

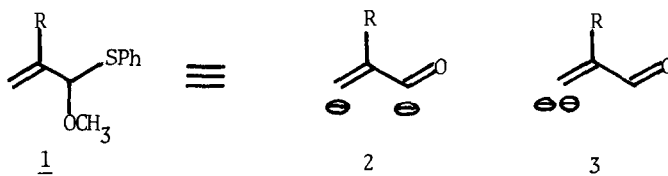
$\alpha$ -METHOXYALLYL SULFIDES AS A NOVEL HOMOENOLATE DIANION EQUIVALENT

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Summary:  $\alpha$ -Methoxyallyl sulfides 1 proved to serve a novel homoenolate dianion equivalent. Introduction of two electrophiles into 1 was realized by successive regiospecific reaction of an allylic moiety with electrophiles intervened by an acid-catalyzed thioallylic rearrangement. Facile desulfurization of the products under mild conditions afforded a variety of  $\alpha,\beta$ -unsaturated carbonyl compounds and 2,3,4-trisubstituted furans.

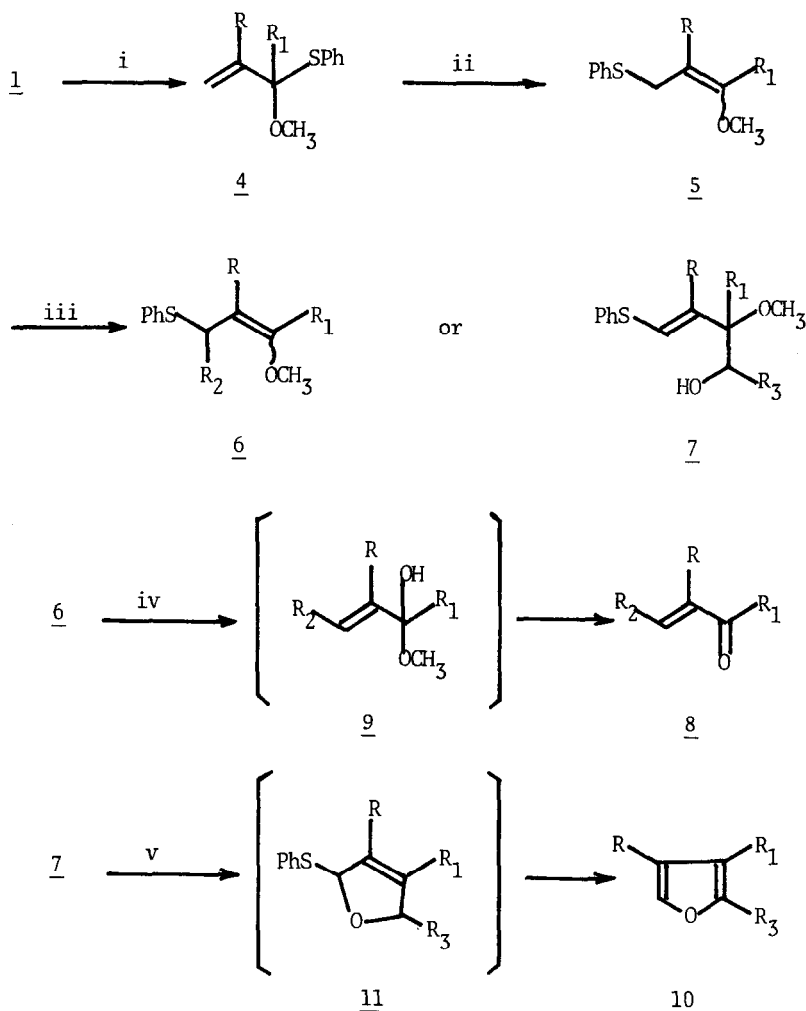
Due to their synthetic utilities, homoenolate anions and their equivalents have received much attention for many years.<sup>1)</sup> Moreover, development of homoenolate dianions and their equivalents seems to be synthetically interesting in view of a possibility of incorporating two electrophiles into ketonic moieties. Although a considerable number of such compounds have been reported,<sup>2)</sup> incorporation of two electrophiles has hardly been realized. To our best knowledge, the only example which exhibits a binucleophilic character is allylic  $\alpha$ -siloxy-phosphonamide,<sup>2i)</sup> which is inevitably thwarted by competing O-alkylation (43-83%), however.

In our continuing studies on the synthetic application of methoxy(phenylthio)methane as a one carbon homologation reagent,<sup>3)</sup> we have found that  $\alpha$ -methoxyallyl sulfides 1 serves as a novel homoenolate dianion equivalent 2 or 3.



As shown in Scheme 1, our strategy consists of a sequence of an exclusive  $\alpha$ -alkylation of 1<sup>3d)</sup> (step i), an allylic rearrangement of a phenylthio group (step ii), and regiospecific reaction of the resultant  $\gamma$ -methoxyallyl sulfides 5 with electrophiles (step iii). Treatment of the anion of 1 generated by LDA (1.5 equiv)<sup>4)</sup> with  $\text{D}_2\text{O}$  or alkyl halides at  $-78^\circ\text{C}$  in THF afforded the  $\alpha$ -deuterated or -alkylated products 4 exclusively (>99% based on  $^1\text{H}$  NMR spectra). It seems of great interest that the reaction proceeds regiospecifically since control of regioselectivity in nucleophilic reaction of an ambident allylic anion is synthetically important.<sup>5)</sup>  $\alpha$ -Methoxy group appears to enhance the nucleophilicity of the  $\alpha$ -carbon. When 4 was heated at reflux in hexane in the presence of silica gel for 4 h, it was found that a facile allylic rearrangement of a phenylthio group takes place to give 5. It should be noted that the presence of silica gel is crucial since no reaction occurred in the absence of this

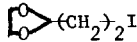
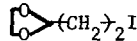
Scheme 1



i) LDA,  $R_1X$ , THF,  $-78^\circ\text{C}$  ii)  $\text{SiO}_2$ , hexane, reflux, 4h iii)  $n\text{-BuLi}$ , TMEDA, THF,  $0^\circ\text{C}$ , 30 min,  $R_2X$  or  $R_3\text{CHO}$ , THF,  $-78^\circ\text{C}$  iv)  $\text{NaIO}_4$ ,  $\text{H}_2\text{O}/\text{dioxane}$ , r.t. v)  $\text{SiO}_2$ , benzene, reflux

material. Further, the fact that the reaction proceeds as well in the dark even in the presence of hydroquinone rules out the photochemical or radical mechanism. Therefore, the reaction may well be accounted for by the intermediacy of an allylic cation.<sup>6)</sup> Apparently, the presence of  $\alpha$ -methoxy group causes a facile cleavage of a phenylthio anion in keeping with our previous observations that a phenylthio group  $\alpha$  to the methoxy group is readily cleaved under mild acidic conditions.<sup>3a-c)</sup> Then, the newly formed allyl sulfide 5 was treated with  $n\text{-BuLi}$  (1.5 equiv) and TMEDA (3 equiv) in THF at  $0^\circ\text{C}$  for 30 min. Reaction of the resultant anion with  $\text{D}_2\text{O}$  and alkyl halides at  $-78^\circ\text{C}$  took place at the  $\alpha$  position exclusively to give 6, while the  $\gamma$ -adduct 7 was the sole product in the reaction with aldehydes.

Table 1. Conversion of 1 into 8 and 10

entry	R	R <sup>1</sup> X	R <sup>2</sup> X or R <sup>3</sup> CHO	<u>5</u> , yield,% <sup>a)</sup>	<u>6</u> or <u>7</u> , yield,% <sup>b)</sup>	<u>8</u> or <u>10</u> , yield,% <sup>c)</sup>
1	C <sub>11</sub> H <sub>23</sub>	D <sub>2</sub> O	 (CH <sub>2</sub> ) <sub>2</sub> I	80 <sup>d)</sup>	<u>6a</u>	<u>8a</u>
2		THPO(CH <sub>2</sub> ) <sub>3</sub> Br	D <sub>2</sub> O	78	<u>6b</u>	<u>8b</u>
3		C <sub>6</sub> H <sub>13</sub> Br	C <sub>4</sub> H <sub>9</sub> I	70	<u>6c</u>	<u>8c</u>
4		THPO(CH <sub>2</sub> ) <sub>3</sub> Br	 (CH <sub>2</sub> ) <sub>2</sub> I	78	<u>6d</u>	<u>8d</u>
5		THPO(CH <sub>2</sub> ) <sub>3</sub> Br	C <sub>5</sub> H <sub>11</sub> CHO	78	<u>7a</u>	<u>10a</u>
6	CH <sub>3</sub>	D <sub>2</sub> O	C <sub>14</sub> H <sub>29</sub> Br	83 <sup>d)</sup>	<u>6e</u>	<u>8e</u>
7		D <sub>2</sub> O	PhCH <sub>2</sub> Cl	83 <sup>d)</sup>	<u>6f</u>	<u>8f</u>
8		THPO(CH <sub>2</sub> ) <sub>3</sub> Br	C <sub>6</sub> H <sub>13</sub> Br	81	<u>6g</u>	<u>8g</u>
9		THPO(CH <sub>2</sub> ) <sub>3</sub> Br	PhCHO	81	<u>7b</u>	<u>10b</u>
10		THPO(CH <sub>2</sub> ) <sub>3</sub> Br	C <sub>5</sub> H <sub>11</sub> CHO	81	<u>7c</u>	<u>10c</u>

- a) Isolated yields based on 1 after column chromatography on silica gel. Column chromatographic purification of 4 was, in general, unsuccessful on account of a partial thioallylic rearrangement.
- b) Isolated yields based on 5 after column chromatography on silica gel.
- c) Isolated yields based on 6 or 7 after column chromatography on silica gel.
- d) Determined on the basis of <sup>1</sup>H NMR spectra.
- e) Contaminated by an undeuterated compound.

Next, we have developed a simple and effective method for transformation of 6 to  $\alpha,\beta$ -unsaturated carbonyl compounds. Treatment of 6 with NaIO<sub>4</sub> (1.2 equiv) in H<sub>2</sub>O/dioxane<sup>7)</sup> at room temperature for 2-10 h resulted in the formation of 8. The reaction may possibly proceed through a hemiacetal intermediate 9 by the Evans rearrangement. On the other hand, 7 was converted into 2,3,4-trisubstituted furan 10 on treatment with silica gel in refluxing benzene for 12-24 h. Hemithioacetal 11 may be a possible intermediate in this reaction. The results are summarized in Table 1. These methods are likely to be synthetically promising because the reaction conditions are mild so that acid-labile functional groups such as tetrahydropyranyl ethers and ketals remain intact during the reaction course.

Of special interest of the present method is to provide conveniently 2,3,4-trisubstituted furans which are difficult-to-obtain according to the reported methods.<sup>8)</sup> Desulfurization-cyclization under almost neutral conditions leads to successful synthesis of furans involving acid-sensitive functional groups.

In summary,  $\alpha$ -methoxyallyl sulfides 1 proved to serve a novel homoenolate dianion equivalent. Successive regiospecific reactions of an allylic moiety with electrophiles intervened by a thioallylic rearrangement result in successful incorporation of two electrophiles. Facile desulfurization of the resulting enol ether 6 or vinyl sulfide 7 under mild conditions affords a variety of  $\alpha,\beta$ -unsaturated carbonyl compounds and trisubstituted furans.

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- (4) Although *n*-BuLi was employed as a base for generation of the anion of 1 previously,<sup>3d)</sup> LDA proved to be preferable.
- (5) For a recent study on this subject, see: Y. Yamamoto, H. Yatagai, Y. Saito, and K. Maruyama, *J. Org. Chem.*, **49**, 1096 (1984).
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