Original synthesis and reactivity of 1,3-benzodiselenolanes

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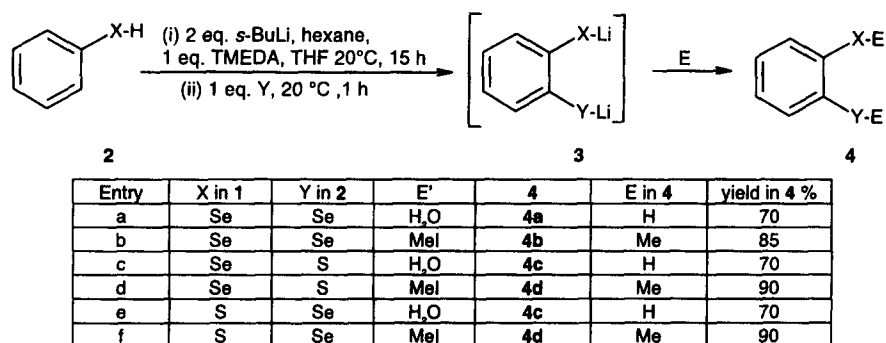
We now report our preliminary results concerning the synthesis of 1,3-benzodiselenolanes 1c which were expected to be more easily prepared than their open chain analogues and the study of their reactivity towards alkyllithiums and LDA (Scheme 1).
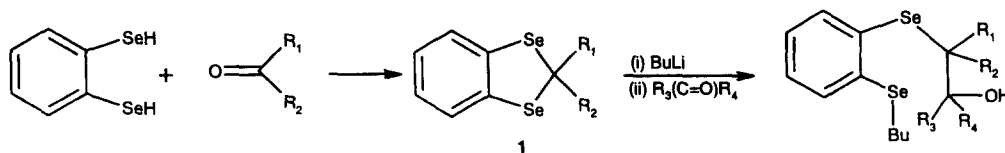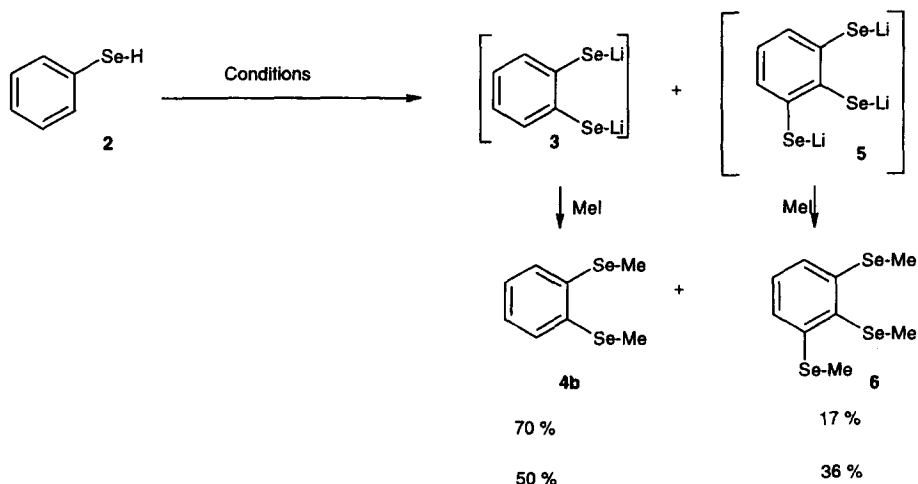

Scheme 1.

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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 (Se°, 1 equiv.) (hexane, 20°C, 12 h, 75% after acid hydrolysis and distillation, Scheme 2) taking advantage of an *ortho*-metalation reaction.[5]

Entry	X in 1	Y in 2	E'	4	E in 4	yield in 4 %
a	Se	Se	H₂O	4a	H	70
b	Se	Se	MeI	4b	Me	85
c	Se	S	H₂O	4c	H	70
d	Se	S	MeI	4d	Me	90
e	S	Se	H₂O	4c	H	70
f	S	Se	MeI	4d	Me	90

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. S°, 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. Se°, 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-thioanisole[7] **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. Se°, 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, CH_2Cl_2, 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). Selenoacatalization 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).
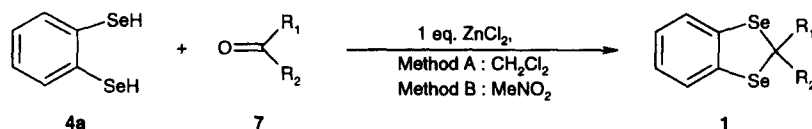
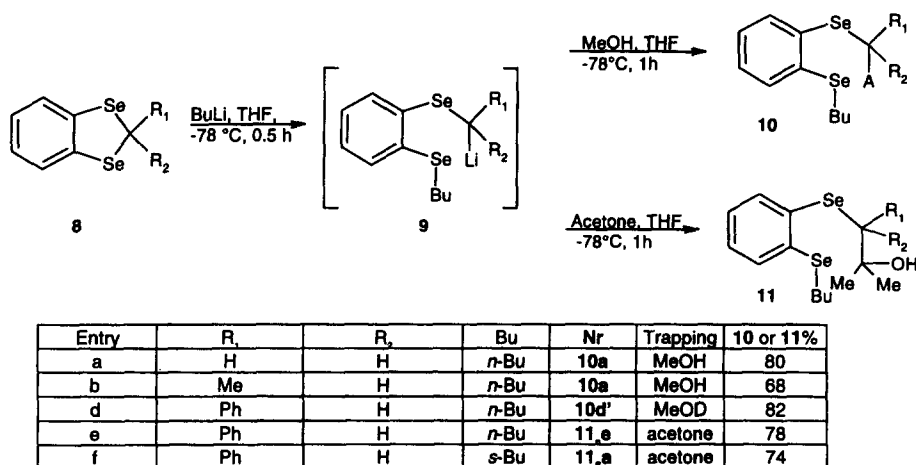| Entry	R₁	R₂	1	Method A 1 % (time/h)	Method B 1 % (time/h)
a	H	H	**1a**	74 (1)	
b	Me	H	**1b**	72 (1)	
c	*t*-Bu	H	**1c**	74 (3)	
d	Ph	H	**1d**	74 (1)	
e	Me	Me	**1e**	74 (1)	
f	*i*-Pr	*i*-Pr	**1f**	0 (24)	70 (10)
g	*t*-Bu	Me	**1g**	76 (24)	
h	*t*-Bu	Et	**1h**	0 (24)	8 (24)
i	Ph	Me	**1i**	66 (10)	
j	Me₂C-CH₂-CH₂-CH₂-C-Me₂		-	0 (24)	0 (24)
k	*t*-Bu	*t*-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]
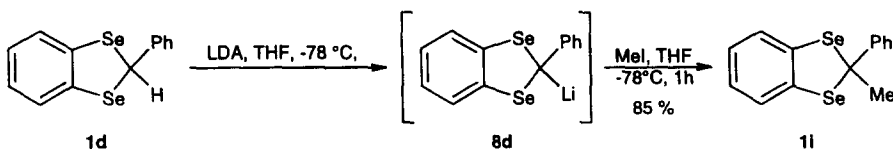
Scheme 5.

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**.

Entry	R₁	R₂	Bu	Nr	Trapping	10 or 11%
a	H	H	*n*-Bu	10a	MeOH	80
b	Me	H	*n*-Bu	10a	MeOH	68
d	Ph	H	*n*-Bu	10d'	MeOD	82
e	Ph	H	*n*-Bu	11,e	acetone	78
f	Ph	H	*s*-Bu	11,a	acetone	74

Scheme 6.

A similar reaction, performed on **1c** with *s*-butyllithium, provides the 2-benzylseleno-1-*sec*-butylseleno benzene **11ₛc** after trapping of the intermediate α-selenoalkyllithium **9ₛc** with methanol and the β-hydroxyalkylselenide **11ₛc** if acetone is reacted instead. Unfortunately, trapping of the α-selenoalkyllithium intermediates **9ₛc** 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

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6. The same compound has already been prepared by reduction of 2-methylseleno-thioanisole.[7]

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8. This compound is identical to the one we have synthesized from acetophenone and 1,2-benzenediselenol (see Scheme 4, entry i).