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Rhodium-catalyzed synthesis of 1-alkynylphosphine oxides from 1-alkynes and tetraphenylbiphosphine

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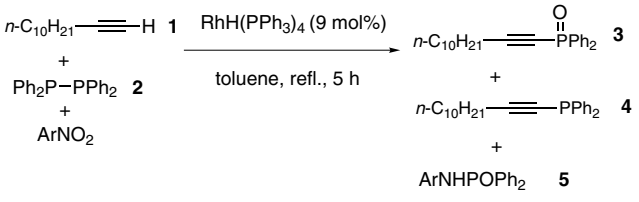
Abstract—A rhodium complex $RhH(PPh_3)_4$ catalyzes the C–P bond forming reaction of 1-alkynes and tetraphenylbiphosphine in the presence of 2,4-dimethylnitrobenzene giving 1-alkynylphosphines and its oxides.

Previously, we reported the C–S bond forming reaction of 1-alkynes and dialkyl disulfides in the presence of $RhH(PPh_3)_4$ giving alkylthioacetylenes,[1] a metathesis reaction of the S–S and C–H bond. It was also found that the same rhodium complex catalyzed the metathesis reaction of biphosphine disulfides (dioxides) and dialkyl disulfides giving dithiophosphinates, in which the S–S and P–P bond exchange took place.[2] It was therefore considered that C–P bond could be formed by the bond metathesis of P–P and C–H, and described here is the rhodium-catalyzed synthesis of 1-alkynylphosphines and its oxides from 1-alkynes and tetraphenylbiphosphine in the presence of 2,4-dimethylnitrobenzene. Reported syntheses of 1-alkynylphosphines from 1-alkynes and phosphine chloride in general employed stoichiometric amounts of organometallic bases of lithium or magnesium.[3] The reaction using a stoichiometric titanium tetrachloride and triethylamine was reported.[4] Beletskaya developed nickel or copper catalyzed reactions in the presence of triethylamine.[5] In some cases, organic bases such as triethylamine or iminophosphines were used for such C–P bond formation.[6] In contrast, the present reaction employs a rhodium catalyst in the absence of any added base but in the presence of a nitrobenzene, which plays several critical roles in the reaction.

When 1-dodecyne **1** was treated with tetraphenylbiphosphine **2** (2 equiv) and 2,4-dimethylnitrobenzene **6** (2 equiv) in the presence of $RhH(PPh_3)_4$ (9 mol %) in refluxing toluene for 5 h, 1-dodecynyldiphenylphosphine oxide **3** and 1-dodecynyldiphenylphosphine **4** were obtained in 74% and 6% yield, respectively (Table 1, entry 6). A considerable part of **6** was converted to a phosphinic amide **5** in 56% isolated yield. The rhodium complex was essential, and no reaction took place in its absence. The nitrobenzene **6** was also required, and, in the absence, (*E*)-1-dodecenylphosphine oxide **7**[7] was formed in 32% yield with no traces of **3** and **4** (entry 1). The

Table 1. Effect of nitrobenzene in the C–P bond formation reaction of **1** and **2**



Entry	Ar	Yield (%)	
		3	**4**
1	None	0[a]	0
2	C_6H_5	57	10
3	*p*-MeC_6H_4	57	13
4	*m*-MeC_6H_4	74	Trace
5	*o*-MeC_6H_4	73	0
6	2,4-$Me_2C_6H_3$ **6**	74	6
7	2,3,4,5-Me_4C_6H	68	16
8	*p*-NCC_6H_4	58	0
9	*p*-$MeOC_6H_4$	46	17

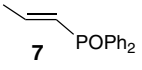
[a] Alkene **7** was formed in 32% yield. 

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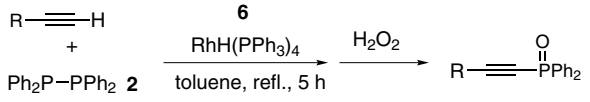
Table 2. Rhodium-catalyzed synthesis of 1-alkynylphosphine oxides from 1-alkynes



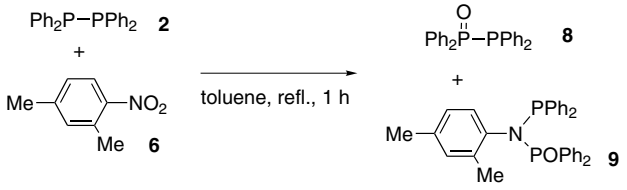
Entry	R	Yield (%)
1	n-C_8H_{17}	84
2	n-$C_{10}H_{21}$	80
3	$Ph(CH_2)_2$	78
4	$MeO(CH_2)_9$	70
5	$BnO(CH_2)_9$	84
6	t-$BuCOO(CH_2)_9$	83
7	n-$C_4H_9CH(C_2H_5)$	83
8	1-Adamantyl	54
9	p-$CH_3C_6H_4$	35[a]

[a] The reaction was conducted at 100 °C for 1 h. (*E*)-2-(*p*-Tolyl)ethenyldiphenylphosphine oxide was also formed in 38% yield.

structure of the nitrobenzene had some effect on the reaction: use of polymethylated nitrobenzenes gave higher yields of **3** and **4** compared to nitrobenzene and *p*-cyanonitrobenzene (entries 2–8); use of 2,3,4,5-tetramethylnitrobenzene and *p*-(methoxy)nitrobenzene increased the amount of **4** (entries 7 and 9).

Several aliphatic 1-alkynes were reacted with **2** (2 equiv) in the presence of **6** (2 equiv) and $RhH(PPh_3)_4$ (9 mol %) giving ca. 1:10 mixtures of 1-alkynylphosphines and its oxides, which were treated with 30% H_2O_2 to convert the small amounts of the phosphines to the oxides (Table 2).[8] The reaction of aromatic 1-alkynes was less efficient; the treatment of *p*-tolylacetylene and **2** in toluene at 100 °C for 1 h followed by H_2O_2 gave (*p*-tolylethynyl)phosphine oxide (35%) and (*E*)-(*p*-tolyl)ethenyldiphenylphosphine oxide (38%).

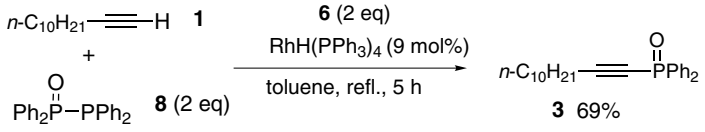
The role of the nitrobenzene is intriguing. As apparent from the formation of phosphinic amide **5**, **6** trapped Ph_2PH, which should formally be formed from **1** and **2**. In addition, **6** was involved in several critical steps in the reaction. When **2** and **6** were reacted in refluxing toluene for 1 h, **2** disappeared with the formation of biphosphine monooxide **8** and an adduct **9**[9] in a 4.5:1 ratio by ^{31}P NMR, the latter of which was isolated in 16% yield (Scheme 1). This oxidation–reduction reaction did not require the rhodium complex. Notably, both **8** and **9** were involved in the C–P bond formation reaction of **1**. The treatment of **1** and **8** (2 equiv) in the presence of $RhH(PPh_3)_4$ (9 mol %) and **6** (2 equiv) in refluxing toluene for 5 h gave **3** in 69% yield, where **4** was not detected (Scheme 2). The rhodium complex and **6** were essential for this reaction. When **9** was reacted with **1** in refluxing toluene for 5 h in the presence of the rhodium complex (9 mol %), **4** (39%) and **3** (13%) were obtained (Scheme 3). The rhodium complex was confirmed to be essential for this reaction. The role of **6** therefore was to activate **2** giving either **8** or **9**, both of which reacted with **1** to form the C–P bond.



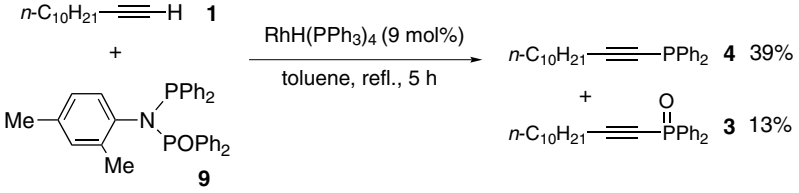
Scheme 1.

The experiments also revealed the presence of two independent processes in the present C–P bond formation (Scheme 4): the phosphine oxide **3** was formed from biphosphine monoxide **8**; the phosphine **4** from **9**. The oxidation of **4** to **3** was unimportant; the treatment of **4** and **6** in refluxing toluene for 2 h gave a very small amount of **3**, which indicated that the oxidation of **4** to **3** was much slower than that of **2** to **8**. The rhodium complex probably activated **9** by the chelate formation between the O and P atoms. Analogous S and P chelating transition metal complexes were reported,[10] and **9** is now shown to function as a novel phosphinylating reagent.

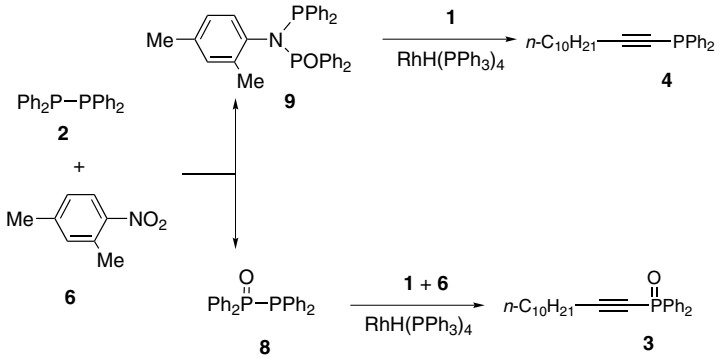
In summary, rhodium-catalyzed C–H and P–P bond metathesis reaction of 1-alkynes and biphosphine giving 1-alkynylphosphine oxide was developed, and a nitrobenzene was found effectively to activate the P–P bond for the transition metal catalysis.



Scheme 2.



Scheme 3.



Scheme 4.

Acknowledgments

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7. The oxygen atom on **7** may be derived from a small amount of oxygen contaminated.
8. In a two-necked flask equipped with a reflux condenser were placed **2** (0.25 mmol, 93 mg), **6** (0.25 mmol, 33.8 μL), and $RhH(PPh_3)_4$ (9 mol %, 13 mg) under an argon atmosphere. Degassed toluene (1 mL) and **1** (0.125 mmol, 27 μL) were added, and the solution was heated at reflux for 5 h. Then, 30% hydrogen peroxide (0.25 mL) in THF (5 mL) was added to the solution at 0 °C, and the mixture was stirred for 1 h at the temperature. Aqueous sodium thiosulfate was added, and the organic materials were extracted with ethyl acetate. The organic layer was washed with water and brine, dried over $MgSO_4$, and filtered. After removal of the solvents, flash chromatography (hexane/ethyl acetate = 2/1) over neutral silica gel gave **3** (36.7 mg, 80%) as pale yellow oil.
9. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13 (3H, s), 2.10 (3H, s), 6.43 (1H, s), 6.65 (1H, d, $J = 8.0$ Hz), 7.10 (1H, d, $J = 8.0$ Hz), 7.11 (2H, dt, $J = 8.0$, 3.6 Hz), 7.20–7.31 (8H, m), 7.43 (1H, dt, $J = 8.0$, 1.6 Hz), 7.49 (2H, dd, $J = 16.8$, 8.0 Hz), 7.54–7.61 (3H, m), 7.69 (2H, dt, $J = 8.0$, 1.6 Hz), 8.17 (2H, dd, $J = 12.0$, 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.9, 20.8, 126.5 (d, $J = 1.5$ Hz), 127.3 (d, $J = 12.1$ Hz), 127.9, 128.0 (d, $J = 15.2$ Hz), 128.1 (d, $J = 3.8$ Hz), 128.3, 130.9, 131.0 (d, $J = 12.1$ Hz), 131.5 (d, $J = 2.3$ Hz), 131.7 (dd, $J = 127.3$, 4.2 Hz), 131.8 (d, $J = 3.8$ Hz), 131.9, 132.7 (dd, $J = 127.3$, 2.5 Hz), 132.9 (d, $J = 18.2$ Hz), 133.8 (dd, $J = 8.4$, 3.0 Hz), 134.1 (d, $J = 8.4$ Hz), 134.2 (d, $J = 8.5$ Hz), 136.0 (d, $J = 6.0$ Hz), 136.1 (d, $J = 27.2$ Hz), 136.6 (d, $J = 1.5$ Hz), 137.6 (d, $J = 21.3$ Hz), 137.7 (d, $J = 3.0$ Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.3 (d, $J = 78.4$ Hz), 54.6 (d, $J = 78.4$ Hz). IR (neat) 3055, 2975, 1492, 1437, 1203, 1119, 913 cm^{-1}. MS (EI) m/z 505 (M^+, 63%), 321 (M^+-184, 100%). HRMS calcd for $C_{32}H_{29}ONP_2$: 505.1724. Found: 505.1716.
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