

Ligand Exchange Reaction of Sulfoxides in Organic Synthesis: Sulfoxide Version of the Julia-Lythgoe Olefination

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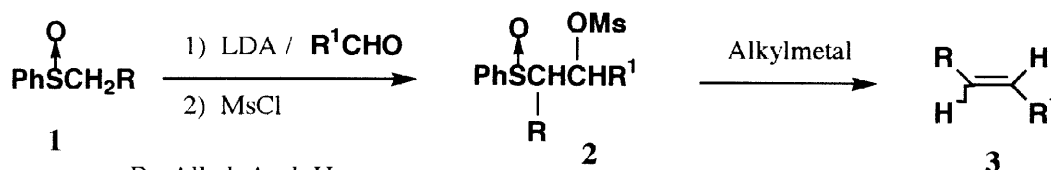
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Abstract: Reaction of β -mesyloxy sulfoxides, derived from alkyl (or arylmethyl) phenyl sulfoxides and aldehydes in two steps, with alkylmetal (*n*-BuLi, *t*-BuLi, or EtMgBr) at -78°C gave olefins in good to excellent yields. This reaction offers a sulfoxide version of the Julia-Lythgoe olefination. © 1998 Elsevier Science Ltd. All rights reserved.

Formation of olefins from sulfones and carbonyl compounds via reductive elimination of β -hydroxy sulfones or their derivatives has been known as the Julia-Lythgoe olefination.¹ Originally, the reductive elimination was carried out with Na-Hg. Later, because of the high toxicity of Hg, this step was improved by replacing Na-Hg with other reducing agents, such as SmI_2 ² or Mg.³ The Julia-Lythgoe olefination incurs another problem in the step of formation of the carbon-carbon bond with α -sulfonyl carbanion and carbonyl compounds. Namely, because the hydrogen on the carbon bearing the sulfonyl group is highly acidic, in some cases the addition reaction of α -sulfonyl carbanion with carbonyl compounds is reversible with the equilibrium lying towards the starting materials.^{2c,4}

We have recently studied the chemistry of the ligand exchange reaction of sulfoxides⁵ and some reductive eliminations were realized.⁶ In continuation of the study, we report herein a sulfoxide version of the Julia-Lythgoe olefination (Scheme 1).

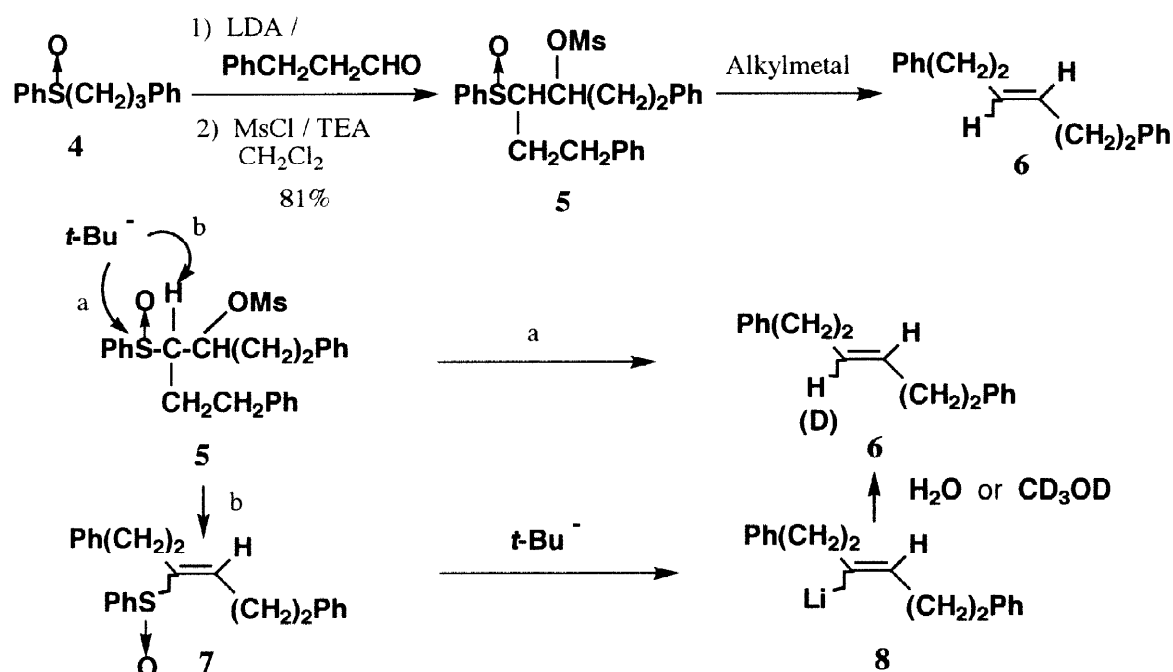


Scheme 1

On treatment of sulfoxides having hydrogens on their α -carbon with alkyllithium, it is expected that the reaction would give α -sulfinyl carbanion. Many examples were reported for the generation of α -sulfinyl carbanions from sulfoxides with alkyllithiums.⁷ However, from our recent studies, alkylmetals react with some sulfoxides at the sulfur very quickly to give an anion of the carbon even at very low temperature (about -100°C).⁸ These results suggested to us that treatment of β -mesyloxy sulfoxides **2**, derived from sulfoxide **1** and aldehydes, with alkyllithium would give olefin **3** via β -mesyloxy carbanion.

Toward this end, we synthesized β -mesyloxy sulfoxide **5** (a mixture of diastereomers) from sulfoxide **4** in two steps in 81% overall yield and treated it with 4 equivalents of *n*-BuLi in THF at -78°C for 5 min (Scheme 2).⁹ Fortunately, the reaction gave a clean reaction mixture, from which the desired olefin **6** (*E/Z*=3:4) was

isolated in 73% yield. *t*-BuLi was also found to be effective in this reaction; however, EtMgBr did not react at all with the β -mesyloxy sulfoxide **5** (see Table 1; entries 1-3).



Scheme 2

In this reaction, two different reaction mechanisms would be expected (Scheme 2). One is the direct β -elimination of the sulfinyl group and mesyloxy group via the ligand exchange reaction of sulfoxide (path a). The other is a two-step mechanism via vinylsulfoxide **7** and vinylolithium intermediate **8** (path b). First, *t*-BuLi eliminates the acidic hydrogen to give vinylsulfoxide **7**, then the vinylsulfoxide again reacts with *t*-BuLi¹⁰ to give vinylolithium **8**, which is protonated to afford the olefin **6**.

To ascertain which path predominantly takes place, the reaction was conducted with *t*-BuLi and after 1 min the reaction was quenched with CD₃OD. No deuterium incorporation was observed in the produced olefin **6** by ¹H NMR. Thus, the elimination proceeds via a direct ligand exchange reaction of the sulfinyl group of the β -mesyloxy sulfoxide **5** (path a).

Preliminary results for the synthesis of olefins from sulfoxides **1** and aldehydes via the ligand exchange reaction of sulfoxide of **2b** are summarized in Table 1. The results in entries 1-3 have been mentioned above. The results using aromatic aldehydes (piperonal and 1-naphthaldehyde; entries 4 and 5) are quite interesting. α -Sulfinyl carbanion reacted with the aromatic aldehydes to give the adduct **2a** in high yields. Mesylation of the adduct, however, gave not the expected mesylate but olefin **3** in moderate yield. The geometry of the olefins was found to be *E*. The exact mechanism of the elimination is not clear now, but it is obvious that the reaction takes place via benzyl cations.

Entries 6-14 show the results by using the sulfoxides having an aromatic group on the carbon bearing the sulfinyl group (**1**; R=aromatic group). Addition of the α -sulfinyl carbanions to 3-phenylpropanal gave almost quantitative yields of the adduct and the mesylation of these alcohols gave the desired mesylates without any

Table 1. Synthesis of Olefins from Sulfoxides and Aldehydes via β -Mesyloxy Sulfoxides

$\text{PhS(O)CH}_2\text{R} \xrightarrow[\text{R}^1\text{CHO}]{\text{LDA}} \text{PhS(O)CH(R)CH(R}^1\text{)OX} \xrightarrow{\text{Alkylmetal}} \text{R-CH=CH-R}^1$ <div style="display: flex; justify-content: space-around; width: 100%;"> <div>1</div> <div>2a X=H b X=Ms</div> <div>3</div> </div>						
Entry	$\frac{1}{\text{R}}$	$\frac{\text{R}^1\text{CHO}}{\text{R}^1}$	$\frac{2a}{\text{Yield / \%}}$	$\frac{2b}{\text{Yield / \%}}$	Alkylmetal ^{a)}	$\frac{3}{\text{Yield}^{b)} / \%(\text{E} / \text{Z})}$
1	PhCH ₂ CH ₂	PhCH ₂ CH ₂	98	83	<i>n</i> -BuLi	73 (3 / 4)
2					<i>t</i> -BuLi	66 (3 / 4)
3					EtMgBr	0
4			87	—	—	56 (E only)
5			95	—	—	47 (E only)
6	Ph	PhCH ₂ CH ₂	92	82	<i>n</i> -BuLi	89 (4 / 1)
7					<i>t</i> -BuLi	92 (4 / 1)
8					EtMgBr	87 (4 / 1)
9		PhCH ₂ CH ₂	98	88	<i>n</i> -BuLi	90 (3 / 1)
10					<i>t</i> -BuLi	68 (3 / 1)
11					EtMgBr	66 (3 / 1)
12	CH ₃ O-	PhCH ₂ CH ₂	99	93	<i>n</i> -BuLi	93 (1 / 0) ^{c)} 73 (1 / 3) ^{d)}
13					<i>t</i> -BuLi	91 (1 / 0) ^{c)} 68 (1 / 3) ^{d)}
14					EtMgBr	75 (1 / 0) ^{c)} 98 (1 / 3) ^{d)}
15	H	CH ₃ O--(CH ₂) ₃	98	98	<i>n</i> -BuLi	31
16					<i>t</i> -BuLi	39
17					EtMgBr	45 ^{e)}
18	H	THPO(CH ₂) ₁₀ CH ₂	85	86	<i>n</i> -BuLi	34
19					<i>t</i> -BuLi	38
20					EtMgBr	39 ^{f)}

a) All the reactions were conducted at -78°C. Unless otherwise noted the β -mesyloxy sulfoxides used in this study are a mixture of diastereomers. b) Isolated purified yield after silica gel column chromatography. c) The result from the crystalline diastereomer of the adduct (see text). d) The result from the mixture of other diastereomers (see text). e) (*E*)-Vinylsulfoxide (25%) and (*Z*)-vinylsulfoxide (24%) were obtained with the olefin. f) In this reaction, the corresponding vinylsulfoxides mentioned above were observed on TLC as the by-products.

problem. Treatment of these mesylates with alkylmetals at -78°C was investigated. As shown in entries 6-8, both *n*-BuLi and *t*-BuLi gave high yields of the desired olefin. In this case, even a Grignard reagent reacted with the mesylate to give olefin in 87% yield.

Entries 9-11 show the results for a synthesis of olefins from the sulfoxide having a 1-naphthyl group. The step for the elimination showed similar results compared with those shown in entries 6-8; however, clearly *n*-BuLi is the reagent of choice. Entries 12-14 show the results by using the sulfoxide having a 4-methoxyphenyl group. In this case, because one of the diastereomers of the adduct **2a** was obtained as a crystalline compound, we carried out this procedure separately with the crystalline diastereomer and a mixture of the other isomers. The results are shown in entries 12-14. Interestingly, the mesylate derived from the crystalline isomer showed high stereospecificity, although we are not sure of the structure of the mesylate now.

Entries 15-20 show the results using methyl phenyl sulfoxide and aldehydes. As shown in the Table, we were able to obtain the desired methylene compound; however, the yields were low to moderate. In these reactions the other products are found to be the vinylsulfoxides. For example, in the reaction shown in entry 17, about 50% yield of both *E* and *Z* vinylsulfoxides was obtained with the desired olefin (45%). In these cases, alkyllithium and Grignard reagent reacted with both the sulfinyl group and the acidic hydrogen on the carbon bearing the sulfinyl group (as seen in Scheme 2).

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9. Typical Experiment: A solution of the β -mesyloxy sulfoxide (0.2 mmol) in minimum amount of THF was added to a solution of *n*-BuLi (0.8 mmol) in 2 ml of THF at -78°C with stirring. The reaction mixture was stirred for 5 min, then the reaction was quenched by adding sat. aq. NH_4Cl . The whole was extracted with ether-benzene and the usual workup followed by silica gel column chromatography (hexane:AcOEt=50:1) gave the olefins in 73% yield as a colorless oil.
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