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Double Phosphinylation of Propargylic Alcohols: A Novel Synthetic Route to 1,2-Bis(diphenylphosphino)ethane Derivatives[†]

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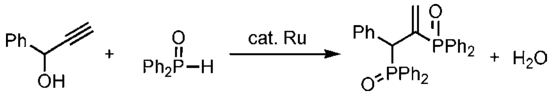
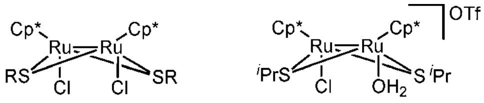
ABSTRACT



Double phosphinylation of propargylic alcohols with diphenylphosphine oxide in the presence of a thiolate-bridged diruthenium complex as catalyst gives the corresponding 2,3-bis(diphenylphosphinyl)-1-propenes in high yields with a complete selectivity.

Recently, we have disclosed the ruthenium-catalyzed efficient propargylic substitution reactions of propargylic alcohols with a variety of heteroatom- and carbon-centered nucleophiles to give the corresponding functionalized propargylic products in high yields with a complete regioselectivity.[1] It is noteworthy that the reactions are catalyzed only by thiolate-bridged diruthenium complexes such as [Cp*RuCl(μ_2-SR)$_2$-RuCp*Cl] (Cp* = η^5-C_5Me_5; R = Me (**1a**), ^{n}Pr (**1b**), ^{i}Pr (**1c**)), and [Cp*RuCl(μ_2-S^{i}Pr)$_2$RuCp*(OH_2)]OTf (OTf = OSO_2CF_3) (**1d**) (Scheme 1).[2] During our continuous study on the propargylic substitution reactions of propargylic alcohols with diphenylphosphine oxide (Scheme 2),[3] we came across the phenomenon that a prolonged reaction of 1-phenyl-2-propyn-1-ol (**2a**) with diphenylphosphine oxide in the presence of 5 mol % of **1a** at higher temperature afforded the corresponding 2,3-bis(diphenylphosphinyl)-3-phenyl-1-propene (**3a**) as a major product together with a small amount of 3-diphenylphosphinyl-3-phenyl-1-propyne (**4a**). This finding prompted us to investigate the double phosphinylation of propargylic alcohols in detail because this double phosphinylation provides a novel synthetic route to 1,2-bis(diphenylphosphino)ethane[4] derivatives, which work as suitable ligands for various transition metals. Preliminary results are described here.

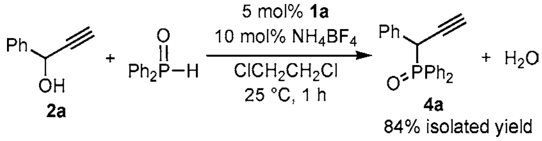
Scheme 1



R = Me (**1a**), ^{n}Pr (**1b**), ^{i}Pr (**1c**)

1d

Scheme 2



Treatment of **2a** with diphenylphosphine oxide in the presence of methanethiolate-bridged diruthenium complex (**1a**) (5 mol %) and NH_4BF_4 (10 mol %) in 1,2-dichloroethane ($ClCH_2CH_2Cl$) at 60 °C for 18 h afforded **3a** in 90% isolated yield (Scheme 3). Neither other products nor regioisomers of **3a** were detected by ^{1}H NMR. The molecular

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[†] Dedicated to Professor Iwao Ojima on the occasion of his 60th birthday.

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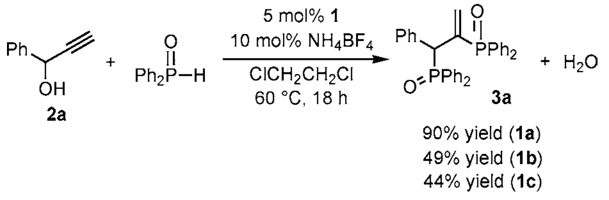
Scheme 3

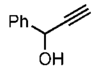
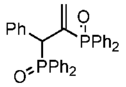
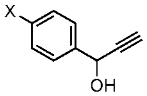
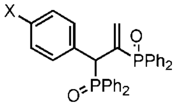
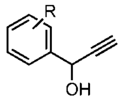
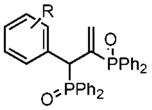
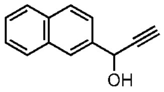
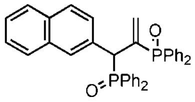


structure of **3a** was unambiguously clarified by preliminary X-ray analysis. An ORTEP drawing of **3a** is shown in Supporting Information as Figure S1. When **1b** or **1c** was used as catalyst in place of **1a**, **3a** was obtained in only 49% or 44% isolated yield, respectively, together with the formation of **4a** in 29 or 30% isolated yield. In the reaction at room temperature for 18 h, **4a** and **3a** were obtained in 77% and 8% isolated yields. Separately, we confirmed that no reaction occurred at all in the absence of **1a**. We have also investigated the reactions of **2a** with diethyl phosphite or diphenyl phosphite under the same reaction conditions, but they resulted in a formation of only some unidentified products unfortunately.

Reactions of various 1-aryl-2-propyn-1-ols (**2**) with diphenylphosphine oxide were carried out in the presence of **1a** (5 mol %) and NH_4BF_4 (10 mol %) at 60 °C for 18 h. Typical results are shown in Table 1. A *p*-halogeno substituent such as fluoro, chloro, or bromo to the benzene ring was tolerant of the catalytic reaction (Table 1, runs 2−4). In sharp contrast, introduction of an electron-donating group such as methyl or methoxy substituent to the benzene ring decreased the yield of double-phosphinylated products (**3**) (Table 1, runs 5−7). In particular, no double phosphinylation occurred when 1-*o*-tolyl-2-propyn-1-ol was used as substrate (Table 1, run 8). In these cases, the corresponding propargylic diphenylphosphine oxides (**4**) were obtained in moderate to good isolated yields. These results indicate that the kind of substituent on the benzene ring has a dramatic influence on the reactivity. Unfortunately, the reaction of 1-cyclohexyl-2-propyn-1-ol did not proceed at all. When other terminal alkynes such as 1-octyne, phenylacetylene, ethyl propiolate, and 4-phenyl-5-hexyn-2-one were used in place of propargylic alcohols, no reaction occurred at all in all cases.

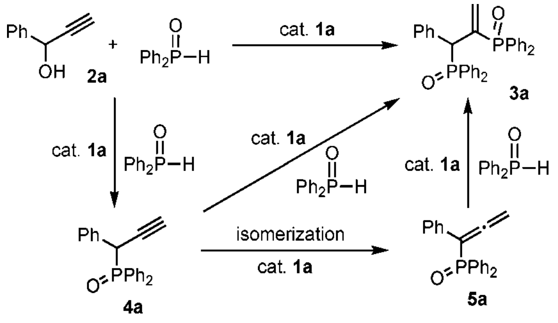
To obtain some information of the reaction mechanism, we monitored the reaction of **4a** with diphenylphosphine oxide in the presence of **1a** (5 mol %) in $ClCD_2CD_2Cl$ at 60 °C for 50 h by ^1H NMR. The conversion of **4a** into an intermediate was observed, and the intermediate was then converted into the double phosphinylated product **3a**. Interestingly, the intermediate was actually isolated in 72% yield in a separate experiment by heating **4a** in the presence of **1a** at 60 °C for 50 h (eq 1), which was characterized as an allenyldiphenylphosphine oxide (**5a**).[5] Separately, we confirmed the transformation of **4a** into **3a** in the presence of **1a** (5 mol %) in $ClCH_2CH_2Cl$ at 60 °C for 18 h, **3a** being obtained in 85% isolated yield (eq 2). The addition of diphenylphosphine oxide to the isolated **5a** was also confirmed by ^1H NMR, **3a** being formed in quantitative yield (eq 3).[6] These results clearly show that the double phosphinylation of **2a** proceeds via pathways shown in Scheme 4.

Table 1. Ru-Catalyzed Double Phosphinylation of Propargylic Alcohols (**2**) with Diphenylphosphine Oxide Affording Double-Phosphinylated Compounds (**3**)[a]

run	propargylic alcohol (**2**)		double phosphinylated product (**3**)		yield (%)[b]
1		**2a**		**3a**	90
2		**2b** X = F		**3b**	71
3		**2c** X = Cl		**3c**	96
4		**2d** X = Br		**3d**	88
5		**2e** R = *p*-OMe		**3e**	15[c]
6		**2f** R = *p*-Me		**3f**	54[d]
7		**2g** R = *m*-Me		**3g**	46[e]
8		**2h** R = *o*-Me		**3h**	0[f]
9		**2i**		**3i**	80

[a] All the reactions of propargylic alcohol **2** (0.60 mmol) with diphenylphosphine oxide (3.00 mmol) were carried out in the presence of **1a** (0.03 mmol) and NH_4BF_4 (0.06 mmol) in $ClCH_2CH_2Cl$ at 60 °C for 18 h. [b] Isolated yield. [c] The corresponding propargylic substituted product (**4e**) was obtained in 72% isolated yield. [d] **4f** in 28% isolated yield. [e] **4g** in 31% isolated yield. [f] **4h** in 79% isolated yield.

Scheme 4



At first, **2a** is transformed rapidly into propargylic substituted product **4a** by the catalysis of **1a**. Isomerization from **4a** into

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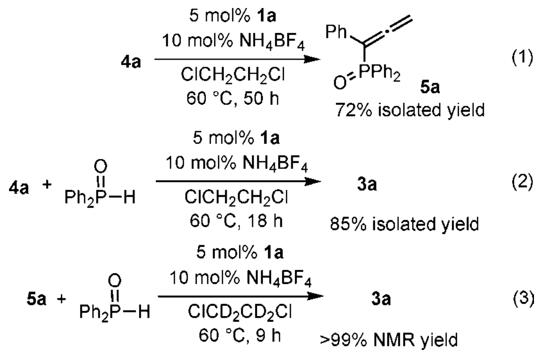
(1) (a) Nishibayashi, Y.; Wakiji, I.; Hidai, M. *J. Am. Chem. Soc.* **2000**, *122*, 11019. (b) Nishibayashi, Y.; Onodera, G.; Inada, Y.; Hidai, M.; Uemura, S. *Organometallics* **2003**, *22*, 873. (c) Nishibayashi, Y.; Imajima, H.; Onodera, G.; Hidai, M.; Uemura, S. *Organometallics* **2004**, *23*, 26. (d) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Hidai, M.; Uemura, S. *J. Org. Chem.* **2004**, *69*, 3408.

(2) (a) The thiolate-bridged diruthenium complexes (**1**) were found to provide an unique bimetallic reaction site for activation and transformation of various terminal alkynes; see: Nishibayashi, Y.; Yamanashi, M.; Wakiji, I.; Hidai, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2909 and references therein. (b) The methanethiolate-bridged diruthenium complex [Cp*RuCl(μ_2-SMe)$_2$RuCp*Cl] (**1a**) is commercially available from Wako Pure Chemical Industries (Japan) as met-DIRUX (*met*hanethiolate-bridged *diru*thenium comple*x*) (130-14581).

(3) Nishibayashi, Y.; Milton, M. D.; Inada, Y.; Yoshikawa, M.; Wakiji, I.; Hidai, M.; Uemura, S. *Chem. Eur. J.*, in press.

5a occurs, and then the addition of another diphenylphosphine oxide to **5a** catalyzed by **1a** gives **3a**.



The direct addition of diphenylphosphine oxide to **4a** catalyzed by **1a** might also be considered as another pathway for this catalytic reaction although we have already confirmed that no catalytic reaction of other terminal alkynes such as 1-octyne and phenylacetylene with diphenylphosphine oxide proceeded even in the presence of catalyst **1a**.

As a preliminary result, we have already found the optical resolution of racemic **3a** by using optically active (2*S*,3*S*)-(+)-2,3-*O*-dibenzoyltartaric acid ((+)-DBTA) as a resolving agent.[7] The result of X-ray analysis of the complex with (+)-DBTA indicates that the absolute configuration of optically active **3a** in the complex is *S*. An ORTEP drawing of (*S*)-**3a**·(+)-DBTA is shown in the Supporting Information as Figure S2. Unfortunately, we have not yet succeeded in practical preparation of the optically active (*S*)-**3a** by using this method. Detailed experimental results will be reported in due course.

In summary, we have found the ruthenium-catalyzed double phosphinylation of propargylic alcohols with diphenylphosphine oxide to give the corresponding 2,3-bis(diphenylphosphinyl)-1-propenes in high yields with a complete selectivity. Although transition metal-catalyzed addition of phosphorus-centered nucleophiles to an alkyne or alkene is known as a synthetic method for the preparation of the compounds with carbon−phosphorus single bond,[8] the double phosphorylation and phosphinylation of alkynes are limited to only a few cases reported by Lin and co-workers.[9] The method reported here provides a more convenient route to the double phosphinylated products from propargylic alcohols and diphenylphosphine oxide.[10] The double phosphinylated products are considered to be precursors of modified chiraphos[11] (2,3-bis(diphenylphosphinyl)-butane derivatives), which have a potential to work as new types of chiral bidentate ligands for asymmetric synthesis. Further studies on the reduction of optically active **3a** into the corresponding 1,2-bis(diphenylphosphino)propanes are currently in progress and the detailed results will be reported in due course.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research for Young Scientists (A) (No. 15685006) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available: Experimental procedures and spectral data for all new compounds. Crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

OL048347K

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[4] ,2-Bis(diphenylphosphino)ethane (dppe) has been used as a typical bidentate ligand for various transition metals, see some recent examples: (a) Arisawa, M.; Yamaguchi, M *J. Am. Chem. Soc.* **2003**, *125*, 6624. (b) Maleczka, R. E.; Shi, F.; Holmes, D.; Smith, M. R. *J. Am. Chem. Soc.* **2003**, *125*, 7792. (c) Kuwano, R.; Kondo, Y.; Matsuyama, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12104.

[5] Representative spectral data of **5a**: IR (KBr, cm^{-1}) 1929, 1953; ^1H NMR ($CDCl_3$) δ 4.72 (d, 2H, $^4J_{PH} = 10.9$ Hz), 7.02−7.12 (m, 3H), 7.27−7.33 (m, 6H), 7.51 (d, 2H, $J = 7.6$ Hz), 7.60−7.68 (m, 4H); ^{31}P NMR ($CDCl_3$) δ 26.4 (s); HRMS calcd for $C_{21}H_{17}OP$ [M] 316.1017, found 316.1015.

[6] (a) Denmark, S. E.; Marlin, J. E. *J. Org. Chem.* **1991**, *56*, 1003. (b) Pravia, K.; White, R.; Fodda, R.; Maynard, D. F. *J. Org. Chem.* **1996**, *61*, 6031.

[7] Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.

[8] Some recent examples: (a) Han, L.-B.; Zhang, C.; Yazawa, H.; Shimada, S. *J. Am. Chem. Soc.* **2004**, *126*, 5080. (b) Jérôme, F.; Monnier, F.; Lawicka, H.; Dérien, S.; Dixneuf, P. H. *Chem. Commun.* **2003**, 696. (c) Depréle, S.; Montchamp, J.-L. *J. Am. Chem. Soc.* **2002**, *124*, 9386. (d) Han, L.-B.; Zhao, C.-Q.; Tanaka, M. *J. Org. Chem.* **2001**, *66*, 5929 (e) Han, L.-B.; Mirzaei, F.; Zhao, C.-Q.; Tanaka, M. *J. Am. Chem. Soc.* **2000**, *122*, 5407. (f) Han, L.-B.; Choi, N.; Tanaka, M. *Organometallics* **1996**, *15*, 3259. (g) Han, L.-B.; Tanaka, M. *J. Am. Chem. Soc.* **1996**, *118*, 1571.

[9] (a) Palladium-catalyzed bisphosphorylation of alkynes with dialkyl phosphites to give the corresponding 1,2-bisphosphonates has been reported: Allen, A., Jr.; Manke, D. R.; Lin, W. *Tetrahedron Lett.* **2000**, *41*, 151. (b) Palladium-catalyzed bisphosphinylation of alkynes with diphenylphosphine oxide to give the corresponding 1,2-bisphosphine oxides has been reported: Allen, A., Jr.; Ma, L.; Lin, W. *Tetrahedron Lett.* **2002**, *43*, 3707.

[10] A related Ni-catalyzed phosphinylation of propargylic alcohols with diphenylphosphine oxide to give the corresponding phosphoroyl-substituted 1,3-butadienes has been reported; Han, L.-B.; Yazawa, H. The 84th Annual Meeting of the Chemical Society of Japan, Kobe, March 2004, Abstract 3PC-193.

[11] Chiraphos (2,3-bis(diphenylphosphinyl)butane) has been widely used as a chiral bidentate ligand for various transition metals. For some recent examples, see: (a) Kimmich, B. F. M.; Somsook, E.; Landis, C. R. *J. Am. Chem. Soc.* **1998**, *120*, 10115. (b) Wicht, D. K.; Zhuravel, M. A.; Gregush, R. V.; Glueck, D. S.; Guzei, I. A.; Liable-Sands, L. M.; Rheingold, A. L. *Organometallics* **1998**, *17*, 1412. (c) Casado, M. A.; Perez-Torrente, J. J.; Ciriano, M. A.; Oro, L. A.; Orejon, A.; Claver, C. *Organometallics* **1999**, *18*, 3035. (d) Kuwano, R.; Sato, K.; Kurokawa, T.; Karube, D.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7614.