



Deprotection of 1,3-oxathiolanes to ketones promoted by base

Biao Du^a, Changchun Yuan^a, Langzhong Zhang^a, Li Yang^a, Bo Liu^{a,b,*}

^aKey Laboratory of Green Chemistry & Technology of Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, China

^bKey Laboratory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, 345 Lingling Road, Shanghai 200032, China

ARTICLE INFO

Article history:

Received 19 December 2012

Revised 30 January 2013

Accepted 19 February 2013

Available online 1 March 2013

Keywords:

Deprotection

1,3-Oxathiolane

Ketone

ABSTRACT

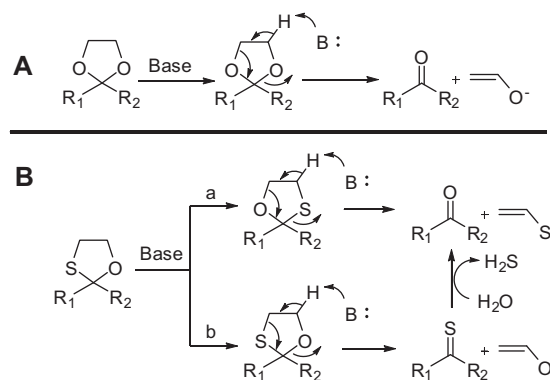
A variety of 1,3-oxathiolanes can be easily converted to the corresponding ketones in good yields with LTMP in THF. This deprotection methodology shows satisfactory chemoselectivity when other protecting groups, such as dimethylketal, 1,3-dioxolane, 1,3-dithiane, and other acid-sensitive groups, are present within the same substrates.

© 2013 Elsevier Ltd. All rights reserved.

Protection and deprotection play important roles and are usually unavoidable in the synthesis of complex molecules. Among the various protecting groups for carbonyl, 1,3-oxathiolane is very useful because of its stability under mild acidic condition, in which the *O,O*-acetals are often not tolerant. Accordingly, many methods have been exploited for the deprotection of 1,3-oxathiolanes. These usual reagents include Lewis acids,¹ oxidants,² and those resulting in sulfonium intermediates,³ such as NBS,^{3a-c} I₂-AgNO₂,^{3d,3e} and Bi(NO₃)₃.^{3h} Moreover, other special reagents^{4–10} proved effective for this deprotection as well, including Raney nickel,⁴ Chloramine-T,⁵ BSP/Tf₂O,⁶ HgO,⁷ and benzyne.⁸ However, to the best of our knowledge, deprotection of 1,3-oxathiolane solely with base has never been explored.

We have previously reported an interesting base-promoted deprotection of 1,3-dioxolanes (Scheme 1A),¹¹ adventitiously discovered during the total synthesis of lindenane-type sesquiterpenoids.¹² In view of reaction mechanism, we anticipated that treating 1,3-oxathiolanes with base should potentially provide the corresponding ketones via either path a or path b (Scheme 1B). Herein we present our results on this deprotection with lithium 2,2,6,6-tetramethylpiperidide (LTMP).

Initially, 1,3-oxathiolane of α -tetralone (**1a**) was selected as the test substrate and treated with various bases in THF (Table 1, entries 1–8). Although potassium *tert*-butoxide and potassium and lithium bis(trimethylsilyl)amides proved ineffective to deprotect **1a** even at 0 °C (entries 1–3), lithium diisopropylamide (LDA) led to a satisfactory 61% yield as a stronger base (entry 4). To our delight, LTMP behaved as the optimal base, affording 79% yield at



Scheme 1.

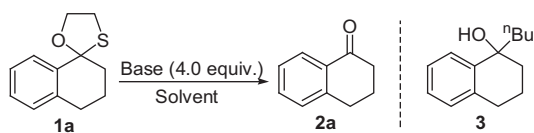
–78 °C (entry 5). However, inferior yields were obtained when we attempted *n*-butyl lithium, *s*-butyl lithium, and *t*-butyl lithium (entries 6–8). To probe the possibility of further optimization, we studied deprotection in different solvents. Interestingly, in the ethereal solvents other than THF, the reaction proceeded sluggish even at 0 °C, as was the situation in toluene (entries 9–12). Finally, we achieved 84% yields with 5.0 equiv of LTMP in THF, while a lower yield was obtained with a less amount of base even at higher reaction temperatures (entries 13–14).

Based on the above optimization, we investigated the substrate scope for this reaction with 5.0 equiv of LTMP in THF. The results are summarized in Table 2. First, aromatic substrates with a different *para*-substituent were screened, showing that both electron-donating and electron-withdrawing groups are tolerable (entries 2–4). Similarly, the *ortho*-substituted bromide also

* Corresponding author. Tel./fax: +86 28 8541 3712.

E-mail address: chembliu@scu.edu.cn (B. Liu).

Table 1
Optimization of the reaction condition^a



Entry	Solvent	Base	Temperature (°C)	Yield of 2a ^b (%)
1	THF	<i>t</i> -BuOK	–78 to 0	NR ^c
2	THF	KHMDS	–78 to 0	NR
3	THF	LHMDS	–78 to 0	NR
4	THF	LDA	–78	61
5	THF	LTMP	–78	79
6	THF	<i>n</i> -BuLi	–78	14 ^d
7	THF	<i>s</i> -BuLi	–78	59
8	THF	<i>t</i> -BuLi	–78	25
9	DME	LTMP	–78 to 0	15
10	<i>t</i> -BuOMe	LTMP	–78 to 0	29
11	Et ₂ O	LTMP	–78 to 0	25
12	Toluene	LTMP	–78 to 0	14
13	THF	LTMP ^e	–78	84
14	THF	LTMP ^f	–78 to rt	69

^a Unless otherwise specified, the reaction was carried out with **1a** (0.5 mmol) and the corresponding base (2.0 mmol) in solvent (4 mL) under argon atmosphere.

^b Isolated yields.

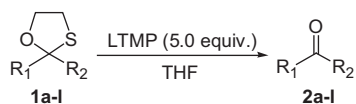
^c NR = no reaction.

^d By-product **3** formed in 58% yield.

^e 2.5 mmol of LTMP was used.

^f 1.5 mmol of LTMP was used.

Table 2
Deprotection of 1,3-oxathiolane of ketones



^a

Entry	Starting material ^b	Temperature (°C)	Product	Yield ^c (%)
1		–78		84
2		–78		77
3		–78		79
4		–78		81
5		–78		74
6		–78		88

Download English Version:

<https://daneshyari.com/en/article/5264130>

Download Persian Version:

<https://daneshyari.com/article/5264130>

[Daneshyari.com](https://daneshyari.com)