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Methane-Derived Polyanionic Synthons from Bis(phenylthio)methane

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Abstract: Successive treatment of bis(phenylthio)methane (**1**) with (a) *n*-butyllithium at 0°C, (b) a carbonyl compound [^{t}BuCHO, Me_2CO, Et_2CO, $(CH_2)_5CO$] at -40°C, (c) lithium and a catalytic amount of DTBB (5%) and (d) a second carbonyl compound [^{i}PrCHO, ^{t}BuCHO, Me_2CO, Et_2CO, $(CH_2)_5CO$], both at -78°C, leads, after hydrolysis, to the expected dihydroxy thioethers **5**. When, after step (d), a second DTBB-catalysed lithiation is performed at temperatures ranging between -78 and 20°C, the corresponding allylic alcohols **7** are isolated. Finally, treatment of compounds **7** with 6 M hydrochloric acid gives 1,3-dienes **10** in almost quantitative yield. © 1999 Elsevier Science Ltd. All rights reserved.

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Since the pioneering reports of Corey and Seebach,[1] the formation of a carbanionic center at a position α-to two sulfur atoms, and further reaction with an electrophile, has played a fundamental role in organic synthesis. Sulfur-stabilised carbanions are one of the most typical acyl anion equivalents[2] showing umpolung reactivity.[3] On the other hand, in the last few years, new methodology for the preparation of organolithium intermediates[4] has been developed consisting of a reductive lithiation of phenyl thioethers,[5] using a stoichiometric[6] or catalytic[7,8] amount of an arene as an electron carrier reagent. Taking into account both these methodologies, α-deprotonation of dithioacetals/sulfur-lithium exchange, we thought it interesting to combine them in order to generate *sp*^{2} or *sp*^{3} polylithium synthons.[9,10] In this paper we explore this possibility starting from a simple precursor bis(phenylthio)methane.

Deprotonation of the dithioacetal **1** with *n*-butyllithium in THF at 0°C followed by reaction with a carbonyl compound [^{t}BuCHO, Me_2CO, Et_2CO, $(CH_2)_5CO$] at -40°C gave an alcoholate **2**, which was lithiated *in situ* by means of an excess of lithium and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB; 5 mol %)[11] at -78°C to give a β-oxido organolithium intermediate **3**.[12] The reaction of this dianion with a second carbonyl compound [^{i}PrCHO, ^{t}BuCHO, Me_2CO, Et_2CO, $(CH_2)_5CO$] at -78°C gave the corresponding dialcoholate **4**

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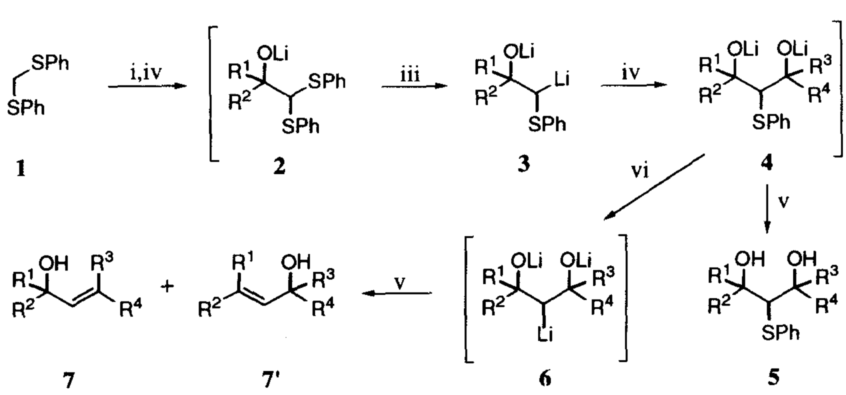
which, after hydrolysis with water, yielded the expected dihydroxy thioethers **5** (Scheme 1 and Table 1). Intermediates **4** were also lithiated using the same procedure as for the transformation **2** → **3**, giving a trianionic species **6**, which was unstable under the reaction conditions used (-78 to 20°C), giving a corresponding mixture of allylic alcohols **7**+**7'**[13] (Scheme 1, Chart 1 and Table 2).



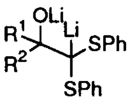
Scheme 1. *Reagents and conditions*: i, ^{n}BuLi, THF, 0°C; ii, ^{t}BuCHO, or Me_2CO, or Et_2CO, or $(CH_2)_5CO$, -40°C; iii, Li, DTBB cat. (5 mol %), -78°C; iv, ^{i}PrCHO, or ^{t}BuCHO, or Me_2CO, or Et_2CO, or $(CH_2)_5CO$, -78°C; v, H_2O; vi, Li, DTBB cat. (5 mol %), -78 to 20°C.

Table 1. Preparation of Phenylthiodiols **5**

Entry	No.	R1	R2	R3	R4	Yield (%)[a]
1	**5a**	H	^{t}Bu	H	^{t}Bu	45[b]
2	**5b**	Me	Me	Me	Me	50
3	**5c**	Et	Et	Me	Me	65
4	**5d**	Et	Et	Et	Et	48
5	**5e**	$(CH_2)_5$		H	^{i}Pr	55[c]
6	**5f**	$(CH_2)_5$		H	^{t}Bu	75[c]
7	**5g**	$(CH_2)_5$		H	Ph	75[c]
8	**5h**	$(CH_2)_5$		Me	Me	46
9	**5i**	$(CH_2)_5$		Et	Et	38
10	**5j**	$(CH_2)_5$		$(CH_2)_5$		52

[a] Isolated yield of pure compounds **5** (≥95% from GLC and/or 300 MHz ^1H NMR) after column chromatography (silica gel, hexane/ethyl acetate), based on the starting dithioacetal **1**. [b] A *ca.* 1:1:1 diastereomeric mixture (75 MHz ^{13}C NMR) was obtained. [c] A *ca.* 1:1 diastereomeric mixture (75 MHz ^{13}C NMR) was obtained.

Attempts to deprotonate intermediates **2** or **4** with *n*-butyllithium *in situ* under different reaction conditions to give polyanionic species **8** or **9**, respectively, failed.



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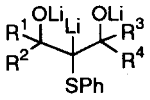

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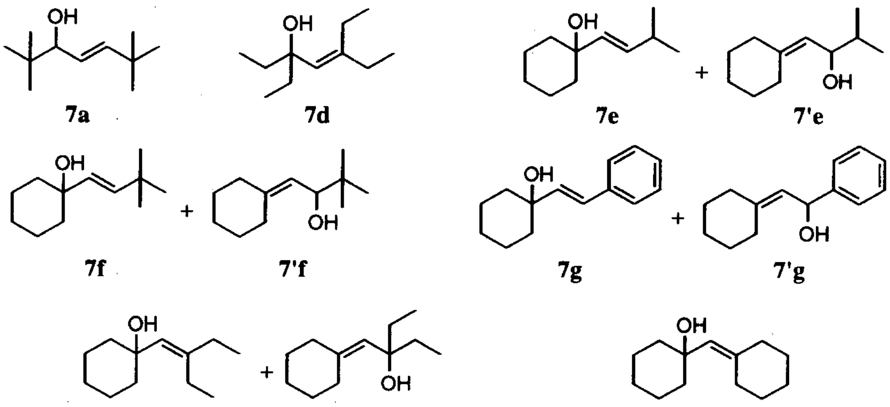
Table 2. Preparation of Allylic Alcohols **7** and Dienes **10**

Entry	Starting material	Allyl alcohol		Diene	
		No.	Yield (%)[a,b]	No.	Yield (%)[a,c]
1	**5a**	**7a**	42	--	--
2	**5d**	**7d**	32	--	--
3	**5e**	**7e+7'e**	62 (0.4:1)	**10e**	>95
4	**5f**	**7f+7'f**	56 (1:1)	**10f**	>95
5	**5g**	**7g+7'g**	29 (0.4:1)	**10g**	>95
6	**5i**	**7i+7'i**	40 (1:1)	**10i+10'i**	>95 (1:0.3)
7	**5j**	**7j**	73	**10j**	>95

[a] Isolated yield of pure compounds **7** or **10** (≥95% from GLC and/or 300 MHz ^{1}H NMR) based on the starting materials **5** or **7**; in parenthesis the corresponding regioisomers ratio from 75 MHz ^{13}C NMR. [b] After column chromatography (silica gel, hexane/ethyl acetate). [c] Crude.



7a **7d** **7e** **7'e** **7f** **7'f** **7g** **7'g** **7i** **7'i** **7j**

Chart 1

Finally, we treated either pure allylic alcohol **7j** (Table 2, entry 7) or the mixture **7+7'** (Table 2, entries 3-6) with a few drops of 6 M hydrochloric acid in chloroform at 20°C, affording 1,3-dienes **10** in almost quantitative yield (Chart 2 and Table 2). Only in one case (**10i+10'i**) was a mixture of regioisomers obtained.

In conclusion, we have reported here a simple way to prepare 1,3-dihydroxythioethers **5**, allylic alcohols **7** and 1,3-dienes **10** starting from a very simple precursor **1** and using a combination of α-deprotonation/sulfur-lithium exchange.

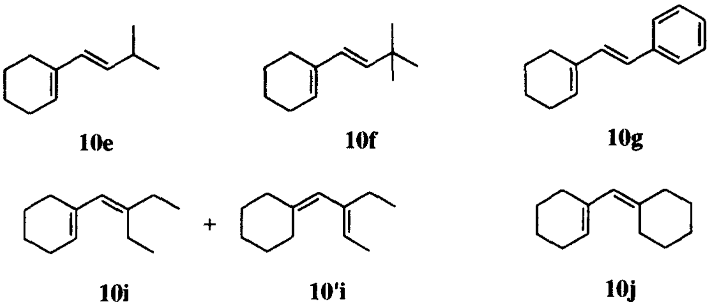


Chart 2

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