A Facile Method for Synthesis of Alkyl Phenyl Selenides. The Reaction of Diphenyl Diselenide with Oxygen-containing Compounds Using $\text{La/Me}_3\text{SiCl/}^{\text{cat.}}\text{I}_2\text{/}^{\text{cat.}}\text{CuI}$ System

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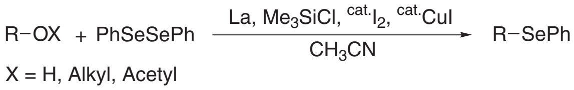
Alcohols, ethers, and esters were directly converted to the corresponding alkyl phenyl selenides by the reaction of diphenyl diselenide and the $\text{La/Me}_3\text{SiCl/}^{\text{cat.}}\text{I}_2\text{/}^{\text{cat.}}\text{CuI}$. It was suggested that alkyl phenyl selenides were formed by the S_H2 type reaction of diphenyl diselenide with alkyl radicals generated from alcohols, ethers or esters.

Since the phenylseleno group can be easily transformed into various useful functional groups, organoselenium compounds are used as valuable intermediates in organic synthesis.[1] In the organoselenium chemistry, alkyl phenyl selenides are often utilized as a key intermediate, and much effort is being devoted to accomplish the synthesis of these selenides. The alkyl phenylselenides are generally synthesized by the following two methods. One of the methods involves the reaction of the phenylselenolate anion with electrophiles such as alkyl halides.[2] Another one consists of the reaction of diphenyl diselenide with carbon nucleophiles such as alkyl or aryl metal compounds and metal enolates.[3] However, there are some disadvantages in both methods; (i) instability of selenium reagents used as selenium sources toward air and moisture, (ii) instability of carbon nucleophiles toward air and moisture, (iii) basic reaction conditions, and (iv) low yield of tertiary alkyl phenyl selenides.

We have recently reported a new method for the deoxygenative dimerization of alcohols, ethers or esters using the $\text{La/Me}_3\text{SiCl/}^{\text{cat.}}\text{I}_2\text{/}^{\text{cat.}}\text{CuI}$ system giving the corresponding alkanes.[4] On the basis of a number of experimental observations, it was suggested that the reaction proceeded via alkyl radical intermediate generated by the reduction of alcohols, ethers or esters using the $\text{La/Me}_3\text{SiCl/}^{\text{cat.}}\text{I}_2\text{/}^{\text{cat.}}\text{CuI}$. It is then expected that if diphenyl diselenide is added to this reaction system as an efficient radical scavenger, alkyl phenyl selenide can be produced by the reaction of the alkyl radical.[5,6] In this study, we show a one-pot synthesis of alkyl phenyl selenides via the S_H2 reaction of diphenyl diselenide with alkyl radicals, generated by the treatment of oxygen-containing compounds, alcohols, ethers and esters, with $\text{La/Me}_3\text{SiCl/}^{\text{cat.}}\text{I}_2\text{/}^{\text{cat.}}\text{CuI}$ (Scheme 1).

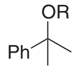
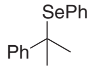
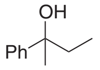
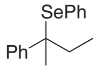
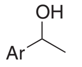
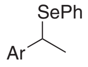
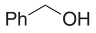
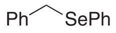
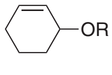
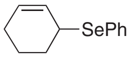
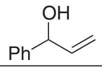
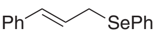


Scheme 1.

When 2-phenyl-2-propanol (**1a**) was treated with lanthanum metal, chlorotrimethylsilane, and a catalytic amount of iodine and copper(I) iodide in the presence of diphenyl diselenide in acetonitrile as the solvent at 82 °C for 1 h, the phenylselenylation of **1a** proceeded to give 2-phenyl-2-phenylselenopropane (**10**) in 86% yield (Entry 1). In the absence of CuI, the yield of **10** was very low (Entry 2). Similarly, 2-methoxy-2-phenylpropane (**1b**) and 2-acetyl-2-phenylpropane (**1c**) were converted into **10** by the addition of a catalytic amount of H_2O (Entries 3 and 4). It is interesting to note that two phenylseleno groups included in diphenyl diselenide were efficiently utilized in the reaction, and furthermore, a tertiary alkyl phenylselenide was successfully obtained in good yield by this method.

Various alcohols, ethers, and esters were allowed to react with diphenyl diselenide using the $\text{La/Me}_3\text{SiCl/}^{\text{cat.}}\text{I}_2\text{/}^{\text{cat.}}\text{CuI}$, and the results are shown in Table 1. Tertiary alkyl phenyl selenides were synthesized in moderate to good yields by this method (Entries 1, 3, 4, and 5). When phenethylalcohol (**3**) and *p*-methyl, *p*-methoxy, and *p*-chloro substituted phenethylalcohols were treated with diphenyl diselenide in this reaction, the corresponding α-phenylselenoethylbenzene derivatives were formed in 41–91% along with the formation of homo coupling products (Entries 6–9). This method is applicable to the conversion of an allylic alcohol into an allylic phenyl selenide. Similar treatment of 2-cyclohexene-1-ol (**8a**) and its ether and ester derivatives with diphenyl diselenide produced 3-phenylseleno-1-cyclohexene (**17**) in moderate yields (Entries 11–13).

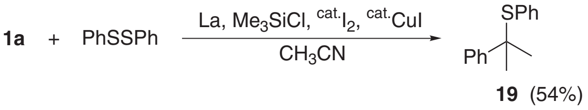
Table 1. Synthesis of benzylic and allylic phenyl selenides[a]

Entry	Substrate		Product		Yield /%[b]
1		**1a**: R = H			86
2[c]		**1a**: R = H		**10**	3
3[d]		**1b**: R = Me			84
4[d]		**1c**: R = Ac			89
5[e]		**2**		**11**	56
6		**3**: Ar = C_6H_5		**12**	48
7		**4**: Ar = *p*-MeC_6H_4		**13**	91
8		**5**: Ar = *p*-$MeOC_6H_4$		**14**	59
9		**6**: Ar = *p*-ClC_6H_4		**15**	41
10		**7**		**16**	27
11		**8a**: R = H		**17**	67
12[d]		**8b**: R = Me			49
13[d]		**8c**: R = Ac			49
14		**9**		**18**	45[f]

[a]Reaction conditions: substrate (1.0 mmol), PhSeSePh (0.5 mmol), La (1.0 mmol), Me_3SiCl (2.0 mmol), I_2 (0.2 mmol), CuI (0.2 mmol), and CH_3CN (3.0 mL) at 82 °C for 1 h. [b]GC yield based on substrate. [c]In the absence of CuI. [d]H_2O (0.2 mmol) was added. [e]For 3 h. [f]3-phenylseleno-1-propene (7%) was formed.

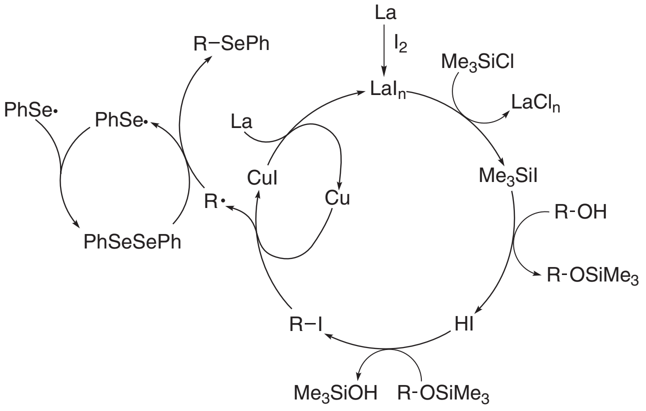
The reaction of 1-phenyl-2-propene-1-ol also gave 1-phenyl-3-phenylseleno-1-propene in 45% yield along with the formation of 3-phenyl-3-phenylseleno-1-propene (7%). The reaction of tertiary aliphatic alcohol such as 2-methyl-2-tridecanol resulted in the formation of 2-methyltridecane, and 2-methyltridecene and 2-methyl-1-tridecene, in 51, 20, and 4% yields, respectively, in preference to phenylselenated product (5%).

A similar method to the synthesis of alkyl phenyl selenides was examined for the synthesis of *tert*-alkyl phenyl sulfide using diphenyl disulfide as the radical scavenger.[7] It was confirmed that tertiary alkyl phenyl sulfides was synthesized by a similar method (Scheme 2).



Scheme 2.

A possible reaction pathway for the formation of alkyl phenyl selenides is shown in Scheme 3 on the basis of the reaction path for the deoxygenative dimerization of oxygen-containing compounds.[4] The first step involves the generation of iodotrimethylsilane by the halogen exchange reaction of chlorotrimethylsilane with lanthanum iodide generated in situ by the reaction of lanthanum metal with iodine. Iodotrimethylsilane reacts with an alcohol forming the corresponding alkyl iodide. Subsequently, the alkyl iodide is reacted with zerovalent copper generated in situ by the reduction of copper(I) iodide[8] with lanthanum metal giving the corresponding alkyl radical followed by the reaction with diphenyl diselenide in an $\mathrm{S_H2}$ fashion to produce alkyl phenyl selenide and phenylseleno radical. The phenylseleno radical is readily dimerized to reproduce the diphenyl diselenide.[9]



Scheme 3. A possible reaction path.

In summary, it was found that alkyl phenyl selenides could be synthesized by the reaction of oxygen-containing compounds with diphenyl diselenide using the $\mathrm{La/Me_3SiCl/^{cat.}I_2/^{cat.}CuI}$. It is interesting to note that the synthesis of tertiary alkyl phenyl selenides was successfully achieved, and two phenylseleno groups involved in diphenyl diselenide molecule are efficiently utilized in this reaction. The present phenylselenylation is considered to proceed via an alkyl radical followed by the $\mathrm{S_H2}$ type reaction with diphenyl diselenide.

The application of the reaction system, $\mathrm{La/Me_3SiCl/^{cat.}I_2/^{cat.}CuI}$, in organic synthesis is now in progress.

References and Notes

1 For recent reviews a) A. Krief and L. Hevesi, in "Organoselenium Chemistry," Springer-Verlag, Belrin (1988), Vol. 1. b) C. Paulmier, in "Selenium Reagents and Intermediates in Organic Synthesis," Pergamon Press, Oxford (1986). c) S. Patai and Z. Rappoport, in "The Chemistry of Organic Selenium and Tellurium Compounds," John Wiley & Sons, New York (1986), Vol. 1. d) S. Patai and Z. Rappoport, in "The Chemistry of Organic Selenium and Tellurium Compounds," John Wiley & Sons, New York (1987), Vol. 2. e) A. Krief, in "Comprehensive Organometallic Chemistry," ed. by B. M. Trost, Pergamon Press, Oxford (1991), pp 85-192. f) T. G. Back, in "Organoselenium Chemistry," Oxford University Press, Oxford (1999) and references cited therein.

2 a) L. Chierci, H. Lumbroso, and R. Passerini, *Bull. Soc. Chim. Fr.*, **1955**, 686. b) K. B. Sharpless and R. F. Lauer, *J. Org. Chem.*, **37**, 3973 (1972). c) K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, **94**, 715 (1972). d) K. B. Sharpless and M. W. Young, *J. Org. Chem.*, **40**, 947 (1975). e) T. Otsubo, F. Ogura, and H. Yamaguchi, *Synth. Commun.*, **10**, 59 (1980) and ref. 1 and references cited therein.

3 a) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am Chem. Soc.*, **97**, 686 (1975). b) P. A. Grieco and M. Miyashita, *J. Org. Chem.*, **39**, 2114 (1974). c) D. Seebach and D. Enders, *J. Med. Chem.*, **17**, 1225 (1974). d) F. M. Hauser, R. P. Rhee, and S. Prasannna, *Synthesis*, **1980**, 72 and ref. 1 and references cited therein.

4 T. Nishino, Y. Nishiyama, and N. Sonoda, *Tetrahedron Lett.*, **43**, 3689 (2002).

5 a) X. Lin, G. D. Artman, D. Stien, and S. M. Weinreb, *Tetrahedron*, **32**, 8779 (1976). b) M. J. Perkins and E. S. Turner, *J. Chem. Soc., Chem. Commun.*, **1981**, 139. c) G. A. Russell and H. Tashtoush, *J. Am. Chem. Soc.*, **105**, 1398 (1983). d) C. Sheu, A. Sobkowiak, L. Zhang, N. Ozbalic, D. H. R. Barton, and D. T. Sawyer, *J. Am. Chem. Soc.*, **111**, 8030 (1989). e) V. F. Patel and G. Pattenden, *J. Chem. Soc., Perkin Trans., 1*, **1990**, 2703. f) A. Ogawa, H. Tanaka, H. Yokoyama, R. Obayashi, K. Yokoyama, and N. Sonoda, *J. Org. Chem.*, **57**, 111 (1992). g) A. Ogawa, R. Obayashi, H. Ine, Y. Tsuboi, N. Sonoda, and T. Hirao, *J. Org. Chem.*, **63**, 881 (1998). h) D. H. R. Barton, M. Jacob, and E. Peralez, *Tetrahedron Lett.*, **40**, 9201 (1999). i) X. Lin, D. Stien, and S. M. Weinreb, *Org. Lett.*, **1**, 637 (1999). j) X. Lin, D. Stien, and S. M. Weinreb, *Tetrahedron Lett.*, **41**, 2333 (2000).

6 For the substitution method of the hydroxy group into the seleno group: a) P. A. Grieco, S. Gilman, and M. Nishizawa, *J. Org. Chem.*, **41**, 1485 (1976). b) P. A. Grieco, J. Y. Jaw, D. A. Claremon, and K. C. Nicolaou, *J. Org. Chem.*, **46**, 1215 (1981). c) T. G. Back and D. J. McPhee, *J. Org. Chem.*, **49**, 3842 (1984). d) H. Abe, A. Yamasaki, H. Fujii, and T. Harayama, *Chem. Pharm. Bull.*, **44**, 2223 (1996). e) H. Abe, A. Yamasaki, and T. Harayama, *Chem. Pharm. Bull.*, **46**, 1311 (1998).

7 For the preparative method of alkyl phenyl sulfide from an alcohol or alkene using diphenyl disulfide as the phenylthio group source: a) H. Suzuki and N. Sato, *Chem. Lett.*, **1981**, 267. b) K. Kano, M. Takeuchi, S. Hashimoto, and Z. Yoshida, *Chem. Lett.*, **1990**, 1381. c) M. Takeuchi, H. Shimakoshi, and K. Kano, *Organometallics*, **13**, 1208 (1994).

8 Ebert et al. reported that benzylic and allylic halides were reduced by activated copper prepared by the reduction of copper salt with lithium naphthalenide, giving the reductive coupling products within few minutes in good yields. see: F. O. Ginah, Jr., T. A. Donovan, S. D. Suchan, D. R. Pfennig, and G. W. Ebert, *J. Org. Chem.*, **55**, 584 (1990).

9 The treatment of diphenyl diselenide with La followed by addition of tertiary alkyl iodide did not provide alkyl phenyl selenide and alkyl iodide was recovered (92%).

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