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Ligand Exchange Reaction of Sulfoxides in Organic Synthesis. A Novel Method for Synthesizing Acetylenes from Carbonyl Compounds through β-Trifluoromethanesulfonyloxy Vinyl Sulfoxides

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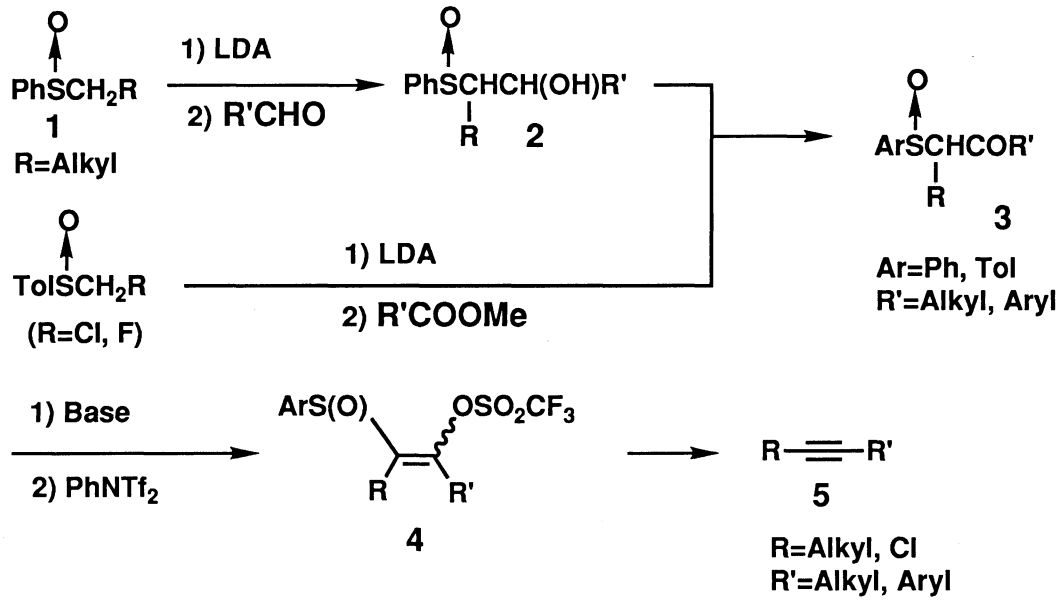
α-Sulfinyl ketones were prepared by the reaction of alkyl phenyl sulfoxide or chloromethyl *p*-tolyl sulfoxide with aldehydes or methyl esters in high yields, and were converted to acetylenes through β-trifluoromethanesulfonyloxy vinyl sulfoxides by the ligand exchange reaction of the sulfinyl group.

Acetylenes are important compounds in organic chemistry and extensive studies have been reported for their chemistry and synthesis.[1] One of the most useful methods for synthesizing acetylenes is a 1,2-elimination of olefins: for example, by abstraction of hydrogen halide from vinylhalides.[2] Reductive 1,2-elimination of enol phosphonates belongs to this category of reaction.[3]

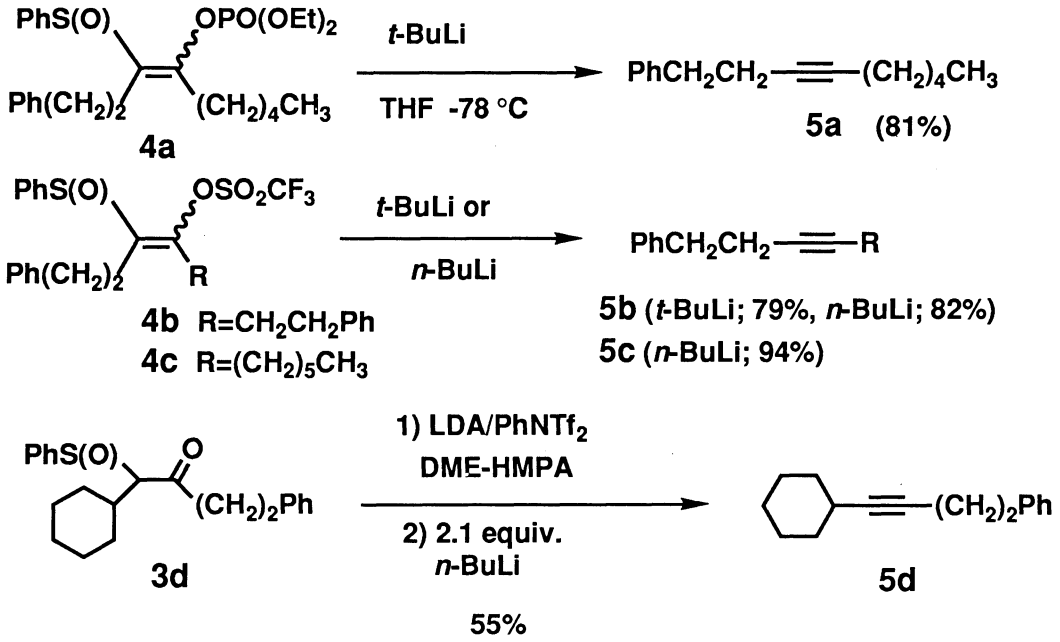
In a previous paper, we reported a novel method for the synthesis of haloalkenes from aldehydes and 1-haloalkyl aryl sulfoxides via ligand exchange of the sulfinyl group with *n*-butyllithium.[4] In continuation of this study and the development of our work for the ligand exchange reaction of sulfoxides in organic synthesis,[5] here we report a new method for the carbonyl to acetylene transformation (Scheme 1).



Scheme 1.

Firstly, 1-phenyl-3-(phenylsulfinyl)-4-nonanone (**3**; Ar=Ph, R=$PhCH_2CH_2$; R'=$(CH_2)_4CH_3$) was synthesized from 3-phenylpropyl phenyl sulfoxide and hexanal via **2** in 93% yield. Enol phosphorylation of the ketone was carried out with the reported procedure[3] to give **4a**; however, the yield was lower than 60%. Ligand exchange reaction of **4a** was investigated with *t*-BuLi in THF at -78 °C. This reaction gave the desired acetylene **5a** in 81% yield. As the synthesis of the enol phosphonate was problematical, we turned our attention to the use of enol triflate.

The enol triflates **4b** and **4c** were synthesized according to the method reported by McMurry[6] from the corresponding ketones **3** in 99% and 95% yields, respectively, as the *E*/*Z*-isomeric mixture. The ligand exchange reaction of **4b** and **4c** was carried out with *t*-BuLi and less expensive *n*-BuLi. Both were found to be effective for the reaction; however, *n*-BuLi gave slightly higher yields (Scheme 2). It is noteworthy that both the stereoisomers showed almost equal reactivity with the alkyllithium to afford the acetylene.



Scheme 2.

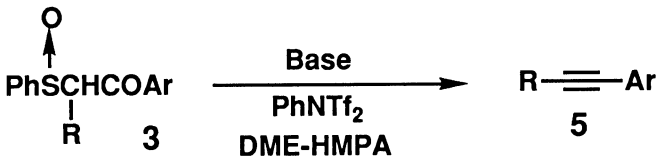
The enol triflate of **3d** showed somewhat different properties compared with **4b** and **4c**. It is rather unstable when contacted with silica gel giving sulfinylallene. In this particular case, the enol triflate of **3d** was treated with excess *n*-BuLi without purification by silica gel column chromatography to afford the desired acetylene **5d** in 55% overall yield.

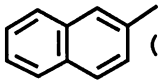
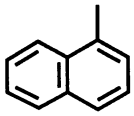
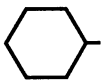
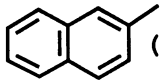
Next, the procedure was applied to the ketone **3** derived from aromatic aldehydes (see Table 1). 1,4-Diphenyl-2-(phenylsulfinyl)-1-butanone **3e** was synthesized from benzaldehyde in two steps in overall 98% yield. Enol triflation of **3e** was carried out in the same conditions as above; however, the reaction was found to be quite sluggish and only a complex mixture was obtained. After some investigation, we found that the reaction took place much more smoothly on addition of about 7 equivalents of HMPA in the solution. At the moment, it was found that the produced enol triflate was converted to the desired acetylene **5e** at room temperature for 20 h

in 64% yield. This case, obviously, the ligand exchange reaction proceeded with the nucleophile other than *n*-BuLi, and also indicated that a one-pot reaction for synthesizing acetylenes from **3** was possible.

Four examples of the results for the transformation of the aromatic ketones (**3e-3h**) to acetylenes (**5e-5h**) are shown in Table 1. This reaction was also possible with KH as a base, although the yields were somewhat lower than those with LDA. From this fact, it is inferred that the nucleophile for the ligand exchange reaction is $PhN^{-}Tf$, but further investigation may be required.

Table 1.

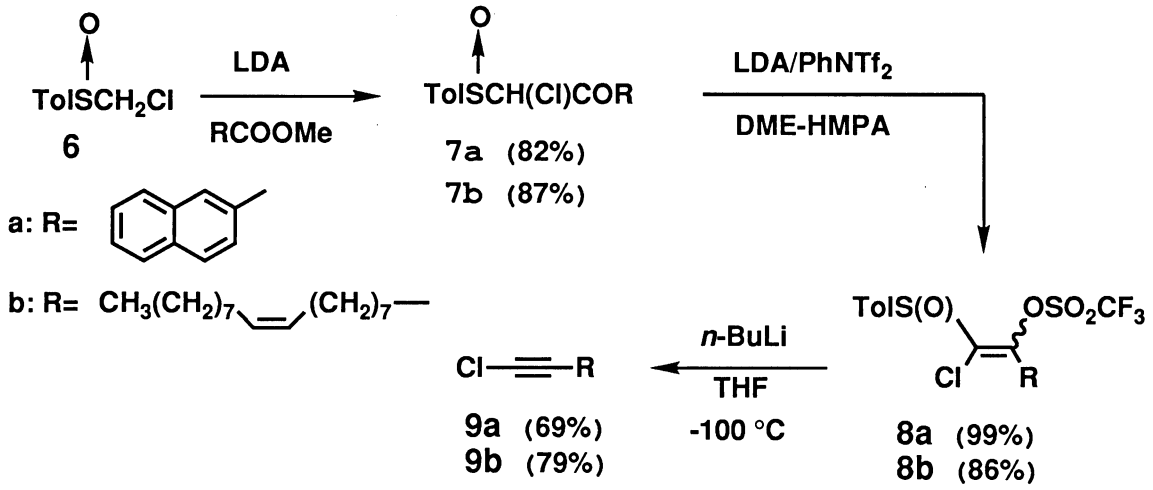


Entry	3			Base	5
		R	Ar (Yield/%)[a]		(Yield/%)
1	3e	$PhCH_2CH_2$	Ph (98)	LDA	5e (64)
2				KH	5e (56)
3	3f	$PhCH_2CH_2$	 (96)	LDA	5f (55)
4				KH	5f (34)
5	3g	$PhCH_2CH_2$	 (81)	LDA	5g (55)
6				KH	5g (47)
7	3h		 (89)	LDA	5h (57)

a) Two-step overall yield from aromatic aldehyde.

Finally, this procedure was applied to the synthesis of chloroacetylenes[7] (Scheme 3). Chloromethyl *p*-tolyl sulfoxide **6** was treated with 2.4 equivalents of LDA in THF at -70 °C, then addition of a methyl ester, to give α-chloro α-sulfinyl ketone **7** in good yield. The enol triflation took place smoothly in DME-HMPA at room temperature to afford **8** in high yield. The conditions for the ligand exchange of the sulfoxide **8** were found to be subtle. Treatment of **8** with 1.4 equivalents of *n*-BuLi in THF at -100 °C for 2 min proved to be the conditions of choice for the reaction and the desired chloroacetylene **9a** and **9b** were obtained in moderate to good yields.

We also tried to synthesize fluoroacetylenes by this method. The enol triflates (**8**; fluorine insted of chlorine) were synthesized in a similar way as described for **8** without any problem. However, the ligand exchange gave a complex mixture, probably due to instability of the fluoroacetylenes.[7]



Scheme 3.

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