Tetrahedron Letters,Vol.28,No.28,pp 3193-3196,1987
Printed in Great Britain

0040-4039/87 $3.00 + .00
Pergamon Journals Ltd.

ALLYLIC 1,3-REARRANGEMENT OF THIOPHENYL SUBSTITUTED SULFONES

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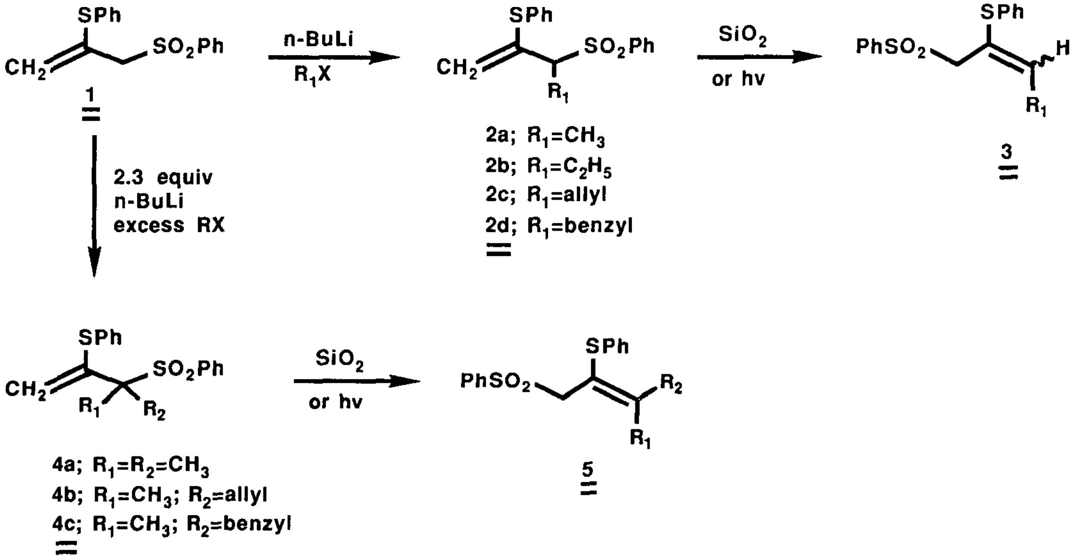
Abstract: Substituted thiophenyl allyl sulfones undergo a 1,3-allylic sulfonyl shift and this rearrangement has been utilized within a metallation-alkylation sequence.

The synthetic application of sulfones to the preparation of natural products has increased enormously during the past several years.[1,2] This increased interest stems from the recognition that sulfones can stabilize anions,[3,4] may be removed reductively[5] and, where appropriate, may be eliminated to form olefins.[6] Lately, there have been several reports in the literature which indicate that substituted allylic sulfones can undergo a 1,3-rearrangement.[7-12] We have been involved in the preparation and utilization of allyl sulfones of the general type **1**, with the objective of performing metallation-alkylation, followed by 1,3-rearrangement, then a further metallation-alkylation and finally hydrolysis of the vinyl sulfide. This would correspond to using **1** as an acetone dianion equivalent. In this communication we report the results of these studies.

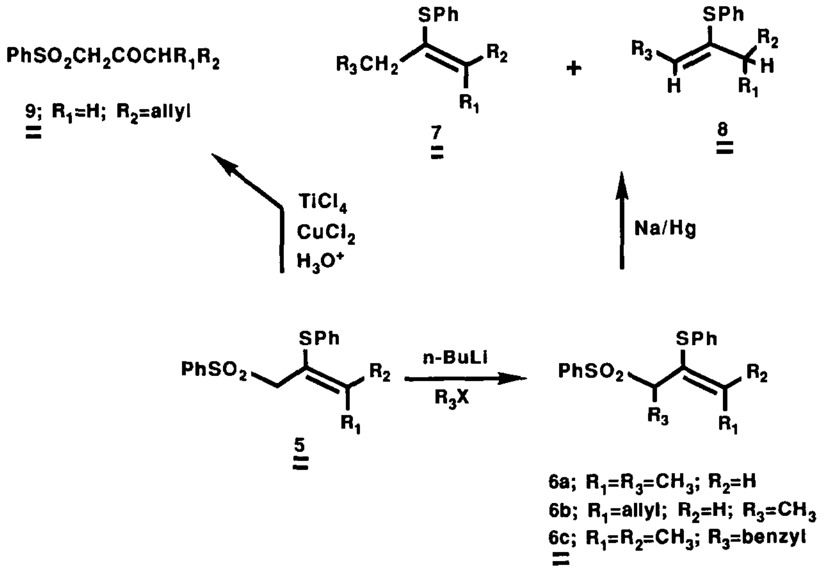
Exposure of allyl sulfone **1**, simply available from the reaction of thiophenoxide with phenylsulfonyl-1,2-propadiene,[13] to n-butyllithium (THF, -78° to 25°C) followed by reaction with



an alkyl halide produced the expected mono-alkylated product **2** in high yield (85-98%). It is well known that the reaction of lithiated allylic sulfones with alkyl halides affords α-alkylated products.[14] When structure **2** was passed through a silica gel packed column, the 1,3-rearranged sulfone **3** (E/Z mixture ca. 3:1) was formed in 98% yield. An alternate way to induce the rearrangement was to heat compound **2** at 80° in solution. At first we thought that this was a thermal reaction, but we found that it did not occur in solution in benzene, chloroform or acetonitrile in the dark. The 1,3-shift does occur in solution on exposure to light, even daylight diffused through the window and a Pyrex flask. It can be prevented simply by wrapping the flask in aluminum foil.

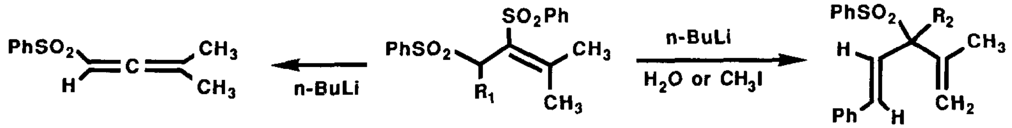
Two different paths can be put forth regarding the mechanism of this rearrangement. One route includes a fairly tight ion-pair which is probably applicable to the silica gel induced rearrangement. The alternate path occurs in solution and involves a radical chain mechanism. The heat and/or light initiates the reaction by bringing about cleavage of the allyl-sulfone bond. The phenyl sulfonyl radical so produced adds to the double bond of another molecule, leading to a new radical which loses the resident phenyl sulfonyl group to generate the rearranged isomer. This path is supported by the fact that the reaction could be completely inhibited by the addition of 5 mole percent of hydroquinone.[15] The α,α'-dialkylated sulfone **4** (formed directly from **1** or via a metallation-alkylation of **2**) also undergoes the 1,3-shift in excellent yield (> 95%). In all cases the thermodynamically rearranged alkene with the more substituted double bond is the exclusive product.

Alkylation of the rearranged sulfone was easily performed under mild conditions. Thus, treatment of **5** with n-butyllithium at -78°C followed by reaction with several alkyl halides proceeded uneventfully and in high yield. The trialkylated sulfone **6c** was transformed into a 2:1



mixture of vinyl sulfides **7** and **8** by reduction with sodium amalgam in methanol. While reductive cleavage of sulfone **5** in protic media effects desulfonylation, subjection of this material to hydrolytic conditions afforded ketosulfone **9** in good yield.

m-Chloroperbenzoic acid oxidation of **5a** readily generates disulfone **10** in high yield. We were interested in the preparation and utilization of allyl anions derived from disulfones related to **10** with the object of cycloadding these 4-electron systems to unsaturated molecules.[16] We found, however, that treating **10** with n-butyllithium results in the elimination of the sulfonyl group to give allene **12** in excellent yield. Reaction of the benzyl substituted disulfone **11** with n-butyllithium resulted in elimination of the allylic sulfonyl group. Quenching the resulting anion with methanol or methyl iodide gave dienes **13** and **14**, respectively.

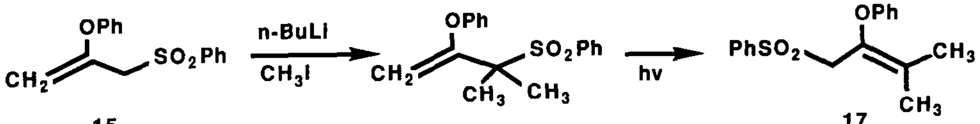


12

10; R_1=H
11; R_1=benzyl

13; R_2=H
14; R_2=CH_3

We have also examined the chemical behavior of the closely related 2-phenoxy substituted sulfone **15**. This compound is readily available from the reaction of phenylsuflonyl-1,2-propadiene and sodium phenoxide. Treatment of **15** with 2 equiv of n-butyllithium in THF at -78°C followed by reaction with excess methyl iodide gave the α,α'-disubstituted sulfone **16**. Irradiation of this material with 3000 A° light results in a quantitative rearrangement to give the isomeric sulfone **17**.



15 **16** **17**

The facility with which these thiophenyl substituted allyl sulfones alkylate and rearrange should open a new dimension to the utility of sulfones in synthesis. Other aspects of the chemistry of thiophenyl allyl sulfones and their application to natural product synthesis will appear in forthcoming papers.

Acknowledgment: We wish to thank the National Science Foundation and the National Cancer Institute, DHEW for generous support of this work.

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(Received in USA 1 April 1987)