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Synthesis of Bulky Phosphines by Rhodium-Catalyzed Formal [2 + 2 + 2] Cycloaddition Reactions of Tethered Diynes with 1-Alkynylphosphine Sulfides

Azusa Kondoh, Hideki Yorimitsu,* and Koichiro Oshima*

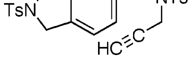
Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyoto-daigaku Katsura,
Nishikyo-ku, Kyoto 615-8510, Japan

Received March 7, 2007; E-mail: yori@orgrxn.mbox.media.kyoto-u.ac.jp; oshima@orgrxn.mbox.media.kyoto-u.ac.jp

In the modern organic synthesis, bulky phosphine ligands play an indispensable role in preparing biologically interesting compounds as well as organic functional materials.[1] Synthesis of such bulky ligands is hence quite important. However, the methods for the synthesis are mostly limited to the reaction of a chlorophosphine with a bulky organometallic reagent[2] and the transition-metal-catalyzed phosphination or phosphinylation of a bulky aryl halide.[3]

We have been focusing on 1-alkynylphosphines as precursors of new phosphines.[4] In the course of our study on the use of 1-alkynylphosphines, we report herein a conceptually different approach to bulky phosphines. Rhodium-catalyzed formal [2 + 2 + 2] cycloaddition reaction[5] of 1,6-diynes and 1-alkynylphosphine sulfides[6] afforded benzene rings having a thiophosphinyl moiety. When substrates are properly designed, the newly formed benzene rings naturally have one or two substituents next to the thiophosphinyl group, which provide sterically congested environment around the phosphorus.[7]

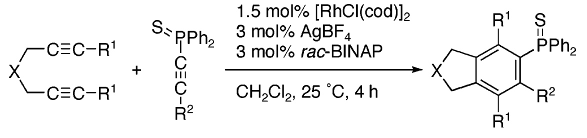
The reaction of 1,6-diyne **1a** with 1-octynyldiphenylphosphine sulfide (**2a**) proceeded smoothly in dichloromethane in the presence of a cationic rhodium catalyst and BINAP (Table 1, entry 1). Among the ligands we screened, BINAP was the best ligand. When DPPE, DPPB, DPPF, or PPh_3 (2 equiv) was used, the yield was moderate. The generation of the cationic rhodium species by the action of silver tetrafluoroborate was essential. Without the silver salt, only **1a** participated in the cycloaddition reaction to form dimerized **4a** and no **3aa** was obtained. The cationic rhodium center would induce the strong coordination of **2a**. Iridium catalysis, $[IrCl(cod)]_2$ with or without the silver salt, for instance, left **2a** untouched and provided **4a** instead. The use of [Cp*RuCl(cod)] only promoted the very slow dimerization of **1a**. The reaction of trivalent 1-octynyldiphenylphosphine with **1a** resulted in no conversion. The highly coordinating nature of the trivalent phosphine would cause deactivation of the catalyst. The reaction of 1-octynyldiphenylphosphine oxide with **1a** provided 40% yield of the corresponding product along with **4a**. The sulfide moiety seems to properly assist the reaction of a rhodacyclopentadiene intermediate with **2a** in the catalytic cycle.[8]



4a

Various combinations of tethered diynes and 1-alkynylphosphine sulfides were examined (Table 1). Dipropargyl ether (**1b**) and a diyne **1c** derived from dimethyl malonate reacted smoothly with **2a**. The latter provided the corresponding triarylphosphine sulfide **3ca** in the highest yield of 97% (entry 3). 1,7-Octadiyne (**1e**) was superior to 1,6-heptadiyne (**1d**) as a substrate.

Table 1. Rh-Catalyzed Formal [2 + 2 + 2] Cycloaddition Reactions of Tethered Diynes with 1-Alkynylphosphine Sulfides



1 (1.2 eq.) **2** **3**

entry	1	X[a]	R¹	2	R²	3	yield
1	**1a**	TsN	H	**2a**	C_6H_{13}	**3aa**	71
2	**1b**	O	H	**2a**	C_6H_{13}	**3ba**	77
3	**1c**	E_2C	H	**2a**	C_6H_{13}	**3ca**	97
4	**1d**	CH_2	H	**2a**	C_6H_{13}	**3da**	60
5	**1e**	CH_2CH_2	H	**2a**	C_6H_{13}	**3ea**	93
6	**1c**	E_2C	H	**2b**	Ph	**3cb**	85
7	**1c**	E_2C	H	**2c**	^iPr	**3cc**	83
8	**1c**	E_2C	H	**2d**	^tBu	**3cd**	74
9	**1c**	E_2C	H	**2e**	*o*-$MeOC_6H_4$	**3ce**	85
10	**1c**	E_2C	H	**2f**	Me_3Si	**3cf**	80
11	**1f**	E_2C	Me	**2a**	C_6H_{13}	**3fa**	87[b]
12	**1g**	E_2C	Ph	**2a**	C_6H_{13}	**3ga**	90[b]
13	**1g**	E_2C	Ph	**2b**	Ph	**3gb**	65[b,c]
14	**1h**	E_2C	^iPr	**2c**	^iPr	**3hc**	70[b,d]
15	**1h**	E_2C	^iPr	**2g**	2-MeO-1-Np[e]	**3hg**	77[b,d]

[a] Ts = *p*-$MeC_6H_4SO_2$, E = CO_2Me. [b] Performed in 1,2-dichloroethane at reflux. [c] Performed for 12 h. [d] $[RhCl(cod)]_2$ (5 mol %), $AgBF_4$ (10 mol %), *rac*-BINAP (10 mol %), 12 h. [e] 2-Methoxy-1-naphthyl.

The scope of 1-alkynylphosphine sulfides (entries 6−10) is wide enough to employ not only phenyl-substituted **2b** but also bulky isopropyl- and *tert*-butyl-substituted **2c** and **2d**. The reactions of *o*-methoxyphenyl-substituted **2e** and trimethylsilyl-substituted **2f** proceeded smoothly. The reaction is so powerful that dialkynylphenylphosphine sulfide **5a** and trialkynylphosphine sulfide **5b** participated in multiple cycloadditions to yield the corresponding products in high yields (eqs 1 and 2).

Reactions of internal diynes ($R^1 \neq H$) did not proceed at all in dichloromethane at 25 °C. Instead, performing the reactions in refluxing 1,2-dichloroethane resulted in smooth conversion to afford the corresponding products in good yields (entries 11−15). The products have a 2,6-disubstituted phenyl group on the phosphorus, which creates a considerable steric effect.[9] Interestingly, the reaction of **1h** with diphenyl[(2-methoxy-1-naphthyl)ethynyl]phosphine sulfide (**2g**) provided phosphine sulfide **3hg**, which has a chiral axis.[10] The use of monosubstituted **1**, where one R^1 is H and the other R^1 is Ph, resulted in self-dimerization of the diyne.

1-Alkynyldicyclohexylphosphine sulfides **7** were less reactive than the corresponding diphenyl analogues **2**. The reaction of terminal diyne **1c** with **7a** provided the desired product **8a** in

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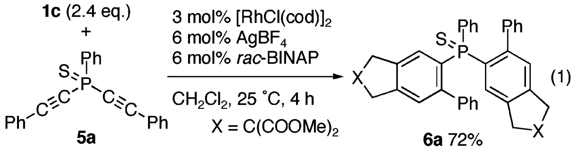
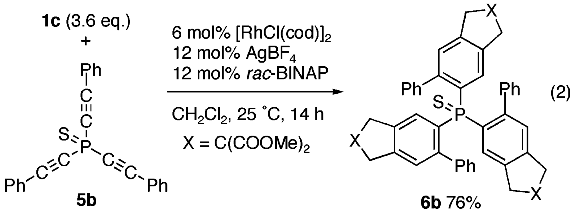
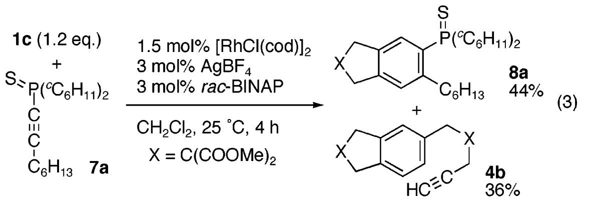
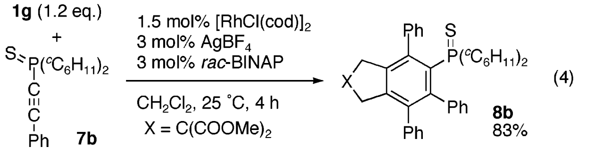




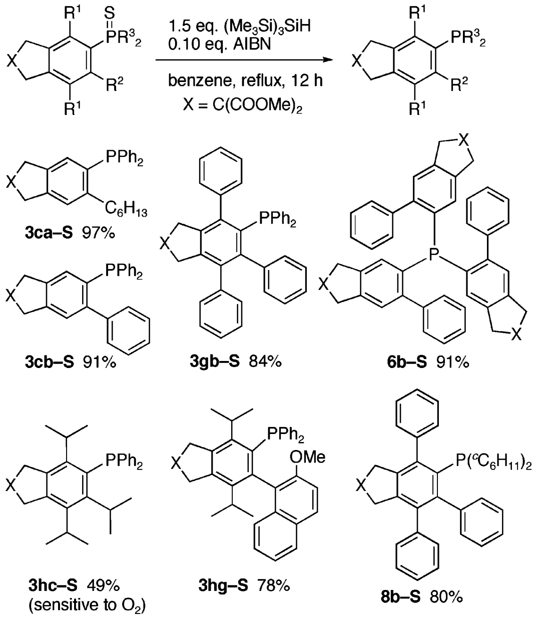
moderate yield with concomitant formation of **4b** (eq 3). The reaction of internal diyne **1g** with dicyclohexylphosphine sulfide **7b** was successful to yield highly crowded **8b** in high yield (eq 4).

The products, phosphine sulfides, were subjected to radical desulfidation conditions[11] to provide the corresponding trivalent phosphines in high yields (Scheme 1). The desulfidation reactions of these bulky phosphines were clean and high-yielding. Except for triisopropyl-substituted **3hc−S**, the phosphines obtained were stable under air. We could perform the purification of the trivalent phosphines on silica gel without any special care. The present method offers a novel access to bulky phosphine ligands.

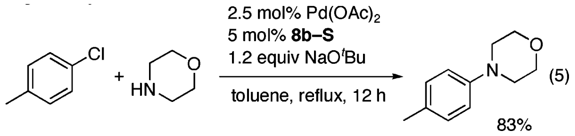




Scheme 1. Desulfidation with TTMSS



Application of the bulky phosphine was examined. The ligand **8b−S** proved to serve as a ligand for the amination of aryl chloride with morpholine (eq 5).[12] The bulky phosphine ligands prepared by this method will find many applications in organic synthesis.



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Supporting Information Available: Experimental details and characterization data for new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) We performed the reaction of 2,6-diphenylphenyllithium with chlorodiphenylphosphine. However, the corresponding bulky phosphine, diphenyl-(2,6-diphenylphenyl)phosphine, was obtained in only 22% yield, along with a significant amount of *m*-terphenyl. See Supporting Information.

(10) When (*R*)-tol-BINAP was used as a ligand, a 55% ee of **3hg** was obtained in 72% yield.

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