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Reaction of 1,3-Diselenanes with Organolithiums

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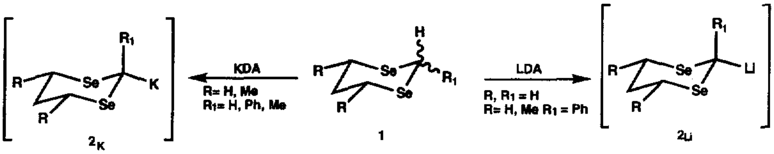
Abstract: Hydrogen / metal or selenium / metal exchange efficiently and selectively takes place on reaction of 1,3-diselenanes with organolithiums. The nature of the two partners directs the reaction. Copyright © 1996 Elsevier Science Ltd

We recently disclosed[1] that 1,3-diselenanes **1** are metallated with KDA or LDA and that the ease of this reaction depends upon the nature of the substituents attached on the 2-, 4- and 6-positions and upon the stereochemistry at C-2 (Scheme 1).

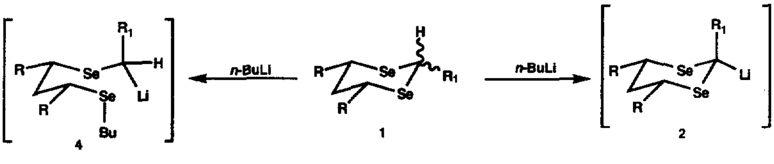
Scheme 1



These results are exceptional since selenoacetals belonging to the alkylseleno- series are not usually metallated with lithium amides and react with alkyllithiums, to produce α-selenoalkyllithiums resulting from the C-Se bond cleavage.[2,3]

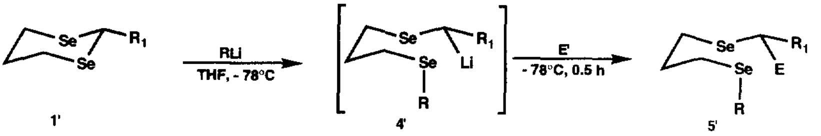
We now report that *n*-butyllithium reacts selectively with 1,3-diselenanes[1] **1** bearing at least one hydrogen at C-2 and leads to products resulting either from the cleavage of the C-Se or of the C-H bond depending upon the nature of the substituents at their 2, 4 and 6-positions (Scheme 2).

Scheme 2



As general trends *n*-butyllithium in THF-hexanes selectively cleaves one of the C-Se bond of 1,3-diselenanes **1'** unsubstituted at C-4 and C-6 and produces α-selenoalkyllithiums bearing a butylseleno group in 3-position.[4] This reaction, usually observed with open chain derivatives,[2,3] takes place with the whole series of compounds bearing hydrogens, one methyl and even one phenyl substituent at C-2 and delivers on further addition of benzaldehyde or acetone, the corresponding β-hydroxyalkyl-(3-butylseleno-propyl) selenides **5'** in fair to good non optimized yields (Scheme 3, entries a-c).

Scheme 3

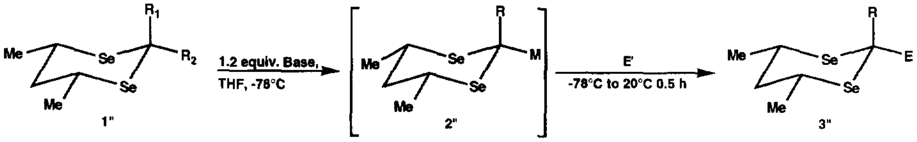


Entry	Starting material	R$_1$	Conditions (RLi)	E'	Product	R	E	Yield in **5'**
a	**1'a**	H	*n*-BuLi, 0.5 h	PhCH=O	**5'a**	*n*-Bu	PhCHOH	60%
b	**1'b**	Ph	*n*-BuLi, 0.25 h	Me$_2$C=O	**5'b**	*n*-Bu	Me$_2$CHOH	87%
c	**1'c**	Me	*n*-BuLi, 0.5 h	PhCH=O	**5'c**	*n*-Bu	PhCHOH	72%
d	**1'b**	Ph	PhLi, 0.75 h	Me$_2$C=O	**5'b'**	Ph	Me$_2$CHOH	85%
e	**1'b**	Ph	MeLi, 0.75 h	Me$_2$C=O	**5'b"**	Me	Me$_2$CHOH	75%

No reaction takes place at -78°C with (i) *n*-butyllithium in ether instead of THF or (ii) *n*-butyllithium TMEDA. The cleavage however efficiently occurs with *sec*- and *tert*-butyllithiums when performed either in THF or in ether.[5] The high propensity of these compounds, especially the one derived from benzaldehyde **1'b**, to be cleaved by organolithium , is so high that even phenyl- and methyl lithium, which are usually inert towards open chain selenoacetals,[3] efficiently react on **1'b** (Scheme 3, entries d,e) .

The reactivity of 4,6-dimethyl-1,3-diselenanes **1"**, bearing two methyl substituents at C-4 and C-6 is more complex and depends upon the nature of the substituent present at C-2. Thus 4,6-dimethyl-1,3-diselenanes derived from formaldehyde **1"a** and acetaldehyde **1"c** are exclusively metallated and provide the 2-lithio-1,3-diselenanes **2"a** and **2"c** (*n*- and *s*-BuLi, THF-hexanes, -78°C) under conditions which lead to the C-Se bond cleavage with other selenoacetals[1-3] including cyclic derivatives **1'** (see above) (Scheme 4).

Scheme 4



Entry	Starting material	R$_1$	R$_2$	Conditions	E'	Product	R	E	Yield in 3" % (*trans/cis* ratio)
a	**1"a**	H	H	*n*-BuLi, 0.5 h	PhCH=O	**3"a**	H	PhCHOH	74% (100/0)
b	**1"c**$_{cis}$[+]	H	Me	*n*-BuLi, 0.5 h	PhCH=O	**1"c**$_{cis}$	H	Me	no reaction
c	**1"c**$_{cis}$	H	Me	*tert*-BuLi, 3h	PhCH=O	**1"c**$_{cis}$	H	Me	no reaction
d	**1"c**$_{cis}$	H	Me	*sec*-BuLi, 2h	PhCH=O	**3"c**	Me	PhCHOH	47% (99/1)
e	**1"c**$_{cis}$	H	Me	*sec*-BuLi, 6h	PhCH=O	**3"c**	Me	PhCHOH	78% (99/1)
f	**1"b**$_{cis}$	H	Ph	PhLi, HMPA, 1 h	MeI	**3"b**	Ph	Me	70% (100/0)
g	**1"b**$_{cis}$	H	Ph	MeLi, HMPA, 1h	MeI	**3"b**	Ph	Me	60% (100/0)
h	**1"b**$_{trans}$	Ph	H	PhLi, 0.75 h	MeI	**3"b**	Ph	Me	68% (100/0)
i	**1"b**$_{trans}$	Ph	H	MeLi, 0.75 h	MeI	**3"b**	Ph	Me	65% (100/0)

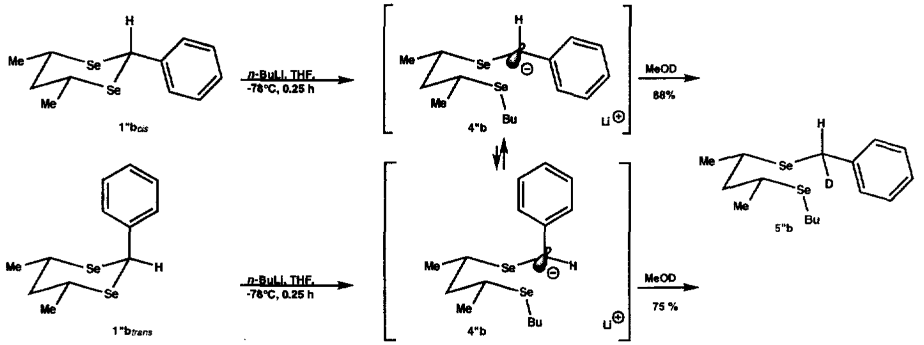
[+] *Trans* and *cis* refer to the stereochemistry of the substituent at C-2 relative to the methyl substituent at C-2 or C-4.

Metallation is effective with the whole set of butyllithiums[5] on the parent compound **1"a** (Scheme 4, entries a) but requires the use of *sec*-BuLi on the 2-methyl substituted derivative **1"c** (Scheme 4, compare entries d,e to b,c). Neither *n*-BuLi nor *tert*-BuLi react in THF with **1"c**$_{cis}$ (Scheme 4, entries b,c). Trapping of the resulting organolithium intermediate **2"c**, with benzaldehyde leads to the corresponding β-hydroxyalkylselenoacetal **3"c** bearing the incoming group in equatorial position (scheme 4, entry d,e). This is produced as a single stereoisomer attesting thus the high propensity of axial lithio derivative **2"c** to epimerise.[1,6]

As expected from our previous work,[1] metallation is slower with the *cis*-2,4,6-trimethyl-1,3-diselenane **1"c**$_{cis}$ than with its *trans*-stereoisomer **1"c**$_{trans}$.[6] The latter is in fact selectively cleaved on reaction of *sec*-BuLi with a 1/1 mixture of *cis/trans* stereoisomers **1"c** and leads on further reaction with benzaldehyde to the β-hydroxyalkylselenoacetal **3"c** (47% yield), besides substantial amounts of unreacted starting material **1"c** in which the *cis*-stereoisomer mainly prevails (*cis/trans* ratio : 90/10).

4,6-Dimethyl-1,3-diselenanes **1"b**$_{cis}$ and **1"b**$_{trans}$ bearing a phenyl group at C-2 are not metallated by butyllithiums but are instead cleaved providing the α-selenoalkyllithium **4"b** then the deuterated selenides **5"b** on further reaction with deuteromethanol (Scheme 5).

Scheme 5



These results are quite surprising since we would have expected that the presence of the phenyl group on the 4,6-dimethyl-1,3-diselenane skeleton **1"** would have enhanced, especially on **1"b**$_{trans}$, their aptitude to be metallated (Scheme 4). The high propensity of 2-aryl-1,3-diselenanes **1"b** to be cleaved might be due to extra stabilization of unshared electrons of the carbanion **4"b** by the phenyl ring if it adopts the conformation presented on Scheme 5.[7,8] *Sec*- as well as *tert*-butyllithiums display[5] the same reactivity as *n*-butyllithium towards **1"b** whereas methyllithium and phenyllithium which are usually not incline to cleave selenoacetals[3] act as bases. The *trans*-derivative **1"b**$_{trans}$ the most acidic of the two diastereoisomers of **1"b** (Scheme 4, entries h,i), is readily metallated in THF at -78 °C whereas its *cis*-stereoisomer **1"b**$_{cis}$ requires the presence of HMPA for the same purpose (Scheme 4, entries f,g).

The reactions described in this section complement those already reported[1] and allows the synthesis of the whole series of 2-lithio-4,6-dimethyl-1,3-diselenanes **2"** unavailable, with the exception of **2b**, from 4,6-dimethyl-1,3-diselenanes **1"** and lithium amides.[1,9]

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4. The cleavage by BuLi of the C-Se bond of diselenanes derived from ketones has been already described : (a) Krief, A.; Badaoui, E.; Dumont, W. *Tetrahedron Lett.* **1993**, *34*, 8517 (b) Reich, H.J.; Bowe, M.D. *J. Am. Chem. Soc.* **1990**, *112*, 8994.
5. These results will be disclosed in the full paper.
6. For related results on 1,3-dithianes : (a) Hartmann, A. A.; Eliel, E. L. *J. Am. Chem. Soc.* **1971**, *93*, 2572 (b) Eliel, E. L.; Abatjoglou, A. G.; Hartmann, A. A. *J. Am. Chem. Soc.* **1972**, *94*, 4786 (c) Eliel, E. L.; Hartmann, A. A.; Abatjoglou, A. G. *J. Am. Chem. Soc.* **1974**, *96*, 1807 (d) Eliel, E. L. *Tetrahedron* **1974**, *30*, 1503 (e) Abatjoglou, A. G.; Eliel, E. L.; Kuyper, L. F. *J. Am. Chem. Soc.* **1977**, *99*, 8262 (f) Jernigan, M. T.; Eliel, E. L. *J. Am. Chem. Soc.* **1995**, *117*, 9638.
7. The authors thank Prof. T. Cohen for a valuable discussion on that matter during his visit to Namur.
8. We have previously described that related 2-phenyl-1,3-dithianes possess also a very high propensity to be cleaved by *n*-BuLi and therefore that this reagent prefers to react on the sulfur atom rather than on the hydrogen attached on C-2, as it is usually the case, with others 1,3-dithianes : Krief, A.; Kenda, B.; Barbeaux, P. *Tetrahedron Lett.* **1991**, *32*, 2509.
9. We nevertheless described that the related potassium derivatives $\mathbf{2}''_{K}$ can be produced on reaction of **1**" with the strongest potassium amide (KDA).[1]

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