

HETEROCYCLES, Vol. 102, No. 7, 2021, pp. 1294 - 1300. © 2021 The Japan Institute of Heterocyclic Chemistry
Received, 25th March, 2021, Accepted, 23rd April, 2021, Published online, 21st May, 2021
DOI: 10.3987/COM-21-14465

NOVEL REACTION COURSE OF THIIRANES TO VINYLOXIRANES: REACTION OF BENZYNE WITH THIIRANES AND ALDEHYDES

Kentaro Okuma,* Yuxuan Qu, and Noriyoshi Nagahora

Department of Chemistry, Fukuoka University, Jonan-ku, Fukuoka 814-0180

e-mail: kokuma@fukuoka-u.ac.jp.

Abstract – Reaction of 2 molar amount of 2-(trimethylsilyl)phenyl triflate with thiiranes and aldehydes in the presence of CsF afforded vinyloxiranes in one-pot operation. Reaction of benzyne with thiiranes gave the corresponding alkenyl phenyl sulfides, which further reacted with another molar of benzyne to afford sulfonium ylide intermediates. Further treatment of aldehydes gave the corresponding vinyloxiranes.

Arynes, as highly electrophilic species, react with various nucleophiles to build heterocycles and complex molecules with high efficacy.¹ Reaction of benzyne prepared from 2-(trimethylsilyl)phenyl triflate **1** with sulfur containing compounds, such as aliphatic sulfides, thiones, and cyclic sulfides afforded sulfur containing organic molecules.² Thiiranes are versatile synthetic intermediates for the synthesis of organosulfur compounds such as aromatic sulfides, cyclic polysulfides, and biopolymers.³ Similar to oxiranes and ethylene imines, the ring strain of thiiranes (18~20 kcal mol⁻¹)⁴ enables to open the ring to afford sulfurous organic molecules or polymerize to give high-refractive-index polymers.⁵ Reactions of benzyne with thiiranes were reported to afford the corresponding phenyl vinyl sulfides in good yields. However, in case of phenylthiirane **2a**, a mixture of regioisomers was obtained (Figure 1a).⁶ We have reported the reaction of triflate **1** with epoxides followed by the addition of pronucleophiles to afford the corresponding three-component products in good yields (Figure 1b).⁷ Li et al. have reported the reaction of arynes with vinyl aryl sulfides **3** having electron-withdrawing groups and water, which gave the corresponding 2-alkenylphenyl aryl sulfides via [3+2] cycloaddition followed by proton abstraction and dehydration. However, by using phenyl styryl sulfide **3a** as a reactant, diphenyl sulfide **4** was obtained in 48% yield (Figure 1c).⁸ These results prompted us to investigate the possibility of formation of phenyl vinyl sulfides or three-component reaction by using thiiranes, arynes, and pronucleophiles. In this communication, we would like to report the novel formation of vinyloxiranes from triflate **1**, thiiranes and aromatic aldehydes in one-pot operation (Figure 1d).

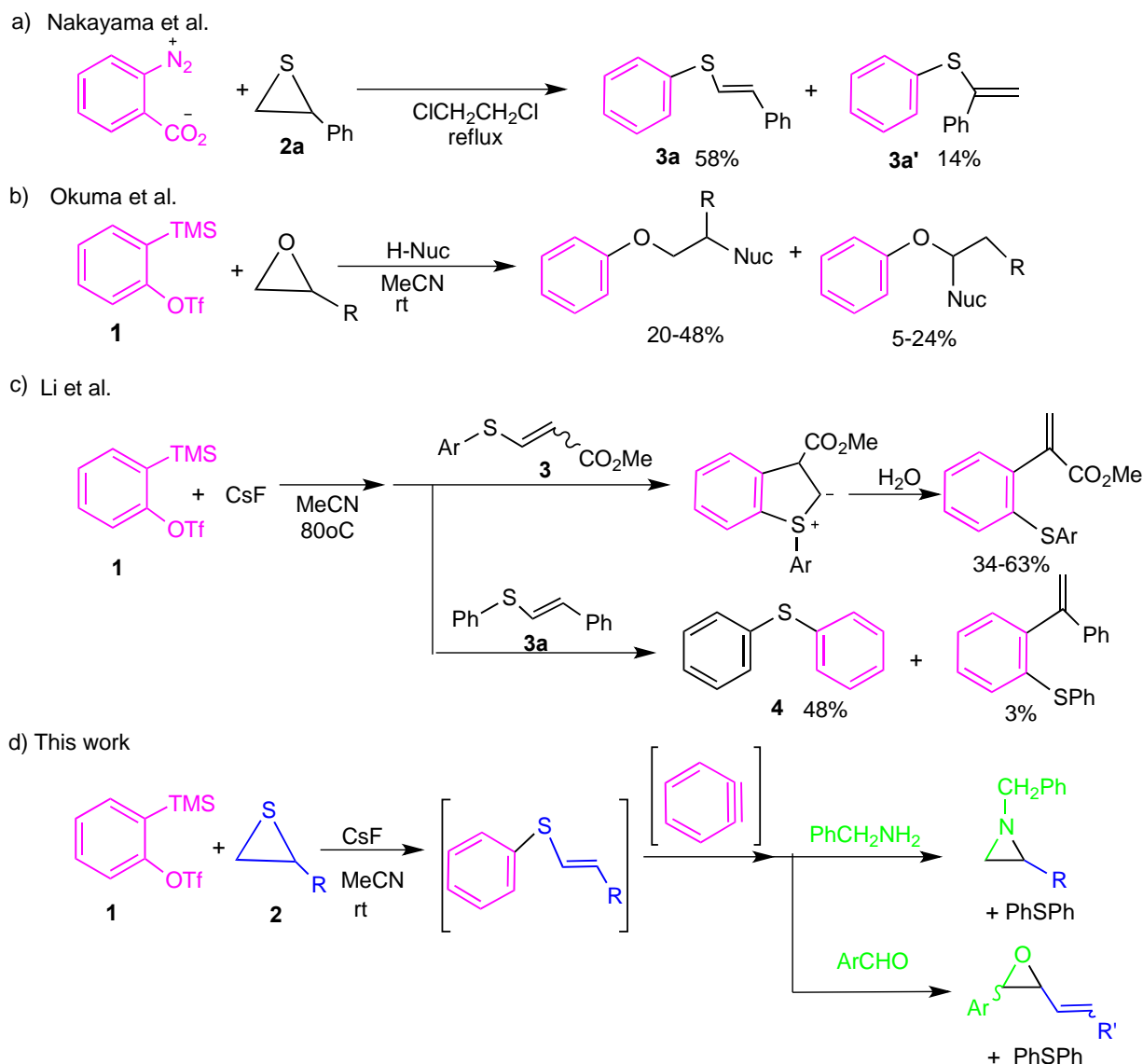
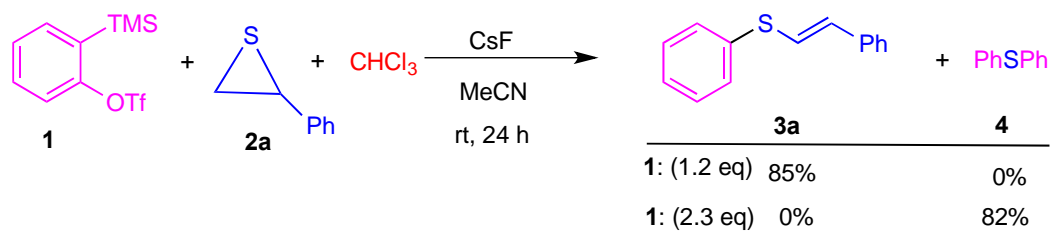


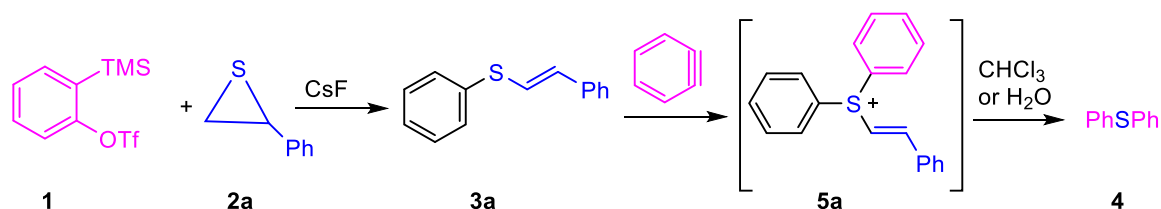
Figure 1. Reaction of benzyne with thiiranes or oxiranes

We initially attempted the reaction of triflate **1** with 2-phenylthiirane **2a** and chloroform whether three-component reaction would proceed. Treatment of triflate **1** with 2-phenylthiirane **2a** and chloroform in the presence of CsF in acetonitrile at rt resulted in the exclusive formation of (*E*)-styrylphenyl sulfide **3a** in 85% yield, the result of which is different from that reported by Nakayama et al.⁶ Presumably, kinetically favored **3a** would be formed at low temperature. No three-component product was observed. This result was quite different from that of cyclic thioethers such as thietanes or tetrahydrothiophenes, which provided the corresponding three-component products.⁹ When 2 molar amount of triflate **1** was used, diphenyl sulfide **4** was obtained as an isolable product, the result of which is similar to Li et al. (Scheme 1).



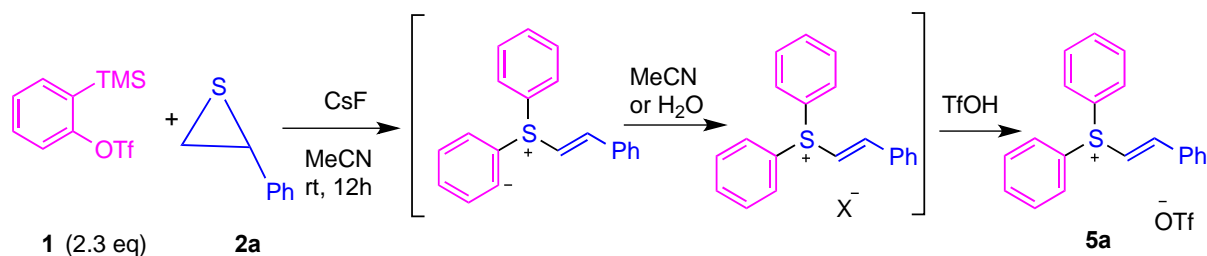
Scheme 1. Reaction of **1** with **2a** and chloroform

How do we account for the formation of diphenyl sulfide **4** by using excess amount of triflate **1**. We speculated that initially formed vinyl sulfide **3a** further reacted another molar of benzyne to give the corresponding zwitter ionic intermediate, which produced diphenylvinylsulfonium salt **5a**. Since vinylsulfonium salt **5a** is unstable under the present reaction conditions, only the decomposed diphenyl sulfide **4** would be formed (Scheme 2).



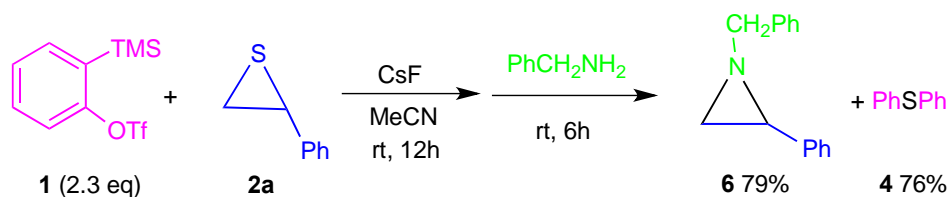
Scheme 2. Plausible reaction mechanism

To confirm this possibility, we have attempted the isolation of diphenylvinylsulfonium triflate **5a**. When triflate **1** (2.3 eq) and 2-phenylthiirane **2a** were treated at rt for 12 h, trifluoromethanesulfonic acid was added. Almost pure diphenylvinylsulfonium triflate **5a** was obtained in 60% yield after repeated precipitations by adding ether (Scheme 3).¹⁰



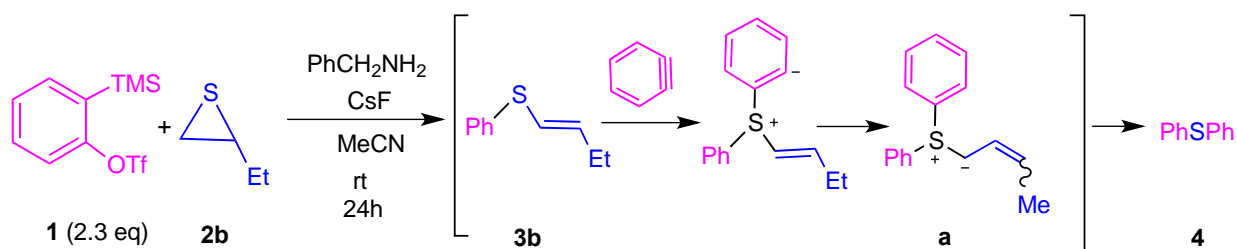
Scheme 3. Reaction of **1** with **2a** and TfOH

Mukaiyama et al. reported the reaction of in situ formed diphenylvinylsulfonium salts with primary amines to afford the corresponding aziridines.¹¹ Thus, we have tried the reaction of triflate **1** with 2-phenylthiirane **2a** followed by the addition of benzylamine. As expected, *N*-benzyl-2-phenylaziridine **6** was obtained in 79% yield (Scheme 4).



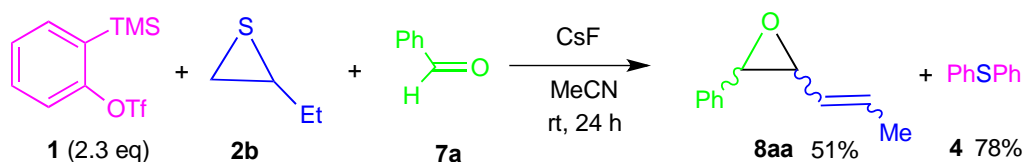
Scheme 4. Reaction of triflate **1** with 2-phenylthiirane **2a** followed by the addition of benzylamine

Since aziridine **6** was easily produced by this reaction, we then tried the reaction of other thiiranes such as 2-ethylthiirane **2b** and 2-methylthiirane **2c**. However, only diphenyl sulfide **4** was isolated. Attempted isolation of aziridines was failed under the same reaction conditions. We thought that more labile vinylsulfonium ylides **a** would be formed under the reaction conditions (Scheme 5).



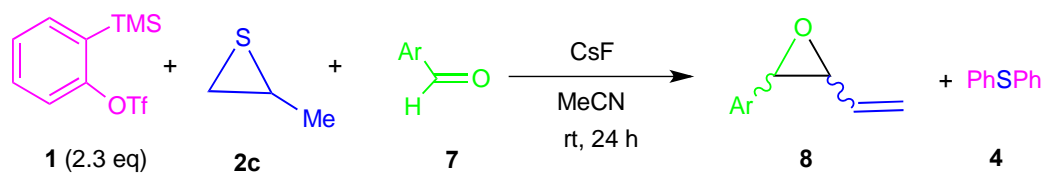
Scheme 5. Reaction of **1** with 2-ethylthiirane **2b**, and benzylamine

To confirm the existence of vinylsulfonium ylide **a**, we then carried out this reaction in the presence of benzaldehyde **7a**.¹² Treatment of 2-ethylthiirane **2b** with triflate **1** and benzaldehyde **7a** in the presence of CsF at rt for 24 h resulted in the formation of isomer's mixture of 2-phenyl-3-(prop-1-en-1-yl)oxirane **8aa** in 51% yield. This result clearly shows that intermediate of the reaction would be ylide **a** (Scheme 6).



Scheme 6. Reaction of **1** with **2b** followed by the addition of benzaldehyde **7a**

Since the obtained mixture of four-isomers **8aa** could not be separated, we then tried the reaction by using 2-methylthiirane **2c**, which would produce only two stereoisomers. Treatment of triflate **1** with 2-methylthiirane **2c** and benzaldehyde **7a** in the presence of CsF at rt for 24 h resulted in the formation of desired vinylloxirane **8ba** in 43% yield. Other aldehydes **7b-7g** also gave the corresponding vinylloxiranes **8bb-8bg**, except for **8be**, in good to moderate yields (Table 1).

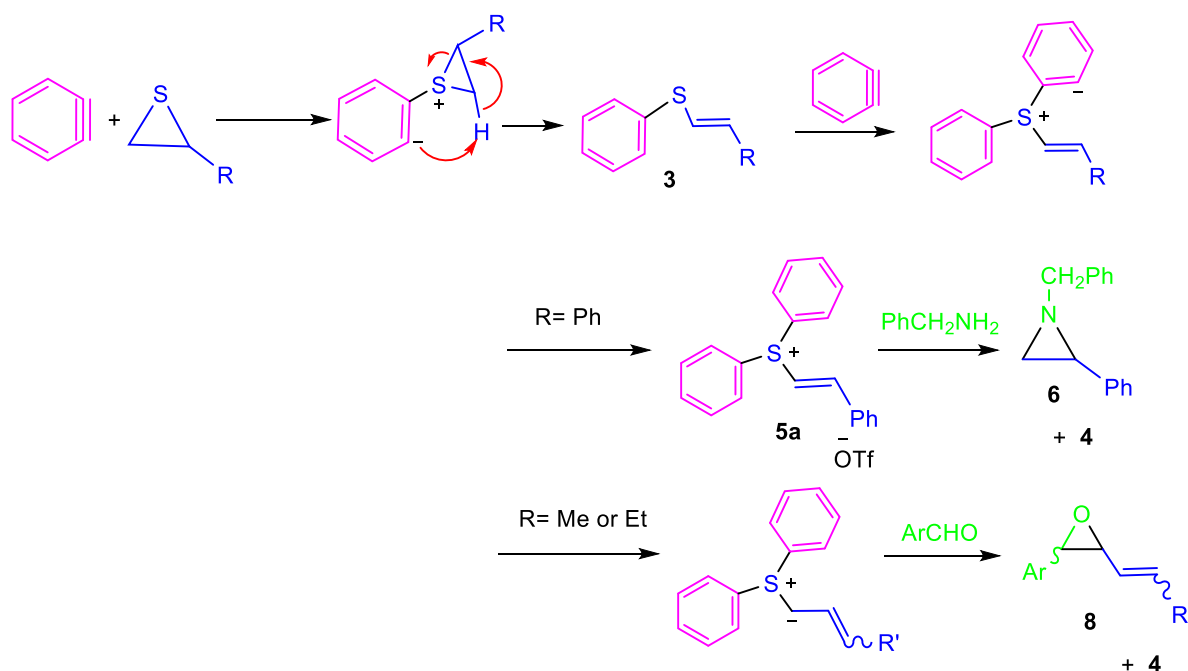
Table 1. Reaction of **1** with thiirane **2c** and aromatic aldehyde **7**

| Entry | 7 | R | 8 | Yield /% | <i>trans</i> : <i>cis</i> |
|-------|-----------|---|------------|----------|---------------------------|
| 1 | 7a | Ph | 8ba | 43 | 40:60 |
| 2 | 7b | 4-MeC ₆ H ₄ | 8bb | 35 | 40:60 |
| 3 | 7c | 4-ClC ₆ H ₄ | 8bc | 57 | 35:65 |
| 4 | 7d | 4-BrC ₆ H ₄ | 8bd | 60 | 40:60 |
| 5 | 7e | 4-MeOC ₆ H ₄ | 8be | 0 | |
| 6 | 7f | 4-NO ₂ C ₆ H ₄ | 8bf | 79 | 35:65 |
| 7 | 7g | 4-FC ₆ H ₄ | 8bg | 66 | 35:65 |

Reaction conditions: **1** (0.7 mmol), **2c** (0.3 mmol), CsF (2.1 mmol), and aldehyde (0.33 mmol) in MeCN (8 mL).

Phenyl and 4-methylphenyl groups gave moderate yields of oxiranes (Entries 1 and 2), whereas 4-anisyl group gave a complex mixture (Entry 5). Electron withdrawing groups such as NO₂, F, Cl, and Br gave better yields of oxiranes (Entries 3, 4, 6, and 7), which clearly suggested that electron deficient aldehydes effectively reacted with vinylsulfonium ylide intermediate. This is the first example of the synthesis of vinyloxiranes from benzyne, thiiranes, and aldehydes.

Thus, the reaction might proceed as follows: Benzyne reacted with thiiranes to give phenyl vinyl sulfide **3**, which further reacted with another molar of benzyne to give the corresponding vinylsulfonium ylide or vinylsulfonium triflate. The ylide reacted with aldehyde to give vinyloxirane **8**. Diphenylstyryl-sulfonium triflate **5a** further reacted with benzylamine to give aziridine **6** (Scheme 7).



Scheme 7. Reaction mechanism

In summary, we have succeeded the synthesis of vinyloxiranes from benzyne, thiiranes, and aldehydes via vinylsulfonium ylide intermediates.

SUPPORTING INFORMATION

Supplementary (Experimental Section, ¹H and ¹³C NMR, MS spectra) data associated with this article can be found, in the online version, at URL: <https://www.heterocycles.jp/newlibrary/downloads/PDFsi/27249/102/7>.

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