

BENZYNE-INDUCED RING OPENING REACTION OF THIIRANES.  
EFFICIENT SYNTHESIS OF PHENYL VINYL SULFIDES

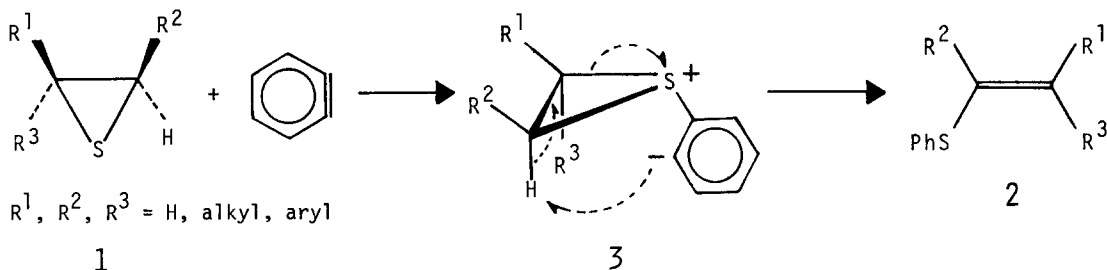
Juzo Nakayama,\* Satoshi Takeue, and Masamatsu Hoshino

Department of Chemistry, Faculty of Science, Saitama University,  
Urawa, Saitama 338, Japan

**Summary:** A series of thiiranes react with benzyne to provide an efficient synthesis of phenyl vinyl sulfides. The reaction is stereospecific, thus producing *cis*-(phenylthio)-stilbene from *cis*-2,3-diphenylthiirane and *trans*-(phenylthio)stilbene from *trans*-2,3-diphenylthiirane.

There is intensive current interest in the development of the preparation of unsaturated sulfides since their versatile usefulness as starting materials or intermediates in organic synthesis has been demonstrated.<sup>1</sup> Herein we report the benzyne-induced ring opening reaction of thiiranes (1) which provides an efficient synthesis of a wide variety of phenyl vinyl sulfides (2) (Scheme 1). Although reactions of benzyne with oxiranes and aziridines were reported,<sup>2</sup> no report on reaction of benzyne with thiiranes has appeared.

Scheme 1

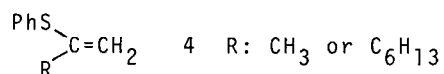


2-Carboxybenzenediazonium chloride<sup>3</sup> and benzenediazonium-2-carboxylate<sup>4</sup> provide a clean source of benzyne and are benzyne precursors chosen. Thus,

either a mixture of 2-carboxybenzenediazonium chloride, a thiirane, and propylene oxide (as hydrogen chloride scavenger) in 1,2-dichloroethane or of benzenediazonium-2-carboxylate and a thiirane in dichloromethane was heated at reflux temperature until all the benzyne precursor disappeared. The resulting mixture was evaporated and purified by appropriate ways (distillation or silica gel chromatography). A series of thiiranes were allowed to react with benzyne in this way.<sup>5</sup> Results summarized in Table 1 show that the reaction is quite general and versatile. The following features are characteristic and noteworthy.

Results in runs 11 and 12 reveal that the reaction is stereospecific, producing *cis*-(phenylthio)stilbene from *cis*-2,3-diphenylthiirane and *trans*-(phenylthio)stilbene from *trans*-2,3-diphenylthiirane with retention of the original stereochemistry of the starting thiiranes. It is known that benzyne reacts with sulfides to yield betaine intermediates as the initial products which collapse to form the final products in several ways.<sup>6</sup> In the light of these facts, the reaction is considered to proceed via the betaine intermediates (3) as shown in Scheme 1. The anionic site of 3 acts as base and abstracts the acidic three-membered ring hydrogen with simultaneous C=C bond formation and C-S bond cleavage, thus affording phenyl vinyl sulfides in which the original stereochemistry of the thiiranes remains retained.<sup>7</sup>

In runs 3, 4, and 8, only 1-(phenylthio)propene and 1-(phenylthio)octene were obtained as mixtures of *cis* and *trans* isomers. No isomeric 2-phenylthio derivatives (4) were produced. This indicates that the more acidic methylene proton of 3 is selectively transferred to the anionic site, thus allowing regioselective bond cleavage between the sulfur and the methine carbon to yield 1-phenylthio derivatives. In the case of styrene sulfide (run 7), the phenyl substituent makes the methine hydrogen acidic and hence both  $\alpha$ - and  $\beta$ -(phenylthio)styrenes are produced.<sup>8</sup>



In conclusion the method developed here provides a versatile general synthesis of a wide variety of phenyl vinyl sulfides since many procedures are available for the preparation of thiiranes.<sup>9</sup>

Table 1 Preparation of Phenyl Vinyl Sulfides by Reaction of Benzyne with Thiiranes

Run	Thiiranes <sup>a</sup>	Source of Benzyne <sup>b</sup>	Phenyl Vinyl Sulfides <sup>c</sup> (Yield, %)
1		A	$\text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{CH}_2$ (74) <sup>d</sup>
2		B	$\text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{CH}_2$ (75) <sup>d</sup>
3		A	$\text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{Me} \\ \diagdown \end{matrix} + \text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{H} \\ \diagdown \end{matrix} \begin{matrix} \text{Me} \\ \text{C} \\ \text{H} \end{matrix}$ (77) <sup>d,f</sup>
4		B	$\text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{Me} \\ \diagdown \end{matrix} + \text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{H} \\ \diagdown \end{matrix} \begin{matrix} \text{Me} \\ \text{C} \\ \text{H} \end{matrix}$ (75) <sup>d,f</sup>
5		A	$\text{PhS} - \text{C}_6\text{H}_{10}$ (89) <sup>d</sup>
6		B	$\text{PhS} - \text{C}_6\text{H}_{10}$ (64) <sup>d</sup>
7		A	$\text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{H} \\ \diagdown \end{matrix} \begin{matrix} \text{Ph} \\ \text{C} \\ \text{H} \end{matrix} + \text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{Ph} \\ \text{C} \\ \text{H} \end{matrix} = \text{CH}_2$ (58) (14.5) <sup>e</sup>
8		A	$\text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{H} \\ \diagdown \end{matrix} \begin{matrix} \text{C}_6\text{H}_{13} \\ \text{C} \\ \text{H} \end{matrix} + \text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{C}_6\text{H}_{13} \\ \diagdown \end{matrix}$ (90) <sup>e,f</sup>
9		A	$\text{Ph} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{Me} \\ \diagdown \end{matrix}$ (78.5) <sup>d</sup>
10		A	$\text{PhS} - \text{C}_7\text{H}_{12}$ (77) <sup>e,g</sup>
11		A	$\text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{H} \\ \diagdown \end{matrix} \begin{matrix} \text{Ph} \\ \text{C} \\ \text{H} \end{matrix}$ (79) <sup>e,h</sup> mp 77-78 °C <sup>i</sup>
12		A	$\text{PhS} \begin{matrix} \diagup \\ \text{C} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix} = \text{C} \begin{matrix} \diagup \\ \text{Ph} \\ \diagdown \end{matrix} \begin{matrix} \text{H} \\ \text{C} \\ \text{H} \end{matrix}$ (71) <sup>e</sup> mp 60.5-61 °C <sup>i</sup>

<sup>a</sup> In runs 1-7 and 9, thiiranes were used in excess (1.5-4.0 mol. equiv.). However, the use of an equimolar amount of thiiranes seems enough. In runs 8, 11, and 12, equimolar amounts of thiiranes and 2-carboxybenzenediazonium chloride were used, and in run 10, 2-carboxybenzenediazonium chloride was used in slight excess (1.2 mol. equiv.).

<sup>b</sup> A: benzyne was generated from 2-carboxybenzenediazonium chloride. B: benzyne was generated from benzenediazonium-2-carboxylate.

(Continued)

Continued (notes added Table 1) <sup>c</sup> Phenyl vinyl sulfides obtained in runs 1-9 are known compounds and their spectral data agreed with those reported.

<sup>d</sup> Yields based on purified materials by distillation with Kugelrohr.

<sup>e</sup> Yields based on purified materials by silica gel column chromatography.

<sup>f</sup> No effort was made to determine the ratio of cis and trans isomers.

<sup>g</sup> <sup>1</sup>HNMR (CDCl<sub>3</sub>) δ 2.0-2.6 (8H, m), 5.3-5.6 (2H, m), 5.8-6.1 (1H, m), and 6.9-7.2 (5H, m).

<sup>h</sup> The formation of trans-(phenylthio)stilbene in a trace amount was detected by <sup>1</sup>HNMR.

<sup>i</sup> The reaction of desoxybenzoin with thiophenol gave a mixture of cis- and trans-(phenylthio)stilbenes: E. Campaigne and J. R. Leal, *J. Am. Chem. Soc.*, **76**, 1272 (1954). Each isomer was separated by silica gel column chromatography followed by repeated recrystallization. The cis isomer melts at 77-78 °C and the trans at 60-61 °C.

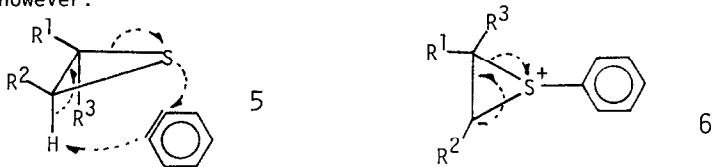
#### References and Notes

- Organic Compounds of Sulphur, Selenium, and Tellurium (Specialist Periodical Report), The Chemical Society, London, Vol. 1 (1970), p. 60, Vol. 2 (1973), p. 25, Vol. 3 (1975), p. 20, Vol. 4 (1977), p. 19, Vol. 5 (1979), p. 23, and Vol. 6 (1981), p. 31.
- R. M. Bryce and J. J. Bernon, *Ad. Heterocycl. Chem.*, **28**, 183 (1981).
- B. H. Klanderman and T. R. Criswell, *J. Org. Chem.*, **34**, 3426 (1969).
- F. M. Logullo and A. H. Seitz, *Org. Synth.*, **48**, 12 (1969).
- Benzenediazonium-2-carboxylate is explosive, and therefore the use of 2-carboxybenzenediazonium chloride is recommended, although caution should also be exercised in the handling of this compound.

The following is typical procedure: A mixture of 1.85 g (10 mmol) of 2-carboxybenzenediazonium chloride, 1.32 g (15 mmol) of isobutylene sulfide, and 4 ml of propylene oxide in 100 ml of 1,2-dichloroethane was refluxed for 1 h. The resulting mixture was evaporated and the residue was purified by distillation with Kugelrohr to give 1.29 g (78.5%) of 2-methyl-1-propenyl phenyl sulfide, bp 110 °C/2.7 mmHg (run 9).

Throughout this work, the only side reaction observed is the formation of diphenyl sulfide by reaction of benzyne with phenyl vinyl sulfides. For reaction of benzyne with phenyl vinyl sulfide, see R. Neidlein and P. Witerzens, *Pharmazie*, **26**, 81 (1971).

- (a) R. Hoffmann, "Dehydrobenzene and Cycloalkynes," Academic Press, New York, 1967, p. 117. (b) T. Ohtsubo and V. Boekelheide, *Tetrahedron Lett.*, 3881 (1975). (c) J. Nakayama, T. Fujita, and M. Hoshino, *Chem. Lett.*, 249 (1983).
- The reaction may proceed concertedly as depicted below (5) without via the betaine intermediates (3) (cf. ene reaction of benzyne with olefin possessing an allylic hydrogen). Incidentally, 3 may collapse to yield ylides (6) which then undergo fragmentation to form phenyl vinyl sulfides. The observed stereochemistry seems not to fit in with this mechanism, however.



- The selective formation of trans-β-(phenylthio)styrene remains as an open question (cf. runs 3, 4, and 8).
- Ref. 1, Vol. 1, p. 109, Vol. 2, p. 100, Vol. 3, p. 85, Vol. 4, p. 186, Vol. 5, p. 187, and Vol. 6, p. 207.

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