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A Convenient One-pot Synthesis of Unsymmetrical Selenium Compounds Using Bis(trimethylsilyl) Selenide

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The reaction of bis(trimethylsilyl) selenide with n-BuLi followed by alkylation with an R^1X gave alkyl silyl selenides. The repetition of a similar one-pot operation with the second n-BuLi and R^2X yielded unsymmetrical selenides (R^1SeR^2) in good yields. This one-pot procedure could be also applicable to the syntheses of selenolesters, selenolcarbonates, and a phosphinothioyl selenide.

In recent years, organoselenium reagents have emerged as potentially important synthetic intermediates.1) Development of convenient and simple methods for the synthesis of these reagents is desirable. Symmetrical selenides are easily prepared by double alkylation of M_2Se where M is an alkali metal,2) whereas unsymmetrical selenides are generally prepared by reduction of symmetrical diselenides to selenolates (RSe^-) and subsequent alkylation,3) in which the starting diselenides must be independently prepared. Another route to unsymmetrical selenides uses the reaction of RLi with elemental selenium followed by alkylation with an appropriate alkyl halide.4) This method is useful only when RLi is easily available.

On the other hand, during the course of our study on the generation of selenoaldehydes,5) which can be directly prepared from aldehydes by using bis(trimethylsilyl) selenide (1)6) in the presence of a catalytic amount of n-BuLi, we have found that lithium trimethylsilyl selenide (2) is generated from the treatment of 1 with 1.0 equiv. of n-BuLi (Eq. 1). We now wish to report in this letter that unsymmetrical selenium compounds (3) can be easily synthesized in a one-pot operation via the simple sequences shown in Eq. 2.

$$\underset{1}{Me_3SiSeSiMe_3} + n\text{-}BuLi \longrightarrow \underset{2}{LiSeSiMe_3} + n\text{-}BuSiMe_3 \qquad (1)$$

A typical reaction was run as follows: butyllithium (1.6 M solution in hexane, 0.53 ml, 0.85 mmol) was added to a solution of 1 (180 mg, 0.80 mmol) in

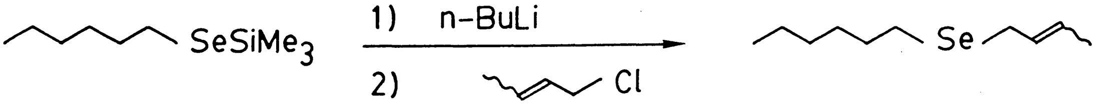
$$\underset{\underset{\sim}{1}}{Me_3SiSeSiMe_3} \xrightarrow[0\ ^\circ C,\ 30\ min,\ THF]{n-BuLi} \underset{\underset{\sim}{2}}{LiSeSiMe_3} \xrightarrow[30\ ^\circ C,\ 2\ h]{R^1X} R^1SeSiMe_3$$

$$\xrightarrow[0\ ^\circ C,\ 30\ min]{n-BuLi} R^1SeLi \xrightarrow[30\ ^\circ C,\ 2\ h]{R^2X} \underset{\underset{\sim}{3}}{R^1SeR^2} \quad R^1, R^2 = alkyl, acyl, etc \qquad (2)$$

THF (20 ml) at 0 °C under nitrogen. After stirring for 30 min at 0 °C, hexyl bromide (140 mg, 0.85 mmol) in THF (5 ml) was added dropwise, and the mixture was stirred for 2 h at 30 °C. After cooling, the second butyllithium (0.85 mmol) and octyl bromide (164 mg, 0.85 mmol) were added in a similar manner as above. Extractive workup followed by flash column chromotography on silica gel (hexane as eluent) yielded hexyl octyl selenide (3b) (215 mg, 0.78 mmol) in 97% yield.

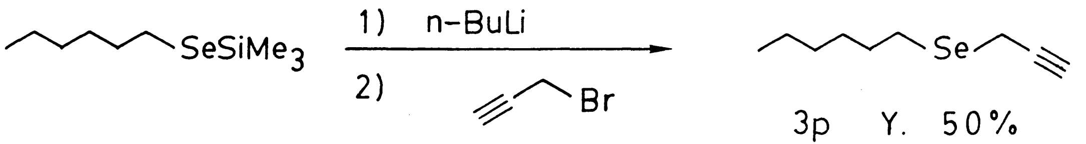
The representative results are listed in Table 1.[7] In most cases hexyl bromide was used as the first alkyl halide R^1X. The yield of simple alkyl selenides exceeded 90% (entries 1 and 2). Benzyl and allyl selenides were also prepared in satisfactory yields (entries 3-5). For the synthesis of secondary alkyl selenides, the addition of 1.0 equiv. of HMPA at the stage of the second alkylation resulted in better yields (entries 6 and 7). Furthermore, as shown in entries 8-14, this procedure can be applicable to a wide range of unsymmetrical selenium compounds. Thus, when acyl chlorides, chloroformates, and phosphinothioyl chloride were used as the second halide R^2X, the corresponding selenolesters (3h-3j), selenolcarbonates (3k-3m), and phosphinothioyl selenide (3n) were yielded, respectively.

The mode of substitution in this reaction was studied in allyllic or propargyllic system. In the second alkylation, crotyl chloride and propargyl bromide were displaced by a clean S_N2 process to give 3o and 3p, respectively, and no products arising from a competitive allyllic rearrangement could be detected (Eqs. 3 and 4).



(3)

3o Y. 70%

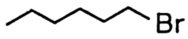
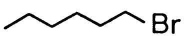
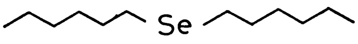
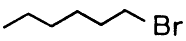
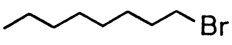
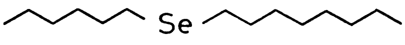
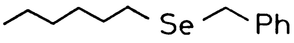
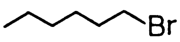
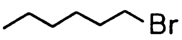
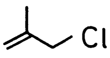
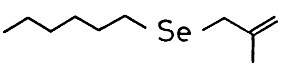
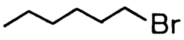
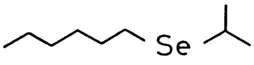
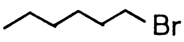
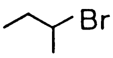
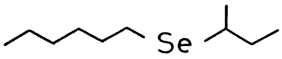
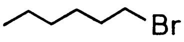
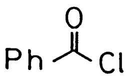
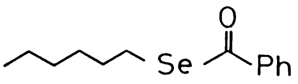
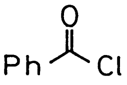
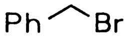
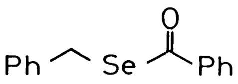
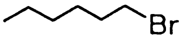
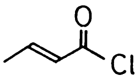
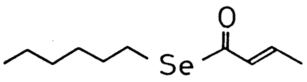
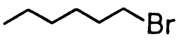
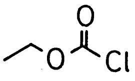
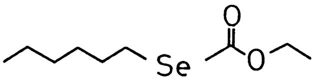
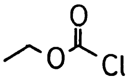
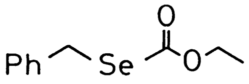
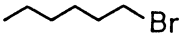
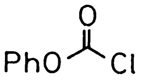
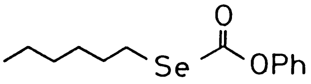
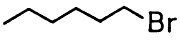
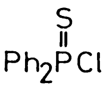
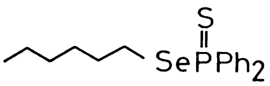


(4)

3p Y. 50%

It seems that in the present reaction, both trimethylsilyl groups of 1 are displaced by butyl anion to give butyltrimethylsilane. To confirm this point, the reaction was followed by ^1H-NMR. The signals corresponding to 2 and butyltrimethylsilane in Eq. 1 appeared as singlets at δ 0.22 and -0.03, respectively, and these two peaks showed about the same hight. After the reaction with the second

Table 1. Preparation of Unsymmetrical Selenium Compounds Using **1** and Various Halides

Entry	R^1X	R^2X	Product		Yield/% [a]
1				(**3a**)	91
2				(**3b**)	97
3				(**3c**)	88[b]
4				(**3d**)	67
5				(**3e**)	65
6				(**3f**)	64[c]
7				(**3g**)	70[c]
8				(**3h**)	79
9				(**3i**)	70[b]
10				(**3j**)	31
11				(**3k**)	75
12				(**3l**)	58[b]
13				(**3m**)	33
14				(**3n**)	63

a) Isolated yield. b) NMR yield. c) 1.0 equiv. of HMPA was added.

BuLi, the hight of the signal at δ -0.03 increased greatly and no other significant peak was observed in Me_3Si region. On the other hand, interestingly, even though **1** was treated with 2.0 equiv. of n-BuLi, the ^{1}H-NMR spectra of the reaction mixture were the same as those obtained from the reaction with 1.0 equiv. of n-BuLi. This result shows that the reaction of **1** with n-BuLi proceeds with a 1:1 stoichiometry and does not afford Li_2Se in situ.[8)]

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6) For synthesis of $(Me_3Si)_2Se$, see: M. R. Detty and M. D. Seidler, J. Org. Chem., 47, 1354 (1982).
7) All new compounds prepared by the present study exhibited satisfactory spectral data (^{1}H-NMR, IR, and mass spectra).
8) Gladysz et al. reported that unsymmetrical selenides cannot be synthesized via sequential addition of R^1X and R^2X to Li_2Se and only symmetrical selenides are detected. See Ref. 2.

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