



Pergamon

Tetrahedron Letters 40 (1999) 6571-6575

TETRAHEDRON
LETTERS

Original synthesis and reactivity of 1,3-benzodiselenolanes

Alain Krief * and Laurent Defrère

Laboratoire de Chimie Organique de Synthèse, Department of Chemistry, Facultés Universitaires Notre-Dame de la Paix,
61 rue de Bruxelles, B-5000 Namur, Belgium

Received 3 June 1999; accepted 25 June 1999

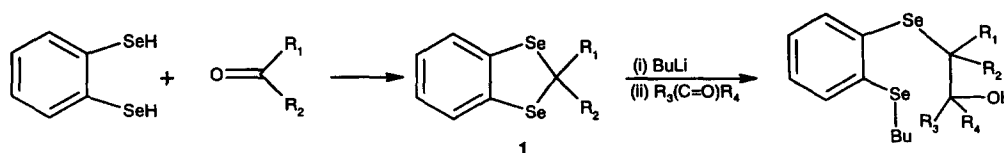
Abstract

Preliminary results concerning the synthesis and reactivity of 1,3-benzodiselenolanes towards lithium diisopropylamide and butyllithiums are described as well as original syntheses of aromatic compounds bearing sulfur and selenium atoms. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Selenoacetals are versatile reagents in organic synthesis.¹ Most of the synthetic work has been carried out with compounds derived from the phenylseleno or the methylseleno series, and only recently results concerning 1,3-diselenanes, their cyclic analogues, have appeared in the literature.² Although both phenylseleno and methylseleno series are efficiently reduced to α -selenoalkyllithiums on reaction with butyllithiums, only the former series can be metallated with metal amides to produce α,α -bis(selenoalkyl)lithiums which play the role of acyl anion equivalents.^{1b-e}

The synthesis of selenoacetals is best achieved from carbonyl compounds and a selenol in the presence of an acid.^{1a,e} The reaction is quite general but we experienced some difficulties with aromatic carbonyl compounds and with the most hindered ketones such as diisopropyl ketone. The latter has been quite properly transformed to the related methylselenoacetal but all the attempts to generate the phenylselenoacetal met with failure.^{1a,e}

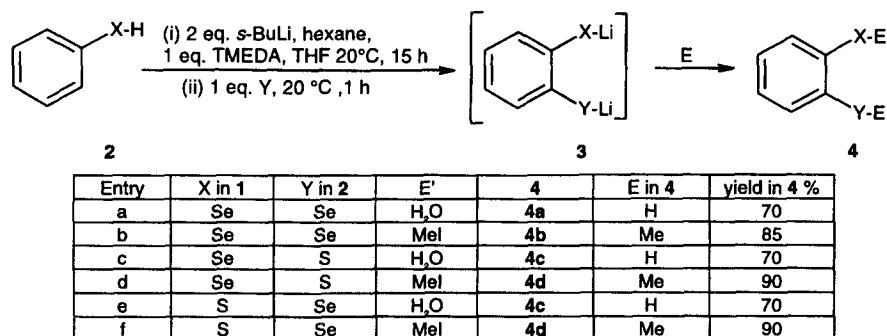
We now report our preliminary results concerning the synthesis of 1,3-benzodiselenolanes **1c** which were expected to be more easily prepared than their open chain analogues and the study of their reactivity towards alkyllithiums and LDA (Scheme 1).



Scheme 1.

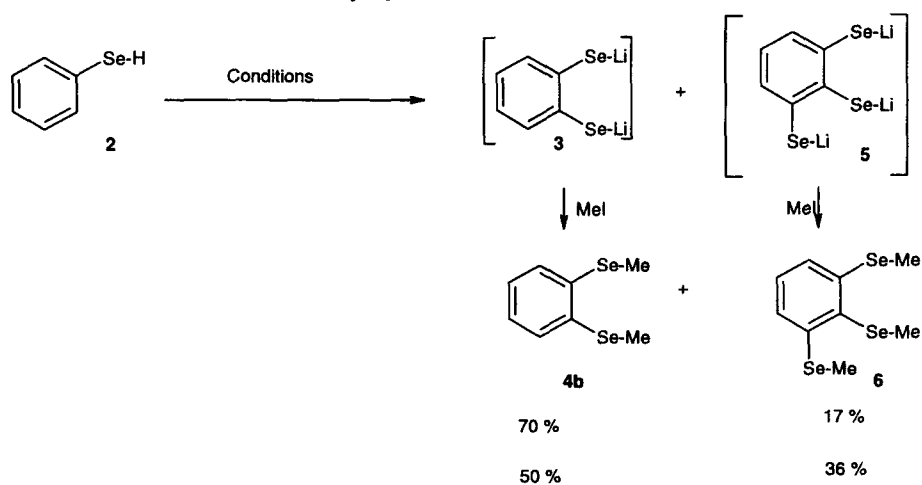
* Corresponding author.

The synthesis of 1,2-benzene diselenol^{3,4} **4a** was readily achieved from phenylselenol, *n*-butyllithium (2 equiv.), TMEDA (1 equiv.) and elemental selenium (Se⁰, 1 equiv.) (hexane, 20°C, 12 h, 75% after acid hydrolysis and distillation, Scheme 2) taking advantage of an *ortho*-metalation reaction.⁵



Scheme 2.

This reaction was extended to the synthesis of the mixed 2-selenol-benzenethiol **4c** (Scheme 2)⁶ and of 1,2,3-benzene triselenolate (Scheme 3). The former compound has been synthesized either from phenylselenol and sulfur [(i) 2 equiv. *s*-butyllithium in hexane, 1 equiv. TMEDA, 1 equiv. S⁰, hexane, 20°C, 12 h; and (ii) acid hydrolysis and distillation, Scheme 2, entry c] or from phenylthiol and selenium [(i) 2 equiv. *s*-butyllithium in hexane, 1 equiv. TMEDA, 1 equiv. Se⁰, hexane, 20°C, 12 h; and (ii) acid hydrolysis and distillation, Scheme 1, entry e].



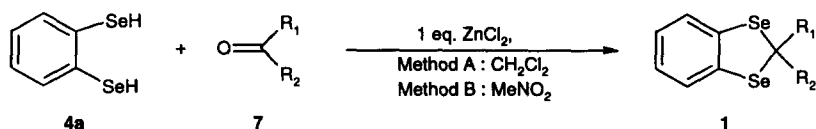
Scheme 3. Conditions A: (i) 3 Equiv. *s*-BuLi, hexane, 2 equiv. TMEDA, 20°C, 15 h; (ii) 2 equiv. Se. 20°C. 1 h. Conditions B: (i) 2 equiv. *s*-BuLi, hexane, 1 equiv. TMEDA, 20°C, 15 h; (ii) 1 equiv. Se, 20°C, 1 h; (iii) 1 equiv. *s*-BuLi, hexane, 1 equiv. TMEDA, 20°C, 15 h; (iv) 1 equiv. Se

Alkylation of **3** with methyl iodide (1 equiv., 20°C, 0.5 h) allows the high yield synthesis of the 1,2-di(methylseleno)-benzene **4b** (Scheme 2, entry b) or the 2-methylseleno-thioanisole⁷ **4d** (Scheme 2, entries d, f).

Introduction of the third selenium atom on the benzene ring was not very efficient. The one-pot reaction implying phenylselenol, *sec*-butyllithium (3 equiv.), TMEDA (2 equiv.) and elemental selenium (2 equiv.), carried out at 20°C, leads after alkylation with methyl iodide (3 equiv.) to 1,2-dimethylselenobenzene **4b** (70%) and a small amount of 1,2,3-trimethylselenobenzene **6** (17%). The yield in the latter was improved (36%) when phenylselenol was treated sequentially: (i) with *s*-

butyllithium in hexane, TMEDA and elemental selenium as described above; (ii) repeating the same process on the *ortho*-dilithiodiselenolate intermediate **3** (1 equiv. *s*-butyllithium in hexane, 1 equiv. TMEDA, 1 equiv. Se⁰, hexane, 20°C, 24 h); and (iii) quenching the reaction with stoichiometric amount of methyl iodide.

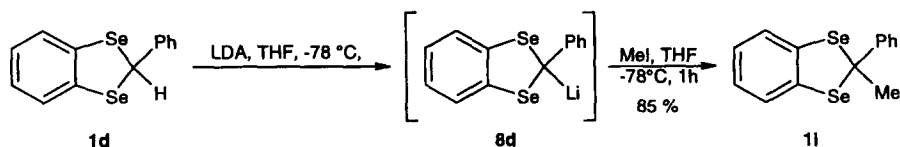
Diselenol **4a** has been used for the selenoacetalization of various aldehydes and ketones using the conditions we routinely used with phenyl and methylselenol (carbonyl compound, 1 equiv. of the diselenol **4a**, 0.5 equiv. of anhydrous zinc chloride, CH₂Cl₂, 20°C).^{1a} The results gathered in Scheme 4 show that the reaction takes place efficiently with: (i) aldehydes including formaldehyde, aromatic or hindered aldehydes such as isovaleraldehyde (Scheme 4, entries a–d); and (ii) dialkyl ketones including quite hindered ketones such as *tert*-butyl methyl ketone (Scheme 4, entries f–g) and methyl phenyl ketone (Scheme 4, entry i). Selenoacetalization using **4a** proved to be far more efficient than the one involving phenylselenol and closely related to the one using methylselenol. This reaction did not, however, work with diisopropyl ketone (Scheme 4, entry f), *tert*-butyl ethyl ketone (Scheme 4, entry h), and even more hindered ketones such as 2,2,6,6-tetramethylcyclohexanone (Scheme 4, entry j) or di-*tert*-butyl ketone (Scheme 4, entry k). Other conditions which proved to be more efficient than the ones used above^{1a} were tested on diisopropyl ketone (Scheme 4, entry f). Titanium tetrachloride allows the synthesis of the desired selenoacetal but in very poor yield, whereas zinc chloride in nitromethane proved to be by far more efficient in this specific case. Unfortunately, however, even these conditions (Method B) do not permit the selenoacetalization of the other hindered ketones with the exception of a symbolic yield from *tert*-butyl ethyl ketone (Scheme 4, Method B, entry h).



Entry	R ₁	R ₂	1	Method A 1 % (time/h)	Method B 1 % (time/h)
a	H	H	1a	74 (1)	
b	Me	H	1b	72 (1)	
c	<i>t</i> -Bu	H	1c	74 (3)	
d	Ph	H	1d	74 (1)	
e	Me	Me	1e	74 (1)	
f	<i>i</i> -Pr	<i>i</i> -Pr	1f	0 (24)	70 (10)
g	<i>t</i> -Bu	Me	1g	76 (24)	
h	<i>t</i> -Bu	Et	1h	0 (24)	8 (24)
i	Ph	Me	1i	66 (10)	
j	Me ₂ C-CH ₂ -CH ₂ -C-Me ₂		-	0 (24)	0 (24)
k	<i>t</i> -Bu	<i>t</i> -Bu	-	0 (24)	

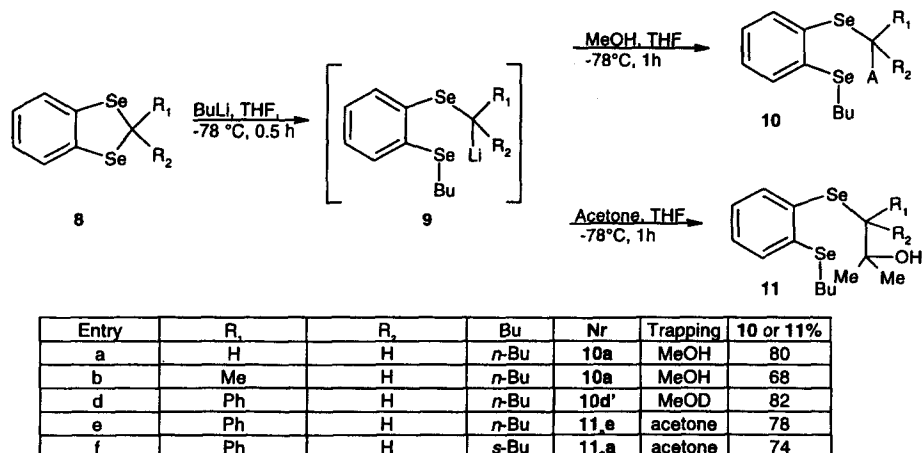
Scheme 4.

We have performed a preliminary screening of the reactivity of the selenoacetals **1** towards LDA and butyllithiums. Thus the selenoacetal **1i** has been synthesized from **1d** by sequential metallation and alkylation ((i) 1.1 equiv. LDA, THF, -78°C, 0.5 h; and (ii) MeI, THF, -78°C to +20°C, 0.5 h, 85% yield, Scheme 5).⁸



Scheme 5.

The Se/Li exchange also takes place efficiently when the selenoacetals **1** are reacted with *n*-butyllithium (1 equiv., THF, -78°C , 1 h) providing after methanolysis at that temperature the corresponding 2-alkylseleno-1-butylseleno benzenes **10** in good yields (Scheme 6). The reaction has been successfully achieved on a wide range of selenoacetals including those derived from formaldehyde **1a**, acetaldehyde **1b**, benzaldehyde **1c** and acetone **1d**.



Scheme 6.

A similar reaction, performed on **1c** with *s*-butyllithium, provides the 2-benzylseleno-1-*sec*-butylseleno benzene **11_c** after trapping of the intermediate α -selenoalkyllithium **9_c** with methanol and the β -hydroxyalkylselenide **11_c** if acetone is reacted instead. Unfortunately, trapping of the α -selenoalkyllithium intermediates **9_c** with methyl iodide was not successful. We are currently trying: (i) to understand the reasons of such behavior; and (ii) to use the β -hydroxyalkylselenides **11** for the synthesis of selenium free compounds.^{1b-e}

Acknowledgements

F.R.I.A. (Fonds pour la Formation à la Recherche dans l'Industrie et l'Agriculture, Bruxelles, Belgium) is greatly acknowledged for its financial support (fellowship to L.D.).

References

- (a) Clarembeau, M.; Cravador, A.; Dumont, W.; Hevesi, L.; Krief, A.; Lucchetti, J.; Van Ende, D. *Tetrahedron* **1985**, *41*, 4793–4812. (b) Krief, A. *Tetrahedron* **1980**, *36*, 2531–2640. (c) Krief, A.; Dumont, W.; Cravador, A.; Denis, J. N.; Halazy, S.; Hevesi, L.; Labar, D.; Lucchetti, J.; Rémon, J.; Sevrin, M.; Van Ende, D. *Bull. Soc. Chim. Fr.* **1980**, *11–12* II, 519–529 (d) Krief, A. In *The Chemistry of Selenium and Tellurium Compounds*; Patai, S., Ed.; John Wiley & Sons, 1987; Vol. 2, pp. 675–764. (e) Krief, A. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G.; McKillop, A., Eds.; Pergamon: Oxford, 1995; Vol. 11, pp. 516–569, and references cited therein.
- (a) Krief, A.; Defrère, L. *Tetrahedron Lett.* **1996**, *37*, 8011–8014. (b) Krief, A.; Defrère, L. *Tetrahedron Lett.* **1996**, *37*, 8015–8018.
- Related strategies have been used for the synthesis of: (a) benzene 1,3-dithiol from phenylthiol and sulfur: Giolando, D. M.; Kirschanbaum, K. *Synthesis* **1992**, 451–452; and (b) aromatic diselenol from trimethylsilylarylselenides and selenium: Ogawa, S.; Kikuchi, T.; Niizuma, S.; Sato, R. *J. Chem. Soc., Chem. Commun.* **1994**, 1593–1594.

4. 1,2-Benzenediselenol or related 1,2-benzenediselenolates have been prepared: (a) from 1,2-dibromo benzene, Mg/Hg-Li and Se⁰: (i) Krief, A. *Tetrahedron*, **1986**, *49*, 1209–1252, (ii) Lestrup, K. A.; Lee, M.; Wiygul, F. M.; Kistenmacher, T. J.; Cowan, D. O. *J. Chem. Soc., Chem. Commun.* **1983**, 294–295; (b) from 1,2-benzenediselenyl dibromide and sodium in liquid ammonia: Lambert, C.; Christiaens, L. *Tetrahedron Lett.* **1984**, *25*, 833–834; and (c) by reduction by sodium borohydride of poly-(1,2-benzenediselenide) itself prepared from 1,2-dibromobenzene and disodium diselenide in DMF: Sandman, D. J.; Stark, J. C.; Acampora, L. A.; Samuelson, L. A.; Allen, G. W.; Jansen, S.; Jones, M. T.; Foxman, B. M. *Mol. Cryst. Liq. Cryst.* **1984**, *107*, 1–8.
5. Snieckus, V. *Chem. Rev.* **1990**, *90*, 879–920.
6. The same compound has already been prepared by reduction of 2-methylseleno-thioanisole.⁷
7. Pierpont, C. G.; Corden, B. J.; Eisenberg, R. *J. Chem. Soc., Chem. Commun.* **1969**, 401–402.
8. This compound is identical to the one we have synthesized from acetophenone and 1,2-benzenediselenol (see Scheme 4, entry i).