# Pathways for decomposition of THF by organolithiums: the role of HMPA

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**The decomposition of THF by organolithiums in the presence of HMPA gives lithium but-3-en-1-oxide by a reverse 5-*endo-trig* ring opening.**

The susceptibility of THF, **1**, to deprotonation by strong organolithium bases[1,2] limits its use in organolithium reactions as temperatures rise above 0 °C. The half-life of *n*-BuLi in THF in the presence of TMEDA, for example, is 50 h at −20 °C, decreasing to 30 min. at +20 °C. *t*-BuLi has a half-life of only 45 min in THF, even at −20 °C.[3]

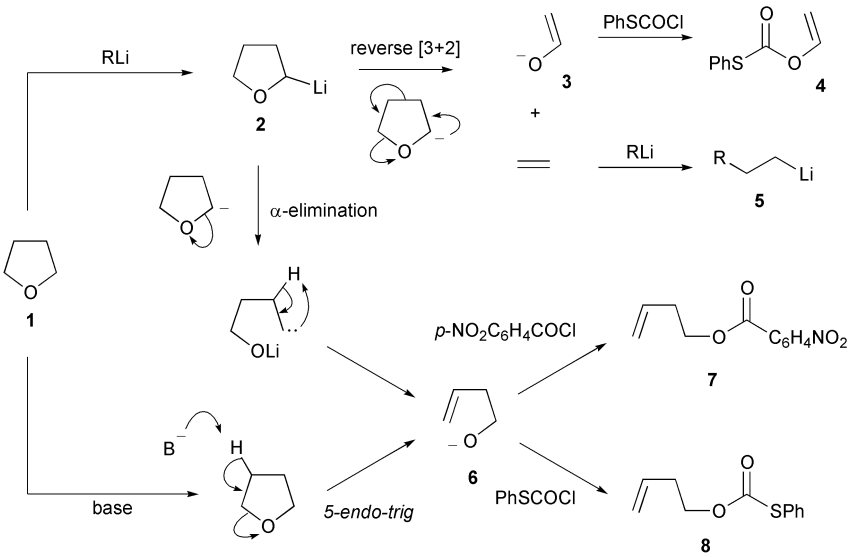
The principal pathway for decomposition of THF by alkyllithiums is deprotonation at C-2, α to oxygen, to give **2**, followed by a reverse [3 + 2] cycloaddition of the resulting anion to yield one molecule of ethylene plus one molecule of the lithium enolate of acetaldehyde, **3** (Scheme 1).[4] Both of these products have been trapped. Treatment of THF with *n*-BuLi and then phenyl thiochlorocarbonate, for example, gives good yields of the enol thiocarbonate **4**,[5] and THF decomposition provides a useful source of clean acetaldehyde enolate.[6,7] Ethylenated by-products from reactions of secondary and tertiary organolithiums in THF[7–11] can be accounted for by the intermolecular carbolithiation of THF-derived ethylene to give species such as **5**.

However, one observation contrasts starkly with these reports. Fleming *et al.*[12] showed that on quenching with *p*-nitrobenzoyl chloride a reaction in THF between phenyldimethylsilyllithium and a tertiary amide, the *p*-nitrobenzoate ester **7** of but-3-en-1-ol was isolated. The only conceivable origin of this ester is lithium but-3-en-1-oxide **6**, formed either by an alternative α-elimination of **2** or by the reverse 5-*endo-trig* (*i.e.*, Baldwin-disfavoured[13]) decomposition of THF initiated by deprotonation of THF at C-3. A similar reactions has been observed in a gas phase reaction between THF and hydroxide or amide ions,[14,15] and 5-*endo-trig* elimination of 3-metallated THF can be enforced by reaction of sodium with 3-chlorotetrahydrofuran.[16]

During some studies of our dearomatising anionic cyclisation,[17–19] which until recently[20] involved a slow reaction with a *t*-BuLi–HMPA mixture, we too observed by-products consistent with the formation of **6** from THF, and in this paper we report the result of a brief study into the factors controlling which decomposition products are formed.

Table 1, entries 1 and 2, shows the results of stirring a solution of *n*- or *t*-BuLi in THF and quenching the resulting solution with phenyl chlorothioformate.[5] In each case, a low to moderate yield of the enol thiocarbonate **4** was isolated. Entry 3 shows the result of adding 6 equiv. of HMPA before mixing *t*-butyllithium and THF. Instead of the enol thiocarbonate **4**, but-3-en-1-yl thiocarbonate **8** was isolated in 29% yield. Thiocarbonate **8** can only be fomed from the alkoxide **6**, the alternative elimination product of THF.

In order to clarify the factors governing the relative importance of these two decomposition pathways for THF, mixtures of THF and various additives were treated with alkyllithiums, quenched with phenyl thiochloroformate, and




**Scheme 1**

**Table 1** Decomposition of THF by alkyllithiums in the presence of additives

| Entry | Alkyllithium | Additive | Equiv. | Yield **4** (%)[a] | Yield **8** (%)[a] |
|---|---|---|---|---|---|
| 1 | *n*-BuLi | – | – | 26[b] | – |
| 2 | *t*-BuLi | – | – | 25[b] | – |
| 3 | *t*-BuLi | HMPA | 6 | – | 29[b] |
| 4 | *t*-BuLi | – | – | 38 | < 1 |
| 5 | *t*-BuLi | HMPA | 6 | < 1 | 62 |
| 6 | *s*-BuLi | HMPA | 6 | < 1 | 42 |
| 7 | *n*-BuLi | HMPA | 6 | < 1 | 24 |
| 8 | *t*-BuLi | HMPA | 3 | 5 | 20 |
| 9 | *t*-BuLi | HMPA | 1 | 54 | 19 |
| 10 | *t*-BuLi | HMPA | 0.1 | 37 | 2 |
| 11 | *n*-BuLi | TMEDA | 1 | 7 | < 1 |
| 12 | *s*-BuLi | TMEDA | 1 | –[c] | –[c] |
| 13 | *t*-BuLi | TMEDA | 1 | (98) | (2) |
| 14 | *s*-BuLi | (−)-sparteine | 1 | (99) | (1) |
| 15 | *t*-BuLi | (−)-sparteine | 1 | (98) | (2) |
| 16 | *t*-BuLi | DMPU | 6 | –[c] | –[c] |

[a] By GC unless otherwise indicated. Figures in parentheses are relative yields, determined by GC. [b] Isolated yield. [c] Neither **4** nor **8** present in complex product mixture.

analysed by gas chromatography. The results are presented in Table 1, entries 4–15. Although all of the additives investigated [DMPU, TMEDA and (−)-sparteine] are commonly used—like HMPA—to increase the basicity and nucleophilicity of organolithium reagents, HMPA is unique among them in its promotion of the 5-*endo*-*trig* ring opening. No qualitative difference was observed between the *n*-, *s*-, and *t*-BuLi-promoted eliminations (entries 5–7): all gave only **8**, and no **4**, in the presence of 6 equiv. HMPA, though yield decreased with organolithium basicity. The yield of **8** drops, however, as the amount of HMPA is decreased, and some **4** is formed when less than 3 equiv. HMPA are present (entries 8–10).

Yields of **4** and **8** were very low when the mixtures contained TMEDA, (−)-sparteine or DMPU, and a range of unidentified by-products was formed, presumably because of competing decomposition of these co-solvents by the organolithiums. However, we were able to quantify the ratio of **4** : **8** formed in some of these reactions, and with both TMEDA and (−)-sparteine, mainly **4** was formed, with only traces of **8**.

Although further experiments are required to elucidate the detailed mechanism by which **6** is formed, the decomposition of THF is evidently one of a number of reactions in which HMPA has a unique role to play.[18,21–25] In a general sense, HMPA appears to function as an extremely strongly binding ligand, breaking up aggregates, saturating lithium's Lewis acidity and weakening any potential coordination with basic substrates[21,22] Perhaps this deaggregation of C-2 lithiated THF promotes the alternative α-elimination, or maybe a lessened requirement for coordination to O directs deprotonation towards C-3 of THF.

## Experimental

### Thiocarbonic acid *O*-but-3-enyl ester *S*-phenyl ester 8

A solution of *t*-butyllithium (1.05 equiv. 1.52 mmol, 1.3 M in hexane, 1.2 mL) was added rapidly to a stirred solution of dry THF (10 mL), HMPA (6 equiv., 8.7 mmol, 1.5 mL) under nitrogen at −78 °C. The reaction mixture was allowed to stir at −78 °C for a further 5 min and then allowed to warm to room temperature over an hour. The mixture was transferred rapidly *via* cannula to a solution of phenyl chlorothioformate (0.2 mL, 1.45 mmol) in THF (10 mL) at −45 °C. The reaction was stirred at this temperature for a further hour, quenched with brine (10 mL) and warmed to room temperature. The organic layer was extracted using hexane (2 × 20 mL) and the combined organic layers dried ($Na_2SO_4$). Removal of solvent *in vacuo* yielded the crude product. $^1$H NMR of the crude material showed an impure sample of the required compound **8**. Purification by flash column chromatography (7 : 1 pet. ether–EtOAc) afforded the pure compound as a yellow oil (2.4165 g, 29%). $R_F$ (7 : 1 pet. ether–EtOAc) 0.44; $\nu_{max}$ ($CH_2Cl_2$) cm$^{-1}$ 3075, 3061, 1713 (amide C=O), 871, 830, 744; $\delta_H$ (300 MHz; $CDCl_3$) 7.46–7.10 (5H, m, Ph–H), 5.78 (1H, m, $H^3$), 5.03 (2H, m, $H^{4a,\,b}$), 4.19 (2H, t, *J* 6.5, $H^{1a,\,b}$) and 2.34 (2H, m, $H^{2a,\,b}$); $\delta_C$ (75 MHz; $CDCl_3$) 169.4 (CO), 135.2, 133.4, 130.1, 129.4, 117.7, 106.6 (aromatic and olefinic C), 67.8 (–$CH_2$–), 66.9 (–$CH_2$–); *m*/*z* (CI) 226 (100%, M + $NH_4^+$), 209 (10%, M + $H^+$); *m*/*z* (EI) 208 (20%, M), 55 (100%, M − $CO_2$SPh). Found $M^+$ 208.0553, $C_{11}H_{12}SO_2$ requires 208.0558.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