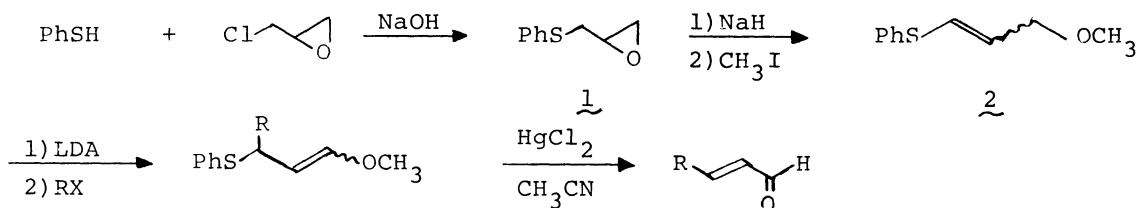


THE WITTIG-TYPE AND THE CLAISEN REARRANGEMENT OF
ALLYLIC 3-PHENYLTHIO-2-PROPEN-1-YL ETHERS

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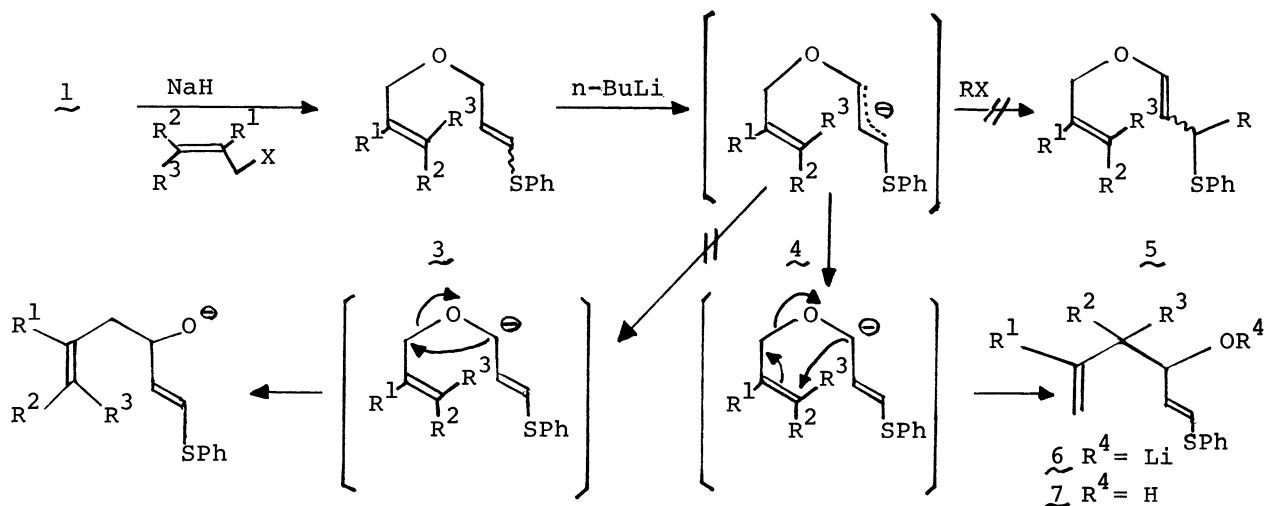
Allylic 3-phenylthio-2-propen-1-yl ethers (3) underwent [2,3]-sigmatropic (Wittig-type) rearrangement by treatment of n-butyllithium in tetrahydrofuran (THF) at $-40 \sim -50^\circ\text{C}$ to give the corresponding allylic alcohols (7). On the other hand, the allylic ethers 3 were treated with potassium *tert*-butoxide in *tert*-butyl alcohol-N,N-dimethylformamide (DMF) at room temperature to give the corresponding allylic enol ethers (12), which isomerized to the corresponding aldehydes (13) on heating in xylene by the Claisen rearrangement.

In the previous paper,¹⁾ it was shown that 3-methoxy-1-phenylthio-1-propene (2) is alkylated exclusively at α -position of the sulfur atom via its lithio derivative and the resulted products afford α,β -unsaturated aldehydes in good yields by hydrolysis in the presence of mercuric chloride.



In connection with the above investigation, we attempted alkylation of allylic ethers 3 to subject the products to the Claisen rearrangement.²⁾

The allylic ethers 3 were synthesized from 1-phenylthio-2,3-epoxypropane (1) by the procedure similar to that described for the methyl ether 2,¹⁾ and yields were listed in Table 1. First, we tried the alkylation of 3-allyloxy-1-phenylthio-1-propene (3a). It was found, however, that treatment of 3a with 1 equivalent of n-butyllithium at -78°C for 2 h and then with benzyl bromide did not afford the expected benzylated product 5, but gave 1-phenylthio-1,5-hexadien-3-ol (7a), isomer of 3a, in 47% yield along with 3a (ca. 26% recovery).



In spite of failure of benzylation, it appeared of interest to investigate this rearrangement, because the product will be used as the synthetic intermediate of certain natural products. Thus, the reaction of 3a with *n*-butyllithium was examined under various conditions. As shown in Table 1, the use of 2 equivalents of *n*-butyllithium gave better results. The lithiation proceeded slowly at -78°C , but when the reaction temperature was raised to -10°C , the reaction mixture became complex. It was found that the most suitable reaction temperature was at $-40 \sim -50^{\circ}\text{C}$.

On the basis of these results together with the fact that it was unable to trap the intermediate carbanion 4 with benzyl bromide, it seemed reasonable that the rearrangement is rather fast and the lithiation is the rate determining step of this reaction.

When 3b was treated with 2 equivalents of *n*-butyllithium at $-40 \sim -50^{\circ}\text{C}$ for 2.5 h in THF, 4-methyl-1-phenylthio-1,5-hexadien-3-ol (7b), isomer of 3b, was isolated.³⁾ From this fact, this rearrangement is not [1,2]-sigmatropic but [2,3]-sigmatropic rearrangement.

In a similar manner, other allylic ethers 3 were rearranged to the corresponding allylic alcohols 7. These results are summarized in Table 1.

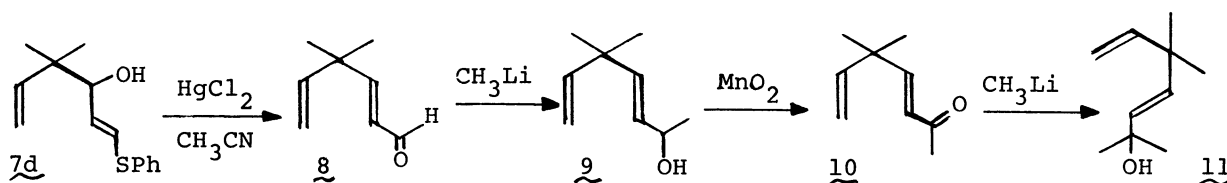
Table 1. Syntheses and the Wittig-type Rearrangement of Allylic Ethers 3

R^1	R^2	R^3	Yield of <u>3</u> ^{a)} (%)	Bp ($^{\circ}\text{C}$)/mmHg	Reaction Conditions n-BuLi (eq)	Temp ($^{\circ}\text{C}$)	Time (h)	Yield ^{d)} of <u>7</u> ^{a)} (%)	Recovery of <u>3</u> (%)
<u>3a</u>	H	H	83 ^{b)}	140/7	1.0	-78	1	50	30
					2.0	-78	1	59	14
					2.0	-78	5	68	9
					2.0	-10	1	63	trace
					2.0	$-40 \sim -50$	5	72	trace
<u>3b</u>	H	CH_3	91 ^{b)}	124-126/2	2.0	$-40 \sim -50$	2.5	76	—
<u>3c</u>	CH_3	H	96 ^{b)}	153-154/8	2.0	$-40 \sim -50$	2.5	80	—
<u>3d</u>	H	CH_3	73 ^{c)}		2.0	$-40 \sim -50$	2.5	71	—

a) Satisfactory IR, NMR, and elemental analysis data were obtained for these compounds. b) Isolated yield by distillation. c) Isolated yield by column chromatography. d) Isolated yield by silica gel TLC.

Typical procedure for the rearrangement is as follows; *n*-butyllithium in hexane (1.36 ml, 2 mmol) was added to a solution of allyl ether 3a (206 mg, 1 mmol) in dry THF (5 ml) with stirring at -78°C under argon. After addition of *n*-butyllithium, the mixture was stirred at $-40 \sim -50^{\circ}\text{C}$ for 5 h. Then the reaction mixture was quenched with NaCl-saturated aqueous solution at the same temperature, and was extracted with ether. The organic layer was dried over anhydrous sodium sulfate. After removal of the solvent, the residue was subjected to TLC (hexane : ethyl acetate = 8 : 1, R_f 0.3) and the allylic alcohol 7a (151 mg) was obtained in 72% yield.

Next, we prepared yomogi alcohol (11) to demonstrate synthetic application of this rearrangement. When allylic alcohol 7d was hydrolyzed in acetonitrile-1*N*-hydrochloric acid (7 : 1) solution in the presence of equimolar amount of mercuric chloride at room temperature for 24 h, the corresponding α,β -unsaturated aldehyde 8 (bp $70^{\circ}\text{C}/28$ mmHg) was obtained in 60% yield. The aldehyde reacted with methyl-lithium at -78°C in THF to give allylic alcohol 9, which, without purification, was treated with 10 equivalents of active manganese dioxide in hexane to afford the corresponding ketone 10 in 62% yield from 8. Yomogi alcohol (11) [bulb to bulb distillation, bp $112\text{--}120^{\circ}\text{C}/22$ mmHg (bath temp)] was obtained in 72% yield by the reaction of 10 with methyl-lithium. IR and NMR data of 11 showed good agreement with those of the natural product⁴⁾ and satisfactory elemental analysis was obtained.



On the other hand, when allylic ethers 3 were allowed to stand with potassium *tert*-butoxide in *tert*-butyl alcohol-DMF at room temperature, double bond isomerization took place and the corresponding allylic enol ethers 12 were obtained in good yields. These compounds 12 were converted to the aldehydes 13 on heating in xylene by the Claisen rearrangement. Some of these results are shown in Table 2.

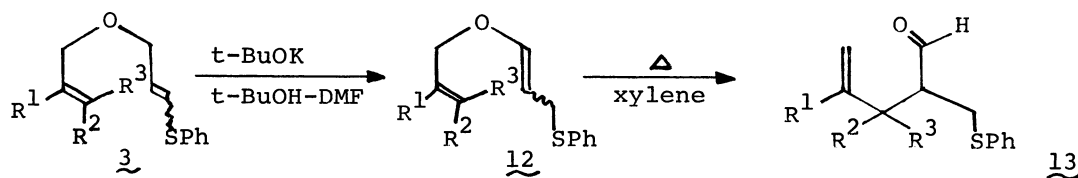


Table 2. Isomerization of Double Bond and the Claisen Rearrangement

	R^1	R^2	R^3	$\underline{12}^{\text{b)}$	Yield ^{a)} (%)	$\underline{13}^{\text{c)}$
<u>3a</u>	H	H	H	82		80
<u>3b</u>	H	CH_3	H	74		88
<u>3c</u>	CH_3	H	H	91		56

a) Isolated yield by silica gel TLC. b) Structure of these compounds were confirmed by IR and NMR spectroscopy.

c) Satisfactory IR, NMR, and elemental analyses data were obtained for these products (see ref. 5).

Typical procedure for isomerization of double bond and the Claisen rearrangement are shown in the following; the allyl ether 3a (206 mg, 1 mmol) in DMF (2 ml) was added into a mixture of potassium tert-butoxide (112 mg, 1 mmol) and tert-butyl alcohol (0.5 ml) in DMF (2 ml) at room temperature and the reaction mixture was stirred for 2.5 h. After being quenched with NaCl-saturated aqueous solution, the reaction mixture was extracted with ether. The allylic enol ether 12a was isolated in 82% yield by silica gel TLC (hexane : benzene = 5 : 2, Rf 0.7). Then, 12a (144 mg, 0.55 mmol) was heated in refluxing xylene (3 ml) for 3 h under argon. After removal of solvent in vacuo, aldehyde 13a (115 mg) was isolated in 80% yield by silica gel TLC (hexane : benzene = 1 : 1, Rf 0.3).

In conclusion, it should be noted that the γ -carbon of allylic halides could be linked regiospecifically to the center or terminal carbon of functionalized three carbon unit ($\text{PhSCH}_2\overset{\text{1}}{\text{C}}\text{HCHO}$ or $-\text{CH}=\overset{\text{2}}{\text{C}}\text{HCHO}$, respectively) via the Wittig and the Claisen rearrangement of allylic ethers 3. The application of these reactions to the syntheses of natural products is now in progress.

REFERENCES AND NOTES

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- 2) Recently, attractive synthetic reactions using sigmatropic rearrangements, including the Cope and the Claisen rearrangement and number of their variations such as the oxy-Cope, thio-Claisen and amino-Claisen rearrangements, have been reported (see follows).
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- 3) 3b, IR(NaCl): 3020, 1100, 965, 740, and 690 cm^{-1} , NMR(CCl_4 , 60 MHz): δ 1.65 (3H, d), 3.71~4.18 (4H, m), 5.47~5.77 (2H, m), 5.80~6.10 (1H, m), 6.41 (1H, d, J = 15 Hz), and 7.23 (5H, m).
7b, IR(NaCl): 3350, 3060, 1640, 950, 740, and 690 cm^{-1} , NMR(CCl_4 , 60 MHz): δ 1.01 (3H, d, J = 7 Hz), 2.03~2.53 (1H, q), 2.97 (1H, s), 3.78~4.17 (1H, m), 4.85~5.28 (2H, m), 5.52~6.07 (2H, m), 6.41 (1H, d, J = 15 Hz), and 7.23 (5H, m).
- 4) a) S.Hayashi, K.Yano, and T.Matsuura, *Tetrahedron Lett.*, 6241 (1968).
b) W.Sucrow and W.Richter, *Ber.*, 103, 3771 (1970).
- 5) 12b (mixture of cis and trans isomers), IR (NaCl): 3050, 2960, 2900, 1660, 1100, 965, and 690 cm^{-1} , NMR(CCl_4 , 60 MHz): δ 1.78 (3H, m), 3.45, 3.60 (2H, ca. 0.4H: 1.6H, d, J = 7 Hz), 4.15 (2H, m), 4.30~4.65 (1H, m), 5.50~5.70 (2H, m), 5.98, 6.25 (1H, ca. 0.8H: 0.2H, d, J = 6 and 12 Hz), and 7.25 (5H, m).
13b (mixture of erythro and threo isomers), IR (NaCl): 3070, 1735, 1580, 1480, 920, 740, and 690 cm^{-1} , NMR(CCl_4 , 60 MHz): δ 0.98 (1.5H, d, J = 7 Hz), 1.05 (1.5H, d, J = 7 Hz) 2.30~2.90 (2H, m), 2.91~3.25 (2H, m), 5.00 (1H, dd, J = 16 Hz and 2 Hz), 5.05 (1H, dd, J = 10 Hz and 2 Hz), 5.43~6.00 (1H, m), 7.17 (5H, s), 9.50 (0.5H, d), and 9.55 (0.5H, d).

(Received March 15, 1977)