[6] J. A. Schlueter, J. M. Seaman, S. Taha, H. Cohen, K. R. Lykke, H. H. Wang, J. M. Williams, *Chem. Commun.* **1993**, 972.

[7] M. Tsuda, T. Ishida, T. Nogami, S. Kurono, M. Ohashi, *Chem. Commun.* **1993**, 1296.

[8] Y. Takaguchi, T. Tajima, K. Ohta, J. Motoyoshiya, H. Aoyama, *Chem. Lett.* **2000**, 1388.

[9] a) A. P. Maierhofer, M. Brettreich, S. Burghardt, O. Vostrowsky, A. Hirsch, S. Langridge, T. M. Bayerl, *Langmuir* **2000**, *16*, 8884; b) M. Brettreich, S. Burghardt, C. Böttcher, T. Bayerl, S. Bayerl, A. Hirsch, *Angew. Chem.* **2000**, *112*, 1915; *Angew. Chem. Int. Ed.* **2000**, *39*, 1845; c) M. Brettreich, A. Hirsch, *Tetrahedron Lett.* **1998**, 2731; d) J.-F. Nierengarten, T. Habicher, R. Kessinger, F. Cardullo, F. Diederich, V. Gramlich, J.-P. Gisselbrecht, C. Boudon, M. Gross, *Helv. Chem. Acta* **1997**, *80*, 2238.

[10] V. J. Catalano, N. Parodi, *Inorg. Chem.* **1997**, *36*, 537.

[11] ^{1}H NMR (400 MHz, [D$_8$]toluene): $\delta = 2.17-2.63$ (m, 24H), 2.32–2.83 (m, 46H), 3.29–3.40 (m, 14H), 3.43 (d, $J = 1.6$ Hz, 2H), 3.48 (s, 24H), 3.48–3.57 (m, 8H), 6.91–7.95 (m, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 32.7$, 33.8, 34.0, 36.1, 37.1, 37.5, 49.2, 49.9, 51.65, 51.67, 52.2, 52.6, 52.9, 55.0, 59.0, 65.9, 74.7, 75.6, 123.7, 125.2, 126.8, 127.8, 128.4, 129.2, 136.5, 137.3, 138.8, 140.1, 141.39, 141.4, 141.6, 141.9, 142.0, 142.1, 142.59, 142.60, 142.62, 142.64, 142.9, 144.5, 144.6, 145.0, 145.18, 145.22, 145.33, 145.37, 145.40, 145.9, 146.1, 146.2, 146.4, 146.5, 152.4, 155.8, 159.52, 159.59, 172.2, 172.4, 173.1; UV/Vis (toluene): $\lambda_{\max}$ (ε) = 434.4 (1500), 702.0 nm (153); LD-TOF MS: $C_{141}H_{127}N_{15}O_{24}$: m/z calcd: 2414.62 [M]$^-$; found: 2414.22.

[12] C. Luo, M. Fujitsuka, A. Watanabe, O. Ito, L. Gan, Y. Hung, C.-H. Hung, *J. Chem. Soc. Faraday Trans.* **1998**, *94*, 527.

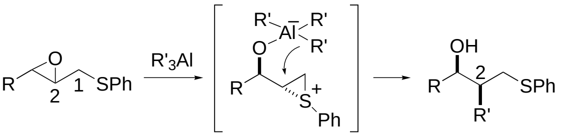
[13] J. W. Arbogast, C. S. Foote, *J. Am. Chem. Soc.* **1991**, *113*, 8886.

Stereospecific Interconversion between *cis* and *trans* 2,3-Epoxysulfides[**]

Atsushi Hirai, Terumichi Tonooka, Kofumi Wakatsuki, Keiji Tanino, and Masaaki Miyashita*

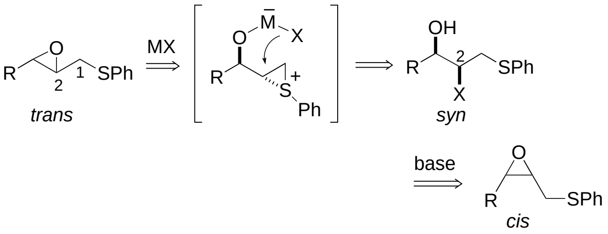
Ring-opening reactions of epoxides with nucleophiles provide a useful method for the stereoselective synthesis of organic compounds.[1] In this type of transformation, the relative stereochemistry of the products reflects that of the parent epoxides, which are usually prepared in the *cis* or *trans* forms from the corresponding *Z* or *E* olefins, respectively.[2] In this connection, however, the interconversion between the *cis* and *trans* epoxides, which contrasts with the configurational isomerization of olefins that is possible by some methods, has not been reported.[3]

Recently, Saigo and co-workers and our group have independently reported that the reaction of a 1-(phenylthio)-2,3-epoxyalkane with an organoaluminum reagent resulted in regio- and stereoselective substitution at C2, with double inversion of configuration (Scheme 1).[4, 5]



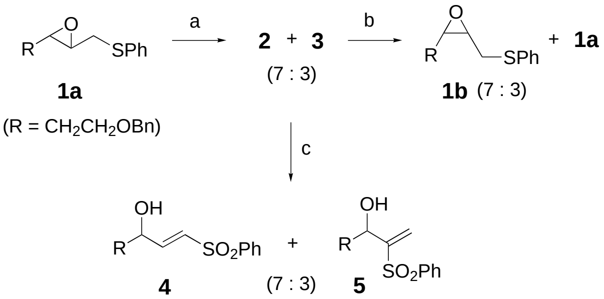
Scheme 1. Proposed reaction mechanism of the alkyl substitution reaction with double inversion of the configuration.

The characteristic stereochemical results, which can be rationalized by assuming an episulfonium ion intermediate, have led us to design a new method for the interconversion between *cis* and *trans* epoxides (Scheme 2): the reaction of a *trans* 2,3-epoxysulfide with a metal halide should afford a *syn* 2-halo-3-alkanol with double inversion of configuration at C2. On treatment with a base, the resulting *syn* halohydrin would undergo an intramolecular S_N2 reaction at C2 to yield the corresponding *cis* 2,3-epoxysulfide. The application of a similar procedure to a simple *trans* epoxide merely results in the recovery of the same *trans* epoxide via an *anti* halohydrin intermediate.[6]



Scheme 2. Interconversion between *cis* and *trans* epoxides (X = halogen).

First, *trans*-5-benzyloxy-2,3-epoxy-1-phenylthiopentane (**1a**) was treated with $MgBr_2 \cdot OEt_2$[7] at 0 °C in toluene, and an inseparable 7:3 mixture of bromohydrins **2** and **3** was obtained (Schemes 3 and 4). The crude product was treated with potassium carbonate in methanol[8] to give a 7:3 mixture of *cis*-epoxide **1b** and *trans*-epoxide **1a**. On the other hand, treatment of the crude bromohydrins **2** and **3** with



Scheme 3. Reagents and conditions: a) $MgBr_2 \cdot OEt_2$, toluene, 0 °C; b) K_2CO_3, MeOH; c) 1. MCPBA, 2. DBU. MCPBA = *meta*-chloroperbenzoic acid; DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

---

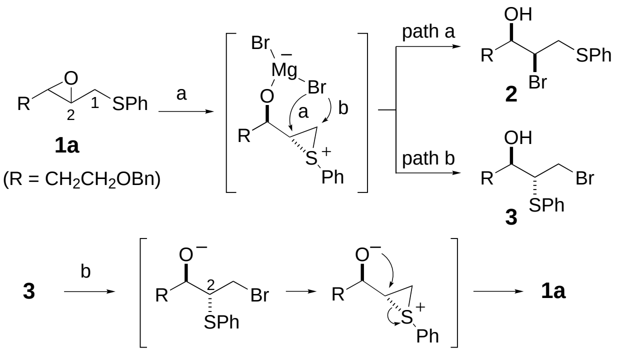
[*] Prof. Dr. M. Miyashita, Dr. A. Hirai, T. Tonooka, K. Wakatsuki, Dr. K. Tanino
Division of Chemistry, Graduate School of Science
Hokkaido University
Sapporo 060-0810 (Japan)
Fax: (+81) 11-706-4920
E-mail: miyasita@sci.hokudai.ac.jp

[**] Financial support from the Ministry of Education, Culture, Sports, Science, and Technology, Japan (a Grant-in-Aid for Scientific Research (A) (No. 12304042) and a Grant-in-Aid for Scientific Research on Priority Areas (A) "Exploitation of Multi-Element Cyclic Molecules" (No. 13029003)) is gratefully acknowledged.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

*m*CPBA followed by DBU afforded a 7:3 mixture of unsaturated sulfones **4** and **5** in almost quantitative yield.

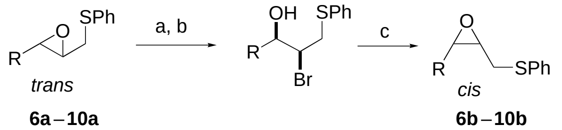
These results can be rationalized by a reaction mechanism that involves an episulfonium ion species as a common intermediate of bromohydrins **2** and **3** (Scheme 4).[9] Since the reaction of **3** with potassium carbonate can not yield an epoxide directly, migration of the phenylthio group at C2 to C1 via an episulfonium ion intermediate would account for the formation of epoxide **1a**. In the course of the studies described above, bromohydrin **3** was found to undergo spontaneous isomerization to **2**, even after aqueous workup.[10] Thus, the ratio of **2** and **3** was changed from 7:3 to 9:1 after standing in $CDCl_3$ at room temperature overnight. The isomerization reaction might proceed through an episulfonium ion intermediate, though the origin of the lower stability of **3** is not clear at present. After further investigation, we found that **3** can be transformed almost completely into **2** by heating the crude bromohydrin at 60 °C in toluene for 3 d. Treatment of the resulting bromohydrin **2** with K_2CO_3 in isopropyl alcohol at room temperature[11] afforded the desired *cis* epoxide **1b** highly stereoselectively (97:3) in 95 % yield from **1a**.



Scheme 4. Reagents and conditions: a) $MgBr_2 \cdot OEt_2$, toluene, −20 °C; b) K_2CO_3, MeOH.

The excellent preliminary results prompted us to examine a variety of *trans* epoxysulfides under these conditions. The results are summarized in Table 1. Epoxysulfide **6**, which has no functional group on its side chain, was converted into the corresponding *cis* epoxide with extremely high stereoselectivity (Table 1, entry 1). Similarly, epoxysulfides that bear oxygen functional groups or a nitrogen functional group also gave excellent results (Table 1, entries 2–5). Conversion of the *cis* epoxides into the corresponding *trans* epoxides was examined by using a similar procedure (Table 2). In these cases, the bromohydrin intermediates were slightly labile in the presence of $MgBr_2 \cdot OEt_2$, and a considerable amount of ketone was formed by means of a 1,2-hydride shift. Fortunately, however, performing the first step at −20 °C effectively reduced the side reaction, and the desired *trans* epoxides were obtained in excellent yields and with high stereoselectivity.

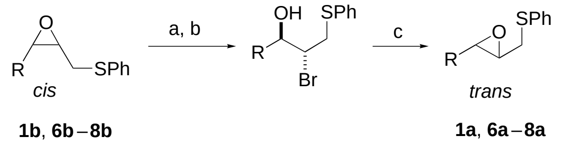
Table 1. Conversion of *trans* epoxides into the corresponding *cis* epoxides.[a]



Entry	Conditions	R	Yield [%][b]	*cis*:*trans*
1	−20 °C, 2 h	$CH_3CH_2CH_2$ (**6**)	99	99:1
2	−20 °C, 2 h	$BnOCH_2$ (**7**)	99	98:2
3	−20 °C, 2 h	$(iPr)_3SiOCH_2$ (**8**)	94	98:2
4[c]	−20 – −10 °C, 8 h	$AdCO_2CH_2CH_2CH_2$ (**9**)	97	98:2
5[c]	−20 – −10 °C, 22 h	$PhtNCH_2CH_2CH_2$ (**10**)	95	99:1

[a] Reagents and conditions: a) $MgBr_2 \cdot OEt_2$, toluene, see column 2; b) toluene, 60 °C, 3 d; c) K_2CO_3, *i*PrOH, room temperature, 1 day. [b] Yield over two steps. [c] Ad = 1-adamantyl, Pht = *o*-$C_6H_4(CO)_2$.

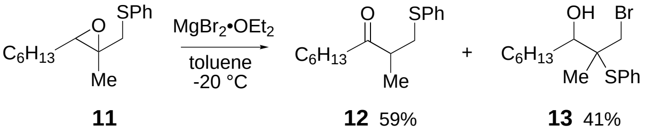
Table 2. Conversion of *cis* epoxides into the corresponding *trans* epoxides.[a]



Entry	Conditions	R	Yield [%][b]	*cis*:*trans*
1	−20 °C, 0.5 h	$CH_3CH_2CH_2$ (**6**)	94	3:97
2	−20 °C, 0.5 h	$BnOCH_2$ (**7**)	98	5:95
3	−20 °C, 3 h	$(iPr)_3SiOCH_2$ (**8**)	83	5:95
4	−20 °C, 2 h	$BnOCH_2CH_2$ (**1**)	96	2:98

[a] Reagents and conditions: a) $MgBr_2 \cdot OEt_2$, toluene, see column 2; b) toluene, 60 °C, 3 d; c) K_2CO_3, *i*PrOH, room temperature, 1 day. [b] Yield over two steps.

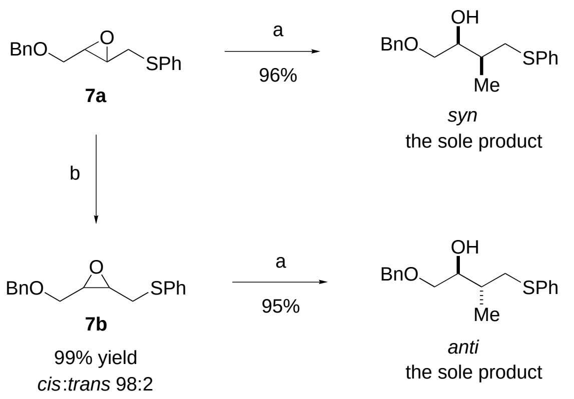
To determine further the scope and limitation of the present transformations, a reaction with trisubstituted epoxysulfide **11** was examined (Scheme 5). However, treatment of **11** with $MgBr_2 \cdot OEt_2$ resulted in the formation of ketone **12** as the major product along with bromohydrin **13**. In this case, the introduction of a bromine atom at C2 might be impeded as a result of increased steric hindrance.



Scheme 5. The reaction of a trisubstituted epoxysulfide.

In conclusion, a novel method for the interconversion of *cis* and *trans* epoxides was developed. To the best of our knowledge, this is the first protocol of this type of transformation. Although the present method can be applied only to disubstituted 1-phenylthio-2,3-epoxyalkanes, these compounds have been demonstrated to be potential intermediates for stereoselective transformations, for example, see Scheme 6.[4, 5] Application of this method in the synthesis of natural products is underway in our laboratory.

Received: September 28, 2001 [Z17988]



Scheme 6. Reagents and conditions: a) Me_3Al (3 equiv), CH_2Cl_2, −30 °C; b) our method.

[1] For reviews, see: a) G. H. Posner, *Org. React.* **1975**, *22*, 253; b) B. H. Lipshutz, S. Sengupta, *Org. React.* **1992**, *41*, 135; c) C. Bonini, G. Righi, *Synthesis* **1994**, 225.

[2] A. S. Rao in *Comprehensive Organic Synthesis*, *Vol. 7* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, p. 357.

[3] The isomerization of *cis* and *trans* olefins has been reported: P. E. Sonnet, *Tetrahedron* **1980**, *36*, 557.

[4] C. Liu, Y. Hashimoto, K. Kudo, K. Saigo, *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2095.

[5] a) M. Sasaki, K. Tanino, M. Miyashita, *Tetrahedron Lett.* **1999**, *40*, 9267; b) M. Sasaki, K. Tanino, M. Miyashita, *J. Org. Chem.* **2001**, *66*, 5388.

[6] R. Bohlmann in *Comprehensive Organic Synthesis*, *Vol. 6* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, p. 203.

[7] C. A. Stewart, C. A. VanderWerf, *J. Am. Chem. Soc.* **1954**, *76*, 1259.

[8] R. P. Hanzlik, *Org. Synth. Coll. Vol.* **1988**, *6*, 560.

[9] The reaction of epoxysulfides with dialkylalkynylaluminum was also found to produce an alkyl adduct at C1 of an episulfonium ion as the minor product. See reference [5].

[10] Isomerization of a β-bromosulfide to the regioisomer via an episulfonium ion intermediate has been reported; see: F. Effenberger, T. Beisswenger, F. Dannenhauer, *Chem. Ber.* **1988**, *121*, 2209.

[11] Conversion of bromohydrins into epoxides in *i*PrOH gave higher chemical yields and stereoselectivity.

Asymmetric Epoxidation of Allyl Alcohol on Organic – Inorganic Hybrid Chiral Catalysts Grafted onto the Surface of Silica and in the Mesopores of MCM-41[**]

Song Xiang, Yiliang Zhang, Qin Xin, and Can Li[*]

Asymmetric epoxidation of allylic alcohols is an important reaction in synthetic organic chemistry.[1] Sharpless and Katsuki[2] have provided an excellent homogeneous catalytic system for this reaction which consists of titanium tetraisopropoxide and a chiral dialkyl tartrate. Heterogeneous systems have tremendous advantages over homogeneous catalytic systems.[3] One of the most attractive advantages is the easy separation of the product from the catalyst without tedious experimental work-up.

Different approaches have been used in the preparation of heterogeneous Sharpless-type catalytic systems for the asymmetric epoxidation of allylic alcohols. An early attempt to develop a polymer-supported system employed a single tartrate ester unit bound to a polystyrene resin;[4a] in this case, the chiral induction was only modest (ca. 50 – 60 % *ee*). Choudary et al.[4b] reported the asymmetric epoxidation of allylic alcohols with a heterogeneous titanium-pillared montmorillonite catalyst in the presence of chiral tartrate ester. However, the preparation of the solids seems to be difficult to reproduce.[5] Hormi and co-workers[4c, 4d] synthesized insoluble branched/crosslinked poly(tartrate ester)s and investigated their use as optically active ligands in the heterogeneous asymmetric epoxidation of allylic alcohols with titanium tetraisopropoxide and *tert*-butyl hydroperoxide. These gel-type polymeric ligands swell during the catalytic reaction. Basset and co-workers[4e] reported silica-supported tantalum catalysts for the enantioselective epoxidation of allylic alcohols in the presence of chiral tartrate derivatives. Their result is comparable to that obtained in the homogeneous Sharpless reaction. However, the organometallic tantalum compound used in the synthesis is not easy to prepare.[6]

The preparation of organic – inorganic hybrid materials is of growing interest.[7, 8] In contrast to organic polymers, organic – inorganic hybrid materials do not swell or dissolve in organic solvents, and have many advantages over most organic polymers because of their superior mechanical and thermal stabilities. Moreover, any leaching could be avoided as the organic moieties are covalently attached to the inorganic supports. For hybrid materials, the design and synthesis of chiral catalytic materials[8] with high enantioselectivities are especially attractive.[8c–e] Highly efficient and enantioselective transition metal complexes have been reported in the literature. The design and synthesis of chiral hybrids with activity and enantioselectivity similar to that of homogeneous catalysts remain a challenge. Few reports have appeared on the synthesis of organic – inorganic hybrid chiral materials and on their use as heterogeneous catalysts in enantioselective reactions.[8c–e] We report herein the synthesis of organic – inorganic hybrid chiral materials by grafting a chiral tartaric acid derivative onto the surface of silica and in the mesopores of MCM-41 material (Scheme 1 b), and provide the first example of their successful application in the heterogeneous asymmetric epoxidation of allyl alcohol. The catalytic systems resulted in enantiomer excesses up to 80 %, which is as good as the homogeneous Sharpless system (Scheme 1 a).

The chiral tartaric derivative was grafted onto inorganic supports in several steps, as outlined in Scheme 2. Tartaric acid (**1**) was converted into the protected tartaric acid dichloride **3**. Treatment of **3** with 3-aminopropyltriethoxysilane gave **4**, which was grafted onto SiO_2 and MCM-41 to afford **5a** and **5b**, respectively. Selective cleavage of the isopropylidene acetal removed the protecting groups and

---

[*] Prof. Dr. C. Li, S. Xiang, Y. Zhang, Prof. Q. Xin
State Key Laboratory of Catalysis
Dalian Institute of Chemical Physics, Chinese Academy of Sciences
Dalian, 116023 (China)
Fax: (+86) 411-4694447
E-mail: canli@dicp.ac.cn

[**] This work was supported by the Natural Science Foundation of China (NSFC, Grant No: 20172051). We thank Prof. Z. Y. Yang for valuable discussions.