Preparation of Enantiomerically Enriched (2*R*,3*R*)- or (2*S*,3*S*)-*trans*-2,3-Diaryloxiranes *via* Camphor-Derived Sulfonium Ylides

An-Hu Li, Li-Xin Dai,* Xue-Long Hou, Yao-Zeng Huang,* and Feng-Wei Li

Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

Received August 3, 1995[⊗]

Easily available D-(+)-camphor-derived sulfides **3**, **4**, **6**, and **7** were employed for enantioselective epoxidation *via* an ylide route. When benzylated or methylated sulfides were used as reagents or mediators for benzylidene transfer, stoichiometric and catalytic epoxidations were realized, respectively. Opposite asymmetric induction was achieved only when sulfides containing *exo*- (**3** and **4**) and *endo*- (**6** and **7**) alkylthio groups were used. That is, both (+)- and (−)-*trans*-diaryloxiranes could be obtained in excellent yields and moderate to good ee values under extremely mild conditions from the same chiral pool-derived reagents. A nonbonded interaction between the free OH in the ylides from sulfides (**3**, **6**, and **7**) and the carbonyl group of aldehydes controls the approach of the substrates to the ylidic carbon preferentially at one specified face and therefore leads to a more efficient asymmetric induction than that in the case of the ylide from methyl-protected hydroxylated sulfides **4**, which cannot cause such an interaction. The same opposite asymmetric induction was also observed in the catalytic reaction with methyl-protected hydroxylated sulfide **4b** and unprotected hydroxylated sulfide **3b**.

Introduction

The notable biological significance[1] and various chemical transformations[2] make nonracemic epoxides one of the most useful synthetic intermediates.[3] The development of methods for the preparation of this type of compound is always a subject of great challenge. The recorded ways for this aim are chiefly as follows: (a) enantiofacially differential oxidation of a prochiral C=C bond;[4] (b) enantioselective alkylidenation of a C=O bond, such as *via* an ylide route or a Darzens reaction. Although the former method has afforded much success, the structural requirements of the substrates are a limiting prerequisite. The latter strategy provides an alternative approach in solving this problem. Enantioselective epoxidation *via* an ylide route is an approach easy to perform but relatively undeveloped to date.[5,6]

After the emergence of an ingenious idea for the first, although failed, attempt[6a] to transfer the methylene group from an optically active sulfonium ylide with a chiral center at the sulfur atom to a C=O bond, several sulfides[6b−h] have been used for producing enantiomerically enriched epoxides. Among them, Durst's sulfides derived from (+)-camphoric acid give the highest levels of enantioselectivity.[6d] However, the long synthetic route led to low overall yields, poor stereoselectivity, a mixture of *trans*- and *cis*- epoxides, and a side reaction, namely β-elimination, which made this method somewhat impractical. Additionally, all other examples either require strict reaction conditions and operations or give only low yields and/or ee values. Our search for convenient methods to prepare functionalized optically active epoxides,[7] combined with our experiences in ylide chemistry,[8] led us to explore enantioselective epoxidation by way

[⊗] Abstract published in *Advance ACS Abstracts,* January 1, 1996.

(1) (a) Hatakeyama, S.; Ochi, N.; Takano, S. *Chem. Pharm. Bull.* **1993**, *41*, 1358−1361. (b) Jerina, D. M.; Daly, J. W. *Science* **1974**, *185*, 573−582. (c) Rokach, J.; Young, R. N.; Kakushima, M.; Lau, C.-K.; Seguin, R.; Frenette, R.; Guindon, Y. *Tetrahedron Lett.* **1981**, *22*, 979−982. (d) Becker, A. R.; Janusz, J. M.; Bruice, T. C. *J. Am. Chem. Soc.* **1979**, *101*, 5679−5687. (e) Sato, F.; Kobayashi, Y. *Synlett* **1992**, 849−857.

(2) For a review on the reactivity of epoxides: Bartók, M.; Lang, K. L. In *The Chemistry of Functional Groups, Supplement E*; Patai, S., Ed.; Wiley: New York, 1980, pp 609−681.

(3) (a) Hudlicky, T.; Tian, X.; Königsberger, K.; Rouden, J. *J. Org. Chem.* **1994**, *59*, 4037−4039. (b) Satake, A.; Shimizu, I.; Yamamoto, A. *Synlett* **1995**, 64−68. (c) Shao, H.; Zhu, Q.; Goodman, M. *J. Org. Chem.* **1995**, *60*, 790−791. (d) Kim, N.-S.; Choi, J.-R.; Cha, J. K. *J. Org. Chem.* **1993**, *58*, 7096−7099. (f) Soulié, J.; Boyer, T.; Lallemand, J. Y. *Tetrahedron, Asymmetry* **1995**, *6*, 625−636.

(4) For a review on Sharpless epoxidations: (a) Johnson, R. A.; Sharpless, K. B. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 7, pp 389−436. For Mn salen complex-catalyzed asymmetric epoxidation: (b) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801−2803. For a review on metalloporphyrin-catalyzed asymmetric epoxidation: (c) Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E. S.; Brauman, J. I. *Science* **1993**, *261*, 1404−1411. Other methods for asymmetric epoxidation: (d) Koch, A.; Reymond, J.-L.; Lerner, R. A. *J. Am. Chem. Soc.* **1994**, *116*, 803−804. (e) Allain, E. J.; Hager, L. P.; Deng, L.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 4415−4416. (f) Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.***1983**, *105*, 3123−3126.

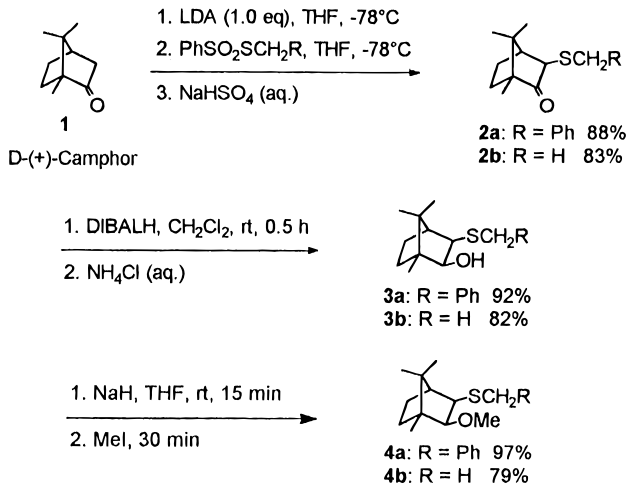
(5) Asymmetric epoxidation with sulfoximine ylides: (a) Johnson, C. R.; Schroeck, C. W. *J. Am. Chem. Soc.* **1968**, *90*, 6852−6854. (b) Johnson, C. R.; Schroeck, C. W. *J. Am. Chem. Soc.* **1973**, *95*, 7418−7423. (c) Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7424−7431. (d) Taj, S. S.; Soman, R. *Tetrahedron, Asymmetry* **1994**, *5*, 1513−1518. With arsonium ylides: (e) Allen, D. G.; Roberts, N. K.; Wild, S. B. *J. Chem. Soc., Chem. Commun.* **1978**, 346−347. (f) Allen, D. G.; Wild, S. B. *Organometallics* **1983**, *2*, 394−399. With dimethylsulfonium methylide in the presence of chiral phase-transfer catalysts: (g) Hiyama, T.; Mishima, T.; Sawada, H.; Nozaki, H. *J. Am. Chem. Soc.* **1975**, *97*, 1626−1627. With chiral sulfimides: (h) Baird, C. P.; Taylor, P. C. *J. Chem. Soc., Chem. Commun.* **1995**, 893−894.

(6) Asymmetric epoxidation with chiral sulfonium ylides: (a) Trost, B. M.; Hammen, R. F.; *J. Am. Chem. Soc.***1973**, *95*, 962−964. (b) Furukawa, N.; Sugihara, Y.; Fujihara, H. *J. Org. Chem.* **1989**, *54*, 4222−4224. (c) Breau, L.; Ogilvie, W. W.; Durst, T. *Tetrahedron Lett.* **1990**, *31*, 35−38. (d) Breau, L.; Durst, T. *Tetrahedron, Asymmetry* **1991**, *2*, 367−370. (e) Solladié-Cavallo, A.; Adib, A. *Tetrahedron* **1992**, *48*, 2453−2464. (f) Aggarwal, V. K.; Kalomiri, M.; Thomas, A. P. *Tetrahedron, Asymmetry* **1994**, *5*, 723−730. (g) Aggarwal, V. K.; Abdel-Rahman, H.; Jones, R. V. H.; Lee, H. Y.; Reid, B. D. *J. Am. Chem. Soc.* **1994**, *116*, 5973−5974. (h) Solladié-Cavallo, A.; Diep-Vohuule, A. *J. Org. Chem.* **1995**, *60*, 3494−3498.

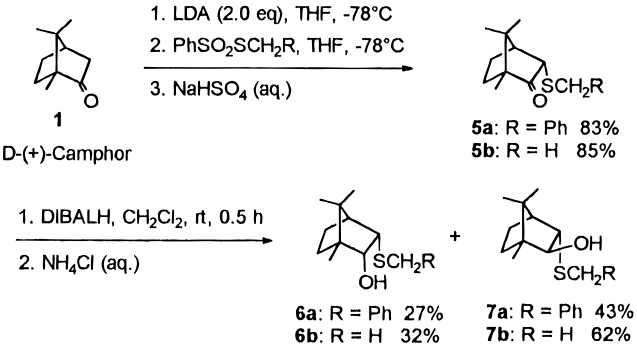
(7) (a) Dai, L.-X.; Lou, B.-L.; Zhang, Y.-Z.; Guo, G.-Z. *Tetrahedron Lett.* **1986**, *27*, 4343−4346. (b) Dai, L.-X.; Lou, B.-L.; Zhang, Y.-Z. *J. Am. Chem. Soc.* **1988**, *110*, 5195−5196. (c) Lai, J.-Y.; Wang, F.-S.; Guo, G.-Z.; Dai, L.-X. *J. Org. Chem.* **1993**, *58*, 6944−6946. (d) Lai, J.-Y.; Shi, X.-X.; Dai, L.-X. *J. Org. Chem.* **1992**, *57*, 3485−3487.

0022-3263/96/1961-0489$12.00/0

Scheme 1



Scheme 2

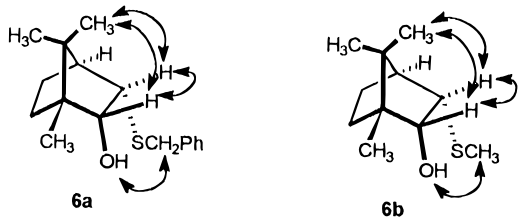


of ylides. We disclose herein our methods for preparing (2*R*,3*R*)-(+)- and (2*S*,3*S*)-(−)-diaryloxiranes through chiral sulfonium ylides with excellent yields and moderate to good ee values.

Results and Discussion

Synthesis of Ylide Precursors 3a, 3b, 4a, 4b, 6a, 6b, 7a, and 7b. Since the appearance of chiral sulfides **2**, **3**, and **5** derived from D-(+)-camphor (**1**), an easily available chiral pool,[9] in 1988,[10] they have found several applications in asymmetric synthesis and reactions.[11] In some cases, satisfactory results could be achieved. In order to examine the effect of these sulfides upon asymmetric induction through ylide epoxidation, we prepared sulfides **3**, **4**, **6**, and **7** by methods similar to that used by Haynes[10] for the preparation of **2**, **3**, and **5** with reasonable yields and optical purity (Scheme 1 and Scheme 2). Sulfides **4**, **6**, and **7** were unreported and were fully characterized. The assignment of the configuration of C_2 connected to the OH group in **6** and **7**[12] was in accordance with the $^1H-^1H$ NOESY maps of **6a** and **6b**. In the NOESY map of **6b** (Scheme 3), the 3.82 ppm doublet of doublet correlates to the 3.39 ppm multiplet. This suggests that the two protons (connected with C_2 and C_3) have a *cis* orientation on the ring, i.e., the OH group is directed to the *endo* position. The same correlation exists in compound **6a**. The OH groups in **7a** and **7b** are therefore assumed to be in the *exo*-position. The configurational assignment of all other compounds was in accordance with the literature results.[10]

Scheme 3



Stoichiometric Enantioselective Epoxidation *via* Ylide of Sulfides 3a, 4a, 6a, and 7a. All reported examples[5,6] of enantioselective epoxidation *via* an ylide route, except those of Furukawa[6b] and Aggarwal,[6g] are stoichiometric reactions, in which sulfonium salts, if sulfonium ylides are involved, must first be prepared. Sometimes silver salts ($AgBF_4$ or $AgClO_4$) are required in preparation of these sulfonium salts.

We found that sulfides **3a**, **4a**, **6a**, and **7a** reacted smoothly with methyl iodide to furnish the corresponding sulfonium salts without the aid of silver salts. This suggested that this ylide reaction could be carried out in one pot. On the basis of our successful experiences with solid−liquid phase-transfer technology in arsonium and telluronium ylide chemistry,[8b,13] we tried the reaction of **3a**, **4a**, **6a**, and **7a** with various aldehydes in the presence of MeI and solid KOH in acetonitrile at room temperature (Table 1).

For aromatic aldehydes, the reaction proceeded perfectly to give completely the *trans* products, with excellent yields in most cases, and moderate to good ee values (19−77%). Any efforts to extend this reaction to aliphatic and heteroaromatic aldehydes and ketones were unsuccessful because of side reactions of aliphatic and heteroaromatic aldehydes, and the low reactivity of ketones.

It is interesting that the opposite asymmetric induction was achieved only when **3a** (benzylthio group at *exo* position) and **6a** or **7a** (benzylthio group at *endo* position) were applied as chiral auxiliaries. This represents an efficient preparation of enantiomerically enriched (+)- and (−)-*trans*-diaryloxiranes from ylides with both high yields and reasonable ee values, although both (+)- and (−)-enantiomers have also been obtained in low yields in some cases.[6b,d] The effect of asymmetric induction from **3a** (*exo*-benzylthio) was generally better than that from **6a** or **7a** (*endo*-benzylthio).

It is noteworthy that the free OH group at C_2 plays an important role; when the OH was converted to a methoxyl group, both the yield and the ee value of the resulting epoxide were greatly lowered. (entry 2 *vs* entry 4 in Table 1). This led us to postulate that there may be a nonbonded interaction between the OH and the car-

(8) (a) Huang, Y.-Z.; Shen, Y.-C. *Adv. Organomet. Chem.* **1982**, *20*, 115−157. (b) Shi, L.; Wang, W.; Wang, Y.; Huang, Y.-Z. *J. Org. Chem.* **1989**, *54*, 2027−2028. (c) Zhou, Z.-L; Huang, Y.-Z.; Shi, L.-L. *J. Chem. Soc., Chem. Commun.* **1992**, 986−988. (d) Wang, W.-B.; Huang, Y.-Z. In *Advances in Organic Synthesis*, Dai, L.-X.; Qian, Y.-L., Eds.; Chemical Industry Press: Beijing, 1993; pp 301−347 (in Chinese).

(9) For a recent review on camphor-derived chiral auxiliaries: Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969−2004.

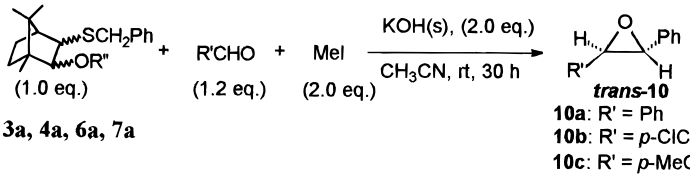
(10) Goodridge, R. J.; Hambley, T. W.; Haynes, R. K.; Ridley, D. D. *J. Org. Chem.* **1988**, *53*, 2881−2889.

(11) (a) Corey, E. J.; Chen, Z.; Tanoury, G. J. *J. Am. Chem. Soc.* **1993**, *115*, 11000−11001. (b) Hung, S.-M.; Lee, D.-S.; Yang, T.-K. *Tetrahedron, Asymmetry* **1990**, *1*, 873−876. (c) Yang, T.-K.; Hung, S.-M.; Chen, C.-Z.; Jiang, Y.-Z.; Mi, A.-Q. *Youji Huaxue* **1993**, *13*, 183−185. (d) Yang, T.-K.; Chen, R.-Y.; Lee, D.-S.; Peng, W.-S.; Jiang, Y.-Z.; Mi, A.-Q.; Jong. T.-T. *J. Org. Chem.* **1994**, *59*, 914−921. (e) Lee, D.-S.; Hung, S.-M.; Lai, M.-C.; Chu, H.-Y.; Yang, T.-K. *Org. Prep. Proc. Int.* **1993**, *25*, 673−679.

(12) The assignment of the configuration at C_3 in **6** and **7** was given in the light of known results.[10]

(13) (a) Huang, Y.; Shi, L.; Yang, J. *Tetrahedron Lett.* **1985**, *26*, 6447−6448. (b) Zhou, Z.-L.; Sun, Y.-S.; Shi, L.-L.; Huang, Y.-Z. *J. Chem. Soc., Chem. Commun.* **1990**, 1439−1440.

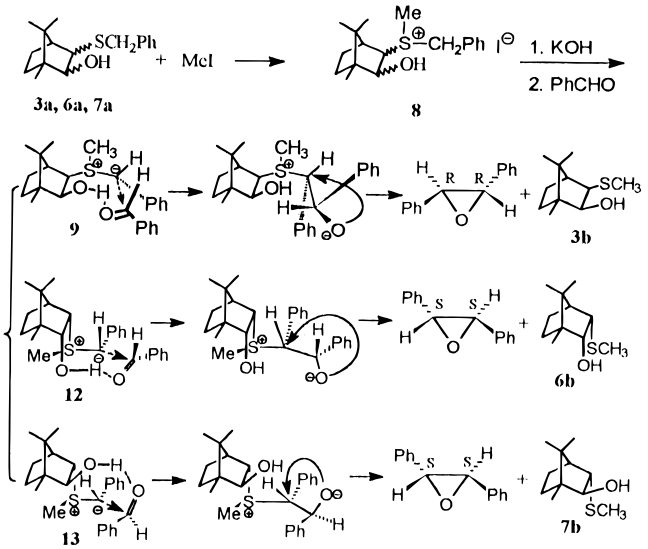
Table 1. Preparation of *trans*-2,3-Diaryloxiranes 10 by Stoichiometric Enantioselective Epoxidation *via* Ylides of Sulfide 3a, 4a, 6a, and 7a[a]



entry	sulfide	R′	yield of **10**,[b] %	$[\alpha]^{20}_D$ of **10** (in EtOH)	ee of **10**,[c] %	configuration of **10**[d]
1	**3a**	Ph	87	+253° (*c*, 0.98)	74	(2*R*,3*R*)
2	**3a**	*p*-ClC_6H_4	96	+279° (*c*, 1.02)	77	(2*R*,3*R*)
3	**3a**	*p*-MeC_6H_4	89	+273° (*c*, 1.22)	72	(2*R*,3*R*)
4	**4a**	*p*-ClC_6H_4	48	+69° (*c*, 1.43)	19	(2*R*,3*R*)
5	**6a**	*p*-ClC_6H_4	94	−127° (*c*, 1.23)	35	(2*S*,3*S*)
6	**6a**	Ph	92	−118° (*c*, 1.37)	35	(2*S*,3*S*)
7	**6a**	*p*-MeC_6H_4	90	−113° (*c*, 1.45)	32	(2*S*,3*S*)
8	**7a**	*p*-ClC_6H_4	98	−115° (*c*, 1.30)	32	(2*S*,3*S*)
9	**7a**	Ph	89	−125° (*c*, 1.09)	37	(2*S*,3*S*)
10	**7a**	*p*-MeC_6H_4	90	−117° (*c*, 0.88)	33	(2*S*,3*S*)

[a] All reactions were carried out under solid−liquid phase transfer conditions at room temperature in acetonitrile (reagent grade, need not be dried before use). [b] Isolated yields based on sulfides. *trans*-**10** was the only product, no *cis*-isomer was detected. [c] Calculated on the basis of the following specific rotations reported for optically pure compounds:[15] (2*R*,3*R*)-2-(*p*-chlorophenyl)-3-phenyloxirane (**10b**), $[\alpha]_D$ +362° (c 1.36, EtOH); (2*R*,3*R*)-2-phenyl-3-phenyloxirane (**10a**), $[\alpha]_D$ +342° (c 1.11, EtOH); (2*R*,3*R*)-2-(*p*-tolyl)-3-phenyloxirane (**10c**), $[\alpha]_D$ +351° (c 1.14, EtOH). [d] The absolute configuration of all products was assigned through comparison of the sign of specific rotations with the literature data.

Scheme 4



bonyl group of aldehydes before attack by an ylide (Scheme 4). This interaction causes the aldehydes to approach the reactive site of the ylide preferentially from the *si*-face, and the aldehyde carbonyl to be attacked on the *re*-face. The stereochemical outcome of our reaction could be rationalized with this assumption (Scheme 4).

Catalytic Enantioselective Epoxidation *via* Ylide of Sulfides 3b, 4b, 6b, and 7b. Since chiral substances other than natural products are generally difficult to obtain, an attempt to make a stoichiometric reaction catalytic is believed to be of practical significance.[8b,14] Clearly, sulfonium salt **8** (Scheme 4) could be prepared either by the methylation of **3a** or by the benzylation of **3b**. In addition, the stoichiometric ylide epoxidation was realized through the transfer of a benzylidene group of ylide **9** instead of a methylene group. Therefore, it is possible to make this reaction catalytic when **3b**, **4b**, **6b**, or **7b** are used to mediate the reaction between benzyl bromide and aldehydes. The catalytic epoxidation proceeded smoothly in the presence of 0.2 equiv of the above-mentioned chiral sulfides. Some results are summarized in Table 2.

In these reactions, the sulfides were converted initially to sulfonium salts **11** by benzyl bromide and then to the corresponding ylide **9** *in situ* under phase-transfer conditions. Ylide **9** was subsequently reacted with aldehydes to furnish epoxides and release **3b** and permit it to enter a new cycle (Scheme 5).

As expected, the opposite asymmetric induction was again observed in the catalytic reaction when **3b**, which contains an *exo*-methylthio group, and **6b** or **7b**, which contains an *endo*-methylthio group, were used (entries 1−3 *vs* entries 7−12 in Table 2).

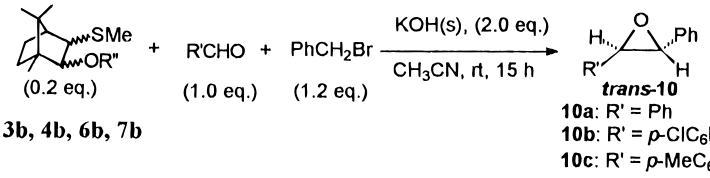
These results are quite reasonable because the catalytic reaction shared the same reactive intermediate sulfonium ylide **9** with the stoichiometric reaction. Surprisingly, the opposite asymmetric induction in the catalytic epoxidation was also observed in the cases using **3b**, which possesses a free OH group, and **4b**, which contains a methyl-protected OH group, although the asymmetric induction of the latter was rather low (entries 1−3 *vs* entries 4−6 in Table 2). This phenomenon had been reported by Furukawa et al.[6b]

To optimize the reaction conditions, the effects of solvents and bases were investigated. In strong polar solvents like DMSO and DMF, the ee values of products were decreased. Under other conditions, the ee values remained nearly the same. In commonly used THF, the yields were reasonably low due to the low solubility of KOH leading to difficulties in producing ylides. Acetonitrile was the best solvent for this reaction, and strong bases like KOH(s), NaOH(s), and aqueous NaOH are useful. Solid KOH seems to be the most suitable base when convenience of operation is taken into account.

The investigation of the effect of the amount of sulfides on this catalytic reaction showed that an increase in the amount of sulfides did not influence the ee values, but did shorten the reaction time and improve the yields (Table 3). From a practical standpoint, 20 mol % of sulfides is suitable for the catalytic reaction. To our knowledge, only two catalytic examples of ylide asym-

(14) (a) Huang, Y.-Z.; Shi, L.-L.; Li; S.-W.; Wen, X.-Q. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2397−2399. (b) Zhou, Z.-L.; Shi, L.-L.; Huang, Y.-Z. *Tetrahedron Lett.* **1990**, *31*, 7657−7660.

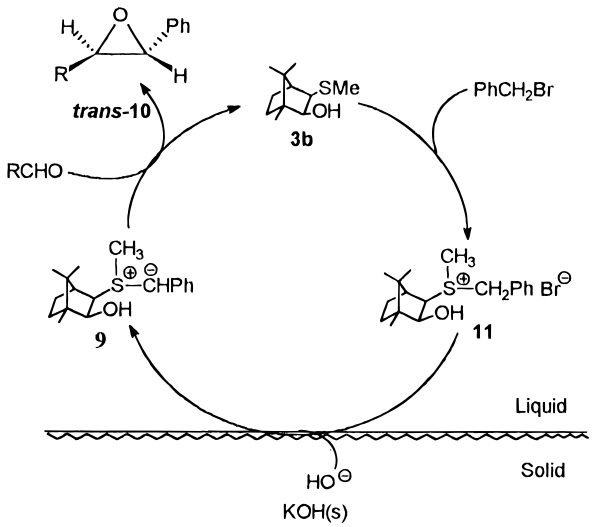
Table 2. Preparation of *trans*-2,3-Diaryloxiranes 10 by Catalytic Enantioselective Epoxidation *via* Ylides of Sulfide 3b, 4b, 6b, and 7b[a]



entry	sulfide	R′	yield of **10**,[b] %	$[\alpha]^{20}_D$ of **10** (in EtOH)	ee of **10**,[c] %	configuration of **10**[d]
1	**3b**	Ph	97 (58[e], 50[f])	+144° (*c*, 1.23)	42 (11[e],47[f])	(2*R*,3*R*)
2	**3b**	*p*-ClC_6H_4	93 (62[e], 50[f])	+217° (*c*, 1.32)	60 (11[e], 43[f])	(2*R*,3*R*)
3	**3b**	*p*-MeC_6H_4	89 (39[f])	+125° (*c*, 1.03)	36 (43[f])	(2*R*,3*R*)
4	**4b**	*p*-ClC_6H_4	97	−17° (*c*, 1.01)	4.7	(2*S*,3*S*)
5	**4b**	Ph	90	−14° (*c*, 0.44)	4.1	(2*S*,3*S*)
6	**4b**	*p*-MeC_6H_4	94	−5° (*c*, 1.08)	1.4	(2*S*,3*S*)
7	**6b**	*p*-MeC_6H_4	94	−119° (*c*, 1.74)	34	(2*S*,3*S*)
8	**6b**	*p*-ClC_6H_4	96	−146° (*c*, 1.35)	40	(2*S*,3*S*)
9	**6b**	Ph	96	−98° (*c*, 1.15)	29	(2*S*,3*S*)
10	**7b**	*p*-ClC_6H_4	94	−53° (*c*, 0.96)	15	(2*S*,3*S*)
11	**7b**	Ph	92	−67° (*c*, 1.0)	20	(2*S*,3*S*)
12	**7a**	*p*-MeC_6H_4	90	−66° (*c*, 2.1)	19	(2*S*,3*S*)

[a] All reactions were carried out under solid−liquid phase transfer conditions at room temperature in acetonitrile (reagent grade, need not be dried before use). [b] Isolated yields based on aldehydes. *trans*-**10** was the only product, no *cis*-isomer was detected. [c] Calculated on the basis of the following specific rotations reported for optically pure compounds:[15] (2*R*,3*R*)-2-(*p*-chlorophenyl)-3-phenyloxirane (**10b**), $[\alpha]_D$ +362° (c 1.36, EtOH); (2*R*,3*R*)-2-phenyl-3-phenyloxirane (**10a**), $[\alpha]_D$ +342° (c 1.11, EtOH); (2*R*,3*R*)-2-(*p*-tolyl)-3-phenyloxirane (**10c**), $[\alpha]_D$ +351° (c 1.14, EtOH). [d] The absolute configuration of all products was assigned through comparison of the sign of specific rotations with the literature data. [e] Taken from reference 6g. A mixture of *trans* and *cis* epoxides (for benzaldehyde, *trans*/*cis*: 86/14; for *p*-chlorobenzaldehyde, *trans*/*cis*: 82/18). In both cases, the ee values belong to the *trans* isomer. [f] Taken from reference 6b.

Scheme 5. Catalytic Cycle for Formation of Oxiranes

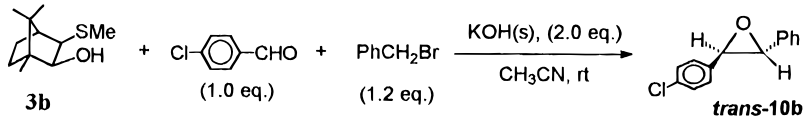


metric epoxidation have appeared in the literature.[6b,g] Furukawa's[6b] method suffered from relatively low yields and ee values; Aggarwal's catalytic epoxidation[6g] had to be carried out under strict conditions, and only 11% ee was observed. Their results may also be found in Table 2. The epoxides obtained by Aggarwal's method are a mixture of *trans* and *cis* isomers, while our epoxides are obtained solely as *trans* compounds.

Conclusions

To examine the effect of asymmetric induction of camphor-derived reagents in ylide epoxidation, chiral sulfides **3**−**7** were synthesized from D-(+)-camphor. When benzylated sulfides **3a**, **4a**, **6a**, or **7a** were employed in the ylide reaction, a stoichiometric enantioselective epoxidation was realized. An efficient catalytic ylide epoxidation was achieved when **3b**, **4b**, **6b**, or **7a** were used as mediators. The opposite asymmetric induction, which led to the synthesis of both (+)- and (−)-*trans*-diaryloxiranes **10**, was achieved only when *exo*-alkylthio-substituted sulfide **3a**, **3b**, or **4a** and *endo*-alkylthio-substituted sulfide **6a**, **6b**, **7a**, or **7b** were used, respectively. An investigation of the function of a free OH group in **3a** and **3b** showed that both yields and ee values were decreased when the OH was methylated in the case of **3a** *vs* **4a**, and the signs of optical rotations were even reversed in the case of **3b** *vs* **4b**. This constitutes a clear

Table 3. Effects of the Amount of Sulfide 3b on the Yields and ee Values of *trans*-10b in Catalytic Enantioselective Epoxidation



entry	amount of **3b**, %	reaction time (h)	yield of **10b**,[a] %	$[\alpha]^{20}_D$ of **10b** (in EtOH)	ee of **10b**,[b] %	configuration of **10b**[c]
1	5	24	24	+186° (*c*, 1.23)	52	(2*R*,3*R*)
2	10	24	61	+208° (*c*, 1.67)	58	(2*R*,3*R*)
3	20	15	93	+217° (*c*, 1.32)	60	(2*R*,3*R*)
4	50	12	95	+193° (*c*, 1.08)	53	(2*R*,3*R*)
5	100	12	97	+201° (*c*, 1.78)	56	(2*R*,3*R*)

[a] Isolated yields based on aldehyde; *trans*-**10b** was the only product, no *cis*-isomer was detected. [b] Calculated on the basis of the following specific rotations reported for optically pure compound:[15] (2*R*,3*R*)-2-(*p*-chlorophenyl)-3-phenyloxirane (**10b**), $[\alpha]_D$ +362° (c 1.36, EtOH). [c] The absolute configuration of the product was assigned through comparison of the sign of specific rotation with the literature data.

example of opposite asymmetric induction in a reaction with two types of reagents prepared through a slight change in reaction conditions from the same chiral starting material. All epoxidation reactions were run under solid−liquid phase-transfer condition with solid KOH as the base in acetonitrile at room temperature in one pot. No moisture-free and oxygen-free manipulations were required.

Experimental Section

Materials and General Procedure. D-(+)-Camphor (>98.0%, mp 178 °C) was obtained from Tokyo Kasei Kogyo Co., LTD, and was used directly in our reactions. All other reagents and solvents, unless otherwise specified, were bought from commercial suppliers and used without further purification. THF was distilled from sodium/benzophenone ketyl under nitrogen. The CH_2Cl_2 was dried over CaH_2 and distilled under nitrogen atmosphere. Proton magnetic resonance spectra, including $^1H-^1H$ NOESY, were recorded on a 300 MHz spectrometer. *S*-Benzyl benzenethiolsulfonate (yield: 95%, mp 42−43 °C) and *S*-methyl benzenethiolsulfonate (yield: 68%, colorless oil) were prepared according to a literature method.[16] The syntheses of sulfides **2a** (yield: 88%, mp 72−75 °C, $[\alpha]_D$: +126° (*c*, 2.88, acetone)), **2b** (yield: 83%, $[\alpha]_D$: +92.7° (*c*, 2.34, acetone)), **3a** (yield: 92%, $[\alpha]_D$: −8.7° (*c*, 2.79, acetone)), **3b** (yield: 82%, $[\alpha]_D$: +7.52° (*c*, 2.12, acetone)), **5a** (yield: 83%, $[\alpha]_D$: −30.2° (*c*, 1.08, acetone), HRMS cacld for $C_{17}H_{22}OS$ (M^+) 274.1391: found: 274.1401), and **5b** (yield: 85%, $[\alpha]_D$: +53.3° (*c*, 2.85, acetone), HRMS cacld for $C_{11}H_{18}OS$ (M^+) 198.1078: found: 198.1059) were performed using Haynes' method.[10]

(−)-(1*R*,2*S*)-2-Methoxy-*exo*-3-(benzylthio)-1,7,7-trimethylbicyclo[2.2.1]heptane (4a). A reaction tube containing a magnetic stirring bar was placed with 306 mg (1.1 mmol) of **3a**[10] and 4 mL of THF. Sodium hydride (55% in oil, 58 mg, 1.32 mmol) was added subsequently at room temperature under N_2. After stirring for 15 min, MeI (0.1 mL, 1.5 mmol) was introduced through a syringe into this reaction mixture. The reaction was worked up after 30 min with the addition of 3 g of silica gel GF_{254} to destroy excess NaH. Chromatography of the product followed on a silica gel column with an eluent of ethyl acetate/petroleum ether (60−90 °C) (1:20) gave 311 mg (97%) of **4a** as a colorless oil: $[\alpha]^{25}_D$: −102.6° (*c*, 1.91, acetone); ^1H NMR ($CDCl_3$) δ 0.76 (s, 3 H), 0.88 (s, 3 H), 1.13 (s, 3 H), 0.93, 0.96, 1.45, 1.66 (m, 4 H), 1.74 (d, J = 3.77 Hz, 1 H), 2.82 (d, J = 7.67 Hz, 1 H), 3.08 (d, J = 7.82 Hz, 1 H), 3.37 (s, 3 H), 3.72 (m, 2 H), 7.22−7.33 (m, 5 H); MS *m*/*z* 290 (M^+, 8), 259 (23), 199 (100), 167 (27), 135 (20), 123 (34), 91 (73), 85 (21), 73 (9), 55 (16), 45 (14); HRMS cacld for $C_{18}H_{26}OS$ (M^+) 290.1704, found 290.1679.

(−)-(1*R*,2*S*)-2-Methoxy-*exo*-3-(methylthio)-1,7,7-trimethylbicyclo[2.2.1]heptane (4b). Prepared as described for the preparation of **4a**. From 301 mg (1.5 mmol) of **3b**[10] was obtained 354 mg (79%) of **4b** as a colorless oil: $[\alpha]^{25}_D$: −90.6° (*c*, 2.46, acetone); ^1H NMR ($CDCl_3$) δ 0.78 (s, 3 H), 0.91 (s, 3 H), 1.13 (s, 3 H), 1.47−1.55 (m, 2 H), 1.72−1.77 (m, 2 H), 1.83 (d, J = 3.98 Hz, 1 H), 2.12 (s, 3 H), 2.88 (d, J = 7.74 Hz, 1 H), 3.20 (d, J = 7.72 Hz, 1 H), 3.44 (s, 3 H); MS *m*/*z* 214 (M^+, 78), 199 (36), 183 (100), 167 (55), 151 (25), 135 (90), 121 (26), 104 (50), 95 (29), 85 (67), 55 (37); HRMS (EI) calcd for $C_{12}H_{22}OS$ (M^+) 214.1391, found 214.1376.

(−)-(1*R*,2*R*)-*endo*-3-(Benzylthio)-1,7,7-trimethylbicyclo-[2.2.1]heptan-2-ol (6a) and (+)-(1*R*,2*S*)-*endo*-3-(Benzylthio)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (7a). Diisobutylaluminum hydride (DIBAL-H, 2.5 M in toluene, 14.3 mL) was introduced through a syringe into a solution of 6.175 g (22.5 mmol) of **5a**[10] in 100 mL of CH_2Cl_2 under N_2 at room temperature. After stirring for 30 min, the reaction mixture was cautiously poured into 360 mL of saturated aqueous NH_4Cl. The organic phase was separated, and the aqueous phase was extracted with ether (3 × 240 mL). The organic phases were combined and washed sequentially with 3 M HCl (3 × 240 mL) and saturated $NaHCO_3$ (3 × 240 mL), dried over anhydrous $MgSO_4$, and purified by chromatography on silica gel column with ethyl acetate/petroleum ether (60−90°C) (1:50) as the eluent to give 1.65 g (27%) of **6a** (colorless oil) and 2.652 g (43%) of **7a** (colorless oil). **6a**: $[\alpha]^{25}_D$: −9.3° (*c*, 2.66, acetone); ^1H NMR ($CDCl_3$) δ 0.83 (s, 3 H), 0.84 (s, 3 H), 1.0 (s, 3 H), 1.50−1.70 (m, 4 H), 2.0 (s, 1 H), 2.02 (s, 1 H), 3.21 (m, 1 H), 3.29 (d, J = 3.80 Hz, 1 H), 3.71 (d, J = 13.19 Hz, 1 H), 3.78 (d, J = 13.21 Hz, 1 H), 7.19−7.37 (m, 5 H); MS *m*/*z* 276 (M^+, 14), 258 (3), 185 (66), 167 (12), 157 (21), 153 (3), 136 (12), 123 (61), 109 (20), 95 (44), 91 (100), 83 (25), 65 (14), 55 (23), 43 (20). **7a**: $[\alpha]^{25}_D$: +5.5° (*c*, 1.81, acetone); ^1H NMR ($CDCl_3$) δ 0.87 (s, 9 H), 1.15 (m, 1 H), 1.47 (m, 2 H), 1.74 (m, 1 H), 1.80 (d, J = 4.0 Hz, 1 H), 2.77 (s, br, 1 H), 3.42 (m, 1 H), 3.68 (m, 2 H), 3.74 (dd, J = 9.19, 1.49 Hz, 1 H), 7.22−7.30 (m, 5 H); MS *m*/*z* 276 (M^+, 11), 258 (5), 185 (65), 167 (14), 157 (29), 153 (3), 136 (13), 123 (73), 109 (22), 95 (23), 91 (100), 83 (20), 81 (19), 65 (14), 55 (18), 43 (17).

(+)-(1*R*,2*R*)-*endo*-3-(Methylthio)-1,7,7-trimethylbicyclo-[2.2.1]heptan-2-ol (6b) and (+)-(1*R*,2*S*)-*endo*-3-(Methylthio)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (7b). Prepared as described for the preparation of **6a** and **7a**. From 9.359 g (47.0 mmol) of **5b**[10] was obtained 2.988 g (32%) of **6b** (colorless oil) and 5.840 g (62%) of **7b** (colorless, oil). **6b**: $[\alpha]^{25}_D$: +22.2° (*c*, 3.16, acetone); ^1H NMR ($CDCl_3$) δ 0.88 (s, 3 H), 0.90 (s, 3 H), 0.94 (s, 3 H), 1.2 (m, 1 H), 1.45 (m, 2 H), 1.74 (m, 1 H), 1.90 (t, J = 4.27 Hz, 1 H), 2.06 (s, 3 H), 2.94 (s, br., 1 H), 3.39 (m, 1 H), 3.82 (dd, J = 9.24, 2.02 Hz, 1 H); MS *m*/*z* 200 (M^+, 47), 185 (13), 183 (4), 172 (93), 157 (29), 153(8), 124 (89), 109 (100), 95 (71), 90 (71), 83 (71), 69 (45), 55 (36), 43 (40). **7b**: $[\alpha]^{25}_D$: +15.6° (*c*, 2.04, acetone); ^1H NMR ($CDCl_3$) δ 0.88 (s, 6 H), 1.08 (s, 3 H), 1.53 (m, 2 H), 1.71−1.84 (m, 3 H), 1.91 (s, br., 1 H), 2.12 (s, 3 H), 3.22 (m, 1 H), 3.31 (d, J = 3.84 Hz, 1 H); MS *m*/*z* 201 (M^+ + 1, 29), 200 (M^+, 91), 183 (23), 172 (36), 157 (20), 152 (36), 137 (26), 124 (70), 109 (87), 95 (100), 90 (72), 83 (89), 69 (45), 55 (67), 43 (50).

General Procedure for Stoichiometric Enantioselective Epoxidation. A reaction tube containing a magnetic stirring bar was charged with sulfides **3a, 4a, 6a, or 7a** (1 mmol), aldehyde (1.2 mmol), MeI (2 mmol), powdered potassium hydroxide (2 mmol), and CH_3CN (4 mL). After stirring for 30 h, the reaction was completed according to TLC. The reaction mixture was then filtered on a short silica gel column to remove inorganic salts. The filtrate was concentrated, and the residue was purified by preparative TLC with a mixture of petroleum ether (60−90 °C) and ethyl acetate (90:10) as the eluent to give pure *trans*-diaryloxiranes **10**.

***trans*-2-Phenyl-3-phenyloxirane (10a)**: mp 67−69 °C (lit.[15] 69 °C); ^1H NMR ($CDCl_3$) δ 3.86 (s, 2 H), 7.29−7.40 (m, 10 H).

***trans*-2-(*p*-Chlorophenyl)-3-phenyloxirane (10b)**: mp 98−99 °C (lit.[15] 100 °C); ^1H NMR ($CDCl_3$) δ 3.79 (d, J = 1.9 Hz, 1 H), 3.82 (d, J = 1.7 Hz, 1 H), 7.21−7.37 (m, 9 H).

***trans*-2-(*p*-Tolyl)-3-phenyloxirane (10c)**: mp 60−62 °C (lit.[15] 62 °C); ^1H NMR ($CDCl_3$) δ 2.36 (s, 3 H), 3.82 (d, J = 1.8 Hz, 1 H), 3.84 (d, J = 1.8 Hz, 1 H), 7.16−7.38 (m, 9 H).

General Procedure for Catalytic Enantioselective Epoxidation. A reaction tube containing a magnetic stirring bar was charged with sulfides **3b, 4b, 6b, or 7b** (0.2 mmol), aldehyde (1.0 mmol), benzyl bromide (1.2 mmol), powdered potassium hydroxide (2.0 mmol), and CH_3CN (4 mL). After stirring for 15−20 h, the reaction was completed according to TLC. The reaction mixture was then filtered on a short silica gel column to remove inorganic salts. The filtrate was concentrated and the residue was purified by preparative TLC with a mixture of petroleum ether (60−90 °C) and ethyl acetate (90:10) as the eluent to give pure *trans*-diaryloxiranes **10**.

Acknowledgment. Financial supports from the National Natural Foundation of China and Chinese Academy of Sciences are gratefully acknowledged.

Supporting Information Available: Copies of NMR spectra (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO951442+

(15) Imuta, M; Ziffer, H. *J. Org. Chem.* **1979**, *44*, 2505−2509.
(16) Hayashi, S.; Furukawa, M.; Yamamoto, J.; Niigata, K. *Chem. Pharm. Bull.* **1967**, *15*, 1188−1192.