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Ruthenium-Catalyzed Formation of Aryl(diphenyl)phosphine Oxides by Reactions of Propargylic Alcohols with Diphenylphosphine Oxide

Gen Onodera,[†] Hideyuki Matsumoto,[†] Marilyn Daisy Milton,[†] Yoshiaki Nishibayashi,*[,‡] and Sakae Uemura[†]

Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Katsura, Nishikyo-ku, Kyoto 615-8510, Japan, and Institute of Engineering Innovation, The University of Tokyo, Yayoi, Bunkyo-ku, Tokyo 113-8656, Japan

ynishiba@sogo.t.u-tokyo.ac.jp

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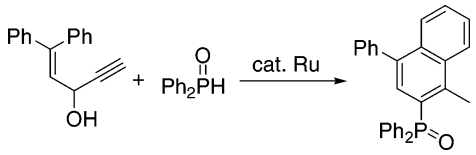
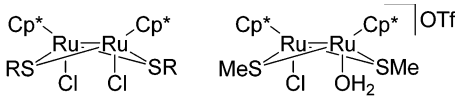
ABSTRACT



1,1-Diaryl-1-penten-4-yn-3-ols react with diphenylphosphine oxide in the presence of a thiolate-bridged diruthenium complex as a catalyst and give high yields of aryl(diphenyl)phosphine oxide products via an initial substitution followed by a cyclization at the produced allene intermediate.

We have been currently interested in the ruthenium-catalyzed propargylic substitution reaction of propargylic alcohols with a variety of heteroatom- and carbon-centered nucleophiles, giving the corresponding propargylated products.[1] These reactions are catalyzed only by thiolate-bridged diruthenium complexes such as $[Cp^*RuCl(\mu_2\text{-}SR)]_2$ ($Cp^* = \eta^5\text{-}C_5Me_5$; R = Me (**1a**), Et (**1b**), ^{n}Pr (**1c**), ^{i}Pr (**1d**)) and $[Cp^*RuCl(\mu_2\text{-}SR)_2RuCp^*(OH_2)]OTf$ (OTf = OSO_2CF_3; R = Me (**1e**), ^{n}Pr, ^{i}Pr) and not by various monoruthenium complexes (Scheme 1).[2] Quite recently, we have disclosed that catalytic phosphinylation of propargylic alcohols with diphenylphosphine oxide (**2**) proceeded smoothly even at room temperature to afford the corresponding propargylic substitution products in high yields[1g] and also that with an excess amount of **2** at higher temperature the corresponding double phosphinylated compounds were obtained in high yields (Scheme 2).[3] As an extension of our study on catalytic phosphinylation

Scheme 1



R = Me (met-DIRUX; **1a**), Et (**1b**), ^{n}Pr (**1c**), ^{i}Pr (**1d**)

met-DIRUX-OTf; **1e**

[†] Kyoto University.
[‡] The University of Tokyo.

(1) (a) Nishibayashi, Y.; Wakiji, I.; Hidai, M. *J. Am. Chem. Soc.* **2000**, *122*, 11019. (b) Nishibayashi, Y.; Wakiji, I.; Ishii, Y.; Uemura, S.; Hidai, M. *J. Am. Chem. Soc.* **2001**, *123*, 3393. (c) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Hidai, M.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 11846. (d) Inada, Y.; Nishibayashi, Y.; Hidai, M.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 15172. (e) Nishibayashi, Y.; Onodera, G.; Inada, Y.; Hidai, M.; Uemura, S. *Organometallics* **2003**, *22*, 873. (f) Nishibayashi, Y.; Inada, Y.; Yoshikawa, M.; Hidai, M.; Uemura, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1495. (g) Nishibayashi, Y.; Milton, M. D.; Inada, Y.; Yoshikawa, M.; Wakiji, I.; Hidai, M.; Uemura, S. *Chem. Eur. J.* **2005**, *11*, 1433. (h) Ammal, S. C.; Yoshikai, N.; Inada, Y.; Nishibayashi, Y.; Nakamura, E. *J. Am. Chem. Soc.***2005**, *127*, 9428.

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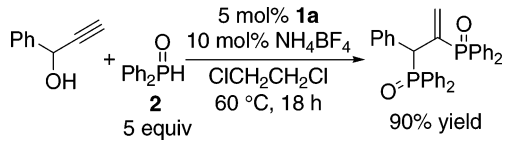
Scheme 2



of propargylic alcohols, we now report the unexpected and high yield formation of aryl(diphenyl)phosphine oxide from 1,1-diaryl-1-pentene-4-yn-3-ol (**3**) (Figure 1) and **2** in the presence of **1** as a catalyst.

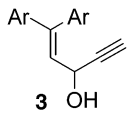
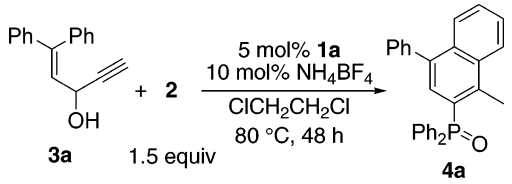


Figure 1.

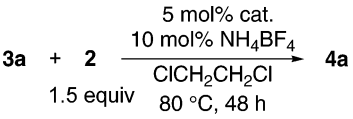
Treatment of **3a** (**3**; Ar = Ph)[4] with **2** in the presence of a catalytic amount of **1a** (5 mol %) and NH_4BF_4 (10 mol %) in 1,2-dichloroethane ($ClCH_2CH_2Cl$) at 80 °C for 48 h gave aryl(diphenyl)phosphine oxide **4a** in 92% isolated yield (Scheme 3).[5] The structure of **4a** was unambiguously clarified

Scheme 3



by X-ray analysis.[6] When **1b**−**1e** or $[Cp^*RuCl(\mu_2\text{-}YMe)]_2$ ($Cp^* = \eta^5\text{-}C_5Me_5$; Y = Se (**1f**), Te (**1g**)) were used as catalysts in place of **1a**, **4a** was obtained in high yields in all cases (Table 1).

Table 1. Reactions of Propargylic Alcohol (**3a**) with Diphenylphosphine Oxide (**2**) Catalyzed by Diruthenium Complexes (**1**)[a]

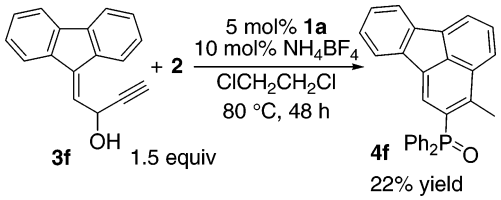


run	catalyst	yield (%)[b]
1	$[Cp^*RuCl(SMe)]_2$ (**1a**)	92
2	$[Cp^*RuCl(SEt)]_2$ (**1b**)	98
3	$[Cp^*RuCl(S^nPr)]_2$ (**1c**)	99
4	$[Cp^*RuCl(S^iPr)]_2$ (**1d**)	98
5	$[Cp^*RuCl(SMe)_2RuCp^*(OH_2)]OTf$ (**1e**)[c]	91
6	$[Cp^*RuCl(SeMe)]_2$ (**1f**)	89
7	$[Cp^*RuCl(TeMe)]_2$ (**1g**)	86

[a] All reactions of propargylic alcohol (**3a**) (0.30 mmol) with diphenylphosphine oxide (**2**) (0.45 mmol) were carried out in the presence of **1** (0.015 mmol) and NH_4BF_4 (0.03 mmol) in $ClCH_2CH_2Cl$ (5 mL) at 80 °C for 48 h. [b] Isolated yield. [c] In the absence of NH_4BF_4.

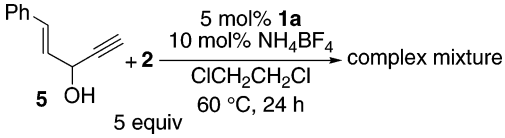
Next, the reactions of various propargylic alcohols **3** with **2** catalyzed by **1a** were investigated. Typical results are shown in Table 2. In all cases, the corresponding aryl(diphenyl)phosphine oxides were produced in high yields (Table 2, runs 1−5). By use of the propargylic alcohol **3f** bearing a fluorene moiety, the corresponding arylphosphine oxide **4f** was obtained in only a low yield (Scheme 4).

Scheme 4



It is noteworthy that from (*E*)-1-phenyl-1-penten-4-yn-3-ol (**5**), the corresponding aryl(diphenyl)phosphine oxide was not obtained (Scheme 5). This result indicates that this

Scheme 5



cyclization reaction requires an aryl group at the C_1 position of the propargylic alcohol in the *cis*-position. The introduction of an aromatic double bond (the use of **6**) only resulted

(2) (a) The thiolate-bridged diruthenium complexes were found to provide a 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) Nishibayashi, Y.; Imajima, H.; Onodera, G.; Hidai, M.; Uemura, S. *Organometallics* **2004**, *23*, 26. (c) Nishibayashi, Y.; Imajima, H.; Onodera, G.; Inada, Y.; Hidai, M.; Uemura, S. *Organometallics* **2004**, *23*, 5100. (d) The methanethiolate-bridged diruthenium complexes are commercially available from Wako Pure Chemical Industries (Japan) as met-DIRUX (*met*hanethiolate-bridged *diru*thenium comple*x*) (**1a**) (130-14581) and met-DIRUX-OTf (**1e**) (132-14781).

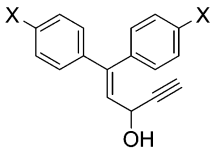
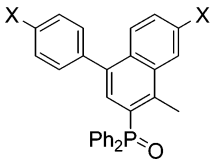
(3) Milton, M. D.; Onodera, G.; Nishibayashi, Y.; Uemura, S. *Org. Lett.* **2004**, *6*, 3993.

(4) The propargylic alcohol **3a** can react with various nucleophiles to afford the corresponding propargylic substituted products; see refs 1b−d,f,g.

(5) Typical results are shown in Supporting Information as Table S1.

(6) An ORTEP drawing of **4a** is shown in Supporting Information as Figure S1.

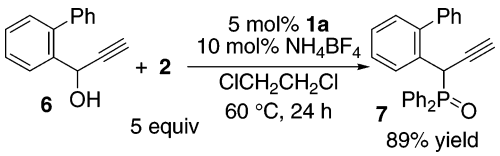
Table 2. Reactions of Propargylic Alcohols (**3**) with Diphenylphosphine Oxide (**2**) Catalyzed by Diruthenium Complex (**1a**)[a]

run	propargylic alcohol (**3**)		cyclization product (**4**)		yield (%)[b]
1		**3a** X = H		**4a**	92
2		**3b** X = F		**4b**	94
3		**3c** X = Cl		**4c**	89
4		**3d** X = Me		**4d**	85
5		**3e** X = MeO		**4e**	88

[a] All reactions of propargylic alcohol **3** (0.30 mmol) with diphenylphosphine oxide **2** (0.45 mmol) were carried out in the presence of **1a** (0.015 mmol) and NH_4BF_4 (0.03 mmol) in $ClCH_2CH_2Cl$ (5 mL) at 80 °C for 48 h. [b] Isolated yield.

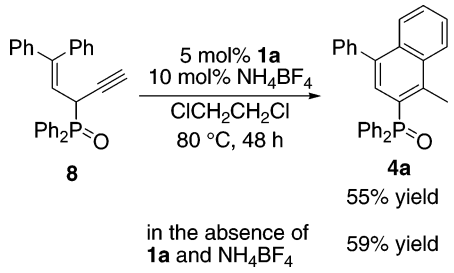
in the expected formation of the propargylic phosphinylated product (**7**) (Scheme 6).

Scheme 6



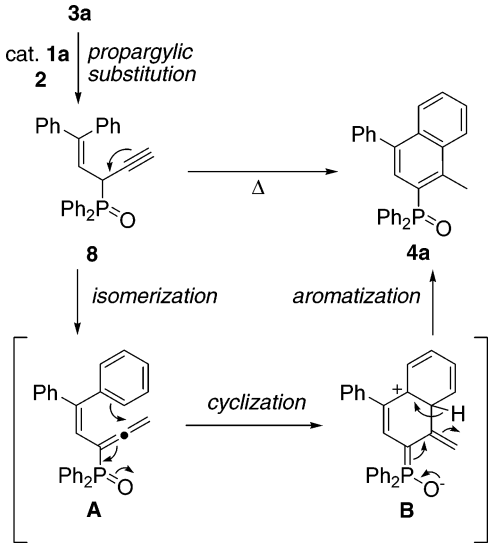
Treatment of the propargylic phosphinylated compound (**8**) in the presence of catalytic amounts of both **1a** and NH_4BF_4 in $ClCH_2CH_2Cl$ at 80 °C for 48 h gave **4a** in 55% isolated yield. However, even in the reaction without catalysts, **4a** was produced in 59% isolated yield. These results indicate that this catalytic cyclization proceeds via the initial formation of **8** and also that the ruthenium complex is not indispensable for the cyclization step of **8** into **4a** (Scheme 7).

Scheme 7



On the basis of these findings, a plausible reaction pathway of this catalytic reaction is shown in Scheme 8. At first, propargylic substitution reaction catalyzed by diruthenium complex occurs to produce **8** followed by isomerization to allene **A**,[7] which is more stable than **7** by 8.50 kcal/mol.[8] The central carbon of an allene moiety is electron-deficient as a result of the electron-withdrawing group of diphenyl phosphine oxide, and so a neighboring phenyl group readily attacks this carbon to give the cyclized product **B**. We consider that this transformation is a Michael-type endo-mode cyclization.[9] Finally, aromatization of **B** affords **4a**. The cyclization step may also be considered as a typical 6π-electrocyclization of allene-diene species.

Scheme 8



Next, we investigated the transformation of **4a** into some other organic compounds. Unfortunately, the reduction of a phosphine oxide moiety did not proceed smoothly when the usual combination of trichlorosilane and triethylamine was employed as a reducing reagent, but it has been achieved smoothly by use of triethoxysilane.[10] Thus, treatment of **4a**

(7) The isomerization of propargylic phosphine oxide to allenyl phosphine oxide was observed, and allenyl phosphine oxide can be isolated; see ref 3.

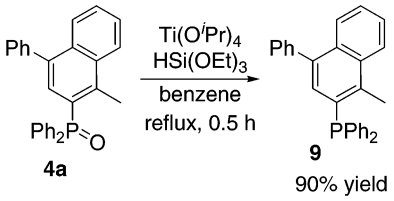
(8) Ab initio molecular orbital calculations of **A** and **8** were carried out.

(9) (a) Mukai and co-workers reported an endo-mode ring-closing reaction of allenyl phosphine oxides: Mukai, C.; Ohta, M.; Yamashita, H.; Kitagaki, S. *J. Org. Chem.* **2004**, *69*, 6867. (b) Maynard and co-workers reported a similar endo-mode ring-closing reaction: Pravia, K.; White, R.; Fodda, R.; Maynard, D. F. *J. Org. Chem.* **1996**, *61*, 6031. (c) Michael-type exo-mode ring-closing reactions have also been reported: Brel, V. K. *Synthesis* **2001**, 1539.

(10) (a) Coumbe, T.; Lawrence, N. J.; Muhammad, F. *Tetrahedron Lett.* **1994**, *35*, 625. (b) Allen, A., Jr.; Ma, L.; Lin, W. *Tetrahedron Lett.* **2002**, *43*, 3707.

with triethoxysilane in the presence of titanium tetraisopropoxide in benzene at 80 °C for 30 min gave the corresponding aryl(diphenyl)phosphine **9** in 90% isolated yield (Scheme 9).

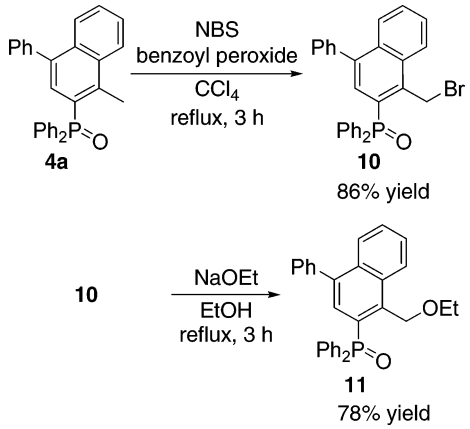
Scheme 9



The methyl group at the C_1 position of the naphthalene ring of **4a** was easily brominated by use of NBS (*N*-bromosuccinimide) with BPO (benzoyl peroxide) to afford the corresponding brominated product **10** (Scheme 10),[11] and the introduced bromine was replaced easily by an ethoxide group by the usual S_N2 reaction to give **11** (Scheme 10). These phosphine compounds may be used as the precursors of a new type of monodentate or bidentate ligands.[12]

In summary, we have explored the scope and limitations of a novel, one-pot ruthenium-catalyzed synthesis of aryl(diphenyl)phosphine oxides (**4**) from propargylic alcohols (**3**) and diphenylphosphine oxide (**2**). A mechanism is proposed that involves the isomerization of an initial propargylic substituted product to an allenyl intermediate, followed by a cyclization and rearomatization to afford the final product.

Scheme 10



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

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(11) For a recent example, see: Oestreich, M.; Schmid, U. K.; Auer, G.; Keller, M. *Synthesis* **2003**, 2725.

(12) For an example, the complex prepared from (*o*-Tol)$_3$P and Pd(OAc)$_2$ is found to work as a highly efficient catalyst for the Heck vinylation of aryl halides: Herrmann, W. A.; Brossmer, C.; Reisinger, C.-P.; Riermeier, T. H.; Öfele, K.; Beller, M. *Chem. Eur. J.* **1997**, *3*, 1357.