

Lithium-Chlorine Exchange Reaction of α -Chloro α -Sulfonyl Ketones

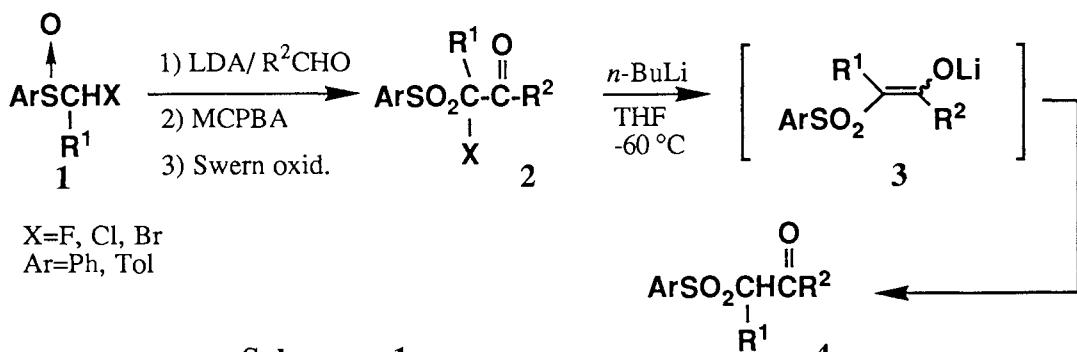
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Lithium-chlorine exchange of α -chloro α -sulfonyl ketones, easily prepared from 1-chloroalkyl aryl sulfoxides and aldehydes in good yields, with *n*-butyllithium gave α -sulfonyl ketones in high yields. Some trials to trap the enolate intermediate were carried out.

Lithium-halogen exchange reactions are well known for the preparation of functionalized and/or unstable alkyl-, vinyl-, and aryllithium reagents.¹⁾ The mechanism²⁾ and application of these reactions to new synthetic methodology³⁾ have been widely studied. Although the lithium-halogen exchange takes place with alkyl, vinyl, and aryl iodides and bromides, a lithium-chlorine exchange is rare.⁴⁾

Recently, α -halogenated sulfur compounds (α -halosulfides,⁵⁾ α -halosulfoxides,⁶⁾ and α -halosulfones⁷⁾ have received much attention in organic chemistry. They are now frequently used in the development of new synthetic methods by several research groups.⁵⁻⁷⁾ We recently focused our attention on the chemistry of α -chlorosulfones and found that the reaction of α -chloro α -sulfonyl ketones with alkylolithium resulted in high yields of lithium-chlorine exchange (Scheme 1).



A typical experiment is reported starting from 1-chloroethyl *p*-tolyl sulfoxide **1** (Ar=Tol, R¹=Me, X=Cl: see Table 1) and *m*-anisaldehyde. Treatment of **1a** with 1.2 equiv. of LDA in THF at -60 °C followed by *m*-anisaldehyde gave the adduct (a

mixture of two diastereomers) in 96% yield. The adduct was oxidized with 3-chloroperoxybenzoic acid (MCPBA) in CH_2Cl_2 at room temperature to afford a mixture of sulfones in 97% yield. Swern oxidation⁸⁾ of the hydroxyl group of the sulfone gave α -chloro α -sulfonyl ketone **2a** quantitatively. All other α -halo α -sulfonyl ketones used in this study were synthesized in the same way in high overall yields.

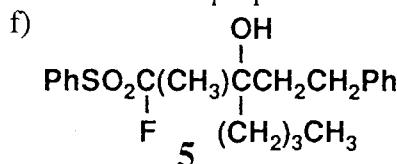
α -Chloro α -sulfonyl ketone **2a** was reacted with *n*-BuLi (1.1 equiv.) in THF at -60 °C and after quenching with aqueous NH_4Cl , **4a** ($\text{Ar}=\text{Tol}$, $\text{R}^1=\text{Me}$, $\text{R}^2=m$ -methoxyphenyl)⁹⁾ was obtained in 85% yield. No product from the reaction of *n*-BuLi with the carbonyl carbon of **2a** was detected. Obviously, this reaction is a lithium-chlorine exchange. The reaction with some other α -halo α -sulfonyl ketones was carried out and the results are summarized in Table 1.

Table 1. Lithium-halogen Exchange Reaction of α -Halo α -Sulfonyl Ketones **2** with Alkyllithium

Entry	2				4		
	Ar	R^1	R^2	X	$\text{RLi}^{\text{a})}$ (equiv.)	Yield/% ^{b)}	
a	Tol	Me	<i>m</i> - $\text{CH}_3\text{OC}_6\text{H}_4$	Cl	<i>n</i> -BuLi (1.1)	4a	85
b	Tol	Me	$\text{Ph}(\text{CH}_2)_2$	Cl	MeLi (1.1)	4b	58(88) ^{c)}
c	Tol	Me	$\text{Ph}(\text{CH}_2)_2$	Cl	<i>n</i> -BuLi (1.1)	4b	95
d	Tol	Me	$\text{CH}_3(\text{CH}_2)_5$	Cl	<i>n</i> -BuLi (1.1)	4d	99
e	Tol	ⁱ Pr	$\text{Ph}(\text{CH}_2)_2$	Cl	<i>n</i> -BuLi (1.1)	4e	69(98) ^{c)}
f	Tol	ⁱ Pr	$\text{CH}_3(\text{CH}_2)_5$	Cl	<i>n</i> -BuLi (1.1)	4f	71(97) ^{c)}
g	Ph	$\text{CH}_3(\text{CH}_2)_6$	$\text{Ph}(\text{CH}_2)_2$	Cl	MeLi (1.1)	4g	56(75) ^{c)}
h	Ph	$\text{CH}_3(\text{CH}_2)_6$	$\text{Ph}(\text{CH}_2)_2$	Cl	<i>n</i> -BuLi (1.1)	4g	90
i	Ph	$\text{CH}_3(\text{CH}_2)_6$	$\text{CH}_3(\text{CH}_2)_5$	Cl	<i>n</i> -BuLi (1.1)	4i	92
j	Tol	Me	$\text{Ph}(\text{CH}_2)_2$	Br ^{d)}	<i>n</i> -BuLi (3.0)	4b	94
k	Ph	Me	$\text{Ph}(\text{CH}_2)_2$	F ^{e)}	<i>n</i> -BuLi (2.1)	5f)	53

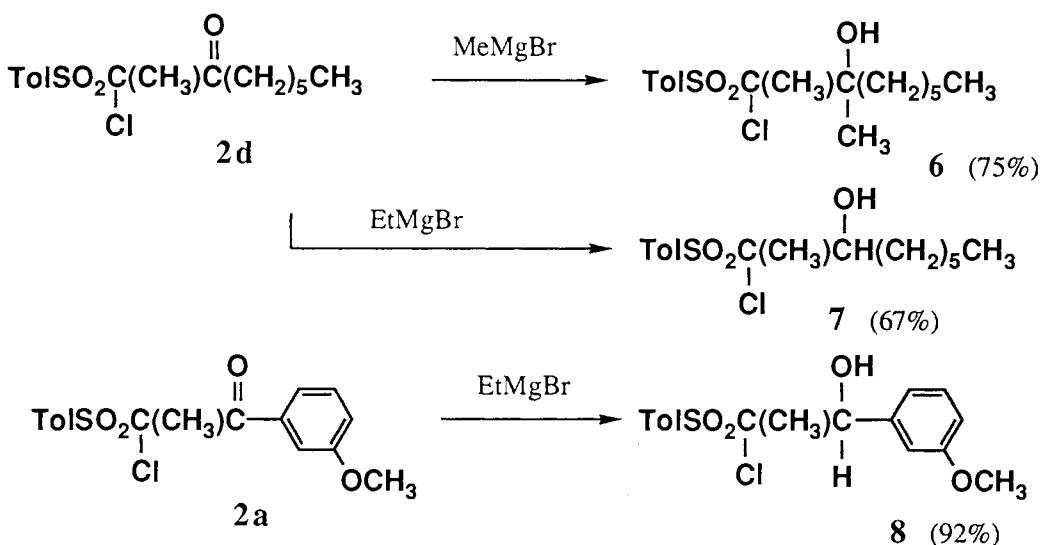
a) All reactions were carried out in dry THF at -60 °C. b) Isolated yield. All α -sulfonyl ketones **4**, and **5** are colorless oily compound.

c) Conversion yield. d) 1-Bromoethyl *p*-tolyl sulfoxide was prepared according to the method by Iriuchijima (Ref. 11). e) 1-Fluoroethyl phenyl sulfoxide was prepared according to the method by Wunk (Ref. 12).

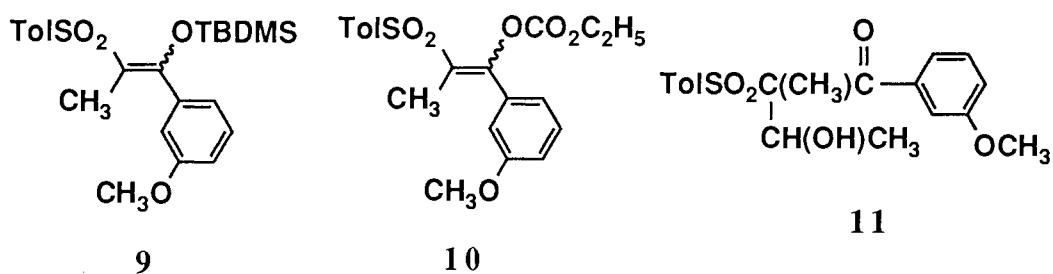


As shown in Table 1, this lithium-chlorine exchange reaction of α -chloro α -sulfonyl ketones is effective with both MeLi and *n*-BuLi; however, *n*-BuLi gave much higher yields. Lithium-bromine exchange¹⁰⁾ of α -bromo α -sulfonyl ketone also gave a good result (entry j). Lithium-fluorine exchange did not take place with α -fluoro α -sulfonyl ketone (entry k); this reaction gave alkylated product 5 in a moderate yield.

Metal-chlorine exchange of α -chloro α -sulfonyl ketones was also studied with Grignard reagents. For example, treatment of **2d** with MeMgBr in THF only gave methylated product **6**. The use of EtMgBr in THF gave a reduced alcohol **7**. Reaction of **2a** with EtMgBr also gave the alcohol **8** in a high yield and no magnesium-chlorine exchange was detected.



The lithium-chlorine exchange of α -chloro α -sulfonyl ketones **2** was thought to take place through an enolate **3**. Actually, the reaction of **2a** with 1.1 equiv. of *n*-BuLi at -60 °C followed by *tert*-butyldimethylsilyl chloride (TBDMS-Cl) and triethylamine gave silyl enol ether **9** (determined by ¹H NMR), which was then hydrolyzed on silica gel to afford β -ketosulfone **4a**. Treatment of the enolate intermediate **3a** with ethyl chloroformate gave the enol carbonate **10** in 29% yield with **4a** (53%). Treatment of the enolate intermediate **3a** with acetaldehyde gave the alcohol **11** in 35% yield with **4a** (64%).



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- 9) 1-(3-Methoxyphenyl)-2-(*p*-tolylsulfonyl)-1-propanone **4a**: colorless oil; IR (neat) 1690 (CO), 1150 (SO₂) cm⁻¹; ¹H NMR δ 1.55 (3H, d, *J*=7 Hz), 2.42 (3H, s), 3.83 (3H, s), 5.10 (1H, q, *J*=7 Hz), 7.0-7.8 (8H, m); MS *m/z* (%) 318 (M⁺, 19), 135 (100).
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