o-(*o*-Iodophenyl)phenylselenenyl Ethers/*t*-BuLi System as an Alkyllithium Equivalent with Structural Variations

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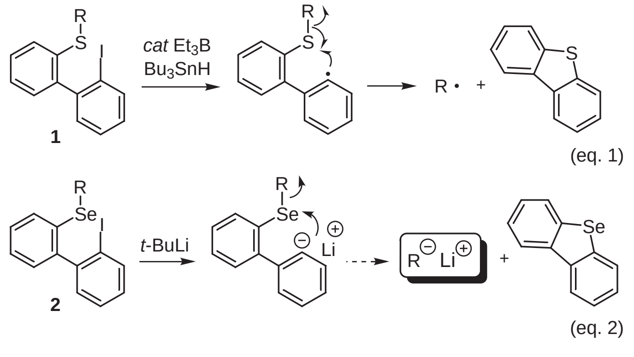
Abstract: *o*-(*o*-Iodophenyl)phenylselenenyl ethers/*t*-BuLi system can function as an alkyllithium equivalent possessing requisite structures based on an anchimeric approach. The synthetic utility as well as the limitation were evaluated in the in situ trapping reaction with carbonyl compounds.

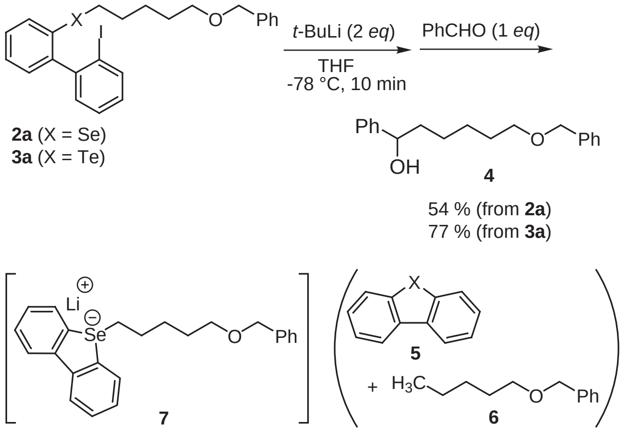
Key words: aldehydes, alkylation, alkyllithiums, anchimeric approach, selenium compounds

Recently we reported the rapid generation of carbon-centered radicals from *o*-(*o*-iodophenyl)phenylthio derivatives **1**, where an initially generated biphenyl radical strongly participates in facilitating the subsequent homolytic cleavage of a carbon-sulfur bond (eq. 1 in Scheme 1).[1] This chemistry led us to investigate the possibility of generating desired alkyl metal species by the utilization of such anchimeric effect. Taking both the versatility and the availability with the limitation of structural types into account,[2,3] we focused on the combined use of *o*-(*o*-iodophenyl)phenylselenenyl derivative **2** and commercially available alkyllithiums, expecting that various alkyllithium reagents could be efficiently prepared through initial Li-halogen exchange and subsequent translocation of the resulting anion as illustrated in Scheme 1 (eq. 2). In this letter, we wish to report the preliminary results of this study and address its utility and limitation in the nucleophilic carbon-carbon bond formation reactions.



Scheme 1

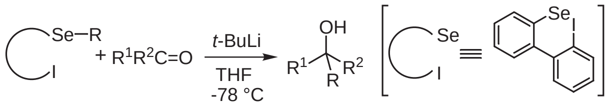
We initiated the examination on the feasibility of generating alkyllithiums by the treatment of *o*-(*o*-iodophenyl)phenylthio ether **1** (R = $(CH_2)_5OBn$) with *t*-BuLi, which turned out to be totally unsuccessful and the main observation was the simple reduction of iodobenzene moiety. This result prompted us to employ phenyselenenyl ether of type **2** on the assumption that selenium would be more susceptible toward the intramolecular attack of initially formed aryl anion.[4] Thus, treatment of *o*-(*o*-iodophenyl)phenylselenenyl ether **2a** with *t*-BuLi (2 equiv) in THF at -78 °C for 10 min and subsequent reaction with benzaldehyde (1 equiv) resulted in the formation of desired *secondary* alcohol **4** in 54% isolated yield along with dibenzoselenophene (**5**, X = Se, 96%) and benzyl pentyl ether (**6**, 7%). Although the clean formation of **5** (X = Se) suggested that the originally expected intramolecular anion translocation process for the generation of $PhCH_2O(CH_2)_5Li$ was operative, the chemical yield difference between **4** and **5** as well as the production of **6** implied the intervention of the selenium ate complex **7** as an alternative reactive species in this alkylation sequence.[5] Here, the use of Te in place of Se increased the chemical yield of **4** (77%) (Scheme 2).[6,7]

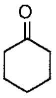


Scheme 2

With the information at hand, we subsequently evaluated the synthetic utility of the present system as an alkyllithium equivalent with a variety of structures in carbonyl alkylations. Here, we employed the in situ trapping method and selected results are listed in the Table. The mixture of **2a** and benzaldehyde (2 equiv) in THF was treated with *t*-BuLi (3 equiv) at -78 °C for 10 min to furnish the alkylation product in 60% yield (entry 1). As expected, siloxy and alkenyl moieties were found to be preserved with this procedure, and the corresponding *secondary* alcohols

Table In situ Alkylation of Carbonyls by *o*-(*o*-Iodophenyl)phenylselenenyl Ethers/*t*-BuLi[a]



entry	R	$R^1R^2C=O$	% yield [b]
1	$(CH_2)_5OBn$ (**2a**)	PhCHO	60
2	$(CH_2)_4CH=CH_2$	PhCHO	81
3	$(CH_2)_5OSiMe_2Bu^t$	PhCHO	74
4	$CH_2C_6H_4CONEt_2$	PhCHO	88
5		*t*-BuCHO	78
6		*c*-HexCHO	67
7			70
8	$(CH_2)_2CONHEt$	PhCHO	35 [c]

[a] Unless otherwise noted, the reaction was carried out with 2 equiv of $R^1R^2C = O$ and 3 equiv of *t*-BuLi in THF at -78 °C for 10 min. [b] Isolated yield. [c] Use of 3 equiv of benzaldehyde and 4 equiv of *t*-BuLi.

were obtained in good yields (entries 2 and 3). The selenenyl benzyl ether with *tertiary* amide functionality, on exposure to the optimized conditions, functioned as the desired benzyllithium equivalent with high efficiency and hence the in situ trapping with several aromatic and aliphatic aldehydes as well as cyclohexanone worked well (entries 4-7). Moreover, the reaction with the selenenyl ether possessing *secondary* amide moiety also appeared feasible, though the chemical yield of the alkylation product was lowered (entry 8).

A typical experimental procedure is as follows (Table, entry 1): To a solution of selenenyl ether **2a** (161 mg, 0.3 mmol) and benzaldehyde (61 μL, 0.6 mmol) in freshly distilled THF (3 mL) was added a 1.51 M pentane solution of *t*-BuLi (596 μL, 0.9 mmol) at -78 °C under argon. After stirring at -78 °C for 10 min, the reaction was quenched by addition of saturated NH_4Cl solution. Extractive workup was performed with ethyl acetate and the organic extracts were dried over Na_2SO_4. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (ethyl acetate/hexane = 1:5 as eluant) gave 6-benzyloxy-1-phenyl-1-heptanol (**4**) as a colorless oil (51 mg, 0.18 mmol, 60% yield).

Acknowledgement

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References and Notes

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(2) Review: (a) D. M. Huryn, In *Comprehensive Organic Synthesis*; B. M. Trost, I. Fleming, L. A. Paquette, Eds., Pergamon Press: New York, 1991, Vol. 1, Chapter 1.2. (b) V. J. Lee, In *Comprehensive Organic Synthesis*; B. M. Trost, I. Fleming, L. A. Paquette, Eds., Pergamon Press: New York, 1991, Vol. 4, Chapter 1.2.

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(4) C. Paulmier, *Selenium Reagents and Intermediates in Organic Synthesis*, Pergamon Press: Oxford, 1986.

(5) We assumed that the ate complex **7** would not be nucleophilic enough to react with benzaldehyde under the reaction conditions and could give **5** and **6** by the workup procedure, lowering the chemical yield of **4**. Although this thought led us to attempt the alkylation at higher temperature, the yield of **4** was not improved. However, involvement of the ate complex of type **7** is still conceivable in this system[8] and the extent would be highly dependent on the structure of substrate, which is difficult to precisely estimate at present.

(6) This result probably stems from more facile lithium-tellurium exchange. For relative rates of lithium-metalloid exchange reactions, see: T. Kanda, S. Kato, N. Kanbe, Y. Kohara, N. Sonoda, *J. Phys. Org. Chem.* **1996**, *9*, 29.

(7) We decided to conduct the following alkylation experiments with selenium derivatives mainly due to the ease of the synthesis.

(8) Alkylation with selenium ate complexes, see, for example: W. Dumont, P. Bayet, A. Krief, *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 804.

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