

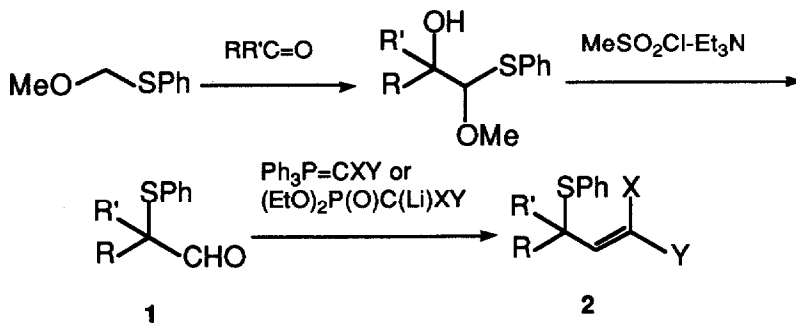
## A VERSATILE METHOD FOR ALLYLIC SULFIDE SYNTHESIS

Tsuneo Sato, Yasuaki Hiramura, Junzo Otera,\* and Hitosi Nozaki  
Department of Applied Chemistry, Okayama University of Science  
Ridai-cho, Okayama 700, Japan

**Abstract.** A practical method for synthesizing a variety of allylic sulfides has been developed through Wittig(-Horner) reaction of  $\alpha$ -sulfenylated aldehydes which are readily accessible from methoxy(phenylthio)methane.

Allylic sulfides which have received much attention as useful building blocks in organic synthesis for many years are usually obtained from allylic halides and alkyl- or arylthiolate ions.<sup>1)</sup> This method is successfully applied to primary allylic derivatives. However, when secondary allylic halides are employed, a serious regiochemical problem arises from competing  $S_N2$  and  $S_N2'$  reactions. The alternative way to arrive at these compounds is alkylation of primary allylic compounds. Unfortunately, this reaction also suffers from ill selectivity providing unseparable  $\alpha$  and  $\gamma$  alkylation products. Still more, incorporation of a sulfenyl group at a tertiary allylic position is virtually impossible. Another class of compounds of great synthetic interest are allylic sulfides with functional groups such as methoxy, sulfenyl, and sulfonyl groups at  $\gamma$ -position. To obtain these compounds which serve as synthetic equivalents, we should have recourse to diverse methodologies suitable for respective purposes. Herein we describe a completely novel route which can afford comprehensively various types of allylic sulfides offering concrete solutions to the above problems.

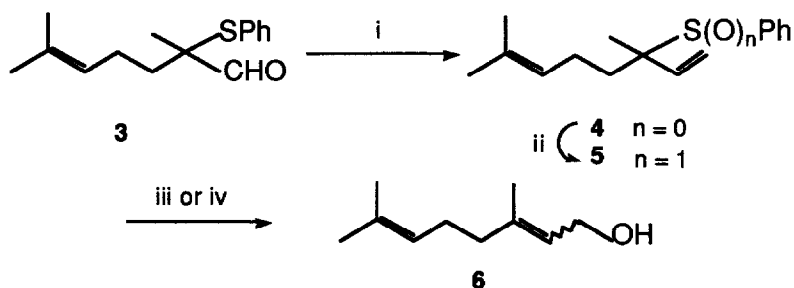
The present method has its foundation on our previous disclosure of general and practical method for preparing  $\alpha$ -sulfenyl aldehydes **1** from methoxy(phenylthio)methane.<sup>2)</sup> Treatment of **1** with Wittig(-Horner) reagents leads to the desired allylic sulfides **2** quite smoothly.



A THF solution (10 ml) containing  $\text{Ph}_3\text{PCH}_2\text{Br}$  (786 mg, 2.2 mmol) and BuLi (1.5 M hexane solution, 1.5 ml, 2.3 mmol) was stirred at 0 °C for 30 min. To this solution was added 2-phenylthiooctanal (236 mg, 1 mmol) dissolved in THF (2 ml) at -78 °C. The reaction mixture was stirred for 6 h during which the temperature was gradually raised up to -30 °C. Aqueous ammonium chloride (2 ml) was added to the mixture, which then was extracted with ethyl acetate (30 ml). The organic layer was washed with aqueous ammonium chloride (10 ml) and brine (10 ml x 2). Drying ( $\text{Na}_2\text{SO}_4$ ) and evaporation provided a crude oil which was purified through column chromatography on silica gel to give 3-phenylthio-1-nonene (150 mg, 64%). The whole results are compiled in Table 1.

A secondary allylic sulfide is obtained without contamination by the primary regioisomer which otherwise forms predominantly (entry 1). Further worthy of note is isolation of the compound of  $\text{R}(\text{SPh})\text{CHCH}=\text{CHR}'$  type in a pure form (entry 2) since alkylation of  $\text{PhSCH}_2\text{CH}=\text{CHR}'$  inevitably leads to regioisomers. Entries 3-7 reveal the effectiveness for allylic sulfides with functional groups at the  $\gamma$ -position. Note that isomerization to the more stable cinnamyl derivative takes place in entry 7. Some of these compounds have been well documented as three carbon homologation reagents.<sup>3-6</sup> More interestingly, a sterically demanding group can be incorporated at the position  $\alpha$  to the phenylthio group (entry 8). Finally, entries 9 and 10 disclose the unprecedented uptake of a phenylthio group at tertiary allylic carbons, the results of great synthetic value since these compounds are the nicest starting materials for Mislow-Evans rearrangement. In his pioneering work on [2,3] sigmatropic rearrangement of allylic sulfoxides, Evans attempted to prepare **5** through alkylation of lithiated 3-phenylsulfinyl-1-butene with 4-methyl-3-pentenyl iodide, but failed to isolate the pure compound: a mixture of  $\alpha$  and  $\gamma$  products resulted.<sup>7</sup> The present method has allowed us to isolate the corresponding sulfide **4** in a pure form from **3**<sup>8</sup>) (Scheme 1). Oxidation of **4** with MoOPH ( $\text{MoO}_5\text{-HMPA-C}_5\text{H}_5\text{N}$ ) and the subsequent [2,3] sigmatropic rearrangement furnished a mixture of geraniol and nerol in satisfactory yield.<sup>9</sup>

Scheme 1



(i)  $\text{Ph}_3\text{P}=\text{CH}_2$  (3 equiv), THF, -78 - 0 °C, 3h, 86%; (ii) MoOPH (1.3 equiv),  $\text{CH}_2\text{Cl}_2$ , rt, 2h; (iii)  $(\text{MeO})_3\text{P-NaHCO}_3$ , MeOH, rt, 11h, 82% based on **4**,  $E:Z = 57:43$ ; (iv)  $\text{Et}_2\text{NH}$ , MeOH, rt, 13h, 80% based on **4**,  $E:Z = 59:41$ .

Table 1. Synthesis of Various Allylic Sulfides **2**.

entry	<b>1</b>	Wittig(-Homer) Reagent (equiv)	<b>2</b>	yield <sup>a)</sup>	<i>E:Z</i> <sup>b)</sup>
1		Ph <sub>3</sub> P=CH <sub>2</sub> (2.2)		64	
2		Ph <sub>3</sub> P=CHCH=CH <sub>2</sub> (2.5)		67	1:2
3		Ph <sub>3</sub> P=CHOCH <sub>3</sub> (2.5)		73	7:3
4		(EtO) <sub>2</sub> P(O)CH(Li)SMe (2.0)		72	>99:1
5		 (1.3)		80	
6		(EtO) <sub>2</sub> P(O)CH(Li)SO <sub>2</sub> Me (3.0)		90	>99:1
7		(EtO) <sub>2</sub> P(O)CH(Li)SO <sub>2</sub> Me (3.0)		78	8:2
8		Ph <sub>3</sub> P=CH <sub>2</sub> (4.0)		66	
9		Ph <sub>3</sub> P=CH <sub>2</sub> (2.0)		65	
10		Ph <sub>3</sub> P=CH <sub>2</sub> (3.0)		76	

<sup>a)</sup> Isolated yields after column chromatography. All compounds gave satisfactory spectroscopic data.

<sup>b)</sup> Determined on the basis of NMR spectra.

**Acknowledgment.** This work was partially supported by Grant-in-Aid from The Ministry of Education, Science, and Culture, Japan.

### References

- (1) D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7**, 147 (1974). O. W. Lever, Jr., *Tetrahedron*, **19**, 1943 (1977). E. Block, "Reactions of Organosulfur Compounds", Academic Press, New York, 1978. N. H. Werstiuk, *Tetrahedron*, **39**, 205.
- (2) T. Sato, H. Okazaki, J. Otera, and H. Nozaki, *J. Am. Chem. Soc.*, **110**, 5209 (1988).
- (3)  $\gamma$ -Methoxyallylic sulfides: C. B. Ruel, B. Ekogha, and S. A. Julia, *Tetrahedron Lett.*, **24**, 4829 (1983). T. Mandai, T. Moriyama, Y. Nakayama, K. Sugino, M. Kawada, and J. Otera, *Tetrahedron Lett.*, **25**, 5913 (1984). T. Sato, H. Okazaki, J. Otera, and H. Nozaki, *Tetrahedron Lett.*, **29**, 2979 (1988).
- (4)  $\gamma$ -Sulfenylallylic sulfides: E. J. Corey and R. Noyori, *Tetrahedron Lett.*, **1970**, 311. E. J. Corey, B.W. Erickson, and R. Noyori, *J. Am. Chem. Soc.*, **93**, 1724 (1971). K. Oshima, H. Yamamoto, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, **48**, 1567 (1975). T. Cohen, D. A. Bennett, and A. J. Mura, Jr., *J. Org. Chem.*, **41**, 2506 (1976). T. Cohen, W. D. Abraham, and M. Myers, *J. Am. Chem. Soc.*, **109**, 7923 (1987).
- (5)  $\gamma,\gamma$ -Disulfenylallylic sulfides: E. J. Corey and A. P. Kozikowski, *Tetrahedron Lett.*, **1975**, 925. E. Dziadulewicz and T. Gallagher, *Tetrahedron Lett.*, **26**, 4547 (1985).
- (6) To the best of our knowledge, no  $\gamma$ -sulfonylallylic sulfides have been available, while the isomeric  $\gamma$ -methylthioallylic sulfones are known: K. Ogura, T. Iihama, K. Takahashi, and H. Iida, *Tetrahedron Lett.*, **25**, 2671 (1984). K. Ogura, T. Iihama, K. Takahashi, and H. Iida, *Bull. Chem. Soc. Jpn.*, **57**, 3347 (1984). K. Ogura, T. Iihama, S. Kiuchi, T. Kajiki, O. Koshikawa, K. Takahashi, and H. Iida, *J. Org. Chem.*, **51**, 700 (1986).
- (7) D. A. Evans, G. C. Andrews, T. T. Fujimoto, and D. Wells, *Tetrahedron Lett.*, **1973**, 1389.
- (8) Prepared from 6-methyl-2-heptenone.
- (9) In contrast to the reported results ( $E:Z = 9:1$ ),<sup>7)</sup> the  $E/Z$  mixture (ca. 6:4) was obtained in our hands. The reason for this discrepancy is not clear to us at present. For the recent relevant study: J.-B. Baudin and S. A. Julia, *Tetrahedron Lett.*, **29**, 3251 (1988).

(Received in Japan 24 March 1989)