Selective mono reduction of bis-phosphine oxides under mild conditions†

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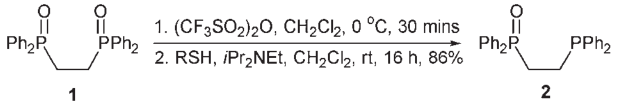
Bis-phosphine oxides can be selectively reduced to bis-phosphine monoxides under exceptionally mild conditions using triflic anhydride and a thiol.

Bis-phosphine monoxides such as **2**, constitute one of the most important classes of hemilabile ligands. Such ligands, which possess both soft and hard Lewis bases within the same molecule, can stabilize various transition metals in low and high oxidation states.[1] If the metal is soft, it will tend to form a strong bond with the phosphine and a weak bond with the oxygen of the phosphine oxide. Conversely, if the metal is hard, it will tend to form a strong bond with the phosphoryl group and a weak bond with the phosphine. Hemilabile transition metal chelates of this type, where a coordinatively unsaturated species is easily generated, can provide exceptional catalysts that combine selectivity with mild reaction conditions.[2]

There are very few methods for preparing bis-phosphine monoxides. For example, direct oxidation of bis-phosphines with conventional oxidants (*e.g.*, H_2O_2) leads to mixtures of the unreacted diphosphine, its monoxide, and its dioxide. More recently, a useful method for the synthesis of monoxides of some of the more common bidentate phosphines has been developed.[3] However, there are no known methods for synthesizing monoxides from bis-phosphine oxides. We now describe a remarkably mild procedure for the selective reduction of bis-phosphine oxides to bis-phosphine monoxides in moderate to high yield.‡

1,2-Bis(diphenylphosphinyl)ethane (**1**) was treated with triflic anhydride (1 equivalent) in dichloromethane (DCM) at 0 °C for 30 minutes, followed by addition of pentanethiol[4] (2 equivalents) and *N*,*N*-diisopropylethylamine (2 equivalents, Scheme 1). 1,2-Bis(diphenylphosphino)ethane monoxide (**2**) was isolated as a white solid, [86%, δ_P −11.6 (d, J = 48.9 Hz), 33.2 (d, J = 48.9 Hz), comparable to literature[3] values].§



Scheme 1 Selective reduction of bis-phosphine oxide **1** (R = pentyl).

The procedure appears to be general, at least for 1,*n*-diphosphine oxides (where *n* = 1–4), and selected BINAP diphosphine oxides. Thus, analogous results were obtained with the corresponding bis-phosphine oxides to give bis(diphenylphosphino)-methane monoxide (52%), 1,3-bis(diphenylphosphino)propane monoxide (71%), 1,4-bis(diphenylphosphino)butane monoxide (71%), (±)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl monoxide (70%, Fig. 1) and (*S*)-2,2′-bis[di(*p*-tolyl)phosphino]-1,1′-binaphthyl monoxide (73%), respectively. The procedure can also be used to reduce simple phosphine oxides to phosphines. For example, treatment of triphenylphosphine oxide with triflic anhydride (0.5 equivalent) followed by excess pentanethiol–diisopropylethylamine gave an approximately 1 : 1 mixture of triphenylphosphine and triphenylphosphine oxide. Triphenylphosphine was isolated in 47% yield. Use of an excess of triflic anhydride (1 equivalent) and the thiol resulted in a decrease in the yield of triphenylphosphine to 30%. This is because triphenylphosphine is oxidised by triflic anhydride.[5] Clearly, with simple phosphine oxides, this procedure can only give a maximum yield of 50%, (or 75% after separating the products and resubjecting the isolated phosphine oxide to a second cycle of the procedure). Elsewhere, full deoxygenation of various phosphine oxides with retention of configuration is described.[6]

Reduction of **1** to give **2** (Scheme 1) is quite a remarkable result, as effectively, a thiol is reducing a phosphoryl group to a phosphine. The P═O bond is extremely stable (dissociation energy ~550 kJ mol^{-1}),[7] and reversion to the phosphine requires a powerful or special reducing agent such as alane (reflux in THF, 30 mins),[8] or trichlorosilane (reflux in benzene, 1–2 h).[9]

The mechanism of the reaction involves initial formation of the phosphonium anhydride **3**[10] (Scheme 2). The formation and reactivity of other phosphonium anhydrides, such as the Hendrickson reagent, is reported elsewhere.[11] Formation of **3** could be followed by attack of the pentanethiolate to give **4a**, which in the presence of excess thiolate could be expected to give

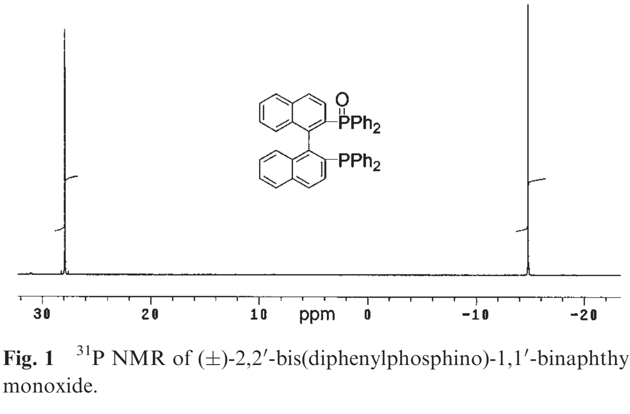


Fig. 1 ^{31}P NMR of (±)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl monoxide.

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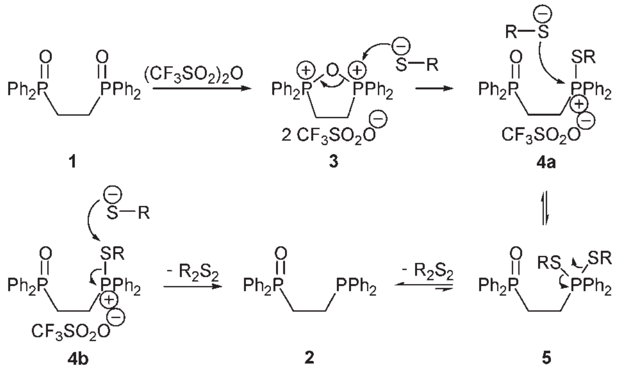

Scheme 2 Mechanism of reduction of bis-phosphine oxides.

the phosphorane **5**. Reductive elimination of the disulfide from **5** would give the phosphine **2**. The phosphorane mechanism is consistent with the mechanism proposed by Zard *et al.*[12] for the reduction of secondary aliphatic nitro compounds to imines by tributylphosphine–diphenyl disulfide. Alternatively, attack by the second thiolate could occur directly on sulfur (as in **4b**) to give the phosphine and the disulfide. Work by Omelanczuk and Mikolajczyk,[13] in which they obtained a phosphine with retention of configuration upon treatment of a chiral alkylthiophosphonium salt with *tert*-butylthiolate, suggests that the second mechanism (**4b**) is the more plausible. Presumably the driving force for the reduction is the activation of the bis-phosphine oxide by the triflic anhydride, and the subsequent transformation of **3** to **4a**, where the thiolate displaces an excellent leaving group (the diphenylphosphinyl group), with the concomitant formation of the very stable P=O bond.

Notes and references

‡ This was a serendipitous discovery. In attempting to convert *N*-(2-mercaptoethyl)benzamide into 2-phenyl-4,5-dihydro-1,3-thiazole using the reagent **3**, we found that bis(2-benzamidoethyl)disulfide was a by-product of the reaction. Upon further investigation, the bis-phosphine monoxide **2** was identified by ^{31}P NMR.

§ **Synthesis of 1,2-bis(diphenylphosphino)ethane monoxide.** Triflic anhydride (199 μL, 1.18 mmol) was added slowly to a solution of 1,2-bis(diphenylphosphinyl)ethane (509 mg, 1.18 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C under a nitrogen atmosphere. A thick white slurry was formed almost immediately which was stirred at 0 °C for 30 min. Consecutive addition of pentane-1-thiol (585 μg, 4.73 mmol) and *N*,*N*-diisopropylethylamine (409 μL, 2.37 mmol) to the slurry gave a pale yellow solution which was allowed to reach room temperature and then left stirring for 16 h. The reaction solution was washed with sodium hydrogen carbonate (5% aqueous solution, 2 × 30 mL), dried (Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue purified by silica column chromatography (CH_3OH–ethyl acetate–hexane, gradient from 0 : 0 : 100 to 10 : 90 : 0). 1,2-Bis(diphenylphosphino)ethane monoxide (**2**) was obtained as a white solid (422 mg, 86%). Mp 193–196 °C (lit.,[14] mp 193–194 °C). δ_P (162 MHz, $CDCl_3$): −11.6 (d, 1P, J = 48.9 Hz), 33.2 (d, 1P, J = 48.9 Hz) [lit.,[3] δ_P (81 MHz, $CDCl_3$): −11.5 (d, 1P, J = 48 Hz), 32.3 (d, 1P, J = 48 Hz)]. 1,2-Bis(diphenylphosphinyl)ethane (**1**) was also isolated (50 mg, 10%). Analogous results were obtained with the corresponding 1,1-, 1,3-, and 1,4-bis-phosphine oxides, 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl monooxide and 2,2′-bis[di(*p*-tolyl)phosphino]-1,1′-binaphthyl monoxide to give, respectively:

Bis(diphenylphosphino)methane monoxide: (142 mg, 52%). Mp 188–190 °C (lit.,[15] mp 191–192 °C). δ_P (162 MHz, $CDCl_3$): −27.3 (d, 1P, J = 51.2 Hz), 30.3 (d, 1P, J = 51.2 Hz) [lit.,[3] δ_P (81 MHz, $CDCl_3$): −26.5 (d, 1P, J = 50.5 Hz), 29.8 (d, 1P, J = 50.5 Hz)]. Bis(diphenylphosphinyl)methane was also isolated (110 mg, 39%).

1,3-Bis(diphenylphosphino)propane monoxide: (217 mg, 71%). Mp 105–107 °C (lit.,[16] mp 106–108 °C). δ_P (162 MHz, $CDCl_3$): −17.3 (s, 1P), 33.2 (s, 1P) [lit.,[3] δ_P (81 MHz, $CDCl_3$): −17.2 (s, 1P), 32.0 (s, 1P)]. 1,3-Bis(diphenylphosphinyl)propane was also isolated (82 mg, 26%).

1,4-Bis(diphenylphosphino)butane monoxide: (170 mg, 71%). Mp 189–191 °C (lit.,[17] mp 190–191 °C). δ_P (162 MHz, $CDCl_3$): −15.8 (s, 1P), 32.6 (s, 1P) [lit.,[3] δ_P (81 MHz, $CDCl_3$): −16.5 (s, 1P), 32.2 (s, 1P)]. Bis(diphenylphosphinyl)butane was also isolated (54 mg, 22%).

(±)-2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl monoxide: (299 mg, 70%). Mp 266–267 °C (lit.,[3,18]). δ_P (162 MHz, $CDCl_3$): −14.1 (s, 1P), 28.7 (s, 1P) [lit.,[3] δ_P (81 MHz, $CDCl_3$): −14.5 (s, 1P), 27.9 (s, 1P)]. (±)-1,1′-(1,1′-binaphthalene)-2,2′-diylbis(1,1-diphenyl) phosphine oxide was also isolated (118 mg, 27%). The ^{31}P NMR spectrum is shown in Fig. 1.

(*S*)-2,2′-Bis[di(*p*-tolyl)phosphino]-1,1′-binaphthyl monoxide: (107 mg, 73%). Mp 267–268 °C (lit.,[19]). δ_P (162 MHz, $CDCl_3$): −15.7 (s, 1P), 28.8 (s, 1P). (*S*)-[1,1′-binaphthalene]-2,2′-diylbis[bis(4-methyl-phenyl)-phosphine oxide] was also isolated (31 mg, 22%).

Triphenylphosphine oxide reduction: triflic anhydride (121 μL, 0.72 mmol), triphenylphosphine oxide (400 mg, 1.44 mmol), pentane-1-thiol (355 μL, 2.87 mmol) and *N*,*N*-diisopropylethylamine (249 μL, 1.44 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to the procedure above. After workup and purification by silica column chromatography (ethyl acetate–hexane, gradient from 0 : 100 to 100 : 0), triphenylphosphine was obtained as a white solid (177 mg, 47%). Mp 79–80 °C (lit.,[16] mp 79–81 °C). δ_P (162 MHz, $CDCl_3$): −5.1 (s, 1P). Triphenylphosphine oxide was also isolated (204 mg, 51%).

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