, DMF, 7 h; (iii) $Pd(OAc)_2$ (1 mol%), dppf (2 mol%), Cs_2CO_3, DMF, 7 h; (iv) $Pd(OAc)_2$ (2.5 mol%), dppf (5 mol%), Cs_2CO_3, DMF, 20 h; (v) $Pd(OAc)_2$ (5 mol%), DPEPhos (10 mol%), Cs_2CO_3, PhMe, 20 h.
[c] At Ph_2POH (1.05 equiv), $Pd(OAc)_2$ (1 mol%), dppf (2 mol%), K_2CO_3, DMF, 7 h, the contents of **3**, **4** and **5** were less than 75%, 72% and 50%, respectively.

Table 2 Synthesis of Mono- and Bis(phosphorylated) Derivatives of Thiazole and Imidazole



Compd	X	R	SPO (equiv)	[Pd]/L (mol%)	Time (h)	Yield (%)[a]
11	S	–	Ph_2POH (0.6)	2/4	5.5	61
12	NMe	–	Ph_2POH (0.8)	4/8	5.5	52[b]
13	S	Oct	Oct_2POH (1.2)	2.5/5	20	71
14	NMe	Oct	Oct_2POH (1.2)	5/10	20	75
15	S	Ph	Ph_2POH (0.6)	2.5/5	5	88[c]
16	NMe	Ph	Ph_2POH (1.2)	10/20	5	85

[a] Isolated yield.
[b] At Ph_2POH (1.1 equiv), $Pd(OAc)_2$ (4 mol%), dppf (8 mol%), Cs_2CO_3, PhMe, 5.5 h, the content of **12** was less than 50%.
[c] At Ph_2POH (1.2 equiv), $Pd(OAc)_2$ (2.5 mol%), DPEPhos (5 mol%), Cs_2CO_3, PhMe, 7 h, the content of **15** was less than 27%.

Having obtained the compounds **11** and **12**, we used them further to synthesize the nonsymmetric TPOs based on the thiazole and imidazole frameworks (**13** and **14**, respectively, Table 2). Yields of target products were higher when using DPEPhos instead of dppf; in addition, to successfully attain the compound **14** it was necessary to use an increased amount of the catalyst.

To study the influence of the substituents at a phosphorus atom in an SPO on the second cross-coupling it was decided to synthesize bis(diphenylphosphine oxides) **15** and **16** from **11** and **12**, respectively. The use of less nucleophilic aromatic SPO (in comparison with *n*-Oct_2POH) is important for the understanding of the reactivity of **11** and **12** in palladium-catalyzed phosphorylation and in particular the relationship between the electron density at a phosphorus atom in an SPO and the rate of debromination.

Analogously to the reaction with Oct_2POH, the cross-coupling of **11** with Ph_2POH was also suffered from the debromination side process (SI: Table S3). In addition, the use of dppf as a ligand led to higher content of debrominated product, than in experiments conducted with DPEPhos (SI: Table S3, No. 4, 5). For the synthesis of the thiazole-based compound the best results were achieved by the use of substoichiometric amount of Ph_2POH (Table 2): under these conditions only **11** and **15** were detected in reaction mixture. The yield of **15** was as high as 88% (based on SPO) and unreacted **11** was recovered successfully.

To our surprise, the reaction between **12** and equimolar amount of Ph_2POH led almost exclusively to **16** (85% isolated yield) without significant debromination, but the reaction was rather slow, so the increased catalyst loading was used in this case (Table 2). It is somewhat unexpected that in the first coupling imidazole framework was more susceptible to debromination than thiazole, while for the second one the reverse situation occurred.

Additional cross-coupling reactions between the two five-membered heterocyclic dibromides and Ph_2POH (2.4 equiv relative to halides) were conducted (SI: Table S2, No. 1–5; Table S4, No. 1–3). No conditions tested previously for single couplings worked in these runs, the desired compounds **11**, **12**, **15**, and **16** presented only in trace amounts while the main products resulted from debromination of either starting dibromides or intermediate bromophosphine oxides. These experiments showed that the debromination is highly and unpredictably dependent on the concentration of the SPO in solution (as well as on its structure) and one-pot double phosphorylation is essentially unattainable for these two azoles.

In conclusion, herein we report on the synthetic route for the preparation of a new type of nonsymmetric tertiary phosphine oxides based on different heterocyclic fragments by successive introduction of phosphine oxide groups by the Pd-catalyzed cross-coupling reaction.[25,26] This approach allows one to obtain the target compounds from readily (either synthetically or commercially) available reagents in two stages with good-to-high yields. In the case of pyridine-type heterocyclic halides the main difficulty was the double coupling at equimolar reagents ratio, while for azoles the key issue was dehalogenation reaction. Both issues were successfully solved by the proper choice of supporting ligand for palladium and reagents stoichiometry.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1706419.

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(25) Scale, halide/SPO ratio, catalytic system loading, and yield are shown in Scheme 1, Table 1, and Table 2 for each tertiary phosphine oxide product.
An oven-dried Schlenk flask was evacuated and back-filled with argon three times. Heteroaryl (di)halide, base (1.3 equiv relative to SPO), and a solution of an SPO in an anhydrous solvent (7 mL/mmol per halogen) were added to the flask. The solution was bubbled with argon for 10 min and $Pd(OAc)_2$ and a phosphine ligand were added to the flask simultaneously. The resulting mixture was stirred and heated at the indicated temperature for the given time. Workup procedures are described below for two different solvents. Final purification of crude products was achieved by column chromatography on silica gel (40–60 um) using CH_2Cl_2–MeOH as eluent.
For Reactions Conducted in DMF
After cooling, the reaction mixture was poured into a fourfold excess of brine. The mixture was extracted three times with CH_2Cl_2 (40 mL/mmol each). The combined organic layers were washed with brine to remove traces of DMF, dried over Na_2SO_4, and then evaporated to dryness.
For reactions Conducted in Toluene
After cooling, the reaction mixture was evaporated to dryness. Then, the mixture was diluted with CH_2Cl_2 (40 mL/mmol) and washed with water and brine (40 mL/mmol). The organic layer was dried over Na_2SO_4 and the CH_2Cl_2 was removed under reduced pressure. Notice that all compounds with two phosphine oxide groups are beige-to-brown solids or slowly solidifying viscous brown oils.
(26) **Analytical Data for Compound 2**
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52–8.57 (m, 1 H, H_{Quin}), 8.42–8.45 (m, 1 H, H_{Quin}), 8.37–8.40 (m, 1 H, H_{Quin}), 8.06 (d, 1 H, *J* = 8.2 Hz, H_{Quin}), 7.77 (t, 1 H, *J* = 7.6 Hz, H_{Quin}), 7.66–7.71 (m, 4 H, 2-H_{Ph}), 7.56–7.60 (m, 2 H, 4-H_{Ph}), 7.45–7.49 (m, 4 H, 3-H_{Ph}), 1.61–1.77 (m, 4 H, H_{Oct}), 1.32–1.45 (m, 2 H, H_{Oct}), 0.97–1.27 (m, 22 H, H_{Oct}), 0.83 (t, 6 H, *J* = 7.2 Hz, H_{Oct}). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 157.39 (d, *J* = 129.3 Hz, 1 C), 146.79 (dd, *J* = 20.5, 7.6 Hz, 1 C), 138.68 (d, *J* = 4.2 Hz, 1 C), 137.55 (d, *J* = 9.0 Hz, 1 C), 132.44 (1 C), 132.37 (d, *J* = 2.4 Hz, 2 C), 132.10 (d, *J* = 9.8 Hz, 4 C), 131.47 (d, *J* = 104.8 Hz, 2 C), 131.61 (1 C), 128.65 (d, *J* = 12.6 Hz, 4 C), 128.30 (d, *J* = 4.2 Hz, 1 C), 128.01 (d, *J* = 10.7 Hz, 1 C), 124.08 (d, *J* = 21.6 Hz, 1 C), 31.70 (2 C), 30.91 (d, *J* = 14.6 Hz, 2 C), 29.80 (d, *J* = 68.9 Hz, 2 C), 29.12 (2 C), 29.01 (2 C), 22.56 (2 C), 21.34 (d, *J* = 4.4 Hz, 2 C), 14.05 (2 C). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 41.64, 27.76. HRMS (ESI+): *m/z* $[M + H]^+$ calcd for $C_{37}H_{49}NO_2P_2 + H^+$: 601.3239; found: 601.3233.
Analytical Data for Compound 7
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38 (t, 1 H, *J* = 6.5 Hz, 3-H_{Py}), 8.18 (t, 1 H, *J* = 5.7 Hz, 5-H_{Py}), 8.00–8.05 (m, 1 H, 4-H_{Py}), 7.76–7.81 (m, 4 H, 2-H_{Ph}), 7.52–7.56 (m, 2 H, 4-H_{Ph}), 7.42–7.46 (m, 4 H, 3-H_{Ph}), 1.78–1.92 (m, 4 H, H_{Oct}), 1.46–1.58 (m, 2 H, H_{Oct}), 1.08–1.33 (m, 22 H, H_{Oct}), 0.86 (t, 6 H, *J* = 7.1 Hz, H_{Oct}). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 157.34 (dd, *J* = 114.6, 17.3 Hz, 1 C), 156.98 (dd, *J* = 128.2, 16.0 Hz, 1 C), 136.47 (t, *J* = 8.0 Hz, 1 C), 131.70 (d, *J* = 104.8 Hz, 2 C), 132.00 (2 C), 131.90 (d, *J* = 8.6 Hz, 4 C), 128.94–129.33 (m, 2 C), 128.21 (d, *J* = 12.3 Hz, 4 C), 31.63 (2 C), 30.88 (d, *J* = 13.6 Hz, 2 C), 28.87–28.92 (m, 4 C), 28.54 (d, *J* = 69.1 Hz, 2 C), 22.49 (2 C), 21.21 (d, *J* = 3.7 Hz, 2 C), 13.98 (2 C). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 42.65, 21.79. HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{33}H_{47}NO_2P_2 + Na^+$: 574.2974; found: 574.2973.
Analytical Data for Compound 8
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.48 (d, 1 H, *J* = 8.1 Hz, H_{Bipy}), 8.32–8.35 (m, 1 H, H_{Bipy}), 8.30 (d, 1 H, *J* = 8.0 Hz, H_{Bipy}), 8.10–8.12 (m, 1 H, H_{Bipy}), 7.99 (td, 1 H, *J* = 7.8, 3.8 Hz, H_{Bipy}), 7.90–7.93 (m, 5 H, 2-H_{Ph}, H_{Bipy}), 7.51 (t, 2 H, *J* = 7.4 Hz, 4-H_{Ph}), 7.41–7.46 (m, 4 H, 3-H_{Ph}), 1.99–2.11 (m, 4 H, H_{Oct}), 1.62–1.71 (m, 2 H, H_{Oct}), 1.36–1.45 (m, 2 H, H_{Oct}), 1.27–1.35 (m, 2 H, H_{Oct}), 1.10–1.22 (m, 16 H, H_{Oct}), 0.78 (t, 6 H, *J* = 6.9 Hz, H_{Oct}). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 156.15 (d, *J* = 117.5 Hz, 1 C), 155.75 (d, *J* = 131.0 Hz, 1 C), 155.34 (d, *J* = 18.9 Hz, 1 C), 155.25 (d, *J* = 17.4 Hz, 1 C), 137.19 (d, *J* = 19.2 Hz, 1 C), 137.13 (d, *J* = 18.1 Hz, 1 C), 132.81 (d, *J* = 104.3 Hz, 2 C), 132.02 (d, *J* = 9.5 Hz, 4 C), 131.88 (d, *J* = 2.0 Hz, 2 C), 128.56 (d, *J* = 20.0 Hz, 1 C), 128.24 (d, *J* = 12.1 Hz, 4 C), 128.13 (d, *J* = 19.0 Hz, 1 C), 122.33 (d, *J* = 9.7 Hz, 1 C), 122.32 (d, *J* = 8.8 Hz, 1 C), 31.63 (2 C), 30.84 (d, *J* = 13.9 Hz, 2 C), 28.89 (2 C), 28.86 (2 C), 28.46 (d, *J* = 68.1 Hz, 2 C), 22.46 (2 C), 21.28 (d, *J* = 4.0 Hz, 2 C), 13.94 (2 C). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 42.64, 21.45. HRMS (ESI+): *m/z* $[M + Na]^+$ calcd for $C_{38}H_{50}N_2O_2P_2 + Na^+$: 651.3240; found: 651.3243.
Analytical Data for Compound 9
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 (dd, 1 H, *J* = 8.1, 4.3 Hz, 3-H_{Phen}), 8.46–8.59 (m, 1 H, 8-H_{Phen}), 8.40–8.45 (m, 2 H, 4-H_{Phen}),

7-H_{Phen}), 8.28–8.34 (m, 4 H, 2-H_{Ph}), 7.89–7.94 (m, 2 H, 5-H_{Phen}, 6-H_{Phen}), 7.47–7.51 (m, 2 H, 4-H_{Ph}), 7.41–7.45 (m, 4 H, 3-H_{Ph}), 2.19–2.36 (m, 4 H, H_{Oct}), 1.68–1.81 (m, 2 H, H_{Oct}), 1.40–1.53 (m, 2 H, H_{Oct}), 1.04–1.33 (m, 20 H, H_{Oct}), 0.77 (t, 6 H, *J* = 7.0 Hz, H_{Oct}). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 157.69 (d, *J* = 118.6 Hz, 1 C), 157.21 (d, *J* = 132.2 Hz, 1 C), 146.12 (d, *J* = 19.0 Hz, 1 C),145.85 (d, *J* = 20.1 Hz, 1 C), 136.05 (d, *J* = 25.6 Hz, 1 C), 135.96 (d, *J* = 24.9 Hz, 1 C), 132.79 (d, *J* = 103.3 Hz, 2 C), 132.03 (d, *J* = 9.0 Hz, 4 C), 131.62 (d, *J* = 2.6 Hz, 2 C), 129.29 (d, *J* = 2.6 Hz, 1 C), 129.22 (d, *J* = 2.6 Hz, 1 C), 128.18 (d, *J* = 12.0 Hz, 4 C), 128.17 (1 C), 127.82 (1 C), 125.99 (d, *J* = 18.8 Hz, 1 C), 125.88 (d, *J* = 21.0 Hz, 1 C), 31.59 (2 C), 30.95 (d, *J* = 13.6 Hz, 2 C), 28.94 (2 C), 28.92 (2 C), 28.71 (d, *J* = 67.8 Hz, 2 C), 22.45 (2 C), 21.40 (d, *J* = 4.2 Hz, 2 C), 13.93 (2 C). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 43.64, 16.55. HRMS (ESI+): *m/z* [M + 1/2Ca^{2+}]$^+$ calcd for $C_{40}H_{50}N_2O_2P_2$ + 1/2Ca^{2+}: 672.3155; found: 672.3159.

Analytical Data for Compound 13

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47 (dd, 1 H, *J* = 2.9, 2.1 Hz, 5-H_{Thz}), 7.83–7.88 (m, 4 H, 2-H_{Ph}), 7.57–7.61 (m, 2 H, 4-H_{Ph}), 7.46–7.51 (m, 4 H, 3-H_{Ph}), 1.95–2.02 (m, 4 H, H_{Oct}), 1.53–1.66 (m, 2 H, H_{Oct}), 1.20–1.41 (m, 22 H, H_{Oct}), 0.87 (t, 6 H, *J* = 7.0 Hz, H_{Oct}). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.64 (dd, *J* = 124.5, 17.9 Hz, 1 C), 154.96 (dd, *J* = 96.2, 19.9 Hz, 1 C), 134.34 (d, *J* = 20.3 Hz, 1 C), 132.65 (d, *J* = 2.4 Hz, 2 C), 131.62 (d, *J* = 10.1 Hz, 4 C), 130.94 (d, *J* = 109.8 Hz, 2 C), 128.55 (d, *J* = 12.9 Hz, 4 C), 31.67 (2 C), 30.83 (d, *J* = 14.4 Hz, 2 C), 29.55 (d, *J* = 69.7 Hz, 2 C), 28.95 (4 C), 22.51 (2 C), 21.35 (d, *J* = 3.7 Hz, 2 C), 14.02 (2 C). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 39.43, 18.92. HRMS (ESI+): *m/z* [M + H]$^+$ calcd for $C_{31}H_{45}NO_2P_2S$ + H^+: 558.2719; found: 558.2711.

Analytical Data for Compound 14

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.80–7.83 (m, 4 H, 2-H_{Ph}), 7.63 (s, 1 H, 5-H_{Im}), 7.55–7.57 (m, 2 H, 4-H_{Ph}), 7.45–7.48 (m, 4 H, 3-H_{Ph}), 4.02 (s, 1 H, H_{Me}), 1.83–1.94 (m, 4 H, H_{Oct}), 1.56–1.65 (m, 2 H, H_{Oct}), 1.23–1.46 (m, 22 H, H_{Oct}), 0.88 (t, 6 H, *J* = 7.1 Hz, H_{Oct}). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 142.66 (dd, *J* = 143.8, 15.2 Hz, 1 C), 136.22 (dd, *J* = 128.5, 14.4 Hz, 1 C), 132.98 (dd, *J* = 24.2, 3.4 Hz, 1 C), 131.19 (d, *J* = 2.8 Hz, 2 C), 131.8 (d, *J* = 111.7 Hz, 2 C), 131.61 (d, *J* = 10.2 Hz, 4 C), 128.33 (d, *J* = 12.9 Hz, 4 C), 35.19 (1 C), 31.72 (2 C), 30.94 (d, *J* = 14.5 Hz, 2 C), 29.50 (d, *J* = 71.1 Hz, 2 C), 29.04 (2 C), 28.99 (2 C), 22.53 (2 C), 21.42 (d, *J* = 4.0 Hz, 2 C), 14.02 (2 C). ^{31}P NMR (243 MHz, $CDCl_3$): δ = 41.48, 21.10. HRMS (ESI+): *m/z* [M + H]$^+$ calcd for $C_{32}H_{48}N_2O_2P$ + H^+: 554.3191; found: 554.3186.