An Efficient, Practical Method for Preparation of Optically Active *erythro*-Epoxy Secondary Alcohols using Sharpless Kinetic Resolution of β-Trimethylsilyl Secondary Allylic Alcohols

Yasunori Kitano, Takashi Matsumoto, Yoshiyuki Takeda, and Fumie Sato*

Department of Chemical Engineering, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

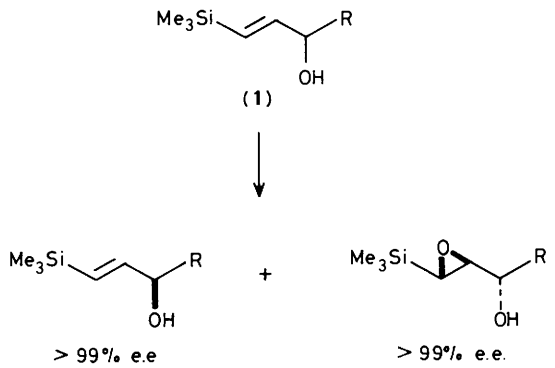
Kinetic resolution of β-trimethylsilyl allylic alcohols by the Sharpless process proceeds with synthetically satisfactory rate differences for the two enantiomers, thus providing a practical, efficient method for preparation of both enantiomers of *erythro*-epoxy secondary alcohols with high optical purity.

Recently we reported that the kinetic resolution of (*E*)-1-trimethylsilylalk-1-en-3-ols (**1**) by the Sharpless asymmetric epoxidation reaction[1] proceeds with large variation in rate for the two isomers; thus both the epoxy alcohol and the allylic alcohol can be obtained simultaneously (Scheme 1) with >99% purity.[2]

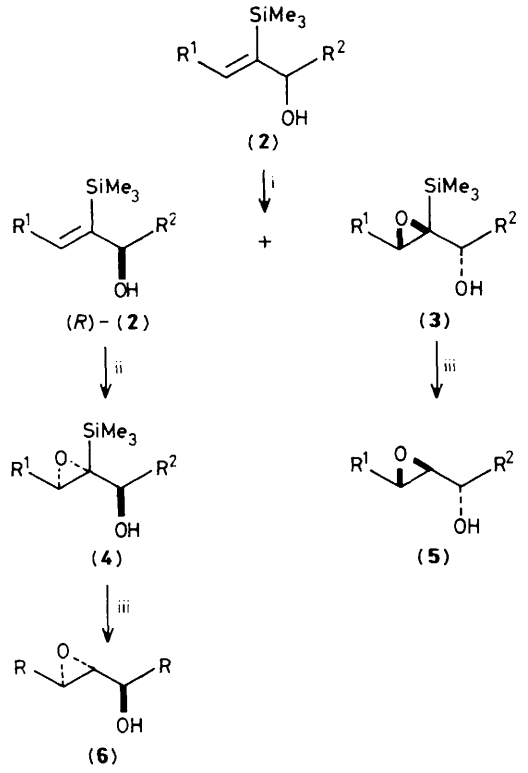
With these results in hand, we were interested in the kinetic resolution of β-trimethylsilyl allylic alcohols (**2**), because if the reaction proceeded with large rate differences for the two enantiomers, it would provide a convenient method for preparation of both enantiomers of *erythro*-epoxy secondary alcohols (**3**) and (**4**) according to the procedure shown in Scheme 2. The alcohols (**3**) and (**4**) thus prepared can be readily converted into *erythro*-epoxy alcohols (**5**) and (**6**), respectively, by protodesilylation.[3]

It has been reported that secondary allylic alcohols with bulky tertiary groups in the α-vinyl position are not good kinetic resolution substrates, and in the reaction with (**7**), the enantiomeric excess (e.e.) of the recovered starting alcohol was only 30% at 60% conversion (Scheme 3).[4] We were thus concerned about the efficiency of kinetic resolution of (**2**), but in practice our concern was unfounded.

Table 1 summarizes the results of the kinetic resolution of (**2**) using L-(+)-di-isopropyl tartrate as chiral source. The relative rates of fast and slowly reacting isomers for (**2**) are not as great as for (**1**), but have the synthetically satisfactory magnitudes of about 24 : 1 for (**2**) in which R^1 is H and near 100 : 1 when R^1 is an alkyl group; these values were calculated



Scheme 1. *Reagents:* Bu^{t}OOH, L-(+)-di-isopropyl tartrate (DIPT), Ti(OPr^i)$_4$, −20 °C, 7 h.

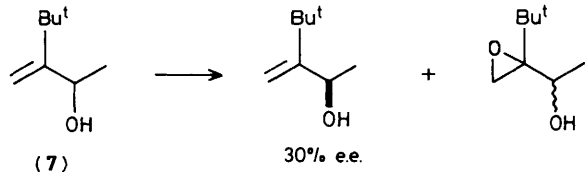


Scheme 2. *Reagents:* i, Bu^{t}OOH, L-(+)-DIPT, Ti(OPr^i)$_4$; ii, Bu^{t}OOH, VO(MeCOCHCOMe)$_2$; iii, Bu^{t}OK, Bu$^n_4$NF, tetrahydrofuran.

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

Run		Substrate (**2**) R^1	R^2	Reaction time/h	Enantiomeric purity (% e.e.) (**3**)[c]	(*R*)-(**2**)	Conversion[b] (%)
1	(**2a**)	H	n-C_5H_{11}	24	79.2[d]	87.4[d,e]	52.5
2	(**2b**)	Bu^n	Me	1	92.4[f]	95.4[f]	50.8
3	(**2b**)	Bu^n	Me	2	83.8[f]	>99[f,g,h]	54.4

[a] Reactions 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 0.6 equiv. of anhydrous Bu^{t}OOH were stirred in dry CH_2Cl_2 (6.1 ml/mmol) at −23 °C. [b] Calculated from %e.e. of (**3**) and (*R*)-(**2**). Total yields of (**3**) and (*R*)-(**2**) were >98% (^{1}H n.m.r. analysis). [c] No *threo* isomer was detected. [d] The alcohols (**3a**) and (*R*)-(**2a**) were resolved by h.p.l.c. [CHIRALPAK OT(+), Daicel Chemical Industries, Ltd.] after conversion into the benzoates of (**5a**) and (**6a**) (see Scheme 2 and text). [e] Absolute configuration was confirmed by conversion into (*R*)-(+)-2-acetoxyheptanal[6] by protodesilylation (NaH, hexamethylphosphoric triamide)[3], and acetylation followed by ozonolysis. [f] The e.e. values were determined by ^{1}H n.m.r. analysis of the corresponding allylic acetate (Ac_2O–pyridine) of (*R*)-(**2b**) in the presence of (−)-Pr(dfpm)$_3$ and of the corresponding epoxy acetate of (**3b**) in the presence of (+)-Eu(dfpm)$_3$ (dfpm = di(perfluoro-2-propoxypropionyl)methanato). [g] Absolute configuration was confirmed by conversion into (*R*)-(−)-octan-2-ol[7] by protodesilylation (NaH, hexamethylphosphoric triamide) followed by hydrogenation. [h] Since (**3b**) and (*R*)-(**2b**) themselves were difficult to separate effectively, they were converted into their acetates and separated by column chromatography on silica gel: (*R*)-(**2b**); $[\alpha]_D^{25}$ +17.5° (*c* 0.96, $CHCl_3$).



Scheme 3. *Reagents:* Bu^{t}OOH, L-(+)-DIPT, Ti(OBu^t)$_4$; 60% conversion.

from the equation which relates the relative rates to the optical purities of (*R*)-(**2**) and (**3**).[5]

As expected, the allylic alcohols (*R*)-(**2**) thus obtained can be readily converted into (**4**) by V^{5+} catalysed epoxidation with Bu^{t}OOH[8] (Scheme 2). Thus (*R*)-(**2a**) and (*R*)-(**2b**) were converted into the corresponding epoxides (**4**) specifically in 87 and 88% yields, respectively. Treatment of (**3**) and (**4**) with Bu^{t}OK and Bu$^n_4$NF in tetrahydrofuran at 0 °C for 5 min resulted in a near quantitative protodesilylation to afford (**5**) and (**6**), respectively[3] (Scheme 2).

Since racemic mixtures of the alcohols (**2**) are readily available by hydromagnesiation of 1-trimethylsilylalk-1-ynes followed by reaction with aldehydes,[9] the present reaction offers a practical synthesis of both enantiomers of *erythro*-epoxy alcohols (**3**) and (**4**), and also (**5**) and (**6**). It is noteworthy that both enantiomers can be prepared by using a single chiral source.

α,β-Epoxysilanes are not only precursors of epoxides but are also useful precursors of carbonyl compounds and heteroatom-substituted alkenes.[10] The synthetic uses of (**3**) and (**4**) are being studied.

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