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New Synthetic Method of Diorganyl Selenides: Palladium-Catalyzed Reaction of $PhSeSnBu_3$ with Aryl and Alkyl Halides

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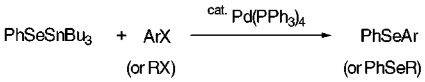
ABSTRACT



$$PhSeSnBu_3 + \underset{\text{(or RX)}}{ArX} \xrightarrow{\text{cat. } Pd(PPh_3)_4} \underset{\text{(or PhSeR)}}{PhSeAr}$$

Palladium complexes such as $Pd(PPh_3)_4$ catalyzed the reaction of phenyl tributylstannyl selenide ($PhSeSnBu_3$) with aryl and alkyl halides, giving the corresponding diaryl and alkylaryl selenides in moderate to good yields.

In the organic chemistry of selenium, the key intermediates are often diorganyl selenides, and much effort is being devoted to accomplishing the synthesis of these compounds.[1] However, many synthetic methods sometimes suffer from the improper handling of selenium reagents used as selenium sources, because of their instability against air and/or moisture. Therefore, the development of new synthetic methods using stable selenium reagents would have significant synthetic value.

Transition metal complex-catalyzed reactions of aryl halides with organoheteroatom compounds having M−M′ (M and M′ = heteroatom) bonds are now widely used for the synthesis of various heteroatom-containing compounds;[2] however, similar reactions of aryl halides with organoselenium compounds containing a selenium−heteroatom bond have not been found. In the course of our study on the utilization of phenyl tributylstannyl selenide ($PhSeSnBu_3$) (**1**),[3,4] which is stable against air and moisture, in organic reactions, we found that the reaction of **1** with aryl and alkyl halides in the presence of a catalytic amount of $Pd(PPh_3)_4$ took place efficiently, giving the corresponding

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(1) Krief, A.; Hevesi, L. In *Organoselenium Chemistry*, Vol. 1; Springer-Verlag: Berlin, 1988. Paulmier, C. In *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986. Patai, S.; Rappoport, Z. In *The Chemistry of Organic Selenium and Tellurium Compounds*, Vols. 1 and 2; 1986. Krief, A. In *Comprehensive Organic Synthesis*, Vol. 3; Trost, B. M., Eds.; Pergamon Press: Oxford, 1991; pp 85−192 and references therein.

(2) There are some reports on the palladium complex-catalyzed reaction of aryl and alkyl halides with organic heteroatom compounds having heteroatom−heteroatom bonds. (i) B−B: Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508. (ii) Si−Si: Matsumoto, H.; Nagashima, S.; Yoshihiro, K.; Nagai, Y. *J. Organomet. Chem.* **1975**, *85*, C1. Matsumoto, H.; Yoshihiro, K.; Nagashima, S.; Watanabe, H.; Nagai, Y. *J. Organomet. Chem.* **1977**, *128*, 401. Matsumoto, H.; Nagashima, S.; Kato, T.; Nagai, Y. *Angew. Chem.* **1978**, *90*, 288. Faboru, C.; Griffiths, R. W.; Pidcock, A. *J. Organomet. Chem.* **1982**, *225*, 331. Nakano, T.; Takahashi, M.; Ashizawa, T.; Arai, T.; Seki, S.; Matsumoto, H.; Nagai, Y. *Chem. Lett.* **1982**, 613. Hiyama, T.; Obayashi, M.; Mori, I.; Nozaki, H. *J. Org. Chem.* **1983**, *48*, 912. Hatanaka, Y. Hiyama, T. *Tetrahdron Lett.* **1987**, *28*, 4715. (iii) Al−Si: Trost, B. M.; Yoshida, J. *Tetrahedron Lett.* **1983**, *24*, 4895. (iv) Si−P: Tunney, S. E.; Stille, J. K. *J. Org. Chem.* **1987**, *52*, 748. (v) Si−Sn: Mori, M.; Kaneta, N.; Shibasaki, M. *J. Org. Chem.* **1991**, *56*, 3486. (vi) S−Sn: Beletzkaya, I. P. *J. Organomet. Chem.* **1983**, *250*, 551. Carpita, A.; Rossi, R.; Scamuzzi, B. *Tetrahedron Lett.* **1989**, *30*, 2699. Juxiang, C.; Crisp, G. T. *Synth. Commun.* **1992**, *22*, 683. (vii) Sn−Sn: Farina, V.; Hauck, S. I. *J. Org. Chem.* **1991**, *56*, 4317. Kosugi, M.; Shimizu, K.; Ohtani, A.; Migita, T. *Chem. Lett.* **1981**, 829.

(3) Nishiyama, Y.; Aoyama, S.; Hamanaka, S. *Phosphorus, Silicon, Sulfur* **1993**, *65*, 1245. Nishiyama, Y.; Ohashi, H.; Itoh, K.; Sonoda, N. *Chem. Lett.* **1998**, 159.

(4) The other applications of organoselenium compounds having a Se−Sn bond are very few due to the lack of methods for the activation of the selenium−tin bond.[5] See: Shimada, K.; Okuse, S.; Takikawa, Y. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2848. Segi, M.; Kato, M.; Nakajima, T.; Suga, S. *Tetrahedron Lett.* **1991**, *32*, 7427. Segi, M.; Kojima, T.; Nakajima, T.; Suga, S. *Synlett* **1991**, 105. Harpp, D. N.; Gingras, M. *J. Am. Chem. Soc.* **1988**, *110*, 7737. Steliou, K.; Mrani, M. *J. Am. Chem. Soc.* **1982**, *104*, 3104. Baudler, M.; Suchomel, H.; Fürstenberg, G.; Schings, U. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 1044. Crosse, B. C.; Hutson, G. V. *J. Chem. Soc. A* **1967**, 2014.

10.1021/ol990233z CCC: $18.00

diaryl and alkylaryl selenides in moderate to good yields (eq 1).

$$\mathrm{PhSeSnBu_3} + \underset{\text{(or RX)}}{\mathrm{ArX}} \xrightarrow{\text{cat. }\mathrm{Pd(PPh_3)_4}} \underset{\text{(or PhSeR)}}{\mathrm{PhSeAr}} \qquad (1)$$

When phenyl tributylstannyl selenide ($\mathrm{PhSeSnBu_3}$) (**1**) (0.25 mmol) was reacted with 1 equiv of iodobenzene (**2**) (0.25 mmol) in the presence of a catalytic amount of $\mathrm{Pd(PPh_3)_4}$ (5 mol %) at 80 °C for 0.5 h, the phenylselenation of **2** efficiently proceeded to give diphenyl selenide (**3**) in 75% yield (entry 3 in Table 1).[6] Table 1 shows the results of the reaction of **1** with **2** under various reaction conditions. At lower reaction temperature (50 and 25 °C), the yield of **3** was markedly decreased (entries 1 and 2). Although the phenylselenation of **2** with **1** proceeded, even upon using DMF, $\mathrm{CH_3CN}$, THF, and $\mathrm{CHCl_3}$, instead of toluene as the solvent, the yields of the product slightly decreased (entries 5−8). The other palladium complexes such as $\mathrm{Pd(Ph_2PCH_2CH_2PPh_2)_2}$, $\mathrm{PdCl_2(CH_3CN)_2}$, $\mathrm{PdCl_2(PhCN)_2}$, $\mathrm{PdCl_2(PPh_3)_2}$, $\mathrm{PdCl_2}$, $\mathrm{Pd(OAc)_2}$, and $\mathrm{PdCl_2(1,5\text{-}C_8H_{12})}$ did not exhibit catalytic activity in this reaction (entries 9−15).

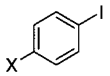
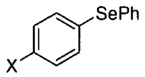
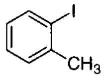
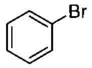
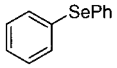
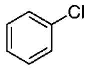
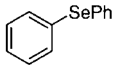
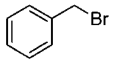
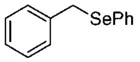
Table 1. Palladium-Catalyzed Reaction of $\mathrm{PhSeSnBu_3}$ with Iodobenzene under the Various Reaction Conditions[a]

$$\underset{\mathbf{1}}{\mathrm{PhSeSnBu_3}} + \underset{\mathbf{2}}{\mathrm{PhI}} \xrightarrow[\text{Toluene}]{\text{Pd-Catayst}} \underset{\mathbf{3}}{\mathrm{PhSePh}}$$

Entry	Pd-Catayst	Temp./°C	Yield/%[b]
1	$\mathrm{Pd(PPh_3)_4}$	25	9
2		50	21
3		80	75 (70)
4		110	74
5[c]		80	60
6[d]		80	35
7[e]		67	42
8[f]		61	7
9	$\mathrm{Pd(Ph_2PCH_2CH_2PPh_2)_2}$	80	trace
10	$\mathrm{PdCl_2(CH_3CN)_2}$	80	trace
11	$\mathrm{PdCl_2(PhCN)_2}$	80	trace
12	$\mathrm{PdCl_2(PPh_3)_2}$	80	0
13	$\mathrm{PdCl_2}$	80	trace
14	$\mathrm{Pd(OAc)_2}$	80	0
15	$\mathrm{PdCl_2(1,5\text{-}C_8H_{12})}$	80	0

[a] Reaction conditions : **1** (0.25 mmol), **2** (0.25 mmol), Pd-complex (5 mol%) and toluene (2 mL) for 30 min. [b] GC yield. The number in parenthesis indicates isolated yield. [c] DMF was used as the solvent. [d] $\mathrm{CH_3CN}$ was used as the solvent. [e] THF was used as the solvent. [f] $\mathrm{CHCl_3}$ was used as the solvent.

Table 2. Synthesis of Various Diorganyl Selenides[a]

Entry	RX	Time/h	Product	Yield/%[b]
				
1	X = $\mathrm{CH_3}$	2		81
2	= $\mathrm{OCH_3}$	4		88
3	= $\mathrm{NO_2}$	0.5		70
4	= OH	5		50
5[c]	= $\mathrm{NH_2}$	5		53
6		5		47
7[d]		8		(79)[f]
8[e]		8		(60)[f]
9		2		57
10	$\mathrm{C_8H_{17}I}$	24	$\mathrm{C_8H_{17}SePh}$	62

[a] Reaction conditions : $\mathrm{PhSeSnBu_3}$ (0.25 mmol), organic halide (0.25 mmol), $\mathrm{Pd(PPh_3)_4}$ (5 mol%) and toluene (2 mL) at 80 °C. [b] Isolated yield. [c] 110 °C. [d] PhBr (0.50 mmol), $\mathrm{Pd(PPh_3)_4}$ (15 mol%) at 110 °C. [e] PhCl (2.50 mmol), $\mathrm{Pd(PPh_3)_4}$ (15 mol%) at 110 °C. [f] GC yield.

Table 2 shows the results of the reaction of $\mathrm{PhSeSnBu_3}$ (**1**) with various aryl and alkyl halides in the presence of a catalytic amount of $\mathrm{Pd(PPh_3)_4}$ in a toluene solution. When 4-methyl- and 4-methoxy-1-iodobenzene were allowed to react with **1** under the same reaction conditions as entry 3 in Table 1, the yields of the diaryl selenides were slightly low (49 and 65%). The yields were improved by a longer reaction time (entries 1 and 2). In the case of 4-nitro-1-iodobenzene, 4-nitrophenyl phenyl selenide was formed in 70% yield (entry 3). In this reaction, the $\mathrm{Pd(PPh_3)_4}$ also catalyzed the reaction of **1** with aromatic iodides bearing hydroxy and amino groups, which have a strong coordination ability to palladium metal, giving the corresponding diaryl selenides in moderate yields (entries 4 and 5). 2-Methylphenyl phenyl selenide was synthesized by the reaction of 2-methyl-1-iodobenzene with **1** in 47% yield (entry 6). The coupling reaction of **1** with bromo- or chlorobenzene was

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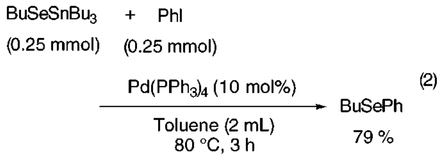
(5) The bond energy of the Se−Sn bond is $D^0_{298} = 98.2 \pm 3$ kcal/mol. See: Ho, K. C. M. In *Thermodynamic Data for Inorganic Sulfides, Selenides, and Tellurides*; Rechhood Press: England, 1974; p 594.

(6) In this reaction, the yield of the product is significantly influenced by the order of the addition of $\mathrm{PhSeSnBu_3}$ and PhI. The reaction of $\mathrm{Pd(PPh_3)_4}$ with PhI in toluene followed by the addition of $\mathrm{PhSeSnBu_3}$ results in a 75% yield of PhSePh. In contrast, when $\mathrm{PhSeSnBu_3}$ was first added to the toluene solution of $\mathrm{Pd(PPh_3)_4}$, PhSePh was formed in only a 20% yield.[7] From these results, we suggested that the oxidative addition of PhI to low-valent palladium species might be the key step to the success of this coupling reaction.

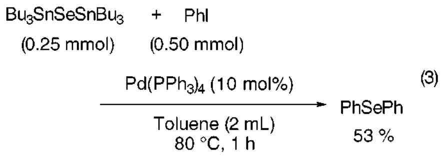
successfully carried out by elevating the reaction temperature (110 °C) and increasing the amounts of palladium catalyst and aryl halides (entries 7 and 8). Aliphatic halides as well as aromatic halide were reacted with **1**, and the corresponding alkyl phenyl selenides were formed in moderate yield (entries 9 and 10).

To further show the usability of this palladium-catalyzed reaction as a practical method for the synthesis of diorganyl selenides, we have examined the reaction of $BuSeSnBu_3$ with iodobenzene. $BuSeSnBu_3$ also acts as a promising reagent for introducing the butylseleno group to the aromatic ring, giving butyl phenyl selenide in 79% yield (eq 2).



$$\underset{(0.25\ \text{mmol})}{BuSeSnBu_3} + \underset{(0.25\ \text{mmol})}{PhI} \xrightarrow[\substack{\text{Toluene (2 mL)}\\ 80\ °\text{C, 3 h}}]{Pd(PPh_3)_4\ (10\ \text{mol\%})} \underset{79\ \%}{BuSePh} \tag{2}$$

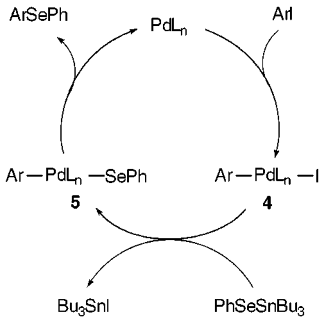
Next, we examined the introduction of two aryl groups to a selenium atom on bis(tributylstannyl) selenide ($Bu_3SnSeSnBu_3$). When bis(tributylstannyl) selenide was allowed to react with 2 equiv of iodobenzene in the presence of a catalytic amount of $Pd(PPh_3)_4$ (10 mol %) at 80 °C for 1 h, diphenyl selenide, in which two phenyl groups were introduced onto the selenium atom, was obtained in 53% yield (eq 3).



$$\underset{(0.25\ \text{mmol})}{Bu_3SnSeSnBu_3} + \underset{(0.50\ \text{mmol})}{PhI} \xrightarrow[\substack{\text{Toluene (2 mL)}\\ 80\ °\text{C, 1 h}}]{Pd(PPh_3)_4\ (10\ \text{mol\%})} \underset{53\ \%}{PhSePh} \tag{3}$$

Although a detailed study on the reaction pathway has not yet been completed, a plausible reaction pathway is shown in Scheme 1. The first step involves the oxidative addition of the aryl iodide to the low-valent palladium species to form an aryl palladium iodide species (**4**).[6–8] The following ligand exchange of **4** with $PhSeSnBu_3$ generates intermediate **5**. The subsequent reductive elimination from **5** affords the coupling product and regenerate the low-valent palladium species.

Scheme 1. Plausible Reaction Path



In summary, the reaction of $PhSeSnBu_3$, which is a stable against air and moisture, with aryl and alkyl halides in the presence of a catalytic amount of $Pd(PPh_3)_4$ proceeded efficiently to give the corresponding diorganyl selenides in moderate to good yields. Various synthetic applications of this reaction system are now in progress.

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(7) Tanaka disclosed that the reaction of $PhSeSnMe_3$ with $Pt(PEt)_3$ took place rapidly (<10 min) at room temperature to afford *trans*-$Pt(SePh)(SnMe_3)(PEt_3)_2$ in 83% isolated yield. See: Han, L.-B.; Shimada, S.; Tanaka, M. *J. Am. Chem. Soc.* **1997**, *119*, 8133.

(8) Rossi has reported the synthesis of (*E*)-1-alkenyl phenyl sulfides by the palladium-catalyzed reaction of 1-alkenyl bromides with trialkylstannyl phenyl sulfide. In this paper, they proposed that the first step of this reaction was the generation of vinyl palladium bromide species by the reaction of 1-alkenyl bromides with low-valent palladium species. See: Carpita, A.; Rossi, R.; Scamuzzi, B. *Tetrahedron Lett.* **1989**, *30*, 2699.