Reaction of Lithium Aluminum Hydride with Elemental Selenium: Its Application as a Selenating Reagent into Organic Molecules

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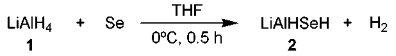
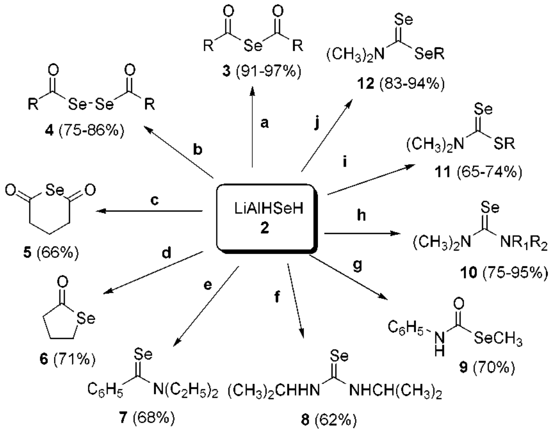
Recently many syntheses of compounds containing selenium have been studied and reported because of the interesting reactivities[1] and their potential pharmaceutical significance.[2] Several methods for the synthesis of selenium-containing compounds using various types of selenating reagents have been developed. The alkali metal salts of hydrogen selenide, which can be readily prepared in situ by the reaction of elemental selenium and a reducing reagent such as Li, $LiBEt_3H$, Na, $NaBH_4$, $NaBEt_3H$, and i-Bu_2AlH, have often been utilized as selenating reagents for the introduction into organic molecules.[3] However, the utilization of these salts as selenating reagents has been limited to the synthesis of either dialkyl diselenides,[3a−c] dialkyl selenides,[3b,c] selenothiocarbamates,[3d] selenoamides,[3e] as well as certain other applications.[4] A selenating reagent, capable of preparing a wide range of selenium-containing compounds, has not been reported yet. Here, we describe the reaction of lithium aluminum hydride with elemental selenium and a wide range of the applications using this reagent.

Scheme 1



$$\underset{\mathbf{1}}{LiAlH_4} + Se \xrightarrow[0^{\circ}C,\ 0.5\ h]{THF} \underset{\mathbf{2}}{LiAlHSeH} + H_2$$

Scheme 2[a]



[a] **a**: RCOCl (2.0 equiv)/THF, 0 °C, 2 h; **b**: (1) RCOCl (1.0 equiv)/THF, 0 °C, 2 h; (2) I_2/KI (1.0 equiv/0.2 equiv), 0 °C, 1.5 h; **c**: $ClCO(CH_2)_3COCl$ (1.0 equiv)/THF, rt, 2.0 h; **d**: $ClCO(CH_2)_3Cl$ (1.0 equiv), 0 °C, 2 h; **e**: $C_6H_5C(=O)N(C_2H_5)_2$ (1.0 equiv)/$(COCl)_2$ (1.0 equiv)/diethyl ether, 0 °C, 1 h, and then rt, 3 h; **f**: $(CH_3)_2CHN=C=NCH(CH_3)_2$ (1.0 equiv), 0 °C, 1 h; **g**: (1) $C_6H_5-N=C=O$ (1.0 equiv), rt, 1 h; (2) CH_3I (1.0 equiv), rt, 2 h; **h**: (1) $[Cl_2C=N(CH_3)_2]Cl$ (1.0 equiv), 0 °C, 1.5 h; (2) amine (2.0 equiv), rt, 2 h; **i**; (1) $[Cl_2C=N(CH_3)_2]Cl$; (2) lithium alkylthiolate (1.0 equiv)/THF, 0 °C, 2 h; **j**: (1) $[Cl_2C=N(CH_3)_2]Cl$; (2) lithium alkylselenolate (1.0 equiv)/THF, 0 °C, 2 h.

Lithium aluminum hydride **1** (1 equiv) was added with stirring to black selenium powder (1 equiv) suspended in THF under an argon atmosphere at 0 °C for 30 min. Considerable hydrogen gas was immediately evolved, and the black selenium powder was consumed in less than 10 min. The reaction mixture became a heterogeneous grayish suspension. (1) Hydrogen gas (1 equiv) was recovered in the present reaction.[5] (2) In the ^1H NMR spectrum of the product **2**, two proton peaks of different chemical shift, 1.86 and 3.75 ppm, were observed. These chemical shifts are close to those of similar compounds in the literatures.[3e,6] From these facts, we inferred that the product generated in the present reaction was LiAlHSeH **2** (Scheme 1). The product **2** formed in situ was ready for further reaction without concentration. We investigated various kinds of solvents and found that THF or diethyl ether could be used in this reaction.

The product **2** in THF, prepared as described above, was applied to the syntheses of many kinds of selenium-containing molecules as a selenating reagent. The compounds prepared in this study are shown in Scheme 2. Reaction of **2** with 2 equiv of acyl chloride gave diacyl selenide **3** in excellent yields. The synthesis of diacyl selenides has been infrequently reported.[7] Jensen et al.[7a] observed the existence of unstable benzoyl selenide, which was obtained by the elimination of hydrogen selenide from selenobenzoic acid at room temperature. The benzoyl selenide was in turn transformed into dibenzoyl diselenide and bis(selenobenzoate). Kato et al. reported the preparation of diacyl selenides by the reaction of *O*-silyl selenocarboxylates with acyl chorides.[7b] We described the preparation of diacyl selenides;[8] however, these methods all required many steps, while the present method is a one-pot reaction from which could be easily isolated

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diacyl selenides **3** in very high yields using silica gel flash column chromatography. Until now it has been relatively difficult to be obtain aliphatic diacyl selenides **3** because of their instability.[8] Both aromatic and aliphatic diacyl selenides **3** were obtained in excellent yields by using **2**. Acyl chloride (1 equiv) and I_2/KI (1.0 equiv/0.2 equiv) yielded diacyl diselenide[9] **4** in 75−86% yields, respectively. Reaction of **2** with glutaryl chloride formed glutaric selenoanhydride **5** in 66%. This method gave **5** in better yield than the first reported synthesis of **5**.[10] γ-Selenobutyrolactone **6** was obtained by adding 4-chlorobutyryl chloride into compounds **2** in 71%. There is only one additional example of the synthesis of a γ-selenobutyrolactone **6** in the literature.[11] The present method requires fewer steps than the previously reported method. Reaction of *N*,*N*-diethyl amide and oxalyl chloride with **2** gave *N*,*N*-diethyl selenoamide **7** in 68% yield. Reaction of **2** with carbodiimide afforded selenourea **8** in 62%. The carbodiimide was previously obtained via oxidation of selenourea using $NaIO_4$ in quantitative yield.[12] This method involves the reverse reaction. The *Se*-methyl *N*-phenylcarbamate **9** was obtained by the reaction of **2** with phenyl isocyanate and methyl iodide. In contrast, **9** could not be prepared using lithium selenide[3b] obtained by lithium triethylborohydride reduction of selenium because of being unable to supply the hydrogen. *N*,*N*-Dimethyl selenocarbamoyl chloride $(CH_3)_2NC(=Se)Cl$ is easily prepared in situ from reaction of **2** with dichloromethylenedimethyliminium chloride $[Cl_2C=N(CH_3)_2]Cl$ and can be trapped with various nucleophiles such as amines, lithium alkylthiolates, and lithium alkylselenolates, to give the corresponding selenoureas **10**, *S*-alkyl selenothiocarbamates **11**, and *Se*-alkyl diselenocarbamates **12** in good to high yields. This is the first reported synthesis of *N*,*N*-dialkyl diselenocarbamates **12**.[13] Previously, selenoureas and selenothiocarbamates bearing limited types of functional groups have been synthesized by using sodium hydrogen selenide.[3d,14] Because the present study can use various carbodiimides, isocyanates, amines, lithium alkylthiolates, or lithium alkylselenolates as nucleophiles, the compounds **8**, **9**, **10**, **11,** and **12** bearing various kinds of alkyl groups are readily prepared.[15]

We have developed a novel and very useful selenating reagent. This communication demonstrates the potential wide-ranging utility of this reagent by the preparation of various organic selenium compounds. Elucidation of the details of the precise reaction mechanism and combined state of **2** requires further study.

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Supporting Information Available: Synthetic procedures for the compounds **2**−**12** prepared in this communication, including spectral characterization (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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