A Practical, Efficient Method for Preparation of Four Possible Stereoisomers of Secondary Allylic Alcohols using Kinetic Resolution of (*E*)-1-Trimethylsilylalk-1-en-3-ol by the Sharpless Process

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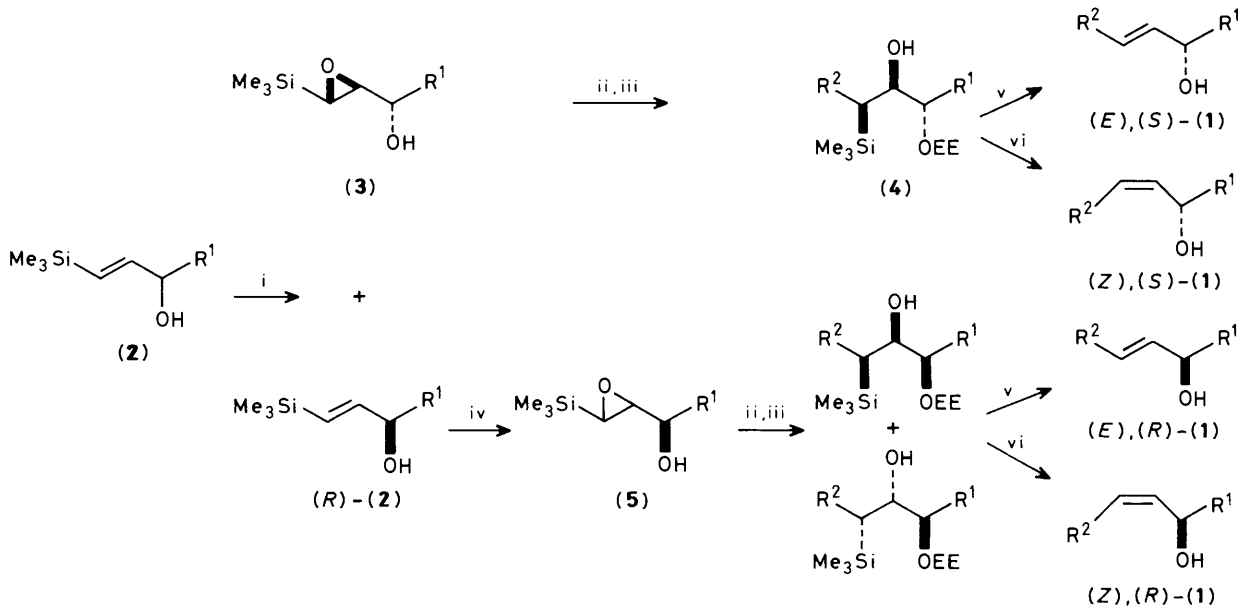
Kinetic resolution of (*E*)-1-trimethylsilylalk-1-en-3-ol by the Sharpless process, which proceeds with very large rate differences for the two isomers, combined with the reactivity of epoxysilyl compounds affords a practical, efficient method for preparation of four possible stereoisomers of secondary allylic alcohols.

Allylic alcohols are valuable intermediates in a number of synthetic organic processes, and their synthesis in an optically active form has attracted much interest in recent years.[1] We now report a practical method for preparation of four possible stereoisomers of secondary allylic alcohols (**1**), *i.e.*, (*E*),(*S*)-(**1**), (*Z*),(*S*)-(**1**), (*E*),(*R*)-(**1**), and (*Z*),(*R*)-(**1**), starting from a single racemic material and using a single chiral source. Our method shown in Scheme 1 involves a highly effective kinetic resolution of (*E*)-1-trimethylsilylalk-1-en-3-ol (**2**) using the Sharpless process as the key step.[1a]

The alcohols (**2**) which have (*E*)-configuration can be prepared specifically by the reaction of lithium trimethylsilylethynylide with aldehydes followed by reduction of the resulting adducts (**6**) *via* $(\eta^5\text{-}C_5H_5)_2TiCl_2$-catalysed hydromagnesiation with Bu^{i}MgBr as exemplified by Scheme 2.[2] We found that the reduction of (**6**) with $LiAlH_4$[3] provided a mixture of (*E*)- and (*Z*)-isomers in a ratio of 5 : 1.

A preliminary experiment revealed that the asymmetric epoxidation of (**2**) proceeds with much variation in rate for the two isomers. Thus, to speed up the reaction, the kinetic



EE = ethoxyethyl

Scheme 1. *Reagents:* i, Bu^{t}OOH, L-(+)-di-isopropyl tartrate, Ti(OPr^i)$_4$; ii, CH_2=CH(OEt), H^+; iii, R^2MgBr, CuI; iv, Bu^{t}OOH, VO(MeCOCHCOMe)$_2$; v, KH, tetrahydrofuran then HCl; vi, H_2SO_4, MeOH.

Table 1. Optical purity of (*R*)-(**2**) and (**3**) in the kinetic resolution of racemic (**2**) *vs.* reaction time.[a]

Entry	Reaction time (h)	Enantiomeric purity (% e.e.)[b] (*R*)-(**2**,R^1 = n-C_5H_{11})	(**3**, R^1 = n-C_5H_{11})[c]
1	7	>99	>99
2	10	>99	98.6
3	18	>99	97.6

[a] Reaction performed as follows, 1.0 equiv. of Ti(OPr^i)$_4$, 1.2 equiv. of L-(+)-di-isopropyl tartrate, 1.0 equiv. of racemic (**2**), and 1.5 equiv. of anhydrous TBHP are stirred in dry CH_2Cl_2 [8.8 ml/mmol of (**2**)] at −20 °C. Yields of recovered (*R*)-(**2**) and (**3**) are respectively more than 49%, checked by ^{1}H n.m.r. analysis. Isolated yields of (*R*)-(**2**) and (**3**) were in the range 39—45%. [b] The enantiomeric excesses were determined by ^{1}H n.m.r. analysis on the corresponding allylic acetate (pyridine/Ac_2O) in the presence of (−)-tris[di(perfluoro-2-propoxypropionyl)methanato]praseodymium(III) [(−)-Pr(DPPM)$_3$] and on the corresponding epoxy acetate in the presence of (+)-Eu(DPPM)$_3$ (ref. 6). [c] No *threo* epoxy alcohol was detected.

resolution was carried out using a rather large excess of t-butyl hydroperoxide (TBHP). Table 1 gives the relationship of the enantiomeric purity of the epoxy alcohol produced and the unreacted allyl alcohol to reaction time when the kinetic resolution of (*E*)-1-trimethylsilyl-oct-1-en-3-ol (**2**, R^1 = n-C_5H_{11}) was carried out using 1.5 equiv. of anhydrous TBHP. Entry 1 in Table 1 shows that the kinetic resolution goes almost to completion in 7 h to afford (**3**, R = n-C_5H_{11}) with more than 99% e.e. and (*R*)-(**2**, R^1 = n-C_5H_{11}) with more than 99% e.e.† Allowing the reaction to run for 10 h (entry 2) or 18 h (entry 3) scarcely alters the enantiometic purity of (**3**, R^1 = n-C_5H_{11}) nor the yield of (*R*)-(**2**, R^1 = n-C_5H_{11}). These results indicate that the rate of the epoxidation reaction between two enantiomers of (**2**) differs significantly. We confirmed this point by carrying out the epoxidation of (*R*)-(**2**, R^1 = n-C_5H_{11}) by using L-(+)-di-isopropyl tartrate (mismatched pair) and 1.5 equiv. of TBHP which afforded the epoxidation product(s) in less than 1.7% yield after 18 h reaction.

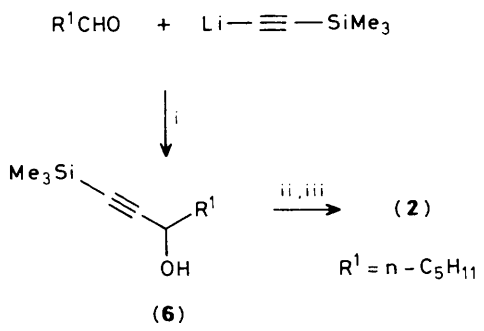
† Preparation of optically active β-methyl-γ-(trimethylsilyl) homoallyl alcohols[4] and γ,δ-epoxy-β-methyl-γ-(trimethylsilyl)-alkanols[5] has been reported.

Table 2. Yields and rotations of (**1**, R^1 = n-C_5H_{11}, R^2 = Pr^n).

Allylic alcohol	Yield (%)	$[\alpha]_D^{25}$ (*c* in $CHCl_3$)
(*E*),(*S*)-(**1**)[a]	77[c]	−5.1° (1.26)
(*Z*),(*S*)-(**1**)	51[c]	−24.3° (0.99)
(*E*),(*R*)-(**1**)	61[d]	+4.9° (1.27)
(*Z*),(*R*)-(**1**)[b]	41[d]	+24.9° (1.06)

[a] The optical purity was confirmed by converting into (*S*)-(−)-acetoxyheptanal *via* ozonolysis after acetylation. $[\alpha]_D^{20}$ −38.3° (*c* 0.58, $CHCl_3$) {lit.[9] $[\alpha]_D^{20}$ −37.8° (*c* 0.5, $CHCl_3$)}. [b] (*R*)-(+)-2-acetoxyheptanal obtained; $[\alpha]_D^{20}$ 38.0° (*c* 0.60, $CHCl_3$). [c] Based on (**3**). [d] Based on (*R*)-(**2**).

Compound (**3**) thus obtained can be readily converted into either (*E*),(*S*)-(**1**) or (*Z*),(*S*)-(**1**) by the procedure shown in Scheme 1.[7] Thus, protection of (**3**, R^1 = n-C_5H_{11}) as an ethoxyethyl ether followed by treatment with Pr^{n}MgBr in the presence of a catalytic amount of CuI (20%) afforded (**4**, R^1 = n-C_5H_{11}, R^2 = Pr^n), from which (*E*),(*S*)-(**1**, R^1 = n-C_5H_{11}, R^2 = Pr^n) or (*Z*),(*S*)-(**1**, R^1 = n-C_5H_{11}, R^2 = Pr^n) was synthesized by treatment with KH in tetrahydrofuran (5 °C for 1.5 h) or H_2SO_4 in MeOH (room temperature for 2 h) respectively. Similarly, two other possible stereoisomers of allylic alcohols (*E*),(*R*)-(**1**, R^1 = n-C_5H_{11}, R^2 = Pr^n) and (*Z*),(*R*)-(**1**, R^1 = C_5H_{11}, R^2 = Pr^n) were prepared from (*R*)-(**2**, R^1 = n-C_5H_{11}) after converting into the epoxy alcohol (**5**, R^1 = n-C_5H_{11}) (*threo*:*erythro* = 1:3) using TBHP–VO(MeCOCHCOMe)$_2$[8] (Scheme 1). Overall yields and the specific rotations of the alcohols (**1**) thus prepared are summarized in Table 2. Although the $[\alpha]_D$ values of the pairs of enantiomers indicate that conversion of (**2**) or (**3**) into (**1**) proceeds without racemization, this was confirmed by con-



Scheme 2. *Reagents:* i, Et_2O, −30—25 °C, 96%; ii, $2Bu^iMgBr/(\eta^5\text{-}C_5H_5)_2TiCl_2$, 27 °C, 7 h; iii, H^+, 96%.

verting (*E*),(*S*)-(**1**, R^1 = n-C_5H_{11}, R^2 = Pr^n) and (*Z*),(*R*)-(**1**, R^1 = n-C_5H_{11}, R^2 = Pr^n) into 2-acetoxyheptanal by ozonolysis after acetylation and comparing the rotation with the literature value (see Table 2).

The present synthesis is characterized as providing a 'selective and operationally simple route to all the possible stereoisomers of secondary allylic alcohols with high optical purity' starting from (*E*)-1-trimethylsilylalk-1-en-3-ol.

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References

1 For a recent preparation of optically active secondary allylic alcohols, see: (a) V. S. Martin, S. S. Woodard, T. Katsuki, Y. Yamada, M. Ikeda, and K. B. Sharpless, *J. Am. Chem. Soc.*, 1981, **103**, 6237; (b) R. Noyori, *Pure Appl. Chem.*, 1981, **53**, 2315; (c) J. Fujiwara, Y. Fukutani, M. Hasegawa, K. Maruoka, and H. Yamamoto, *J. Am. Chem. Soc.*, 1984, **106**, 5004; (d) T. Sato, Y. Gotoh, Y. Wakabayashi, and T. Fujisawa, *Tetrahedron Lett.*, 1983, **24**, 4123.

2 F. Sato, H. Watanabe, Y. Tanaka, and M. Sato, *J. Chem. Soc., Chem. Commun.*, 1982, 1126; F. Sato and H. Katsuno, *Tetrahedron Lett.*, 1983, **24**, 1809.

3 E. J. Corey, J. A. Katzenellenbogen, and G. H. Posner, *J. Am. Chem. Soc.*, 1967, **89**, 4245.

4 Y. Kobayashi, Y. Kitano, and F. Sato, *J. Chem. Soc., Chem. Commun.*, 1984, 1329.

5 Y. Kobayashi, H. Uchiyama, H. Kanbara, and F. Sato, *J. Am. Chem. Soc.*, 1985, **107**, 5541.

6 N. Ishikawa, H. Honda, and F. Yamaguchi, presented at the Annual Meeting of Japan Chemical Society, April 1983, Tokyo.

7 E. W. Colvin, 'Silicon in Organic Synthesis,' Butterworths, London, 1981, ch. 12; W. P. Weber, 'Silicon Reagents for Organic Synthesis,' Springer-Verlag, New York, 1983, ch. 6; P. F. Hudrlik, D. Peterson, and R. J. Rona, *J. Org. Chem.*, 1975, **40**, 2263.

8 H. Tomioka, T. Suzuki, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, 1982, **23**, 3387; A. S. Narula, *ibid.*, 1982, **23**, 5579.

9 R. Noyori, I. Tomino, and M. Nishizawa, *J. Am. Chem. Soc.*, 1984, **106**, 6717.