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Sulfoxide synthesis from sulfinate esters under Pummerer-like conditions†

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A facile synthetic method for the preparation of allyl sulfoxides by *S*-allylation of sulfinate esters proceeds through sulfonium intermediates without [3,3]-sigmatropic rearrangement and further Pummerer-type reactions of the resulting allyl sulfoxides. On the basis of the plausible reaction mechanism involving sulfonium salt intermediates, *S*-alkynylation and *S*-arylation were also accomplished.

Organosulfur compounds have gained attention in a broad range of research fields such as pharmaceutical sciences, agrochemistry, and materials science.[1,2] The recent remarkable successes of synthetic chemistry using sulfoxides have enhanced the accessibility of highly functionalized compounds by virtue of the significant transformability of sulfoxides.[3–8] For example, the preparations of diverse compounds **2–5** were achieved by a variety of transformations of allyl aryl sulfoxides **1** through C–S bond cleavage (Fig. 1A).[6,7,8h,j] In particular, multisubstituted aromatic sulfides **4** and **5** were synthesized from sulfoxides **1** by a reaction with aryne intermediate **I** in the presence of electrophiles and the [3,3]-sigmatropic rearrangement of allyl sulfonium intermediate **II**, respectively.[6,7] Similar interrupted Pummerer reactions of sulfoxides **6** and **8** with trifluoromethanesulfonic anhydride (Tf$_2$O) in the presence of allyltrimethylsilane were also accomplished through the [3,3]-sigmatropic rearrangement, showing the notable reactivity of allyl sulfonium intermediates **III** and **IV** (Fig. 1B and C).[4b,d,e,n] Herein, we describe an efficient synthesis of various allyl sulfoxides by allylation of sulfinate esters[9] using allyltrimethylsilane under the Pummerer-like conditions[4] through sulfonium intermediate **V** having a methoxy group, enabling to avoid the [3,3]-sigmatropic rearrangement and further Pummerer-type reactions of the resulting allyl sulfoxides (Fig. 1D).

Sulfinate esters hitherto have served in the sulfoxide synthesis with Grignard reagents.[9a] Recently, Lewis acid-mediated

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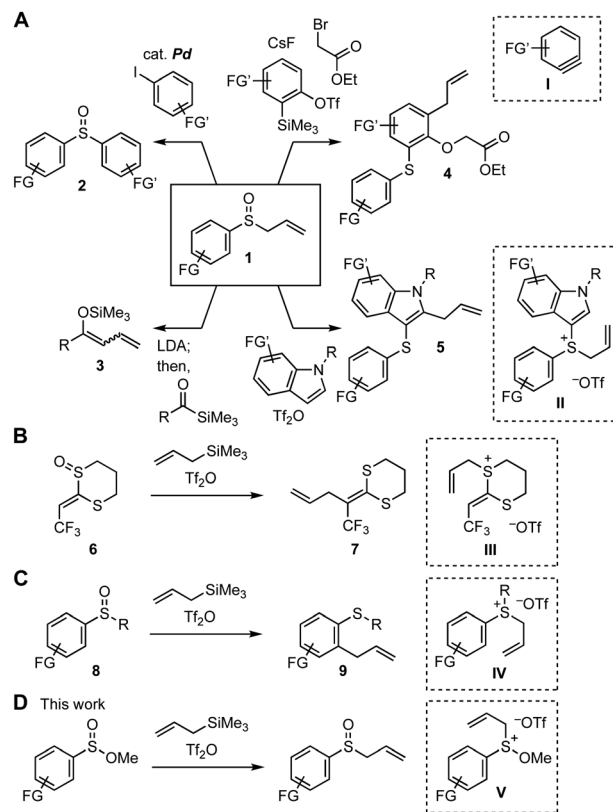

Fig. 1 Transformations through the Pummerer-type activation of sulfoxides and sulfinate esters. (A) Versatile transformations using allyl sulfoxides **1**. (B) Interrupted Pummerer reaction of ketenedithioacetal monoxide **6**. (C) Interrupted Pummerer reaction of aromatic sulfoxide **8**. (D) This work.

Friedel–Crafts-type sulfinylation of electron-rich arenes using sulfinate esters was developed.[9b] Taking the sulfinate ester chemistry into account, we envisioned that the Pummerer-type activation of sulfinate esters **10** in the presence of allylsilanes **11** and stability of methoxy sulfonium intermediates[10] would allow for the facile synthesis of allyl sulfoxides **12**, considering that the hydrolysis of methoxy sulfonium intermediates **V′** can

afford sulfoxides (Fig. 2A). As a result of screening the reaction conditions, we found that treatment of methyl benzenesulfinate (10a) with Tf$_2$O in the presence of allyltrimethylsilane (11a) followed by addition of aqueous sodium bicarbonate provided allyl phenyl sulfoxide (12a) in high yield (Fig. 2A and 2B). Examinations using a variety of acid anhydrides or Lewis acids showed the remarkable reactivity of Tf$_2$O in the S-allylation of sulfinate ester 10a.[11,12] A wide range of allyl sulfoxides 12b–12j were prepared by the S-allylation under the Pummerer-like conditions, where C-allylation products through the [3,3]-sigmatropic rearrangement were not obtained. Indeed, not only electron-rich aromatic sulfinate esters bearing methyl and methoxy groups but also electron-deficient substrates with chloro and nitro groups were efficiently allylated to furnish sulfoxides 12b–12e. Sulfoxides 12f and 12g were obtained uneventfully by the reactions of bulky 2-bromo- and 2,6-dimethyl-substituted benzenesulfinate esters. Furthermore, S-allylations of 2-naphthyl-, benzyl-, and n-pentyl-substituted sulfinate esters also took place smoothly to provide sulfoxides 12h–12j.

Various functionalized allylsilanes 11 participated in the S-allylation of sulfinate ester 10a (Fig. 2A and C).[13] Sulfoxides 12k and 12l were efficiently synthesized by 2-methyl- and 2-phenyl-allylation, respectively. It is worth noting that the C–S bond formation enabled to prepare allyl chloride 12m, allyl acetate

12n, ester 12o, and bromoalkene 12p leaving highly electrophilic functional groups untouched, while it is not easy to synthesize sulfoxides having electrophilic moieties by the conventional allyl sulfoxide synthesis via allylation of thiols and subsequent oxidation. Moreover, transformable sulfoxides 12q and 12r possessing a silyl and boryl groups were obtained in moderate to good yields without damaging these reactive functional groups.

To gain insight into the reaction mechanism of the S-allylation of sulfinate esters under the Pummerer-like conditions, we then examined control experiments (Fig. 3). Firstly, the reaction using [^{18}O]H$_2$O in the hydrolysis using aqueous sodium bicarbonate was conducted to clarify the origin of the oxygen atom of sulfoxide 12a (Fig. 3A). The result showed that ^{18}O-incorporated 12a′ was obtained selectively, indicating that the sulfoxide oxygen was derived from water in the hydrolysis. We then attempted to isolate sulfonium intermediate 13 (Fig. 3B). As a result, after sulfinate ester 10a was treated with Tf$_2$O in the presence of allylsilane 11a, an addition of solid sodium bicarbonate, filtration of the resulting mixture, removal of the solvent of the filtrate, and washing with diethyl ether afforded sulfonium salt 13 quantitatively. Hydrolysis of sulfonium salt 13 with aqueous sodium bicarbonate underwent uneventfully to give sulfoxide 12a. In addition, reduction of sulfonium salt 13 with sodium borohydride successfully provided allyl phenyl sulfide (14) in good yield.[10c] On the basis of these results, we proposed a reaction mechanism of the S-allylation (Fig. 3C). The Pummerer-type activation of sulfinate ester by virtue of the remarkable reactivity of Tf$_2$O,[14] and following S-allylation of the resulting sulfonium intermediate VI would furnish sulfonium intermediate 13 along with trimethylsilyl triflate. Then, hydrolysis of sulfonium salt 13 with aqueous sodium bicarbonate involving the nucleophilic attack of external water to the sulfur atom leads
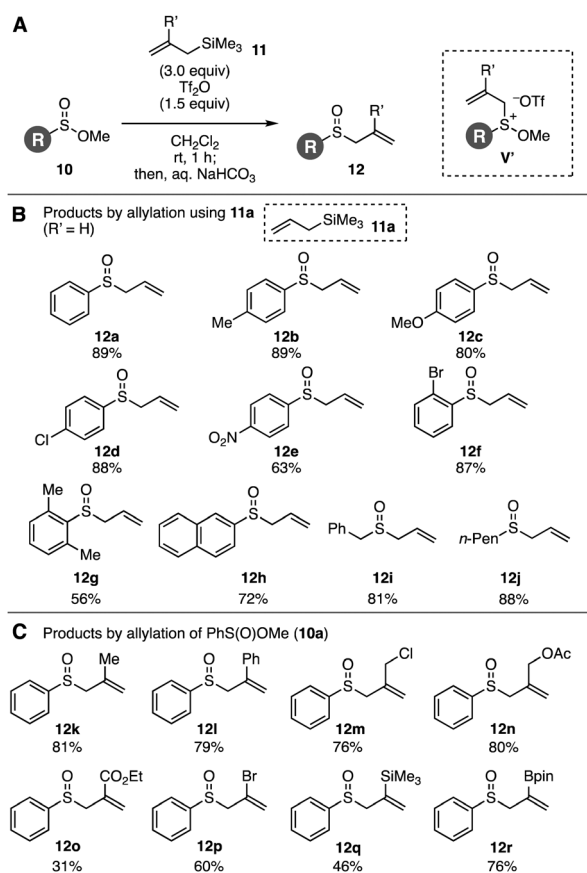

Fig. 2 Allyl sulfoxide synthesis from sulfinate esters 10 and allylsilanes 11. (A) General scheme. (B) Results using various sulfinate esters 10 with 11a. (C) Results using allylsilanes 11 with 10a.
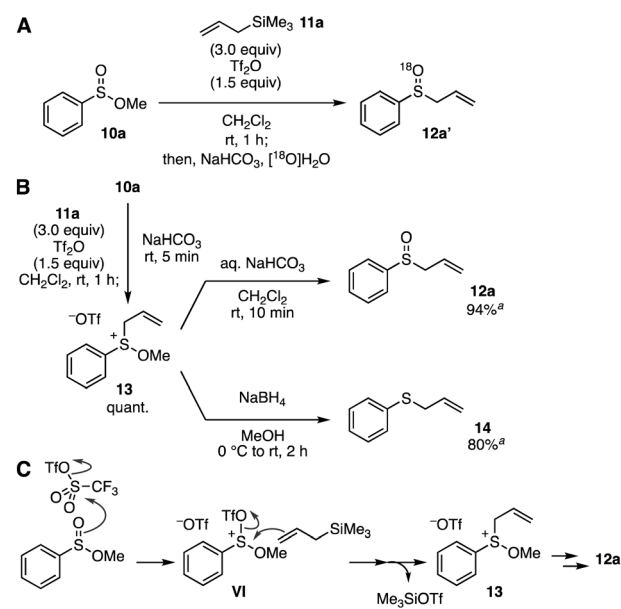

Fig. 3 Control experiments. (A) Reaction using [^{18}O]H$_2$O. (B) Isolation of sulfonium salt 13, hydrolysis of 13, and reduction of 13. (C) Plausible reaction mechanism. ^{a} ^{1}H NMR yield.
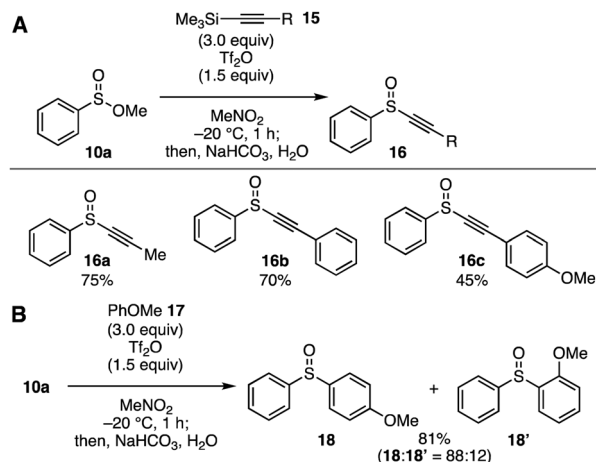
Fig. 4 Alkynylation and arylation of sulfinate ester **10a**. (A) Alkynylation with alkynylsilanes **15**. (B) Arylation with anisole (**17**).

Fig. 5 Transformations of allyl sulfoxides. (A) Benzofuran synthesis. (B) Trisubstituted phenol synthesis. (C) Multisubstituted indole synthesis.

to sulfoxide **12a**. Although the role of methoxy group is still unclear, the stability of sulfonium salt **13** would achieve the sulfoxide synthesis without [3,3]-sigmatropic rearrangement or the Pummerer-type reactions of allyl sulfoxide **12a** and further Pummerer-type reactions of the resulting allyl sulfoxides.[15]

Our attention then directed toward novel transformations through the cationic intermediates generated by the Pummerer-type activation of sulfinate esters with Tf_2O (Fig. 4). In this context, we have developed a facile synthetic method of alkynyl sulfoxides **16** using alkynyl silanes **15** (Fig. 4A). Indeed, treatment of sulfinate ester **10a** dissolved in nitromethane with Tf_2O in the presence of ethynylsilanes **15** at −20 °C furnished alkynyl sulfoxides **16** in moderate to high yields. This novel transformation enabled the preparation of alkynyl sulfoxides **16a–16c** having a methyl, phenyl, and 4-anisyl group. Since alkynyl sulfoxides serve in a variety of reactions including carbometallation, [2+2] cycloaddition, and cyclopropanation, the alkynyl sulfoxide synthesis developed in this study would allow for the preparation of a range of organosulfur compounds.[4k,16] In addition, Friedel–Crafts-type arylation of sulfinate ester **10a** also took place smoothly to afford a regioisomeric mixture of diaryl sulfoxides **18** and **18'** in good yield (Fig. 4B).[9b]

Wide transformability of allyl aryl sulfoxides synthesized from sulfinate esters was showcased by the syntheses of multi-substituted aromatic compounds (Fig. 5). Modifying the conditions for the trifunctionalization of aryne intermediates reported by Li and coworkers[6] (Fig. 1A, **1** to **4**), we found that 2,3,6-trisubstituted phenol **20a** was obtained in moderate yield with avoiding further arylation between phenol **20a** and 3-methoxybenzyne when the aryne trifunctionalization was performed in hot 1,4-dioxane[5d] in the absence of electrophiles such as ethyl bromoacetate (Fig. 5A). Iodine-mediated cyclization of the resulting phenol **20a** and subsequent elimination with a base successfully furnished benzofuran **21**.[17] Methallylation of sulfinate ester **10d** followed by the aryne trifunctionalization led to the synthesis of highly functionalized phenol **20b** (Fig. 5B). Furthermore, tetrasubstituted indole **23** was prepared through 2-bromoallylation
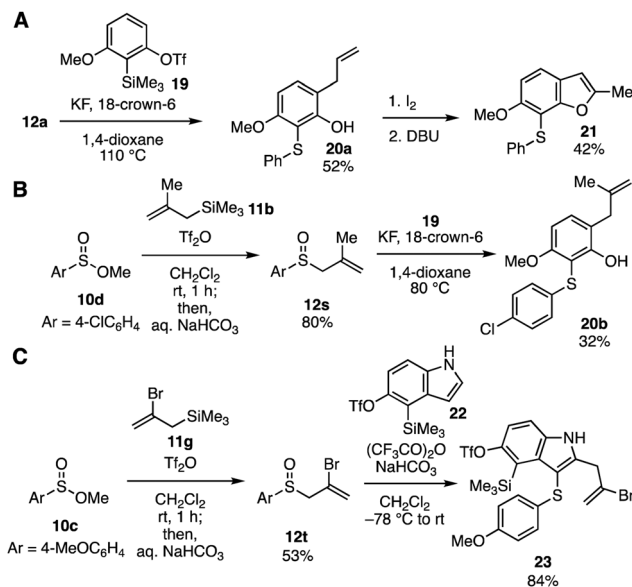
of sulfinate ester **10c** and following 2,3-difunctionalization of indole **22** according to the reports by Procter and coworkers[7] (Fig. 5C). Functionalized allyl aryl sulfoxide **12t** and indole **22** bearing *o*-silylaryl triflate moiety[18] for the aryne generation participated in the 2,3-disubstituted indole synthesis leaving the reactive functional groups intact. Thus, a wide variety of indoles would be synthesized by *S*-allylation of sulfinate esters, 2,3-difunctionalization of indoles, and further transformations through indolyne intermediates with a number of arynophiles.[18,19]

In summary, we have developed a facile synthetic method of allyl sulfoxides by *S*-allylation of sulfinate esters through sulfonium intermediates without [3,3]-sigmatropic rearrangement and further Pummerer-type reactions of the resulting allyl sulfoxides. On the basis of the plausible reaction mechanism, *S*-alkynylation and *S*-arylation were also accomplished. Further studies to expand the scope of these transformations using sulfinate esters under the Pummerer-like conditions, chiral sulfoxide synthesis, and the applications to the synthesis of bioactive compounds are now in progress.

Conflicts of interest

There are no conflicts to declare.

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