JOCNote

Highly Regioselective Simultaneous Introduction of Phosphino and Seleno Groups into Unsaturated Bonds by the Novel Combination of (Ph$_2$P)$_2$ and (PhSe)$_2$ upon Photoirradiation

Shin-ichi Kawaguchi, Takamune Shirai, Takashi Ohe,
Akihiro Nomoto,* Motohiro Sonoda, and Akiya Ogawa*

Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, 1-1 Gakuen-cho, Nakaku, Sakai, Osaka 599-8531, Japan

ogawa@chem.osakafu-u.ac.jp

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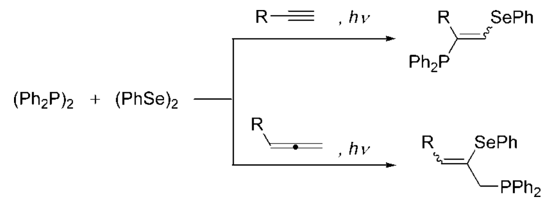
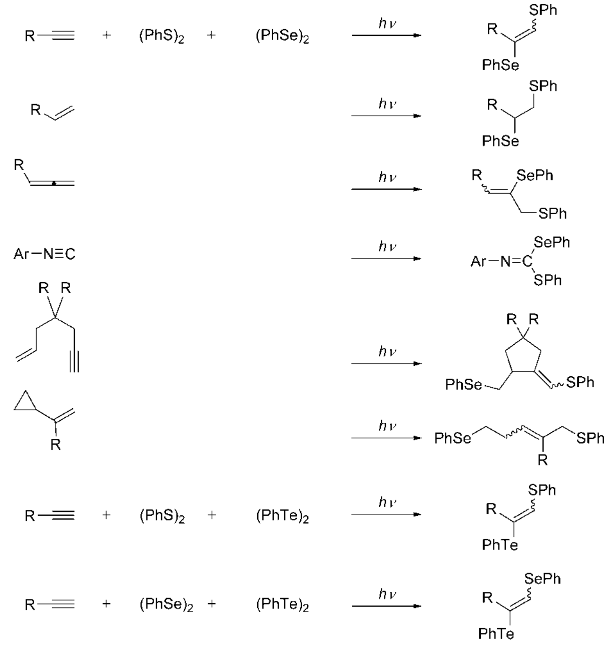


A novel combination of tetraphenyldiphosphine and diphenyl diselenide under photoirradiation conditions attains simultaneous introduction of diphenylphosphino and phenylseleno groups into carbon−carbon unsaturated bonds such as terminal alkynes or allenes, regioselectively.

Highly selective introduction of different heteroatom-including functional groups into unsaturated bonds provides a useful tool to synthesize multifunctionalized heteroatom compounds in one portion.[1−5] We have revealed that group 16 heteroatom-mixed systems under photoirradiation conditions realize convenient synthesis of a wide variety of group 16 heteroatom compounds, as indicated in Scheme 1.[6] By using a (PhS)$_2$−(PhSe)$_2$ mixed system, for example, a series of unsaturated compounds such as alkynes, alkenes, allenes, and isocyanides undergo regioselective thioselenation to give the corresponding thioselenated products without formation of the dithiolated adducts or diselenated adducts. The higher reactivity of phenylthio radical compared with phenylseleno radical ($k_{S}/k_{Se} = 10-50$)[7] and the higher carbon radical capturing ability of diphenyl diselenide compared with diphenyl disulfide ($k_{Se}/k_{S} = 160$)[8] contribute to the excellent regioselectivity and product selectivity. In the case of enynes, the photoinduced thioselena-

SCHEME 1. Group 16 Heteroatom-Mixed Systems



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(1) For books concerning the recent advance of radical chemistry in organic synthesis, see, for example: (a) Nanni, D. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vols. *1 and 2*. (b) *Stereochemistry of Radical Reactions*; Curran, D. P., Porter, N. A., Giese, B., Eds.; VCH: Weinheim, 1996. (c) Giese, B.; Kopping, B.; Göbel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. *Org. React.* **1996**, *48*, 301. (d) *Free Radicals in Organic Chemistry*; Fossey, J., Lefort, D., Sorba, J., Eds.; Wiley: Chichester, 1995.

(2) For books concerning the chemistry of organoselenium compounds, see, for example: (a) Ogawa, A. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 2, Chapter 15. (b) *Topics in Current Chemistry*; Wirth, T., Ed.; Springer: Berlin, 2000; Vol. 208. (c) *Organoselenium Chemistry—A Practical Approach*; Back, T. G., Ed.; Oxford University Press: Oxford, 1999.

(3) For books concerning the chemistry of organophosphorous compounds, see, for example: (a) *A Guide to Organophosphorus Chemistry*; Quin, L. D., Ed.;Wiley-Interscience: New York, 2000. (b) Postigo, A.; Barata, S.; Ogawa, A.; Sonoda, M. In *Electronic Encyclopedia of Reagents for Organic Synthesis*; John Wiley & Sons, Ltd.: New York, 2008.

(4) For radical addition reactions via simultaneous introduction of different two heteroatom moieties into unsaturated bonds, see, for example: (a) Toru, T.; Seko, T.; Maekawa, E.; Ueno, Y. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1927. (b) Back, T. G.; Brunner, K.; Krishna, M. V.; Lai, E. K. Y.; Muralidharan, K. R. In *Heteroatom Chemistry*; Block, E., Ed.; VCH Publishers, Inc.: New York, 1990; Chapter 4. (c) Back, T. G. *Phosphorous Sulfur, Silicon, Relat. Elem.* **1992**, *67*, 203. (d) Wada, T.; Kondoh, A.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2008**, *10*, 1155.

(5) For a radical reaction involving the bond cleavage between two different heteroatoms, see, for example: (a) Carta, P.; Puljic, N.; Robert, C.; Dhimane, A.-L.; Fensterbank, L.; Lacôte, E.; Malacria, M. *Org. Lett.* **2007**, *9*, 1061. (b) Vaillard, S. E.; Mück-Lichtenfeld, C.; Grimme, S.; Studer, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 6533.

(6) (a) Ogawa, A.; Hirao, T. *Rev. Heteroatom. Chem.* **1998**, *18*, 1. (b) Ogawa, A.; Tanaka, H.; Yokoyama, H.; Obayashi, R.; Yokoyama, K.; Sonoda, N. *J. Org. Chem.* **1992**, *57*, 111. (d) Ogawa, A.; Sonoda, N. *Phosphorus, Sulfur, Silicon* **1994**, *95−96*, 331. (e) Ogawa, A.; Obayashi, R.; Ine, H.; Tsuboi, Y.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1998**, *63*, 881. (f) Ogawa, A.; Obayashi, R.; Sonoda, N.; Hirao, T. *Tetrahedron Lett.* **1998**, *39*, 1577. (g) Ogawa, A.; Obayashi, R.; Doi, M.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1998**, *63*, 4277. (h) Ogawa, A.; Ogawa, I.; Obayashi, R.; Umezu, K.; Doi, M.; Hirao, T. *J. Org. Chem.* **1999**, *64*, 86. (i) Tsuchii, K.; Tsuboi, Y.; Kawaguchi, S.-i.; Takahashi, J.; Sonoda, N.; Nomoto, A.; Ogawa, A. *J. Org. Chem.* **2007**, *72*, 423. (j) Mitamura, T.; Tsuboi, Y.; Iwata, K.; Tsuchii, K.; Nomoto, A.; Sonoda, M.; Ogawa, A. *Tetrahedron Lett.* **2007**, *48*, 5953.

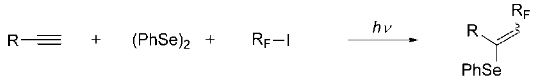
(7) (a) Ito, O.; Matsuda, M. *J. Am. Chem. Soc.* **1979**, *101*, 1815. (b) Ito, O.; Matsuda, M. *J. Am. Chem. Soc.* **1979**, *101*, 5732. (c) Ito, O.; Matsuda, M. *J. Am. Chem. Soc.* **1981**, *103*, 5871. (d) Ito, O. *J. Am. Chem. Soc.* **1983**, *105*, 850. (e) Ito, O.; Matsuda, M. *J. Org. Chem.* **1984**, *49*, 17. (f) Ito, O.; Matsuda, M. *Prog. Polym. Sci.* **1992**, *17*, 827. (g) Ito, O. In *The Chemistry of Free Radicals: S-Centered Radicals*; Alfassi, Z. B., Ed.; Wiley: Chichester, 1999; Chapter 6.

(8) (a) Perkins, M. J.; Turner, E. S. *J. Chem. Soc., Chem. Commun.* **1981**, 139. (b) Russell, G. A.; Tashtoush, H. *J. Am. Chem. Soc.* **1983**, *105*, 1398. (c) Russell, G. A.; Ngoviwatchai, P.; Tashtoush, H. I.; Pla-Dalmau, A.; Khanna, R. K. *J. Am. Chem. Soc.* **1988**, *110*, 3530.

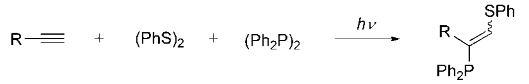
10.1021/jo8020067 CCC: $40.75

tion proceeds through the 5-*exo* cyclization, affording the corresponding five-membered ring compounds bearing both thio and seleno groups. On the other hand, the thioselenation of vinylcyclopropanes takes place via the ring-opening of cyclopropane ring. Not only the thioselenation but also the thiotelluration and selenotelluration of alkynes can be attained by using $(PhS)_2-(PhTe)_2$ mixed system and $(PhSe)_2-(PhTe)_2$ mixed system, respectively.

Very recently, we have succeeded in application of this methodology to a novel combination of group 16 heteroatom compounds and others such as group 17 and group 15 heteroatom compounds: perfluoroalkylselenation by using a $(PhSe)_2-R_FI$ mixed system[9] and thiophosphination by using a $(PhS)_2-(Ph_2P)_2$ mixed system[10] take place successfully with excellent regioselectivity (eqs 1 and 2).

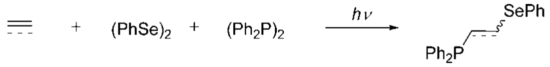


(1)



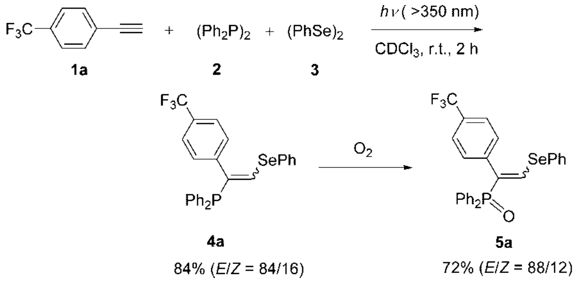
(2)

In this paper, we report novel selenophosphination of carbon−carbon unsaturated compounds by the combination of $(PhSe)_2$ and $(Ph_2P)_2$ upon photoirradiation (eq 3).



(3)

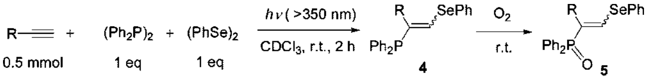
1-Ethynyl-4-trifluorobenzene (**1a**, 0.5 mmol), tetraphenyldiphosphine (**2**, 0.5 mmol), and diphenyl diselenide (**3**, 0.5 mmol) in $CDCl_3$ (0.6 mL, degassed) were placed in an NMR (ϕ = 4 mm, Pyrex) tube filled with nitrogen, and then the tube was sealed. Irradiation through a filter with a xenon lamp ($h\nu$ > 350 nm) was conducted at room tempetature for 2 h. A novel selenophosphination successfully took place with excellent regioselectivity, affording the corresponding phosphine oxide (**5a**) by air-oxidation during workup (eq 4).

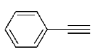
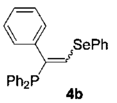
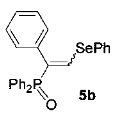
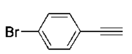
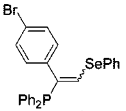
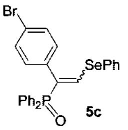
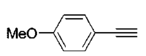
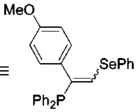
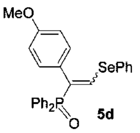
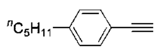
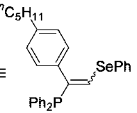
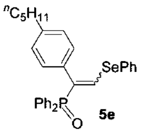
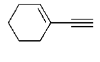
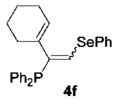
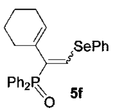


(4)

X-ray crystallographic analysis of **5a** clearly indicates the regioselectivity of this selenophosphination: the seleno group and phosphine oxide group are located selectively at the terminal and the inner positions of the triple bond of **1a**, respectively. In this reaction, the corresponding regioisomer,[11] the diphosphination product,[12] and the diselenation product[13] are not obtained at all, and the selenophosphination product (**5a**) is obtained with excellent selectivity.

TABLE 1. Photoinduced Selenophosphination of Alkynes with $(Ph_2P)_2$ and $(PhSe)_2$



entry	alkyne	yield (%) [*E*/*Z*] 4[a]		5	
1	 **1b**	 **4b**	83 [89/11]	 **5b**	68 [91/9]
2	 **1c**	 **4c**	96 [85/15]	 **5c**	77 [91/9]
3	 **1d**	 **4d**	78 [93/7]	 **5d**	60 [93/7]
4	 **1e**	 **4e**	77 [93/7]	 **5e**	74 [89/11]
5	 **1f**	 **4f**	83 [89/11]	 **5f**	68 [91/9]

[a] Determined by ^{1}H NMR.

Table 1 shows the representative results of the selenophosphination of several alkynes. When aromatic alkynes were employed as the substrates, the desired selenophosphination smoothly proceeded in good yield, regioselectively (entries 1−4). A conjugated alkyne such as 1-ethynylcyclohexene also gave the corresponding selenophosphination product in good yield (entry 5). In the case of the aliphatic alkyne such as 1-octyne, unfortunately, the desired selenophosphination did not occur. In general, the addition to aromatic alkynes proceeds via the formation of vinylic π-radical intermediate,[14] whereas the addition to aliphatic alkynes involves the formation of less stable vinylic σ-radical intermediate.[15] The difference of the stability between these radical intermediates may contribute to the difference of the reactivity between aromatic alkynes and aliphatic ones.

Similarly, in an NMR tube, a mixture of cyclohexylallene (**6a**, 0.5 mmol), tetraphenyldiphosphine (**2**, 0.5 mmol), and diphenyl diselenide (**3**, 0.5 mmol) was placed in $CDCl_3$ (0.6 mL, degassed), and then the tube was sealed. Upon irradiation with a xenon lamp

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(9) (a) Tsuchii, K.; Ogawa, A. *Tetrahedron Lett.* **2003**, *44*, 8777. See also: (b) Ogawa, A.; Imura, M.; Kamada, N.; Hirao, T. *Tetrahedron Lett.* **2001**, *42*, 2489. (c) Tsuchii, K.; Imura, M.; Kamada, N.; Hirao, T.; Ogawa, A. *J. Org. Chem.* **2004**, *69*, 6658. (d) Nomoto, A.; Ogawa, A. In *Handbook of Reagents for Organic Synthesis:Fluorine-Containing Reagents*; Paquette, L. A., Ed.; John Wiley & Sons Ltd.: New York, 2007; p 289.

(10) Shirai, T.; Kawaguchi, S.-i.; Nomoto, A.; Ogawa, A. *Tetrahedron Lett.* **2008**, *49*, 4043.

(11) The palladium-catalyzed selenophosphorylation of terminal alkynes provides (*Z*)-1-phosphoryl-2-seleno-1-alkenes: Han, L.-B.; Choi, N.; Tanaka, M. *J. Am. Chem. Soc.* **1996**, *118*, 7000.

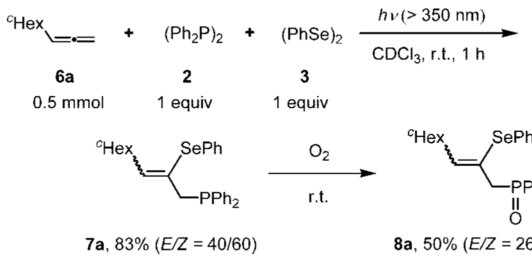
(12) For the photoinduced addition of tetraphenyldiphosphine to alkynes, see: Kawaguchi, S.; Nagata, S.; Tsuchii, K.; Nomoto, A.; Ogawa, A. *Tetrahedron Lett.* **2006**, *47*, 3919.

(13) For the photoinduced addition of diphenyl diselenide to alkynes, see: (a) Back, T. G.; Krishna, M. V. *J. Org. Chem.* **1988**, *53*, 2533. (b) Ogawa, A.; Yokoyama, H.; Yokoyama, K.; Masawaki, T.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 5721.

(14) Singer, L. A.; Chen, J. *Tetrahedron Lett.* **1969**, *10*, 4849.

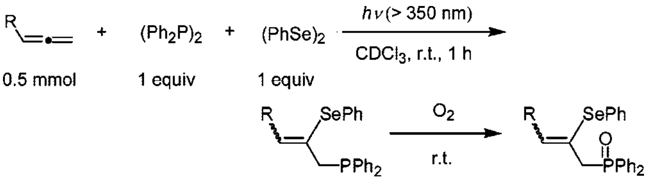
(15) Fessenden, R. W.; Schuler, R. H. *J. Chem. Phys.* **1963**, *39*, 2147.

(500 W) though the filter ($h\nu$ > 350 nm) at room temperature for 1 h, the desired selenophosphination of the allene took place regioselectively at the terminal double bond, affording the adduct (**7a**) in 83% yield (eq 5). A trace amount of diselenation product[16] was obtained, but no formation of the regioisomers of the selenophosphination product was detected. The selenophosphination product provided the corresponding phosphine oxide **8a** by air-oxidation during workup. The location of seleno group and phosphino group of the selenophosphination product was determined by X-ray crystallographic analysis of **8a**.

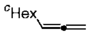
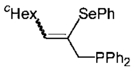
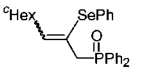
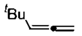
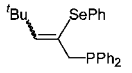
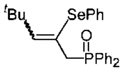
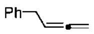
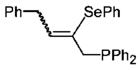
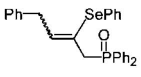
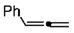
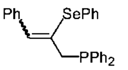
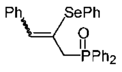
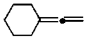
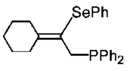
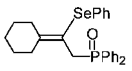
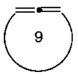


(5)

TABLE 2. Photoinduced Selonophosphination of Allenes with $(Ph_2P)_2$ and $(PhSe)_2$



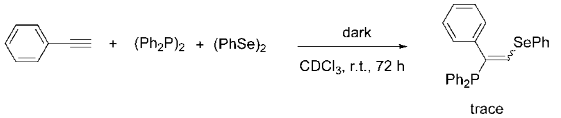
7 8

entry	allene	yield [E/Z]			
		7^a		8	
1	 6a	 7a	83% [40/60]	 8a	50% [26/74]
2	 6b	 7b	82% [34/66]	 8b	44% [32/68]
3	 6c	 7c	78% [37/63]	 8c	42% [33/67]
4	 6d	 7d	73% [40/60]	 8d	28% [33/67]
5	 6e	 7e	92%	 8e	42%
6				N.R.	

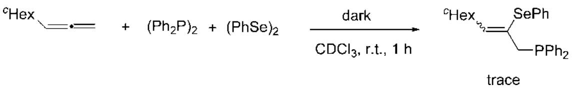
^{a} Determined by ^{1}H NMR.

Similar conditions can be employed with several allenes (**6a**–**e**) (Table 2). In the case of aliphatic allenes (entries 1–3), selenophosphination proceeded smoothly, and Z isomers were obtained preferentially. Aromatic allene also underwent the regioselective selenophosphination (entry 4). The disubstituted terminal allene such as vinylidenecyclohexane also provided the corresponding selenophosphination product smoothly (entry 5). When the internal allene such as cyclonona-1,2-diene was employed, the selenophosphination did not proceed (entry 6). Isolation of the selenophosphination products was conducted by preparative TLC. The reason for the lower isolated yields of **8** is probably due to the relative instability of allylic phosphine.

The selenophosphination of alkynes or allenes did not proceed in the dark (eqs 6 and 7). Therefore, we assume the present selenophosphination may proceed via a radical mechanism. Diphenyl diselenide (**3**) has its absorption maximum (λ_{max}) at 340 nm ($\epsilon = 10^3$)[17] and the absorption reaches to 450 nm, whereas the absorption of tetraphenyldiphosphine (**2**) (λ_{max} = 260 nm, ϵ = 41.3) reaches to 330 nm.[18] Therefore, irradiation with the light of wavelength over 350 nm induces selective homolysis of diselenide (**3**) generating phenylseleno radical (PhSe•) at least in the initial stage. The seleno radical (PhSe•) can also be formed by the photoinduced homolysis of Ph_2PSePh (**9**), which is gradually generated in situ under photoirradiation conditions. In the case of alkynes, the PhSe• attacks the terminal carbon of alkynes, generating vinyl radical intermediate, and then trapping with Ph_2PSePh[19] leads to the selenophosphination products **4**. In the case of allenes, the PhSe• attacks the central carbon of allenes,[20] generating allylic radical intermediate. The subsequent S_H2 reaction of the allyl radical intermediate with Ph_2PSePh[19] affords the adduct **7**, regioselectively. (Scheme 2).

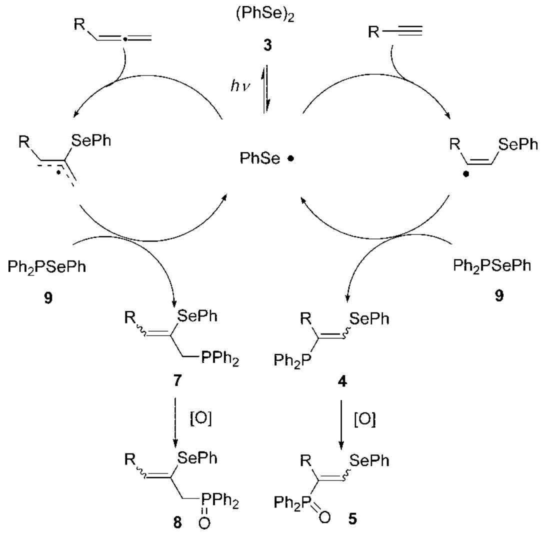


(6)



(7)

SCHEME 2. A Plausible Pathway of Selenophosphination of Alkynes or Allenes



We have demonstrated the first simultaneous and regioselective selenophosphination to carbon–carbon unsaturated bonds

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(16) (a) Ogawa, A.; Yokoyama, K.; Yokoyama, H.; Sekiguchi, M.; Kambe, N.; Sonoda, N. *Tetrahedron Lett.* **1990**, *31*, 5931. (b) Kamiya, I.; Nishinaka, E.; Ogawa, A. *Tetrahedron Lett.* **2005**, *46*, 3649. (c) Kodama, S.; Nishinaka, E.; Nomoto, A.; Sonoda, M.; Ogawa, A. *Tetrahedron Lett.* **2007**, *48*, 6312.

(17) Schmidt, U.; Müller, A.; Markau, K. *Chem. Ber.* **1964**, *97*, 405.

by using the $(Ph_2P)_2$−$(PhSe)_2$ mixed system upon photoirradiation under the mild reaction condition. This $(Ph_2P)_2$−$(PhSe)_2$ binary system is well-controlled by taking advantage of the different reactivity between phosphino atom and seleno atom in radical reactions. We are now investigating the other combinations of heteroatom compounds in radical addition reactions.

Experimental Section

General Procedure for Photoinduced Selenophosphination of Alkynes or Allenes. $(Ph_2P)_2$ (188 mg, 0.5 mmol), $(PhSe)_2$ (156 mg, 0.5 mmol), and alkyne or allene (0.5 mmol) were placed in $CDCl_3$ (0.6 mL) in a sealed Pyrex glass NMR tube under nitrogen atmosphere. The mixture was stirred for 30 s, and then the mixture was irradiated with a xenon lamp (500 W) though the filter ($h\nu > 350$ nm) at room temperature for 1−2 h. The reaction mixture was left under air overnight. Purification of the crude was performed by preparative TLC.

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Supporting Information Available: X-ray structure details for compounds **5a** and **5m** (CIF). Spectral and analytical data, ORTEP plots, Crystal Data and Structure Analysis Results for **(*E*)-5a** and **(*Z*)-9a**, and copies of ^1H NMR and ^{13}C NMR spectra of **5a−f** and **8a−e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Troy, D.; Turpin, R.; Voigt, D. *Bull. Soc. Chim. Fr.* **1979**, 241.

(19) Alternatively, the formed vinyl or allyl radical may abstract diphenylphosphino group from $(Ph_2P)_2$. In this case, $Ph_2P\bullet$ concomitantly reacts with $(PhSe)_2$ generataing Ph_2PSePh and $PhSe\bullet$.

(20) Masawaki, T.; Ogawa, A.; Kambe, N.; Ryu, I.; Sonoda, N. *Chem. Lett.* **1987**, *12*, 2408.