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Unexpected cleavage of tetrahydrofuran by catalytic reductive lithiation[†]

Stéphane Streiff, Nigel Ribeiro and Laurent Désaubry*
UMR 7509, Centre de Neurochimie, 5, rue Blaise Pascal, 67084 Strasbourg Cedex, France.
E-mail: desaubry@chimie.u-strasbg.fr; Fax: +33 (0)3 88 60 76 20; Tel: +33 (0)3 88 45 67 33

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DBB, an electron transporter, can open THF at room temperature under sonication without any Lewis acid activation. This feature was successfully exploited in the straightforward synthesis of bis-silanes.

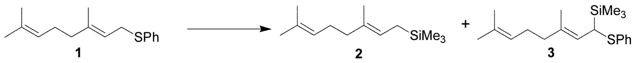
Over the past two decades, reductive lithiations catalyzed by electron transporters, such as naphthalene or 1,4′-di-*tert*-butylbiphenyl (DBB), have been established as some of the most general and versatile methods of organolithium production.[1] Reductive lithiation of phenylthioethers, in particular, has found many useful applications. These reactions are performed in THF. The only alternative solvent that has been used successfully is dimethyl ether.[2]

During the course of our studies on the synthesis of allylsilanes by catalytic reductive lithiation, we observed that allylthioethers were deprotonated and not reduced, depending on reaction conditions. The reductive lithiation of phenylthioethers has been known for over 20 years, and our observation was in apparent contradiction with previous reports.[1,3] This led us to investigate the cause of this aberrant behaviour.

We examined the conditions of formation of the reducing agent LiDBB (Table 1). To prepare this reagent, an excess of lithium and a catalytic amount of DBB were sonicated for less than 5 minutes at room temperature to afford a dark-green solution (conditions A). This was immediately cooled to the desired temperature. In the second procedure (conditions B) the time of sonication was extended to 1 h.

When LiDBB was prepared within 5 minutes, the reductive lithiation of **1** occurred exclusively (Table 1, entries 1–2). On the other hand, when it was prepared according to conditions B, we obtained a substantial amount of silylated thioether **3** at −42 °C (entry 4). This reaction was exclusive at −78 °C (entry 3). One possible reason for these observations which came to mind is that THF might be cleaved into 4-lithiobutoxide, which would deprotonate the thioethers. Such a reductive cleavage of THF has been reported, albeit under more drastic conditions. Eisch was the first to note that THF could be cleaved by lithium in presence of an arene.[4]

Table 1 Effect of the preparation of LiDBB on the reductive silylation of thioether **1**



Entry	Conditions[a]	T/°C	Isolated yield (%)	**2** : **3**
1	A	−78	71	100 : 0
2	A	−42	72	100 : 0
3	B	−78	69	0 : 100
4	B	−42	59	88 : 12

[a] Conditions A: a mixture of Li and DBB in THF was sonicated for less than 5 minutes at r.t.; conditions B: sonication for 1 hour at r.t. **1** was then added at the indicated temperature. When the medium recovered its dark-green colour, TMSCl was added.

This author showed that refluxing a mixture of biphenyl and lithium in THF affords some butanol after hydrolysis of the reaction system. At that temperature, 4-lithiobutoxide decomposed, and its formation was not quantified. Later, Cohen showed that, in presence of boron trifluoride etherate, LiDBB cleaves THF instantaneously at a temperature as low as −78 °C.[5] This reactivity stems from the complexation of the oxygen atom by this strong Lewis acid. More recently, Yus and coworkers reported that the dilithium naphthalene dianion reacts slowly with THF at room temperature for 24 hours, affording after hydrolysis small amounts of butanol as well as products of condensation of naphthalene with THF.[6]

When we analyzed a solution of LiDBB prepared according to conditions B, we were pleased to notice the formation of a substantial amount of *n*-butanol (0.27 M). We quantitatively monitored, after hydrolysis, the formation of *n*-butanol by GC (Fig. 1). The efficiency of this process accounts well for the deprotonation of **1**, as depicted in Scheme 1. Entry 4 in Table 1 shows that the reductive lithiation of **1** is faster than its deprotonation by 4-lithiobutoxide at −42 °C. At −78 °C, it is the opposite (entry 3).

With few exceptions,[7] DBB-catalyzed lithiations do not involve extended sonication at room temperature, this may be why our observation had not been reported.[8]

We took advantage of the property of DBB to catalyse the reductive lithiation of both THF and thioethers, to synthesize the bis-silane **4** (Scheme 2). Thioether **1** was first treated as in entry 1 in Table 1, to afford the intermediary adduct **3**, which underwent a subsequent reductive lithiation overnight before it was quenched by TMSCl. The bis-silane **4** was obtained in 68% yield. This procedure

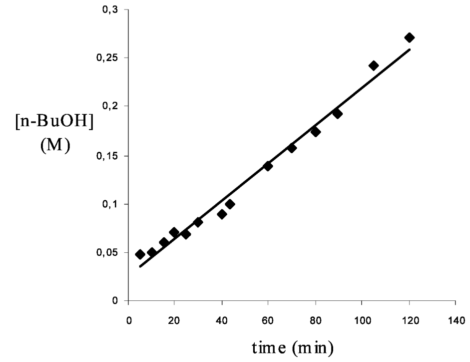
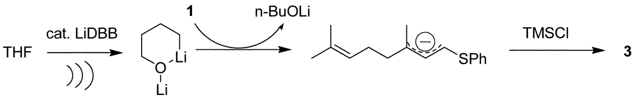
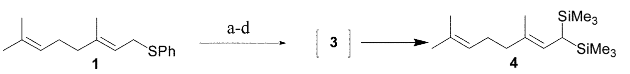


Fig. 1 Formation of n-butanol after hydrolysis of 0.1 M solution of DBB sonicated at r.t.



Scheme 1 Mechanism of formation of the silylated thioether **3**.



Scheme 2 (a) Li, cat. DBB, −78 °C, 4-lithiobutoxide, 30 min; (b) TMSCl, −78 °C; (c) 12 h, −78 °C; (d) TMSCl, −78 °C.

[†] Electronic supplementary information (ESI) available: experimental procedures, THF cleavage kinetics and the synthesis of compounds **2, 3, 4** and **6**. See http://www.rsc.org/suppdata/cc/b3/b312972a/

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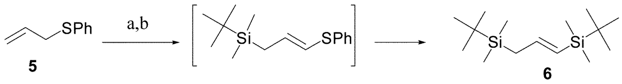
is particularly convenient. Compared to other methods, it does not require any preliminary titration and manipulation of a sensitive reagent. The reappearance of the original dark-green colour indicates that the deprotonation of the thioether is completed and the chlorosilane may be added. When this colour reappears, the reductive lithiation is completed and the second portion of TMSCl is added.

Gratifyingly, we were able to apply the same strategy to allylthioether **5** (Scheme 3). The bis-silane **6** was obtained in a 67% yield. This synthesis represents therefore an improvement of the published procedures that involved two steps.[9] This class of dinucleophilic reagents is useful in organic synthesis.[10]



Scheme 3 (a) Li, cat. DBB, −78 °C, 4-lithiobutoxide, 30 min; (b) TBDMSCl, −78 °C.

In summary, we have provided the first evidence that an electron transporter can cleave THF at room temperature by sonication. This feature was successfully exploited in the straightforward synthesis of bis-silanes **4** and **6**. Due to their usefulness in organic synthesis, the reductive lithiation reactions are still the subject of intensive development. Our finding that THF can be cleaved in mild conditions should be taken into account in the design of new lithiation reactions.

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Notes and references

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