Efficient One-Pot Synthesis of Mono- and Bis[di(2-pyridyl)phosphine Oxides] from Tris(2-pyridyl)phosphine

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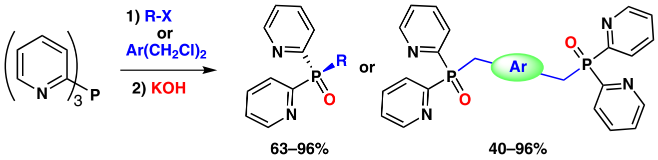

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Abstract An efficient one-pot access to di(2-pyridyl)phosphine oxides $Py_2P(R){=}O$ and bis[di(2-pyridyl)phosphine oxides] $Py_2P(O)–Z–P(O)Py_2$ has been developed based on the reaction of available tris(2-pyridyl)phosphine with various organic halides, followed by treatment of the resulting phosphonium salts with alkali *in situ*. The isolated yields of the phosphine oxides were in the range 40–96%.

Key words dipyridylphosphine oxides, bisphosphine oxides, phosphonium salts, ligands, halo compounds, chemoselectivity

Pyridylphosphine oxides are currently attracting increasing attention due to their importance in materials science, catalysis, and coordination chemistry.[1] Most studies relate to tris(2-pyridyl)phosphine oxide, a useful ligand and building block for functional materials.[2] The closest analogues of tris(2-pyridyl)phosphine oxide, the bis(2-pyridyl)phosphine oxides $Py_2P(R){=}O$, have been much less explored, although they are of particular interest as intriguing ligands for the assembly of unique metal complexes. For example, Cu(I)[3] and Ln(III)[4] complexes based on bis(2-pyridyl)phosphine oxides have been proposed as advanced materials for light-emitting devices. In a series of works,[5] Espinet and co-workers identified peculiarities in the dynamic behavior of Pd(II) and Pt(II) complexes of $Py_2P(Ph){=}O$. Also, Rh(I)[6] and Mo[7] complexes that are catalytically active in the hydrogenation of olefins were prepared from this ligand.

The studies discussed above dealt only with phenylbis(2-pyridyl)phosphine oxide; other bis(2-pyridyl)phosphine oxides $Py_2P(R){=}O$ remain neglected because of their unavailability. Bis[di(2-pyridyl)phosphine oxides] $Py_2P(O)–Z–P(O)Py_2$ are virtually unknown, other than the compound in which Z = $(CH_2)_2$,[4a] although they would be of interest as bridging ligands for the design of coordination polymers.[8] $Py_2P(Ph){=}O$ is generally synthesized by H_2O_2 oxidation of the corresponding phosphine, which, in turn, is generated by the reaction of either $PhPCl_2$ with 2-pyridyllithium at –90 °C (60% yield)[9] or $PhPLi_2$ with 2-chloropyridine (83% yield).[10] [(*E*)-alkenyl]bis(2-pyridyl)phosphine oxides have recently been prepared in 45–56% yield by the reaction of tris(2-pyridyl)phosphine with electron-deficient alkynes in water.[11]

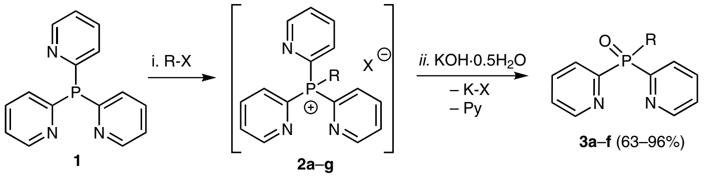
Here, we report an efficient one-pot synthesis of tertiary bis(2-pyridyl)phosphine oxides and bis[di(2-pyridyl)phosphine oxides] from the appropriate organic halides and tris(2-pyridyl)phosphine, which is now readily available by the direct reaction of elemental phosphorus with 2-bromopyridine.[12]

After a series of test experiments, we established that the phosphonium salts **2a**–**g**, prepared *in situ* by the reaction of tris(2-pyridyl)phosphine (**1**) with organic halides (1:10 molar ratio, 24–140 °C, 0.5–1.5 h, no solvent) reacted readily with KOH (1:1.1 ratio, r.t., 0.5 h) to provide the corresponding bis(2-pyridyl)phosphine oxides **3a**–**f** in 63–96% preparative yield (Table 1).[13] We also showed that the treatment of the specially prepared intermediate phosphonium salts **2a**–**g** with alkali under similar conditions also led to the phosphine oxides **3a**–**f** in comparable yields (for details, see the Supporting Information).[14]

The one-pot synthesis has a general character for organic chlorides, bromides, and iodides (Table 1) and permits the synthesis of diverse bis(2-pyridyl)phosphine oxides bearing alkyl (Table 1, entries 1–4) or benzylic substituents (entries 5–7). Secondary and tertiary alkyl halides, e.g. *i*-PrI, *s*-BuI, or *t*-BuBr, were ineffective in the reaction.

In the reaction of the phosphonium salts **2a**–**g** with alkali (step *ii*), GC/MS analysis of the reaction mixture showed that, in addition to potassium halides, pyridine and 2,2′-bipyridine were formed as byproducts of the reaction.

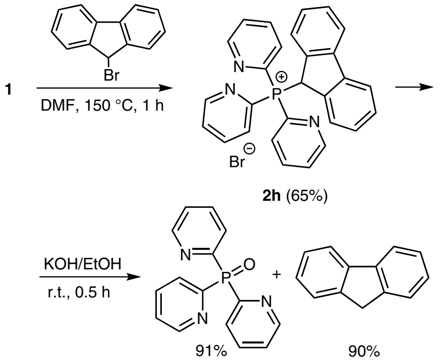
Table 1 One-Pot Synthesis of Phosphine Oxides **3a**–**f** from Tris(2-pyridyl)phosphine[a]



Entry	Conditions for quaternization of phosphine **1** [step (i)]			Product	Yield[b] (%)
	RX	Temp (°C)	Time (h)		
1	MeI	24–25	0.5	**3a**	96
2	EtI	45	0.5	**3b**	63
3	BuI	70	1	**3c**	75
4	$Me(CH_2)_8I$	140	1	**3d**	88
5	BnCl	140	1.5	**3e**	74
6	BnBr	140	1.5	**3e**	78
7[c]	$1\text{-}NaphCH_2Cl$	140	1	**3f**	65

[a] Reaction conditions: *i.* phosphine **1** (0.5 mmol), RX (5.0 mmol), stirring, inert atmosphere; *ii.* $KOH\cdot 0.5H_2O$ (0.55 mmol), r.t., 0.5 h, stirring.
[b] Isolated yield.
[c] A 1:1 molar ratio of **1** to 1-(chloromethyl)naphthalene was used with DMF (3 mL) as solvent.

Interestingly, decompositions of similar salts in acetone in the absence of alkali gave 2,2′-bipyridine hydrobromide, along with $PyP(R)(O)C(Me_2)OH$.[15] Apparently, the formation of the phosphine oxides **3a**–**f** occurs through nucleophilic substitution of one of the pyridyl groups in the organyl[tris(2-pyridyl)]phosphonium cation by a hydroxide anion. In all the above cases, the reaction is strictly chemoselective in terms of the leaving group on the phosphorus atom in **2a**–**g**: no alternative nucleophilic substitution of a benzyl or 2-naphthylmethyl group (or of an alkyl group) by HO^- was observed. However, 9-fluorenyl, a better leaving group, was replaced by the hydroxide anion more easily than the 2-pyridyl unit. Thus, the phosphonium salt **2h**, prepared from phosphine **1** and 9-bromo-9*H*-fluorene (65% yield), reacted with alkali in a 1:1.1 molar ratio to give tris(2-pyridyl)phosphine oxide and 9*H*-fluorene in nearly quantitative yield (Scheme 1).[14] The expected (9*H*-fluoren-9-yl)bis(2-pyridyl)phosphine oxide was not identified among the reaction products.



Scheme 1 Synthesis of phosphonium salt **2h** and its reaction with alkali

To prepare the previously unknown bis[di(2-pyridyl)phosphine oxides] **5**, we extended the substrate scope of our approach to organic dihalides (Table 2). The reaction of tris(2-pyridyl)phosphine (**1**) with bis(chloromethyl)-substituted aromatics (2:1 molar ratio, DMF, 150 °C, 1 h), and subsequent treatment of the resulting bis(phosphonium) salts **4a**–**d** with KOH *in situ* (1:2.2 molar ratio, EtOH, r.t., 0.5 h) gave the corresponding bis(phosphine oxides) **5a**–**d** in moderate to high yields (Table 2, entries 1–4).[14] DMF was used as a solvent because both reactants were solids. Bis(phosphine oxides) **5a**–**d** are promising ligands for the design of functional coordination polymers and supramolecular structures of a new generation. The intermediate salts **4a**–**d** were optionally isolated in 54–85% yield,[14] with the exception of **4b**, which readily converted into **5b** upon handling.

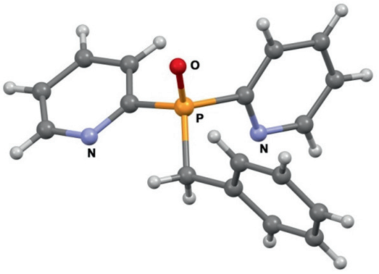
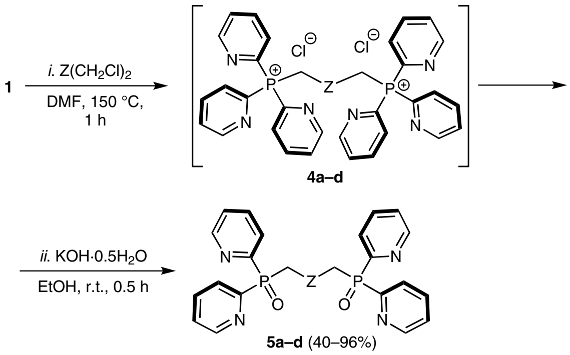
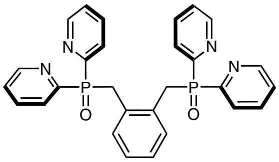
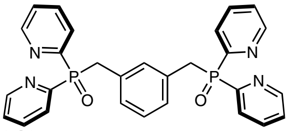
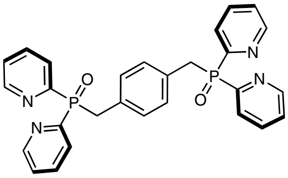
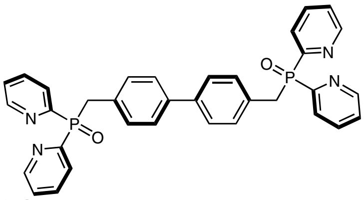


Figure 1 X-ray crystal structure of phosphine oxide **3e**

Table 2 One-Pot Synthesis of Bis(phosphine oxides) **5a–d** from Tris(2-pyridyl)phosphine (**1**)[a]



Entry	$ClCH_2$–Z–CH_2Cl	Product	Yield[b] (%)
1	1,2-$(ClCH_2)_2C_6H_4$	 (**5a**)	40
2	1,3-$(ClCH_2)_2C_6H_4$	 (**5b**)	75
3	1,4-$(ClCH_2)_2C_6H_4$	 (**5c**)	96
4	$[4\text{-}(ClCH_2)C_6H_4]_2$	 (**5d**)	67

[a] Reaction conditions: *i*. phosphine **1** (0.5 mmol) , $ClCH_2$–Z–CH_2Cl (0.25 mmol), DMF (3 mL), 150 °C, 1 h, stirring; *ii*. KOH·0.5H_2O (1.1 mmol), r.t., 0.5 h, stirring.
[b] Isolated yield.

The phosphine oxides **3a**–**f** and **5a**–**d** are air-stable crystals or oils, readily soluble in common organic solvents and almost insoluble in water. All the synthesized compounds (including the intermediate phosphonium salts) were fully characterized by NMR (^{1}H, ^{13}C, and ^{31}P), Fourier-transform IR spectroscopy, and elemental analysis. For compound **3e**, the structure was also determined by X-ray crystallography (Figure 1).[16]

In summary, we have elaborated an efficient one-pot access to di(2-pyridyl)phosphine oxides **3** and bis[di(2-pyridyl)phosphine oxides] **5** from tris(2-pyridyl)phosphine, which is now available.[11] Quaternization of tris(2-pyridyl)phosphine with organic mono- or dihalides and subsequent treatment of the resulting phosphonium salts with alkali *in situ* gave the corresponding phosphine oxides in up to 96% isolated yield. The products might be useful as ligands for the design of functional metal complexes, as potential extractants for rare-earth metals, and as one-step precursors to pyridylphosphines. We have synthesized a series of complexes $\{Cu_2(\mu\text{-}I)_2(\mathbf{3a}\text{–}\mathbf{f})\}$ that exhibited a strong yellow photoluminescence at room temperature (these results will be published elsewhere).

Acknowledgment

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1562485.

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(13) **Phosphine Oxides 3a–f; General Procedure**
A mixture of tris(2-pyridyl)phosphine (**1**; 133 mg, 0.5 mmol) and the appropriate organic halide (5.0 mmol) was stirred at 24–140 °C for 0.5–1.5 h (see Table 1). When the reaction was complete (^{31}P NMR), the mixture was cooled to 20–25 °C and powdered KOH·0.5 H_2O (36 mg, 0.55 mmol) was added. The mixture was stirred for another 30 min at this temperature until the ^{31}P NMR resonance from the phosphonium salts **2a–g** disappeared. $CHCl_3$ (5 mL) was then added to the resulting mixture, the undissolved residue was removed by filtration, and the filtrate was concentrated. The residue was mixed with anhyd Et_2O (3 mL) and the mixture was filtered. The volatiles were evaporated from the filtrate and the residue was dried in vacuo (1 Torr).
Methylbis(2-pyridyl)phosphine Oxide (**3a**)
Yellow-brown oil; yield: 105 mg (96%). FT-IR (film): 3048, 2992, 2918, 2854, 1661, 1575, 1455, 1426, 1292, 1197, 1133, 1084, 1045, 990, 885, 761, 706, 618, 513 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): $\delta = 2.20$ (d, $^{2}J_{PH} = 13.6$ Hz, 3 H, Me), 7.34–7.38 (m, 2 H, H-3 in Py), 7.76–7.81 (m, 2 H, H-4 in Py), 8.04–8.07 (m, 2 H, H-5 in Py), 8.77 (d, $^{3}J_{6-5} = 4.5$ Hz, 2 H, H-6 in Py). ^{13}C NMR (100.62 MHz, $CDCl_3$): $\delta = 13.57$ (d, $^{2}J_{PC} = 76.6$ Hz, Me), 125.42 (d, $^{4}J_{PC} = 1.9$ Hz C-5 in Py), 127.12 (d, $^{2}J_{PC} = 19.8$ Hz, C-3 in Py), 136.11 (d, $^{3}J_{PC} = 8.5$ Hz, C-4 in Py), 150.33 (d, $^{3}J_{PC} = 19.1$ Hz, C-6 in Py), 156.55 (d, $^{1}J_{PC} = 127.6$ Hz, C-2 in Py). ^{31}P NMR (161.98 MHz, $CDCl_3$): $\delta = 32.28$; Anal. Calcd for $C_{11}H_{11}N_2OP$: C, 60.55; H, 5.08; N, 12.84. Found: C, 60.47; H, 5.16; N, 12.65.

(14) Detailed experimental protocols for the synthesis of all new compounds and the corresponding spectroscopic data are provided in the Supporting Information.

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(16) Details of this X-ray analysis are provided in the Supporting Information. CCDC 1477937 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.