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# Communications

## Efficient Stereocontrol in the [2,3] Sigmatropic Rearrangement of Allylic Sulfoxides

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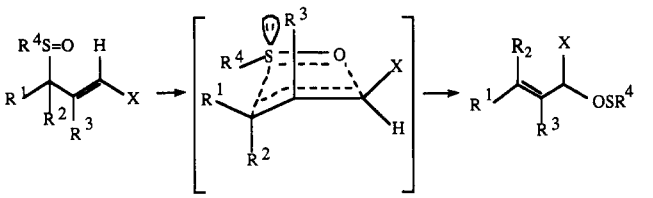
*Summary:* The [2,3] sigmatropic rearrangement of allylic sulfoxides occurs with an extremely high *E* preference when a substituent branched at the $\beta$ position of a sulfinyl group is involved.

*Sir:* The [2,3] sigmatropic rearrangement of allylic sulfoxides has found versatile utility in the synthesis of allylic alcohols[1] and $\alpha,\beta$-unsaturated compounds.[2] Unfortunately, however, with this method one cannot always control the stereochemistry about the double bond. The present paper is concerned with an effective solution to this problem.

A five-membered transition state has led one to postulate that the selectivity for the *E* isomer should increase as $R^1$ becomes larger than $R^2$ since the $R^1$ group would preferentially occupy a pseudoequatorial position.[1b,c]



$R^1 > R^2$ (1)

Indeed this is the case for 2,3-disubstituted allylic compounds ($R^2$ and $R^3$ = H). High *E* selectivity had also been attained for 2,2,3-trisubstituted allylic alcohols ($R^1$, $R^3 \neq$ H, $R^2$ = H),[3,4] but Hoffmann pointed out later that this was not a consequence of a kinetic effect:[1c] the *E* isomers are thermodynamically favored in these compounds. On the other hand, stereocontrol in the preparation of 2,3,3-trisubstituted allylic systems ($R^1$, $R^2 \neq$ H, $R^3$ = H) which are most frequently encountered in organic synthesis has met with little success. Evans and his co-workers commented that the increased *E* selectivity for $R^1 = (CH_3)_2C{=}CHCH_2$ and $(CH_3)_2C{=}CH(CH_2)_2$ as compared with $R^1 = C_2H_5$ where $R^2 = CH_3$ was "quite surprising in view of other previous published work on [2,3] sigmatropic rearrangements leading to olefins having a similar substitution pattern".[4,5] Although this unusual outcome has not yet been fully accounted for, it apparently has nothing to do with the conformational energy difference between the transition states since the two groups do not differ so significantly in bulkiness. Now we report, for the first time, conclusive evidence disclosing the importance of the bulkiness of $R^1$ and $R^2$ in determining the stereochemical outcome. In addition, the concepts outlined here have been found effective even for the preparation of tetrasubstituted double bonds.

In the course of studies on the synthetic applications of 3-alkoxyallyl sulfides **1**,[2d] we have found that their carbonyl adducts **2** are converted into (*E*)-4-hydroxy-2-alkenals **3** in a highly stereoselective manner (Scheme I). A typical procedure is as follows. To a THF solution (3 mL) containing **1** (1 mmol) and HMPA (3.9 mmol) was slowly

(1) (a) Bickart, P.; Carson, F. W.; Jacobus, J.; Miller, E. G.; Mislow, K. *J. Am. Chem. Soc.* **1968**, *90*, 4869. (b) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147. (c) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 563.

(2) (a) Ortiz de Montellano, P. R.; Hsu, C. K. *Tetrahedron Lett.* **1976**, 4215. (b) Yamagiwa, S.; Sato, H.; Hoshi, N.; Kosugi, H.; Uda, H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 570. (c) Mandai, T.; Moriyama, T.; Nakayama, Y.; Sugino, K.; Kawada, M.; Otera, J. *Tetrahedron Lett.* **1984**, *25*, 5913. (d) Sato, T.; Okazaki, H., Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1988**, *29*, 2979.

(3) Grieco, P. A. *J. Chem. Soc., Chem. Commun.* **1972**, 702. Grieco, P. A.; Finkelhor, R. S. *J. Org. Chem.* **1973**, *38*, 2245.

(4) Evans, D. A.; Andrews, G. C.; Fujimoto, T. T.; Wells, D. *Tetrahedron Lett.* **1973**, 1389.

(5) The [2,3] sigmatropic rearrangements of sulfur ylides derived from acyclic terpenoids also gave rise to high *E* preference for trisubstituted double bonds: Blackburn, G. M.; Ollis, W. D. *Chem. Commun.* **1968**, 1261. Blackburn, G. M.; Ollis, W. D.; Smith, S.; Sutherland, I. O. *Chem. Commun.* **1969**, *99*. These results suggest the possibility that a prenyl moiety serves for improving the stereoselectivity. More recently, however, Julia and his co-workers have failed to bias the stereochemistry in the [2,3] sigmatropic rearrangement of the allylic sulfenate with $R^1 = (CH_3)_2C{=}CH(CH_2)_2$ and $R^2 = CH_3$: Baudin, J.-B.; Julia, S. A. *Tetrahedron Lett.* **1988**, *29*, 3251.

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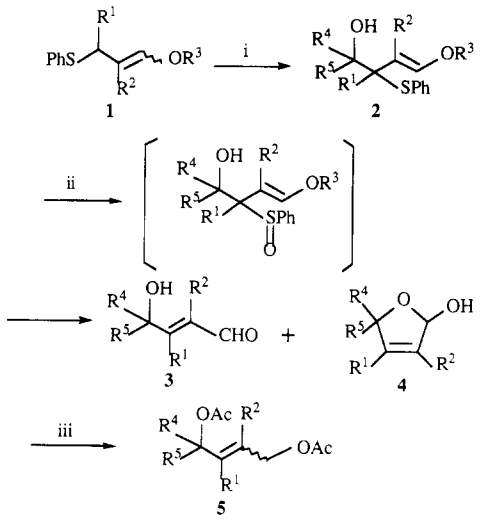
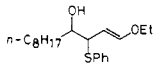
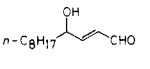
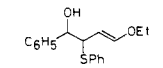
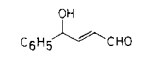
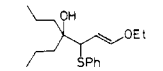
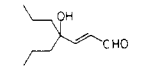
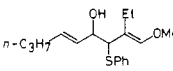
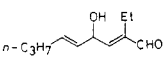
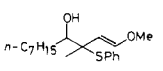
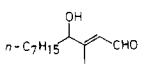
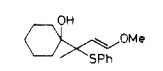
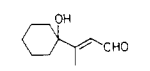
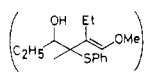
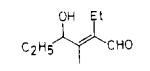
**Scheme I**[a]



[a] (i) *t*-BuLi, HMPA, $R^4R^5C{=}O$, THF −78 °C; (ii) $NaIO_4$, dioxane–water, room temperature, or $MoO_5$–$C_5H_5N$–HMPA, $CH_2Cl_2$, 0 °C; (iii) $LiAlH_4$, THF, −78 °C and $Ac_2O$–$C_5H_5N$–$Me_2NC_5H_4N$, 0 °C.

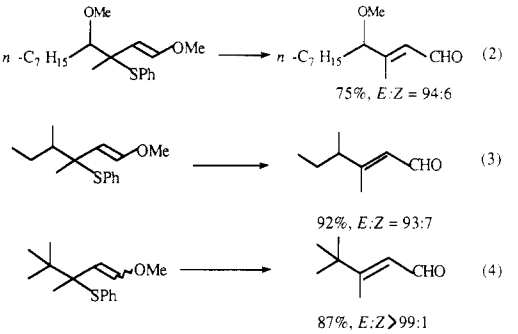
**Table I. Conversion of 2 into 3**[a]

| entry | 2[b] | reactn time, h | 3 | yield[c] | *E*:*Z* of 5[d] |
|---|---|---|---|---|---|
| 1 |  | 20 |  | 81 | 94:6 |
| 2 |  | 1.5 |  | 93 | 99:1 |
| 3 |  | 4 |  | 97 | 99:1 |
| 4 |  | 1[e] |  | 75 | 99:1 |
| 5 |  | 1.5 |  | 75 | 95:5 |
| 6 |  | 1.5[f] |  | 60 | 95:5 |
| 7 |  | 2.5[f] |  | 36[g] | 93:7 |

[a] Reaction conditions unless otherwise noted: $NaIO_4$ (2 equiv), 5:1 dioxane–water, room temperature. [b] Diastereomeric mixtures (ca. 1:1) were obtained for the aldehyde adducts. [c] Isolated yields as pure (*E*)-3 after column chromatography. [d] Determined by capillary GC. [e] MoOPH (2 equiv), $CH_2Cl_2$, 0 °C. [f] $NaHCO_3$ (2 equiv) was added. [g] Yield based on 1 since 2 was used without purification due to its instability.

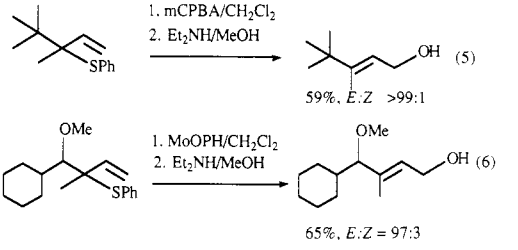
added *t*-BuLi (1.3 mmol) during a period of 10 min at −78 °C. After the solution was stirred for 3 min, aldehyde or ketone (1.3 mmol) was added during a period of 5 min at this temperature. The reaction mixture was stirred for 15 min and quenched with aqueous $NH_4Cl$ (1 mL). The usual aqueous workup and column chromatography on silica gel gave 2. Exposure of 2 (1 mmol) to $NaIO_4$ (2 mmol) in dioxane (5 mL)–water (1 mL) at room temperature or to $MoO_5$–$C_5H_5N$–HMPA (MoOPH) (2 mmol) in $CH_2Cl_2$ (5 mL) at 0 °C and the subsequent aqueous workup provided good to excellent yields of 3 as sole products (Table I).[6] Although no *Z* isomers were detected at all after column chromatography, these isomers were actually formed: reduction of the crude reaction products with $LiAlH_4$ and acetylation afforded small amounts of (*Z*)-diacetates 5 along with their *E* counterparts. The *E*:*Z* ratios are compiled in the last column of the table. Failure to detect the *Z* isomers of 3 in the crude products suggests formation of lactols 4,[2a] which we could not isolate through column chromatography. The present procedure enables one to obtain di-, tri-, and tetrasubstituted 4-hydroxy-2-alkenals in the stereochemically pure forms, indicative of its generality and synthetic usefulness.

Comparison with our previous results on the alkylation products of 1, where *E*,*Z* mixtures of tri- and tetrasubstituted α-enals were produced,[2d] indicates that substitution at the position β to a phenylthio group in 2 plays a pivotal role in controlling the stereochemistry of the subsequent [2,3] sigmatropic rearrangement. The importance of this effect was exemplified by the following reactions. Protection of a hydroxy group as a methyl ether induced little change in both the yield and stereochemical outcome (eq 2); cf. entry 5 in Table I. Incorporation of secondary and tertiary alkyl groups induced high *E* preference as well (eq 3 and 4). These results lead us to conclude that the



bulkiness of the substituents located β to the phenylthio group is primarily responsible for the high stereoselectivity.

The generality was further attested by the conventional Mislow–Evans rearrangement (eq 5 and 6). Allylic sulfides with a bulky substituent were converted into the corresponding *E* allylic alcohols with high stereoselectivity under ordinary reaction conditions. Note that allylic sulfides with less bulky substituents provide thermodynamically controlled *E*:*Z* mixtures of allylic alcohols (ca. 6:4).



In summary, [2,3] sigmatropic rearrangement of allylic sulfoxides proved to occur with an extremely high *E* preference when a substituent branched at the β-position of a sulfinyl group was involved. We presume that the concept could be applied to other [2,3] sigmatropic rearrangements. The generality and simplicity of the present method will undoubtedly meet a variety of synthetic demands.

**Acknowledgment.** Thanks are due to H. Okazaki and Y. Hiramura for their assistance.

**Supplementary Material Available:** Preparation and spectral data of 11 compounds 2 and 3 (4 pages). Ordering information is given on any current masthead page.

(6) All compounds in this study gave satisfactory NMR and HRMS spectral data.