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A Novel Deselenation in the Reaction of Selenoamides with Organolithium Reagents

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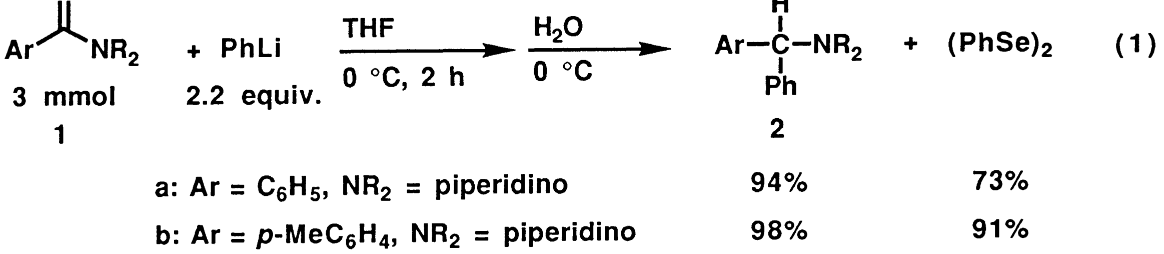
The reaction of selenoamides with organolithium reagents proceeds in a carbophilic manner, and more interestingly, the presence of excess lithium reagents causes a novel deselenation reaction from the carbophilic adducts.

Although much effort is being devoted to the preparation of selenocarbonyl compounds and to make a comparison with their sulfur analogues,[1)] reports on the fundamental reactivities of selenocarbonyl compounds are still rare. For example, thiophilic addition has been well-documented to take place in the reaction of thiocarbonyl compounds with various nucleophiles,[2)] but in contrast, only very limited information is currently available on the reactivity of selenocarbonyl compounds toward nucleophiles. Recently, Okazaki et al. reported that the heterophilic addition of organolithium and organomagnesium reagents is much more significant in the reaction with selenoketone than with thioketone.[3,4)] In this letter, we report that the reaction of selenoamides, as heteroatom-substituted selenocarbonyl compounds,[5)] with organolithium reagents proceeds in a carbophilic manner, and more interestingly, that the presence of excess lithium reagents causes a novel deselenation reaction from the carbophilic adducts.

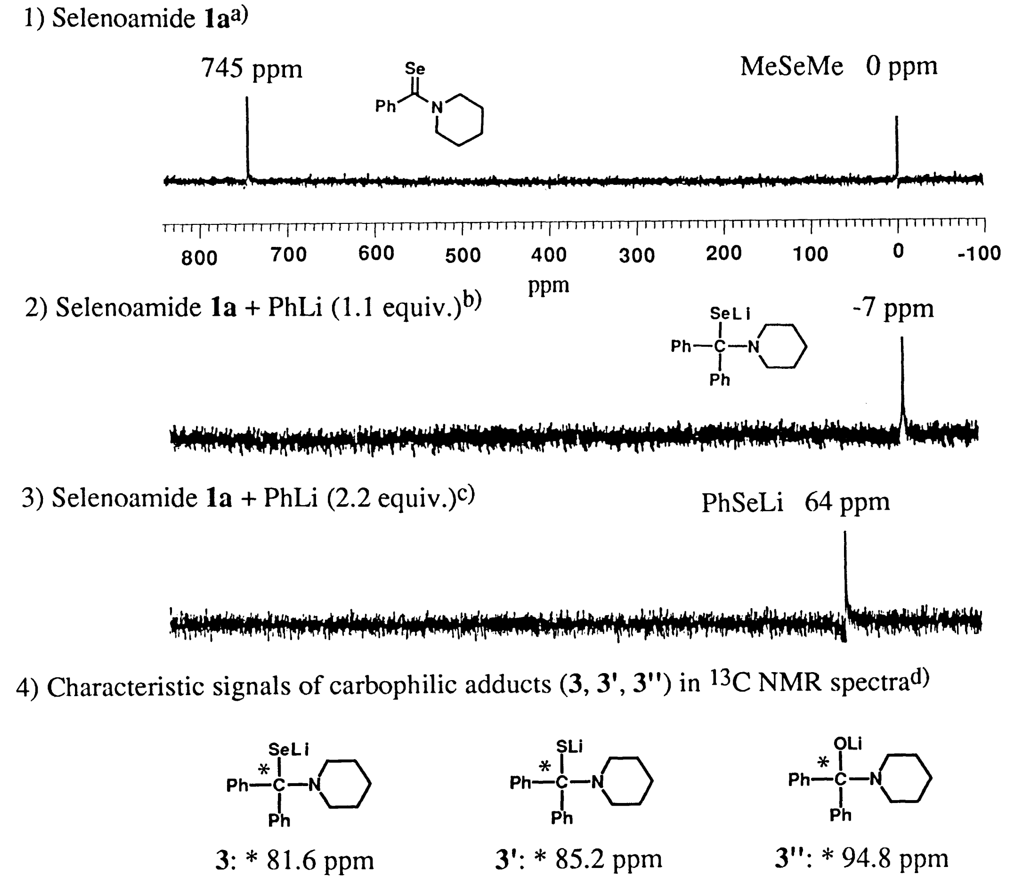
To a stirred THF (15 mL) solution of 1-selenobenzoylpiperidine (**1a**, 3 mmol) was added dropwise 2.2 equivalents of phenyllithium over 20-min period at 0 °C. After 100 min, the reaction mixture was quenched with water and extracted with diethyl ether (3 x 30 mL). The combined extracts were dried over $MgSO_4$, and the solvent was removed *in vacuo*. Flash chromatography on silica gel (eluting with hexane/Et_2O = 10/1) provided 1-benzhydrylpiperidine (**2a**) in 94% yield along with diphenyl diselenide (73%) (Eq. 1).



a: Ar = C_6H_5, NR_2 = piperidino	94%	73%
b: Ar = *p*-MeC_6H_4, NR_2 = piperidino	98%	91%
c: Ar = C_6H_5, NR_2 = 1-pyrrolidinyl	95%	91%
d: Ar = C_6H_5, NR_2 = dimethylamino	82%	90%

Some other selenoamides bearing no hydrogen at α to the selenocarbonyl underwent a similar deselenation with 2.2 equivalents of PhLi. In the case using equimolar amounts of PhLi, amine **2** was not formed at all.[6)]

To gain insight into the reaction course of this deselenation, we attempted to follow the reaction of selenoamide **1a** with PhLi by taking the ^{13}C and ^{77}Se NMR (Fig. 1). The solution of **1a** in THF showed characteristic peaks at δ 202.9 in ^{13}C NMR and δ 745 in ^{77}Se NMR, which are assigned to the selenocarbonyl carbon and selenium, respectively. On treatment of the solution with equimolar amounts of PhLi at -50 °C,[7)] the peaks immediately disappeared and new peaks appeared at δ 81.6 in ^{13}C NMR[8)] and δ -7 in ^{77}Se NMR, which apparently indicates the clean formation of carbophilic adduct **3**. Addition of another one equivalent of PhLi to the solution at 0 °C caused disappearance of the signals of carbophilic adduct **3**, and appearance of a peak at δ 64 in ^{77}Se NMR, which can be assigned to lithium benzeneselenolate.


1) Selenoamide **1a**[a)]

2) Selenoamide **1a** + PhLi (1.1 equiv.)[b)]

3) Selenoamide **1a** + PhLi (2.2 equiv.)[c)]

4) Characteristic signals of carbophilic adducts (**3**, **3'**, **3''**) in ^{13}C NMR spectra[d)]

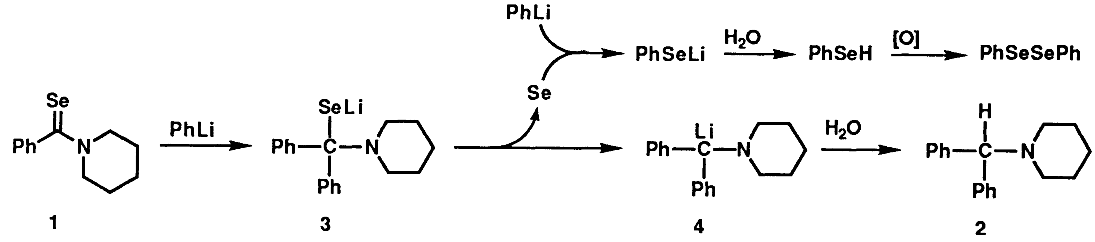
3: * 81.6 ppm

3': * 85.2 ppm

3'': * 94.8 ppm

Fig. 1. ^{77}Se NMR Spectra in THF at -40 °C measured with MeSeMe (neat) or PhSeSePh (0.5 M $CDCl_3$ solution) as an external standard. a) THF solution of selenoamide **1a** (0.8 mmol, 0.53 mol dm^{-3}). b) ^{77}Se NMR spectrum obtained on addition of PhLi (0.88 mmol) to the solution of **1a** in THF. c) Another 1.1 equiv. of PhLi was added to the solution including carbophilic adduct **3**. d) Adducts were prepared *in situ* by the reaction of selenoamide, thioamide, and amide with PhLi (1.1 equiv.) .

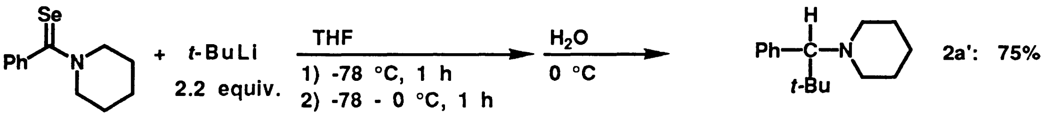
A possible reaction path is shown in Scheme 1: The reaction of selenoamide **1** with PhLi leads to formation of carbophilic adduct **3**, which undergoes deselenation[9)] by the action of another one equivalent of PhLi to form benzylic lithium **4** and lithium benzeneselenolate. The formation of diphenyl diselenide is explained by hydrolysis of PhSeLi and the subsequent air-oxidation of benzeneselenol during workups.



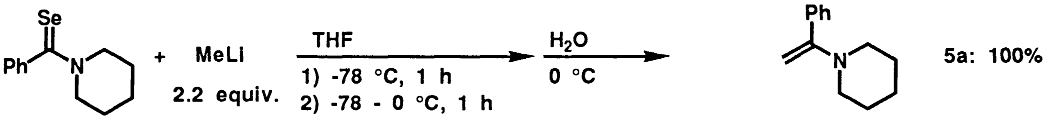
Scheme 1. A possible reaction path.

In sharp contrast, the corresponding amide and thioamide did not undergo deoxygenation and desulfurization by a similar treatment with excess PhLi (2.2 equiv.), and instead, benzophenone and thiobenzophenone were formed in high yields, respectively (> 80%, GLC yield).[10] The measurement of ^{13}C NMR spectra of the solution of amide or thioamide with one equivalent of PhLi showed the formation of carbophilic adducts **3'** and **3"** in analogy with selenoamide (Fig. 1). However, thus formed carbophilic adducts **3'** and **3"** did not show any change on the spectrum of ^{13}C NMR by treating with excess PhLi. Presumably, weaker bond energy of C-Se may partly contribute to occurrence of deselenation.[11]

The reactions of selenoamide with some alkyllithiums (2.2 equiv.) were also carried out (Eqs. 2-4). In the case using *t*-BuLi, a similar deselenation *via* carbophilic adduct took place as well as the case using PhLi. Contrary to this, the reaction with MeLi gave 1-phenyl-1-piperidinoethene (**5a**), the formation of which is understandable as resulting from the elimination of selenolate anion (Li_2Se or LiSeH) from the carbophilic adducts. In the reaction with *n*- and *s*-BuLi, deselenation to benzylic amines **2a"** and **2a'''** was in competition with elimination to enamines **5b** and **5c**.



(2)



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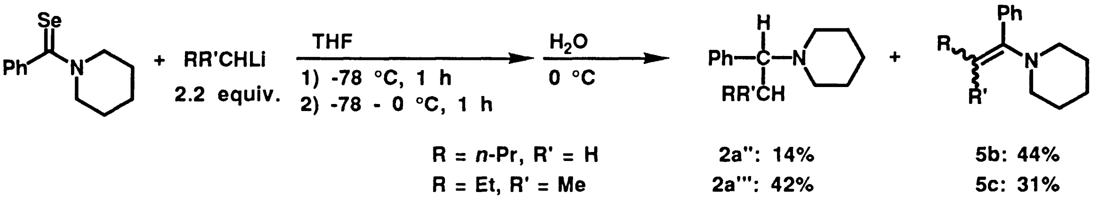

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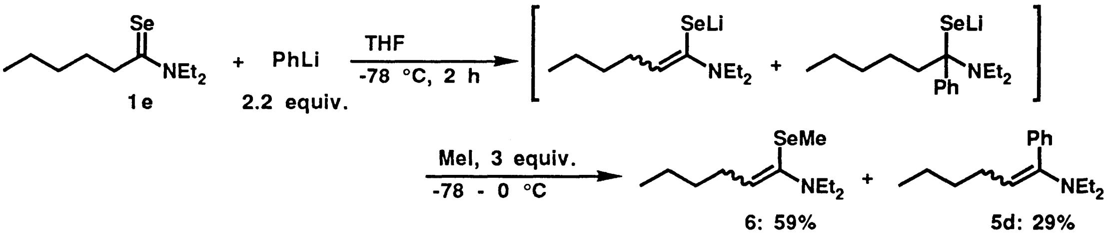

(5)

Moreover, the reaction of aliphatic selenoamide **1e** with PhLi (2.2 equiv.), followed by alkylation with methyl iodide was found to provide α-(methylseleno) enamine **6** and α-phenyl enamine **5d**; this suggests that the α-hydrogen abstraction from selenoamide took place in preference to carbophilic attack.

In conclusion, the reaction of aromatic selenoamides with organolithiums predominantly provided carbophilic adducts, which underwent novel deselenation on treatment of excess lithium reagents unlike related amides and thioamides. Further investigation on precise mechanism of the deselenation and its possible application to organic synthesis are under way.

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6) The reaction of selenoamide **1a** with one equivalent of PhLi provided benzophenone (42%) and dibenzhydryl diselenide (40%) after aqueous workup. It was confirmed that hydrolysis of carbophilic adduct **3** led to benzophenone (40%) and dibenzhydryl diselenide (41%).
7) At 0 °C, the carbophilic adduct **3** gradually decomposed.
8) ^{13}C NMR (THF-d_8) for **3**: δ 26.5 (N-CH_2-CH_2-$\underline{C}H_2$), 27.7 (N-CH_2-$\underline{C}H_2$), 51.4 (N-$\underline{C}H_2$), 81.6 (Se-$\underline{C}$-N), 124.5 (p), 126.5 (m), 130.6 (o), 154.3 (ipso).
9) If the carbophilic adduct **3** is to decompose to piperidinomethyllithium **4** and elemental selenium, PhLi may trap the selenium to give PhSeLi.
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11) Bond dissociation energies *D* [kJ mol^{-1}] for diethyl chalcogenides are as follows: *D* (Se-C) = 251; *D* (S-C) = 292; *D* (O-C) = 362, see: L. Batt, "The Chemistry of Organic Selenium and Tellurium Compounds," ed by S. Patai and Z. Rappoport, John Wiley & Sons, New York (1986), Vol. 1, Chap. 4.

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