Chiral sulfide-mediated enantioselective epoxidation of aldehydes

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Dedicated to Professor Binne Zwanenburg on the occasion of his 70th birthday

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Abstract

Non-racemic epoxides were prepared via enantioselective Corey-Chaykovsky epoxidation of aromatic, heteroaromatic and cinnamic aldehydes with chiral sulfonium ylides. One-pot epoxidation using aldehydes, alkyl bromides and chiral sulfide in the presence of a base was also investigated. The chiral sulfide was easily synthesized in five steps from *d*-camphor through hetero Diels-Alder reaction as a key step.

Keywords: Epoxidation, epoxides, oxiranes, stilbene oxides, sulfides, sulfonium ylides

Introduction

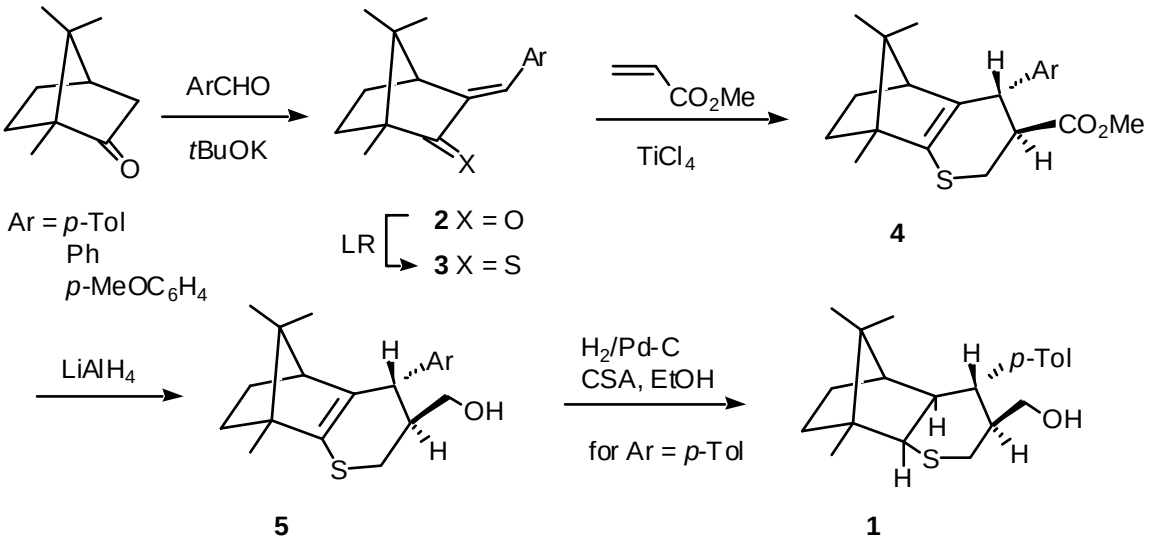
Epoxides are useful and important synthetic intermediates and found diverse applications in organic synthesis.[1] Great concern focuses on development of synthetic methods for asymmetric epoxidation, as exemplified by the Sharpless, Katsuki, and Jacobsen olefin oxidations and Darzens approaches using carbonyl compounds.[2] Chiral sulfonium ylide-mediated enantioselective epoxidation of aldehydes and ketones, an asymmetric version of so-called "Corey-Chaykovsky reaction,[3]" has recently begun to receive much attention as an alternative method for asymmetric synthesis of epoxides.[4-10] The methodology involves the formation of sulfonium ylide which can be *in situ* generated via essentially two independent routes, *viz*. (i) alkylation of a sulfide, followed by deprotonation of the resulting sulfonium salt (salt method),[4-9] and (ii) coupling of a sulfide with a carbenoid (metal carbene) generated *in situ* from diazo compound or its precursor (e.g. tosyl hydrazone salt).[4,10] The efficiency of asymmetric induction for the epoxidation undoubtedly depends largely upon chiral sulfides used. In very recent reports, efforts have been made on the synthesis of new chiral sulfides/sulfonium ylides as well as their use in not only epoxidation[11] but also aziridination[12] and cyclopropanation.[13] Thus, information on a variety of new chiral sulfides and/or sulfonium ylides regarding the efficiency on yields and stereoselectivities for these reactions is necessary to understand chemistry from the synthetic and mechanistic points of view.[14] The attractive advantages of exploiting natural *d*-camphor in

asymmetric synthesis are its relatively inexpensive and easy availability, potent transformation ability, and promising asymmetric induction due to the topological differentiation efficiency apparently by virtue of the rigid framework of its derivatives.[15] With this in mind, we envisioned that camphor framework-connected cyclic chiral sulfide would be of high potential as an asymmetric induction mediator in the epoxidation. In this full paper we describe our results in the enantiomeric Corey-Chaykovsky epoxidation with optimization of various factors and reaction conditions employing such camphor-derived homochiral tricyclic sulfide **1**.[16]

Results and Discussion

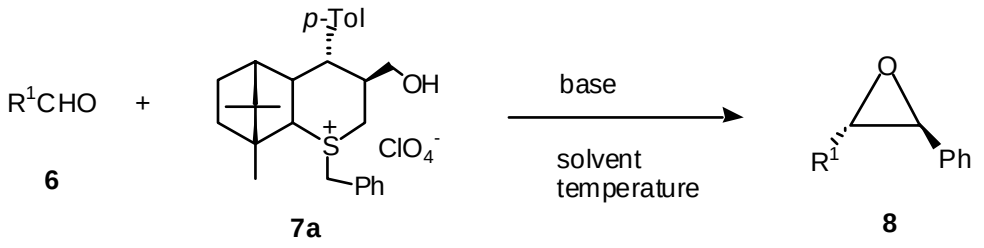
Preparation of Chiral Sulfide 1

The sulfide **1** was readily prepared from natural *d*-camphor in five steps in 50-60% overall yields (Scheme 1). The key step was the highly *exo* selective and complete π-face-selective hetero Diels-Alder reaction of 3-arylmethylenecamphorthiones **3** with methyl acrylate.[17] The stereochemistry of cycloadducts **4** was unequivocally established by X-ray crystallographic analysis of **4** (Ar = Ph) and ^{1}H-NMR spectroscopic study.[17] Although cycloadducts **4** or alcohols **5** essentially neither reacted with benzyl bromide to give sulfonium salts nor mediated epoxidation with aldehydes in the presence of a base, it was hoped that chiral sulfide **1** obtained by highly π-face-selective hydrogenation of **5** would act efficiently as a mediator in the epoxidation. Indeed, sulfide **1** worked well in the epoxidation by both methods, (A) the epoxidation of aldehydes using sulfonium salt prepared in advance and (B) the one-pot epoxidation starting from aldehyde, alkyl halide and sulfide **1** in the presence of a base.



Scheme 1

(A) Epoxidation using sulfonium salt



Scheme 2. For specification of the substituent R^1, see Table 6.

Sulfonium perchlorate **7a**, which was prepared by the reaction of chiral sulfide **1** with benzyl bromide and silver perchlorate, was allowed to react with aldehyde **6b** (R^1 = *p*-$NO_2C_6H_4$) as a model reaction to find first a suitable base under the conditions (Table 1). In all the cases *trans* epoxide (*trans*-**8b**) was obtained as the major product with enantiomeric excess (ee) of 71-79 %. Among the bases used KOH seems to be the best of choice in the balance of yield and enantioselectivity.

Table 1. Effects of base in epoxidation of **6b** (R^1 = *p*-$NO_2C_6H_4$) with **7a** to afford **8b** [a]

Run	Base (equiv.)	Yield (%)[b]	Trans: cis[c]	*Trans* ee (%)[c]
1	KOH (1.2)	95	>99 : <1	79
2	*t*-BuOK (1.2)	57	>99 : <1	71
3	*n*-BuLi (1.5)	33	>99 : <1	79

[a] Reactions were carried out in THF at -78 °C for 6 h using 1.0 equiv. **6a** and 1.2 equiv. **7a**. [b] Yields based on consumed amounts of *p*-nitrobenzaldehyde (**6b**). [c] Determined by HPLC [Chiralcel OD, *i*-PrOH-hexane (1:30)].

Table 2. Epoxidation of **6b** (R^1 = *p*-$NO_2C_6H_4$) with **7a** to afford **8b** under various reaction conditions [a]

Run	Reaction conditions	Yield (%)[b]	Trans : cis[c]	*Trans* ee (%)[c]
1	CH_2Cl_2, r. temp, 2 h	99	97 : 3	27
2	THF, r. temp, 2 h	99	97 : 3	18
3	THF, 0 °C, 3 h	99	98 : 2	35
4	THF, -15 °C, 5 h	99	98 : 2	56
5	THF, -40 °C, 6 h	50 [98]	99 : 1	77
6	THF, -78 °C, 6 h	31 [99]	>99 : <1	79
7	MeCN, r. temp, 1.5 h	99	97 : 3	41
8	MeCN, 0 °C, 2 h	99	97 : 3	62

Table 2. Continued

Run	Reaction conditions	Yield (%)[b]	Trans : cis[c]	*Trans* ee (%)[c]
9	MeCN, -15 °C, 3 h	99	98 : 2	71
10	MeCN, -40 °C, 9 h	89 [98]	99 : 1	81
11	*t*-BuOH, r. temp, 1.5 h	99	82 : 18	80
12	THF-MeCN (2:1), -78 °C, 9 h	43 [98]	99 : 1	79
13	THF-*t*-BuOH (2:1), -78 °C, 9 h	37 [98]	99 : 1	79
14	MeCN-*t*-BuOH (2:1), -40 °C, 9 h	89 [98]	94 : 6	82

[a] KOH (1.2 equiv) was used as a base. [b] Isolated yields. In square brackets yields based on consumed amounts of **6b**. [c] Determined by HPLC [Chiralcel OD, *i*-PrOH-hexane (1:30)].

Then, we explored the same reaction in the presence of KOH to optimize reaction conditions by varying solvent, temperature and reaction time. The results are shown in Table 2. In every case high *trans:cis* selectivity was obtained. As the reaction temperature becomes lower (runs 2-6 and 7-10), the *trans:cis* selectivity and the enantioselectivity both become higher in the same solvent, as expected. As for the solvent effect on the enantioselectivity and the diastereoselectivity, higher ee's values could be attained in more polar solvents than in less polar solvents, whereas the reverse propensity was observed for the diastereoselectivity. This effect would not simply arise from solubility of the sulfonium perchlorate **7a** because **7a** is soluble enough in either solvent under the conditions applied. Quite recently, an excellent rationale has been proposed by Aggarwal et al. to explain origins of both of the stereoselectivities by unraveling the mechanism.[10a] This tendency of the solvent effect was also observed in the reaction of benzaldehyde (**6a**) to give epoxide **8a** (Table 3).

Table 3. Effects of solvent in epoxidation of **6a** (R^1 =Ph) with **7a** to afford **8a** [a]

Run	Solvent	Yield (%)[b]	Trans : cis[c]	*Trans* ee (%)[c]
1	CH_2Cl_2	52 [86]	99 : 1	22
2	MeCN	80 [94]	95 : 5	34
3	*t*-BuOH	85 [>99]	94 : 6	69

[a] Reactions were carried out at room temperature (22-25 °C) for 2 days using KOH (1.2 equiv) as a base. [b] Isolated yields. In square brackets yields based on consumed amounts of benzaldehyde (**6a**). [c] Determined by HPLC [Chiralcel OD, *i*-PrOH-hexane (1:100)].

Table 4. Effects of water added as a co-solvent in epoxidation of **6b** (R^1 = *p*-$NO_2C_6H_4$) with **7a** to afford **8b** [a]

Run	Reaction conditions (ratio in volume)	Yield (%)[b]	Trans : cis[c]	*Trans* ee (%)[c]
1	MeCN, room temp, 1.5 h	99	97 : 3	41
2	MeCN-H_2O (9:1), room temp, 2 h	99	88 : 12	76
3	MeCN-H_2O (5:5), room temp, 2 h	99	80 : 20	79
4	MeCN-H_2O (3:7), room temp, 2 h	99	78 : 22	80
5	MeCN-H_2O (1:9), room temp, 2 d	85	76 : 24	80
6	MeCN-H_2O (7:3), -40 ^oC, 9 h	69 [98]	92 : 8	86
7[d]	MeCN-H_2O (7:3), -40 ^oC, 9 h	32 [97]	97 : 3	91
8	H_2O, r. temp, 4 d	18	69 : 31	80
9	*t*-BuOH, r. temp, 1.5 h	99	82 : 18	80
10	*t*-BuOH-H_2O (9:1), room temp, 2 h	99	76 : 24	83
11	*t*-BuOH-H_2O (5:5), room temp, 2 h	99	70 : 30	84

[a] KOH (1.2 equiv) was used as a base. [b] Isolated yields. In square brackets yields based on consumed amounts of **6b**. [c] Determined by HPLC [Chiralcel OD, *i*-PrOH-hexane (1:30)]. [d] *p*-Chlorobenzaldehyde (**6c**) was used instead of **6b**.

Since in more polar solvents higher enantioselectivity was obtained as described above, we further examined the reaction by adding water as a co-solvent. The results are summarized in Table 4. As the ratio water/solvent increases (runs 1-5 and 9-11), the enantioselectivity goes up, while the *trans:cis* ratio gradually decreases.[18] At a temperature of -40 ^oC in MeCN-H_2O (7:3) (runs 6 and 7), the highest ee's of 86% and 91% were achieved albeit in lower isolated yield. In the reaction in the medium of water (run 8) equally good enantioselectivity of 80 % ee was obtained, though the isolated yield was very low. The low yield may be due to sparing solubility of the aldehyde **6** and/or generated sulfonium ylide into the water, since considerable amounts of **6** unreacted was recovered.

Furthermore, effects of the counter anion of the sulfonium salts for the epoxidation were also checked. As a result, no significant differences of the yields and both the stereoselectivities were observed (Table 5).

Table 5. Effects of the counter anion of **7** in epoxidation of **6b** (R^1 = *p*-$NO_2C_6H_4$) to afford **8b** [a]

Run	**7**	Counter anion	Time (h)	Yield (%)[b]	Trans : cis[c]	*Trans* ee (%)[c]
1	**a**	ClO_4^-	1.5	99	88 : 12	80
2	**b**	TfO^-	2	99	88 : 12	78
3	**c**	BF_4^-	3	99	88 : 12	76
4	**d**	Br^-	6	97	87 : 13	77
5	**e**	I^-	6	98	84 : 16	78

[a] Reactions were carried out in *t*-BuOH at room temperature (22-25 ^oC) using KOH (1.2 equiv.) as a base. [b] Isolated yields. [c] Determined by HPLC [Chiralcel OD, *i*-PrOH-hexane (1:30)].

In order to examine the generality of this epoxidation, the reaction of **7a** with aldehydes **6** bearing a variety of substituents (R^1) was performed under the conditions optimized above in terms of balance of the reactivity (yield) and the diastereo- and enantioselectivities. The results are shown in Table 6. Apparently, the electron-withdrawing substituents accelerate the reaction, whereas the electron-repelling ones retard the reaction. By using 2.0 equimolar amounts of **7a**, the results could be somewhat improved (runs **d** and **e**).

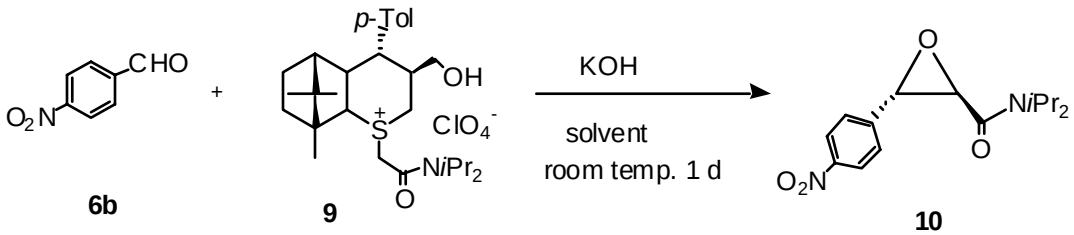
It is noteworthy that chiral sulfide **1** was recovered enantiomerically pure in good yields in the cases that good isolated yields of epoxides **8** were obtained (Tables 2 -6) and could be reused.

By employing this epoxidation method, *trans*-oxiranylcarboxamide **10** could be synthesized in high *trans* : *cis* selectivity with fairly good enantioselectivity (Scheme 3, Table 7), which are comparable to those in recent report.[5a,11e] However, it was found that an electron-withdrawing group such as a nitro group in aldehyde **6** is necessary to activate the formyl group in the epoxidation with this amide-stabilized sulfonium ylide generated from salt **9**.

Table 6. Epoxidation of **6** bearing a variety of substituents with **7a** to afford **8** [a]

Run	R^1	Time (h)	Yield (%)[b]	Trans : cis[c]	*Trans* ee (%)[c]		*Cis* ee (%)[c]
a	Ph	48	85	94 : 6	69	[S,S]	69
b	*p*-$NO_2C_6H_4$	1.5	99	82 : 18	80	[S,S]	99
c[d]	*p*-ClC_6H_4	4	99 (32)	92 : 8 (97 : 3)	70 (91)	[S,S]	nd
d[e]	*p*-Tol	96 [48]	88 [89]	93 : 7 [93 : 7]	56 [62]	[S,S]	nd
e[e]	*p*-$MeOC_6H_4$	96 [48]	44 [82]	96 : 4 [95 : 5]	62 [68]	[S,S]	nd
f	2-Naphtyl	24	99	89 : 11	74	[S,S]	nd
g	β-Styryl	18	95	95 : 5	80	[S,S]	nd
h	2-Furyl	3	96	82 : 18	80	[S,R]	80
i	2-Thienyl	3	95	94 : 6	70	[S,R]	63
j	2-Pyridyl	2	99	68 : 32	56	[S,S]	57

[a] Reactions were carried out in *t*-BuOH at room temperature (22-25 °C) using KOH (1.2 equiv.) as a base. [b] Isolated yields. [c] Determined by HPLC [Chiralcel OD or AD, *i*-PrOH-hexane (1:20-200) or EtOH-hexane (1:20-300)]. The absolute configuration of *trans* isomers was assigned by comparison of the (-) sign of specific rotation with literature data or by assumption. [d] In parentheses values taken from run **7** in Table 4. [e] In square brackets values when 2.0 equiv. **7a** was used.



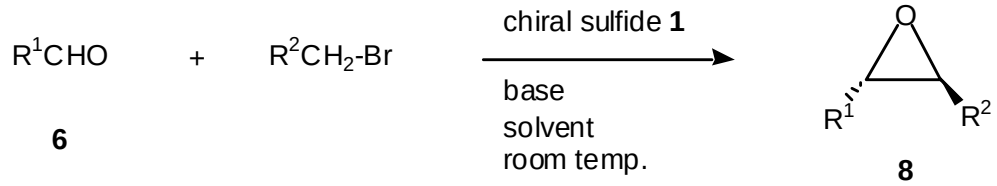
Scheme 3

Table 7. Enantioselective synthesis of *trans*-oxiranylcarboxamide **10** by epoxidation of **6b** with **9** [a]

Run	Solvent	Yield (%)[b]	Trans : cis[c]	*Trans* ee (%)[c]
1	CH_2Cl_2	41	>99 : <1	50
2	MeCN	68	>99 : <1	58
3	*t*-BuOH	50	>99 : <1	55

[a] Reactions were carried out using 1.0 equiv. **6b** and 1.2 equiv. **9** in the presence of 1.2 equiv. KOH. [b] Isolated yields. [c] Determined by HPLC [Chiralcel AS, EtOH-hexane (1:50)].

(B) One-pot epoxidation of aldehyde with alkyl bromide and sulfide 1



6 **8**

Scheme 4

Establishing the method (A) using sulfonium salt **7** or **9** prepared beforehand, we next performed three-component one-pot epoxidation of **6** with alkyl bromide and chiral sulfide **1**. A model reaction using benzaldehyde **6a** (1.0 equiv), benzyl bromide (3.0 equiv) and chiral sulfide **1** (1.0 equiv) in acetonitrile under the conditions furnished the desired epoxide **8a** in 72 % yield with high diastereoselectivity (*trans:cis* = 96:4) and with moderate enantioselectivity (56 % ee) of the *trans* isomer, when K_2CO_3 was used as a base (Table 8, run 1). Cs_2CO_3 can also be a candidate as a base. Encouraged by this result, we next screened solvents for better stereoselectivities (Table 9). Among the solvents used, the reaction in *t*-butyl alcohol showed the best enantioselectivity of 71 % ee of the *trans* isomer albeit in lower isolated yield and with somewhat decreased diastereoselectivity (run 4). The reaction in tetrahydrofuran or acetone gave only a trace amount of epoxide **8a**. Acetonitrile and *t*-butyl alcohol can be the solvent of choice for diastereo- and enantioselectivities, whereas water-containing acetonitrile was less effective in contrast to the above results in Table 4. At a higher temperature of 83 ^oC the reaction was indeed accelerated (2 h, in *t*-BuOH) but the enantioselectivity of *trans* isomer was depressed to 44% ee.

Table 8. Effects of base in one-pot epoxidation to afford **8a** [a]

Run	Base [a]	Yield / %[b]	Trans : cis [c]	*Trans* ee / % [c]
1	K_2CO_3	72 [99]	96 : 4	56
2[d]	Cs_2CO_3	99	97 : 3	43
3	NaH	25 [99]	92 : 8	32
4	KOH	trace	-	-

[a] Reactions were carried out in MeCN at room temperature for **4** days using 1.0 equiv. **6a**, 3.0 equiv. benzyl bromide and 1.0 equiv. **1** in the presence of a base (3.0 equiv.). [b] Isolated yields. In square brackets, yields based on consumed amounts of benzaldehyde **6a**. [c] Determined by HPLC [Chiralcel OD, *i*-PrOH-hexane (1:100)]. The absolute configuration was assigned [*S*,*S*] by comparison of the sign (-) of specific rotation with the literature data. [d] For 1 day.

Table 9. Effects of solvent in one-pot epoxidation to afford **8a** [a]

Run	Solvent	Yield / %[b]	Trans : cis [c]	*Trans* ee / % [c]
1	CH_2Cl_2	54 [99]	94 : 6	51
2	MeCN	72 [99]	96 : 4	56
3[d]	MeCN/H_2O (v/v 9:1)	43 [51]	77 : 23	47
4	*t*-BuOH	30 [99]	77 : 23	71

[a] Reactions were carried out in the presence of K_2CO_3 (3.0 equiv.) at room temperature for **4** days using 1.0 equiv. **6a**, 3.0 equiv. benzyl bromide and 1.0 equiv. **1**. [b] Isolated yields. In square brackets, yields based on consumed amounts of benzaldehyde **6a**. [c] Determined by HPLC [Chiralcel OD, *i*-PrOH-hexane (1:100)]. The absolute configuration was assigned [*S*,*S*] by comparison of the sign (-) of specific rotation with the literature data. [d] For 1 week.

In order to see possibility of the catalytic process of this one-pot epoxidation, the reactions of **6a**,**b** with benzyl bromide in the presence of varied quantities of chiral sulfide **1** were examined. The results are shown in Table 10. Obviously, degrees of the diastereo- and enantioselectivities in each reaction were not so markedly decreased by reducing the amounts of **1** added, while the reaction became slow (runs 1-4 and 5-8). The electron-withdrawing *p*-nitro substituent of benzaldehyde obviously accelerated the reaction and good yield of epoxide **8b** was obtained. Although sub-stoichiometric amounts of sulfide **1** are necessary to obtain higher yields and stereoselectivities, a merit of this epoxidation is that after the reaction, chiral sulfide **1** was recovered optically pure in good yield and could be reused.

Table 10. Dependence on stoichiometry of chiral sulfide **1** in one-pot epoxidation of **6a**,**b** to afford **8a**,**b**

Run	R^1 (R^2 = Ph)	n (equiv.) **1**	Time (d)	Yield (%)	Trans : cis [c]	*Trans* ee (%) [c]
1	Ph	1.0	4	72 [99]	96 : 4	56
2		0.5	4	63 [96]	94 : 6	55
3		0.2	4	36 [45]	94 : 6	46
4		0.1	4	35 [41]	91 : 9	44
5	*p*-$NO_2C_6H_4$	1.0	1	99	96 : 4	57
6		0.5	1.5	99	98 : 2	52
7		0.2	3.5	99	90 : 10	48
8		0.1	6	99	88 : 12	48

[a] Reactions were carried out in the presence of K_2CO_3 (3.0 equiv.) in MeCN at room temperature using 1.0 equiv. **6a**,**b**, 3.0 equiv. benzyl bromide and n equiv. **1**. [b] Isolated yields. In square brackets, yields based on consumed amounts of benzaldehyde **6a**. [c] Determined by HPLC [Chiralcel OD, *i*-PrOH-hexane (1:50-100)]. The absolute configuration was assigned [*S*,*S*] by comparison of the sign (-) of specific rotation with the literature data.

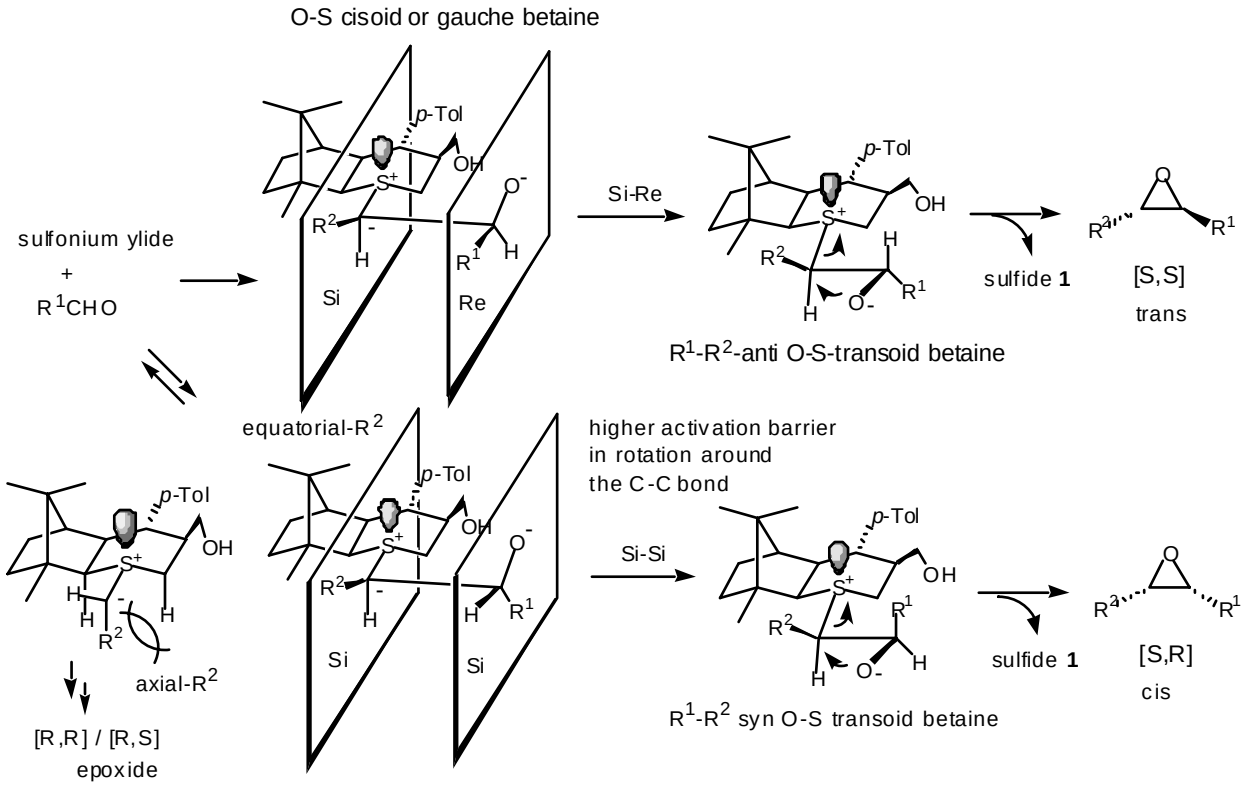
Finally, the reactions of variously substituted aromatic aldehydes **6** and alkyl bromides were carried out in the presence of an equimolar amount (n =1.0) of **1** under the optimized reaction conditions. The epoxides **8** were obtained in fairly good yields and stereoselectivities (Table 11). From the viewpoint of enantioselectivity, it is suggested that recommended are the reactions with benzyl bromide in *t*-BuOH for syntheses of *trans*-epoxides **8a-c**,**e** and **8g** (runs 12-14, 16, and 17), whilst the reaction with *p*-methylbenzyl bromide in MeCN (run 10) is preferable to those of runs 4 and 15 for synthesis of *trans*-2-phenyl-3-*p*-tolyl epoxide **8d**. In this one-pot method, the chiral sulfide **1** used was again virtually quantitatively recovered enantiomerically pure after the reaction and could be used repeatedly.

Table 11. One pot epoxidation of **6** bearing a variety of substituents with benzyl bromide to afford **8** [a]

Run	R^1	R^2	Time (d)	Epoxide	Yield (%)[b]	Trans : cis[c]	*Trans* ee (%)[c]	
	< In MeCN >							
1	Ph	Ph	4	**8a**	72 [99]	94 : 6	56	[S,S]
2	*p*-$NO_2C_6H_4$	Ph	1	**8b**	99	95 : 5	57	[S,S]
3	*p*-ClC_6H_4	Ph	2	**8c**	99	90 : 10	46	[S,S]
4	*p*-Tol	Ph	4	**8d**	84 [90]	81 : 19	75	[S,S]
5	*p*-$MeOC_6H_4$	Ph	4	**8e**	33 [89]	83 : 17	61	[S,S]
6	β-Styryl	Ph	4	**8g**	68	>99 : <1	40	[S,S]
7	*o*-HOC_6H_4	Ph	4	**8k**[d]	57 [99]	97 : 3	47	[S,S]
8	2-Pyridyl	Ph	1	**8j**	99	>99 : <1	45	[S,S]
9	Ph	*p*-$NO_2C_6H_4$	4	**8b**	73 [99]	72 : 28	22	[S,S]
10	Ph	*p*-Tol	4	**8d**	58 [69]	80 : 20	91	[S,S]
11	Ph	β-Styryl	3	**8g**	66	79 : 21	20	[S,S]
	< In *t*-BuOH >							
12	Ph	Ph	4	**8a**	24 [99]	77 : 23	71	[S,S]
13	*p*-$NO_2C_6H_4$	Ph	1	**8b**	99	76 : 24	76	[S,S]
14	*p*-ClC_6H_4	Ph	3	**8c**	99	79 : 21	75	[S,S]
15	*p*-Tol	Ph	4	**8d**	51 [99]	76 : 24	66	[S,S]
16	*p*-$MeOC_6H_4$	Ph	4	**8e**	47 [85]	77 : 23	65	[S,S]
17	β-Styryl	Ph	3	**8g**	80	90 : 10	78	[S,S]
18	Ph	*p*-$NO_2C_6H_4$	4	**8b**	36 [90]	73 : 27	22	[S,S]

[a] Reactions were carried out at room temperature (22-25 ^oC) using 1.0 equiv. **6** and 3.0 equiv. alkyl bromide in the presence of K_2CO_3 (3.0 equiv.) as a base. [b] Isolated yields. In square brackets, yields based on consumed amounts of aldehyde **6**. [c] Determined by HPLC [Chiralcel OD or AD, *i*-PrOH-hexane (1:20-200) or EtOH-hexane (1:20-50)]. The absolute configuration of *trans* isomers was assigned [*S,S*] by comparison of the sign (-) of specific rotation with the literature data or by assumption. [d] *ortho-O*-benzylated epoxide was obtained.

Rationale for enantio- and diastereoselectivities



Scheme 5

Recently, mechanisms of carbonyl epoxidation with sulfonium ylide based on computational studies have been proposed by Aggarwal et al.[14a] and Koskinen et al..[14b] On the basis of their proposal, the predominant formation of (*S,S*)-*trans*-stilbene oxides observed in the epoxidation with the sulfonium ylide derived from chiral sulfide **1** can essentially be explained as illustrated in Scheme 5. (i) The sulfonium ylide adopts two dominant conformations in which the filled orbital on the ylide carbon is orthogonal to the sulfur lone pair. (ii) The conformation having the R^2 group in an equatorial position is favored over the other one with an axial R^2 group due to steric repulsion between the R^2 group and the diaxial protons in the thiane ring. (iii) The aldehyde attacks the ylide carbon preferably from the less hindered *Si* face with an arrangement of the aldehyde as to be attacked from the *Re* face or the *Si* face in a manner of *cisoid* ([2+2]) or *gauche* addition with coulombic interaction to form the *cisoid* betaines. The former (*Si-Re*) *cisoid* betaine forms the anti-*transoid* betaine *via* the rotation around the C-C bond. The internal nucleophilic substitution with *trans* elimination of sulfide **1** leads to a stereoselective formation of (*S,S*)-*trans*-epoxides, while the syn-*transoid* betaine formed from the syn-*cisoid* betaine (*Si-Si*) leads to (*S,R*)-*cis*-epoxide. The higher becomes the activation barrier in the tortional rotation step from the syn-*cisoid* (*Si-Si*) to the syn-*transoid* betaine, the greater increases the degree of reversibility to the starting materials; thus, it leads to high *trans* selectivity. The distribution of

these key species involved in the pathways is significantly influenced by the factors such as substituents (electronic property, steric hindrance) and solvents (charge solvation).† Although the sense of asymmetric induction and diastereoselectivity could be thus explained, the observed enantioselectivity was not so high than that expected. This is ascribable most likely to partial release of controlling the ylide conformation as the factor (ii),[11c] nevertheless, much better enantioselectivity was observed in the imino Corey-Chaykovsky aziridination by the use of the same ylides derived from sulfide **1**.[12a] It is also noteworthy that a simple, relatively less congested C_2-symmetric sulfide (2,5-dimethylthiolane, 2,5-diethylthiolane) is an efficient catalyst for the epoxidation *via* the ylide route.[6]

Conclusions

The present study demonstrates diastereo- and enantioselective synthesis of optically active epoxides *via* the Corey-Chaykovsky reaction. Although the stereoselectivities observed were moderate to good, the methods are promising because of the easy and simple but efficient preparation of the chiral sulfide with good crystallinity and the feasible introduction of a variety of substituents to the tetrahydrothiopyran ring to tune up the stereoselectivities by further manipulation. Moreover, the chiral sulfide can be recovered optically pure and essentially quantitatively and reused.

Experimental Section

General Procedures. Melting points are uncorrected. Analytical TLC was carried out on Merk silica gel 60 F254 plates. Visualization was performed with UV light, *p*-anisaldehyde/sulfuric acid, phosphomolybdic acid, and/or $KMnO_4$. Column chromatography was conducted on silica gel (100-200 mesh) or on alumina (100-200 mesh). IR spectra were recorded on a Hitachi Model 270-30 instrument. ^{1}H NMR and ^{13}C NMR spectra were measured at 100, 270 and/or 500 MHz for ^{1}H, and at 25, 67.8 and/or 125.65 MHz for ^{13}C using JEOL JNM-FX 100, JEOL JNM-EX 270 and JEOL JNM-LA 500 spectrometers. Chemical shifts from tetramethylsilane (TMS) as an internal standard are given in ppm and coupling constants, *J*, in Hz. Mass spectra (EI or FAB) were obtained with a Hitachi Model M-80B double focusing mass spectrometer with a data processing system M-0101. Elemental combustion microanalyses were performed on a Perkin-Elmer 2400 CHNS/O Elemental Analyzer. Optical rotations were recorded on a Nippon Bunko Model DIP-370 digital Polarimeter and are reported in units of 10^{-1} degcm^{2}g^{-1}. Enantiomeric excesses and ratios of *trans* and *cis* isomers were determined by HPLC measurement using

† Aggarwal et al. proposed a general rationalization for the origins of diastereo (*trans* vs. *cis*)- and enantioselectivities including their dependence on substituents and solvents in the sulfur ylide-carbonyl epoxidation. For further discussion, see literature [10a,14a].

chiralcel OD, AD and AS columns (0.5-20 % *i*-PrOH-hexane, 0.3-5 % EtOH-hexane) on a Millipore-Waters 996 instrument or Shiseido Model S-MicroChrom instrument.

Preparation of chiral sulfide (1). [(1*R*, 2*R*, 5*S*, 6*R*, 7*R*, 8*R*)-(1,11,11-Trimethyl-6-*p*-tolyl-3-thia-tricyclo[6.2.1.$0^{2,7}$]undec-5-yl)-methanol]. A mixture of *d*-camphor (30 mmol, 4.57 g), *p*-tolualdehyde (36 mmol, 4.33 g) and potassium *t*-butoxide (39 mmol, 4.38 g) was heated in *t*-butyl alcohol (37 mL) for 5 h under reflux. The reaction mixture was neutralized with aq. HCl, extracted with ethyl acetate (20 mL x 3) and the combined extracts was washed with saturated aq. NaCl solution and dried over $MgSO_4$. Evaporation of the solvent and column chromatography of the residue on silica gel using EtOAc-hexane (1:5) as an eluent to give 3-(*p*-tolylmethylene)camphor **2** (6.25 g, 82 % yield) as a colorless solid after crystallization from hexane, mp 97.2-98.2 ^oC; IR (KBr disk, cm^{-1}) 2916, 1704, 1628, 1506, 1436, 1368, 1320, 1250, 1144, 1102, 1056, 1012, 958, 918, 808 and 744; ^1H-NMR (100 MHz, $CDCl_3$) δ 0.80 (3H,s), 0.99 (3H, s), 1.02 (3H, s), 1.48-1.60 (2H, m), 1.77 (1H, dt, *J* 3.1, 12.2), 2.14-2.20 (1H, m), 2.36 (3H, s), 3.10 (1H, d, *J* 4.0), 7.19 (2H, d, *J* 7.9), 7.21 (1H, s), 7.38 (2H, d, *J* 7.9); ^{13}C-NMR (25 MHz, $CDCl_3$, DEPT) δ 9.23 (CH_3), 18.27 (CH_3), 20.16 (CH_3), 21.30 (CH_3), 25.85 (CH_2), 30.67 (CH_2), 46.63 (C), 49.15 (CH), 56.97 (C), 127.48 (CH), 129.31 (CHx2), 129.69 (CHx2), 132.73 (C), 138.84 (C), 141.16 (C), 208.17 (C); MS (FAB) m/z 255 ($M+H^+$, 100), 254 (40), 105 (14); HRMS (FAB) Calcd for $C_{18}H_{22}OH$: M+H 255.1749. Found, 255.1746. Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 85.03; H, 8.96.

A mixture of 3-(*p*-tolylmethylene)camphor **2** (10 mmol, 2.54 g) and Lawesson's reagent (6 mmol, 2.42 g) was heated in benzene under reflux for 2 h. Evaporation of the solvent and column chromatography of the residue on silica gel [benzene-hexane (1:4)] gave 3-(*p*-tolylmethylene)camphorthione **3** (2.14 g, 79 % yield) as blue needles after recrystallization from hexane, mp 146-147 ^oC; IR (KBr disk, cm^{-1}) 2962, 2920, 1626, 1606, 1312, 1278, 1261, 1240, 1062 and 912; ^1H-NMR (100 MHz, $CDCl_3$) δ 0.75 (3H, s), 1.05 (3H, s), 1.20 (3H, s), 1.24-2.33 (4H, m), 2.36 (3H, s), 3.22 (1H, d, *J* 4.0), 7.17 (2H, d, *J* 8.0), 7.43 (2H, d, *J* 8.0), 7.56 (1H, s); ^{13}C-NMR (25 MHz, $CDCl_3$, DEPT) δ 13.50 (CH_3), 19.02 (CH_3), 20.25 (CH_3), 21.55 (CH_3), 25.71 (CH_2), 34.17 (CH_2), 49.19(C), 50.89 (CH), 67.75 (C), 129.10 (CH), 129.51 (CHx2), 130.27 (CHx2), 133.47 (C), 139.21 (C), 149.37 (C), 252.70 (C); MS (EI, 70eV) m/z 270 (M^+, 69), 269 (M^+-1, 66), 255 (M^+-CH_3, 100); HRMS (FAB) Calcd for $C_{18}H_{22}SH$: M+H 271.1520. Found: 271.1522. Anal. Calcd for $C_{18}H_{22}S$: C, 79.94; H, 8.20. Found: C, 79.82; H, 8.44.

To a solution of methyl acrylate (3.0 mmol, 0.296 mL) in dichloromethane (29 mL) was added a 1.0 M titanium tetrachloride dichloromethane solution (0.3 mL) at rt with stirring for **1** h. 3-(*p*-Tolylmethylene)camphorthione **3** (3.0-3.6 mmol, 0.81-0.97 g) was then added to the solution with stirring at rt. After 10 min the reaction was quenched with water. The mixture was extracted with dichloromethane (15 mL x 2), washed with saturated aq. NaCl solution and dried over $MgSO_4$. Evaporation of the solvent and short column chromatography of the residue [83:17 ratio of *trans* and *cis* isomers (^1H NMR)] on silica gel using EtOAc-hexane (1: 3) as an eluent to give a mixture of *trans*- and *cis*-isomers **4** (1.06 g, 99 % yield), which was used for the next step (LAH reduction) without separation of the isomers. Alternatively, thin layer chromatography or

column chromatography [silica gel, EtOAc-hexane (1: 10)] of the mixture afforded the major *trans*-cycloadduct **4** (0.87 g) as a yellowish oil. $[\alpha]_D$ +171 ($CHCl_3$, c 0.23); IR (neat, cm^{-1}) 2952, 2870, 1741, 1621, 1512, 1436, 1170, 1021, 910, 821, 788 and 734; ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.72 (3H, s), 0.85 (3H, s), 0.75-2.30 (4H, m), 0.96 (3H, s), 2.05 (1H, d, *J* 2.8), 2.30 (3H, s), 2.87 (1H, dt, *J* 4.5, 4.5), 3.08 (2H, d, *J* 4.5), 3.63 (3H, s), 3.98 (1H, d, *J* 4.5), 7.01 (2H, d, *J* 7.9), 7.09 (2H, d, *J* 7.9); ^{13}C-NMR (25 MHz, $CDCl_3$) δ 11.01 (CH_3), 19.15 (CH_3), 19.50 (CH_3), 21.01 (CH_3), 25.29 (CH_2), 26.46 (CH_2), 33.39 (CH_2), 42.84 (CH), 46.15 (CH), 51.81 (CH_3), 55.90 (CH), 56.10 (C), 57.46 (C), 126.62 (CHx2), 129.01 (CHx2), 132.96 (C), 135.39 (C), 136.27 (C), 139.58 (C), 172.82 (C); MS (EI, 70 eV) m/z 356 (M^+, 100). *Cis*-cycloadduct **4** (0.17 g) was also separated pure as yellowish needles after crystallization from dichloromethane-hexane, mp 58-59 °C, $[\alpha]_D$ +201 ($CHCl_3$, c 3.0); IR (KBr disk, cm^{-1}) 2952, 2872, 1738, 1620, 1512, 1434, 1248, 1170, 1024 and 808; ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.75 (3H, s), 0.88 (3H, s), 0.59–2.30 (4H, m), 1.00 (3H, s), 2.10 (1H, d, 3.3), 2.28 (3H, s), 2.70-3.20 (3H, m), 3.51 (3H, s), 3.94 (1H, d, 3.8), 6.86 (2H, d, 8.6) 7.01 (2H, d, 8.6); ^{13}C-NMR (25 MHz, $CDCl_3$) δ 10.87 (CH_3), 19.25 (CH_3), 19.45 (CH_3), 21.05 (CH_3), 22.13 (CH_2), 26.81 (CH_2), 33.29 (CH_2), 43.38 (CH), 45.18 (CH), 51.37 (CH_3), 56.00 (C), 56.93 (CH), 57.46 (C), 128.72 (CHx2), 129.15 (CHx2), 133.15 (C), 135.49 (C), 136.71 (C), 136.95 (C), 172.97 (C); MS (EI, 70 eV) m/z 356 (M^+, 100).

To a suspension of lithium aluminum hydride (2.25 mmol, 0.085 g) in dry THF (20 mL) was added a THF solution (15 mL) of *trans*-**4** (3.0 mmol, 1.07 g) at 0 °C. The reaction mixture was warmed to rt with stirring. After 10 min, the reaction mixture was treated with dilute aq HCl on cooling, extracted with EtOAc (15 mL x 3) and dried over $MgSO_4$. Evaporation and column chromatography of the residue on silica gel [EtOAc-hexane (1: 9)] afforded alcohol **5** (82 % yield) as colorless needles after recrystallization from EtOAc-hexane, mp 144.1-144.6 °C, $[\alpha]_D$ +112 ($CHCl_3$, c 2.96); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.73 (3H, s), 0.84(3H, s), 0.93-1.01 (1H, m), 0.99 (3H, s), 1.32-1.38 (1H, m), 1.49 (1H, br s), 1.53-1.67 (2H, m), 2.01(1H, d, *J* 3.2), 2.01-2.08 (1H, m), 2.32 (3H, s), 2.77 (1H, dd, *J* 5.4, 12.9), 3.12 (1H, dd, *J* 2.7, 12.9), 3.33 (1H, d, *J* 3.4), 3.64 (1H, dd, *J* 5.6, 10.5), 3.74 (1H, dd, *J* 8.3, 10.5), 6.97-7.13 (4H, m); ^{13}C-NMR (125.65 MHz, $CDCl_3$) δ 10.97 (CH_3), 19.48 (CH_3), 19.50 (CH_3), 20.96 (CH_3), 24.83 (CH_2), 26.53 (CH_2), 33.45 (CH_2), 42.41 (CH), 43.14 (CH), 56.12 (CH), 56.17 (C), 57.26 (C), 64.37 (CH_2), 128.46 (CHx2), 128.91 (CHx2), 132.55 (C), 135.40 (C), 135.98 (C), 141.04(C); MS (EI, 70 eV) m/z 328 (M^+, 72), 300 (M^+-CH_2CH_2, 100); HRMS Calcd for $C_{21}H_{28}OS$: M 328.1862. Found: 328.1858. Anal. Calcd for $C_{21}H_{28}OS$: C, 76.78; H, 8.59. Found: C, 76.65; H, 8.76.

A mixture of alcohol **5** (3.0 mmol, 0.986 g), 5 % Pd/C (0.0986 g) and camphorsulfonic acid (0.3 mmol, 0.07 g) in ethanol (5 mL) was vigorously stirred overnight under a hydrogen atmosphere at rt. The mixture was neutralized with aq. $NaHCO_3$ and extracted with dichloromethane. The combined organic layer was washed with saturated aq. NaCl and dried over $MgSO_4$. Evaporation and column chromatography of the residue on silica gel [benzene-hexane (1: 3)] afforded sulfide **1** (82 % yield). Recrystallization from EtOAc-hexane gave optically pure chiral sulfide **1** as colorless needles mp 128.6-129.6 °C, $[\alpha]_D$ +21 ($CHCl_3$, c 1.97); IR (KBr disk, cm^{-1}) 3276, 2872, 1428, 1388, 1298 and 998; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.75 (3H, s), 0.93 - 0.99 (1H, m), 0.97 (3H, s), 1.27-1.31 (2H, m), 1.45 (3H, s), 1.56-1.67 (2H, m),

1.90-1.97 (1H, m), 1.92 (1H, dd, 9.2, 13.4), 2.33 (3H, s), 2.77 (1H, dd, 10.7, 13.4), 2.80 (1H, dd, 7.6, 14.0), 2.92 (1H, dd, 1.5, 14.0), 3.35 (1H, dd, 7.6, 10.4), 3.38 (1H, dd, 10.4, 10.4), 3.40 (1H, d, 9.2), 7.06 (2H, d, 7.9), 7.11 (2H, d, 7.9); ^{1}H-NMR (500 MHz, C_6D_6) δ 0.51 - 0.57 (1H, m), 0.66 (3H, s), 0.83 (1H, dd, 8.1, 9.2), 1.05 (3H, s), 1.16 (1H, dd, 8.1, 9.5), 1.36 (1H, d, 3.1), 1.47-1.50 (1H, m), 1.56 (3H, s), 1.66 (1H, dd, 9.5, 12.8), 1.71 - 1.77 (1H, m), 2.16 (3H, s), 2.63 (1H, dd, 7.3, 14.0), 2.77 (1H, dd, 10.7, 12.8), 2.95 (1H, ddd, 0.3, 1.5, 14.0), 3.17-3.22 (2H, m), 3.23 (1H, d, 9.5), 6.94 (2H, d, 7.9), 6.99 (2H, d, 7.9) (OH peak was not detected); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.27 (CH_3), 20.99 (CH_3), 22.36 (CH_3x2), 30.09 (CH_2), 30.52 (CH_2), 38.23 (CH_2), 42.81 (CH), 44.51 (CH), 47.82 (C), 47.90 (CH), 49.63 (C), 51.76 (CH), 59.13 (CH), 64.73 (CH_2), 129.16 (CHx4), 135.79 (C), 141.60 (C); HRMS (EI) Calcd for $C_{21}H_{30}OS$: M 330.2019. Found: 330.2013. Anal. Calcd for $C_{21}H_{30}OS$: C, 76.31; H, 9.15. Found: C, 76.19; H, 9.21.

Preparation of sulfonium salt (7). Typical procedure. To an acetone solution (3 mL) of sulfide **1** (0.30 mmol, 0.099 g) was successively added benzyl bromide (0.33 mmol, 0.039 g) and silver perchlorate (0.33 mmol, 0.0684 g). The mixture was stirring at rt for 0.5-1 h and then dichloromethane (20 mL) was added to filter insoluble materials. The filtrate was evaporated and the residual fine crystals were washed with dry diethyl ether-hexane to give sulfonium perchlorate **7a** as colorless fine crystals (70 % yield). In the preparation of the other sulfonium salts **7b-e**, evaporation of the filtrate gave viscous oil, which was then treated with hexane to solidify, followed by recrystallization from diethyl ether to give pure **7b-e** for the epoxidation. Sulfonium bromide **7d** was not sufficiently stable to allow NMR measurement.

Sulfonium perchlorate (7a). Colorless needles, mp (dec.) 207.9-208.4 ^{o}C, IR (KBr disk, cm^{-1}) 3468, 2920, 1440 and 1072; ^{1}H-NMR (500 MHz, CD_3CN) δ 0.85 (3H, s), 1.05 (3H, s), 1.11-1.13 (1H, m), 1.25 (3H, s), 1.51-1.52 (1H, m), 1.57-1.68 (3H, m), 2.33 (3H, s), 2.44-2.48 (1H, m), 2.75 (1H, dd, 9.5, 13.1), 2.88 (1H, dd, 11.3, 13.1), 3.17 (1H, dd, 5.2, 9.5), 3.30 (1H, dd, 5.2, 10.7), 3.32 (1H, dd, 4.9, 13.4), 3.78 (1H, dd, 7.0, 13.4), 4.14 (1H, d, 9.5), 4.71 (1H, d, 12.8), 4.86 (1H, d, 12.8), 7.11-7.14 (5H, m), 7.44-7.49 (2H, m), 7.52-7.55 (2H, m); ^{13}C-NMR (125 MHz, CD_3CN) δ 14.18, 21.02, 21.48, 28.98, 36.40, 37.25, 39.26, 44.34, 47.94, 48.65, 49.43, 50.71, 51.32, 66.05, 70.10, 72.97, 127.55x2, 127.73, 128.35x2, 129.78x2, 130.60x2, 136.99, 137.53, 138.38. Anal. Calcd for $C_{28}H_{37}ClO_5S$: C, 64.54; H, 7.16. Found: C, 64.31; H, 7.22.

Sulfonium triflate (7b). Colorless solid; ^{1}H-NMR (500 MHz, CD_3CN) δ 0.81 (3H, s), 0.86 (3H, s), 0.92-1.01 (1H, m), 1.16 (3H, s), 1.36-1.47 (2H, m), 1.60-1.67 (2H, m), 1.95-1.98 (1H, m), 2.25 - 2.33 (2H, m) 2.31 (3H, s), 2.64 (1H, dd, 9.8, 12.8), 2.78 (1H, dd, 11.3, 12.8), 3.02 (1H, dd, 6.1, 11.3), 3.54 (1H, dd, 6.1, 13.4), 3.84 (1H, d, 9.8), 4.66 (1H, d, 12.8), 4.86 (1H, d, 12.8), 7.14-7.18 (4H, m), 7.52-7.59 (5H, m).

Sulfonium tetrafluoroborate (7c). Colorless needles; ^{1}H-NMR (500 MHz, CD_3CN) δ 0.83 (3H, s), 0.93 (3H, s), 0.95-1.01 (1H, m), 1.19 (3H, s), 1.36-1.47 (2H, m), 1.58-1.73 (2H, m), 2.25 (3H, s), 2.65 (1H, dd, 9.6, 12.9), 2.80 (1H, dd, 11.2, 12.9), 3.16 (2H, m), 3.25 (2H, m), 3.40 (1H, dd, 6.3, 13.5), 3.73 (1H, d, 9.6), 4.52 (1H, d, 13.0), 4.77 (1H, d, 12.9), 7.11 (2H, d, 8.1), 7.19 (2H, d, 8.1), 7.52-7.58 (5H, m).

Sulfonium iodide (7e). Yellowish solid; ^{1}H-NMR (500 MHz, CD_3CN) δ 0.75 (3H, s), 0.79 (3H, s), 1.11-1.22 (2H, m), 1.18 (3H, m), 1.47-1.65 (3H, m), 2.30 (3H, s), 2.68-2.85 (2H, m), 3.45-3.50 (2H, m), 3.65-3.68 (1H, m), 3.77-3.80 (1H, m), 3.88-3.91 (1H, m), 4.04-4.06 (1H, m), 4.70-4.95 (2H, m), 7.01-7.56 (9H, m). Anal. Calcd for $C_{28}H_{37}IOS$: C, 61.31; H, 6.80. Found: C, 61.61; H, 7.03.

Sulfonium perchlorate (9). Colorless needles, mp (dec.) 109.0-111.6 ^{o}C; IR (KBr disk, cm^{-1}) 3448, 2920, 1618, 1442, 1246, 1072 and 808; ^{1}H-NMR (500 MHz, CD_3CN) δ 0.89 (3H, s), 1.05-1.13 (1H, m), 1.22 (3H, s), 1.29 (3H, d, 2.1), 1.31 (3H, s), 1.33 (3H, d, 2.1), 1.40 (3H, d, 1.7), 1.43 (3H, d, 1.7), 1.49 (1H, d, 1.8), 1.58-1.78 (3H, m), 2.33 (3H, s), 2.38-2.49 (1H, m), 2.69 (1H, dd, 9.7, 13.2), 2.97 (1H, dd, 11.4, 13.2), 3.23 (1H, dd, 5.9, 10.9), 3.31-3.33 (2H, m), 3.35-3.40 (1H, m), 3.57-3.72 (2H, m), 3.85 (1H, dd, 4.6, 13.0), 3.98 (1H, dd, 6.6, 13.0), 4.09 (1H, dd, 4.6, 14.2), 7.13-7.22 (4H, m); ^{13}C-NMR (125 MHz, CD_3CN) δ 13.89, 20.50, 20.53, 20.58, 20.64, 20.69, 20.79, 21.07, 21.13, 21.89, 22.03, 29.91, 37.64, 40.53, 43.20, 45.03, 47.94, 51.74, 52.21, 52.49, 63.14, 64.32, 130.44, 130.52x3, 138.04, 139.82, 162.49.

Epoxidation using sulfonium salt [Method (A)]. A typical procedure (Table 6, Run **a**). - A mixture of benzaldehyde (**6a**) (0.05 mmol, 0.0051 mL), sulfonium perchlorate **7a** (0.06 mmol, 0.0313 g) and powdered KOH (0.06 mmol, 0.0034 g) in *tert*-butyl alcohol (3 mL) was stirred at rt for 48 h. The reaction was quenched with water and the reaction mixture was extracted with dichloromethane (10 mL x 3). The combined extracts was washed with saturated aq. NaCl and dried over $MgSO_4$. Evaporation of the solvent and column chromatography of the residue on silica gel (40 cm^3) using EtOAc-hexane (1: 9) as an eluent gave 2,3-diphenyloxirane (**8a**) in 85 % yield in a *trans:cis*-isomers ratio of 94:6 with 69 % ee of *trans* isomer. The other epoxidation reactions were similarly carried out under the conditions stated in corresponding Tables and runs.

One-pot epoxidation [Method (B)]. A typical procedure (Table 11, Run **b**). - A mixture of *p*-nitrobenzaldehyde (**6b**) (0.10 mmol, 0.0151 g), benzyl bromide (0.30 mmol, 0.036 mL), chiral sulfide **1** (0.10 mmol, 0.0331 g) and powdered K_2CO_3 (0.30 mmol, 0.042 g) in *tert*-butyl alcohol (5 mL) was stirred at rt for **1** h. The work-up similar to that described above in Method (A) gave 2-(*p*-nitrophenyl)-3-phenyloxirane (**8b**) in 99 % yield in a *trans:cis* ratio of 76:24 with 76 % ee of *trans*–isomer.

Column chromatography conditions and chiral HPLC analyses conditions and data for various epoxides are listed below.

Column Chromatography			HPLC data for epoxides					
	Column	Eluent [a]	Column	Eluent [a] (1.00mL/min)	Retention time / min *Cis*(major)	*Cis*(minor)	*Trans*(major)	*Trans*(minor)
8a	Silica gel	E:H = 1: 9	OD	P:H = 1:100	7.43	-	20.73	9.39
8b	Silica gel	E:H = 1: 9	OD	P:H = 1:30	16.28	12.80	29.14	23.60
8c	Silica gel	B	OD	P:H = 1:20	6.07	6.07	8.09	7.32
8d	Silica gel	E:H = 1: 20	OD	P:H = 1:200	13.06	13.06	31.24	16.05
8e	Alumina	E:H = 1: 50	OD	P:H = 1:50	8.30	8.30	21.97	11.04
8f	Silica gel	E:H = 1: 9	OD	Et:H = 1:50	6.97	6.97	10.12	8.45
8g	Silica gel	E:H = 1: 9 [b]	AD	Et:H = 1:20	5.94	5.41	11.17	7.24
8h	Alumina	H	OD	Et:H = 1:300	8.36	10.49	11.44	26.07
8i	Alumina	H	OD	Et:H = 1:300	10.45	12.54	14.27	23.55
8j	Silica gel	E:H = 1: 9	AD	Et:H = 1:50	13.87	15.14	22.69	39.36
8k	Silica gel	E:H = 1: 9	OD	Et:H = 1:50	10.56	10.56	15.38	14.66
10	Silica gel	E:H = 1: 9	AS	Et:H = 1:50	-	-	19.82	25.61

[a] E = ethyl acetate; Et=EtOH; H = hexane; P = isopropyl alcohol; B = benzene. [b] + 5 % Et_3N was added.

2,3-Diphenyloxirane (8a). [6,7a,9,10a] Colorless solid; m.p. 66.0-67.0 °C; $[\alpha]_D$ -251 (EtOH, c 5.82, 85 % ee) (Calcd. -295); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 3.86 (2H, s), 7.32 - 7.37 (10H, m); MS (FAB) m/z 197 ($M+H^+$, 82), 196 (M^+, 100); HRMS (EI) Calcd for $C_{14}H_{12}O$: M 196.0888. Found: 196.0881.

2-(*p*-Nitrophenyl)-3-phenyloxirane (8b). [6,7a,9,10a] Colorless solid; m.p. 125.5-128.7 °C; $[\alpha]_D$ -192 (EtOH, c 1.013, 74% ee) (Calcd. -260); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 3.85 (1H, d, 1.65), 3.97 (1H, d, 1.65), 7.25 (7H, m), 8.23 (2H, d, 8.7); MS (FAB) 242 ($M+H^+$, 23), 154 (100), 136 (100); HRMS (EI) Calcd for $C_{14}H_{11}NO_3$: M 241.0739. Found: 241.0743.

2-(4-Chlorophenyl)-3-phenyloxirane (8c). [6,7a,9,10a] Colorless solid; m.p. 89.5-91.3 °C; $[\alpha]_D$ -241 (EtOH, c 1.020, 96 %ee) (Calcd. -251); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 3.80 (1H, d, 1.65), 3.83 (1H, d, 1.65), 7.24-7.35 (9H, m).

2-Phenyl-3-tolyloxirane (8d). [6,7a,9,10a] Colorless solid; m.p. 57.5-59.1 °C; $[\alpha]_D$ -261 (EtOH, c 1.867, 90 % ee) (Calcd. -290) ^{1}H-NMR (270 MHz, $CDCl_3$) δ 2.37 (3H, s), 3.84 (1H, d, 1.9), 3.87 (1H, d, 1.9), 7.18-7.39 (9H, m).

2-(Methoxyphenyl)-3-phenyloxirane (8e). [6,10a] Colorless solid; m.p. 76.0-78.2 °C; $[\alpha]_D$ -94 (EtOH, c 0.453, 41 % ee) (Calcd. -229); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 3.74 (3H, s), 3.77 (1H, d, 1.98), 3.81 (1H, d, 1.98), 6.83-6.89 (2H, m), 7.20-7.24 (2H, m), 7.27-7.34 (5H, m).

2-Naphthyl-3-phenyloxirane (8f). [6] Colorless solid; m.p. 120.7-121.2 °C; $[\alpha]_D$ -236 ($CHCl_3$, c 0.867, 97 % ee) (Calcd. -243).; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 3.96 (1H, d, 1.8), 4.03 (1H, d, 1.8),7.23-7.49 (8H, m), 7.75-7.83 (4H, m); MS (FAB) 247 ($M+H^+$, 47), 154 (100); HRMS (EI) Calcd for $C_{18}H_{14}O$: M 246.1045. Found: 246.1049.

2-Phenyl-3-β-styryloxirane (8g). [5d,6,10a] Colorless solid; m.p. 73.1-74.4 °C; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 3.52 (1H,dd, 1.71, 7.81), 3.89 (1H, d, 1.71), 6.06 (1H, dd, 7.81, 16.1), 6.82 (1H, d, 16.1), 7.23-7.39 (8H, m), 7.66 (2H, d, 7.56).
2-Furyl-3-phenyloxirane (8h). [6,7d,10a] Yellow oil; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 3.87 (1H, d, 2.0), 4.34 (1H, d, 2.0), 6.37 (1H, dd, 1.8 , 3.1), 6.47 (1H, d, 3.1), 7.11 - 7.41 (6H, m); MS (FAB) m/z 187 ($M+H^+$, 41), 105 (100); HRMS (FAB) Calcd for $C_{12}H_{10}O_2H$: M+H 187.0759. Found: 187.0758.
2-Phenyl-3-thienyloxirane (8i). [6,10a] Colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 4.03 (1H, d, 1.3), 4.07 (1H, d, 1.3), 6.99 - 7.32 (8H, m); MS (FAB) 203 ($M+H^+$, 100); HRMS (FAB) Calcd for $C_{12}H_{10}OSH$: M+H 203.0531. Found: 203.0531.
2-Phenyl-3-pyridyloxirane (8j). [7d,10a] Yellow oil; $[\alpha]_D$ -140 ($CHCl_3$, c 0.55, 55 % ee) (Calcd. -252); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 4.05 (1H, d, 1.9), 4.07 (1H, d, 1.9), 7.23-7.39 (7H, m), 7.71 (1H, ddd, 1.8, 7.8, 7.8), 8.59 (1H, ddd, 0.83, 0.83, 4.8).
2-(o-Benzyloxy)-3-phenyloxirane (8k). Colorless solid; m.p. 64.0-65.8 °C; $[\alpha]_D$ -27 (EtOH, c 3.107, 47 % ee) (Calcd. -57); IR (KBr disk, cm^{-1}) 2992,1582, 1448, 1368, 1222, 1102, 1008, 844, 728 and 692;^{1}H-NMR (270 MHz, $CDCl_3$) δ 3.79 (1H, d, 1.98), 4.30 (1H, d, 1.98), 5.05 (2H, s), 6.89 (1H, d, 8.25), 6.97 (1H, dd, 7.43, 7.43), 7.21-7.34 (12H, m); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 58.44, 62.05, 69.94, 111.82, 121.02, 125.18, 125.64 (x2), 126.21, 126.80 (x2), 127.68, 128.07, 128.39 (x4), 128.82, 136.80, 137.30, 157.02; MS (FAB) m/z 303 ($M+H^+$, 7), 91 (100); HRMS (FAB) Calcd for $C_{28}H_{18}O_2H$: M+H 303.1385. Found: 303.1383.
2-(*N*,*N*-Diisopropylcarbamoyl)-3-(4-nitrophenyl)oxirane (10). Colorless solid; m.p. 98.4-99.6 °C; $[\alpha]_D$ -8.64 ($CHCl_3$, c 2.40, 73 % ee) (Calcd. -11.68); IR (KBr disk, cm^{-1}) 2932, 1636, 1598, 1516, 1430, 1300, 1206, 1102, 1040 and 832; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 1.27 (3H, d, 6.6), 1.30 (3H, d, 6.8), 1.40 (3H, d, 6.8), 1.41 (3H, d, 6.6), 3.56 (1H, d, 2.0), 3.71 (1H, sept, 6.8), 4.14 (1H, sept, 6.6), 4.22 (1H, d, 2.0), 7.51 (2H, d, 8.3), 8.23 (2H, d, 8.3); ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 20.16 (CH_3), 20.31 (CH_3), 21.34 (CH_3x2), 46.28 (CH), 47.85 (CH), 56.60 (CH), 59.49 (CH), 123.92 (CHx2), 126.42 (CHx2), 143.39 (C), 148.04 (C), 164.36 (C); MS (FAB) m/z 293 ($M+H^+$, 79), 86 (100); HRMS (FAB) Calcd for $C_{15}H_{20}N_2O_4H$: M+H 293.1501. Found: 293.1501. Anal. Calcd for $C_{15}H_{20}N_2O_4$: C, 61.63; H, 6.90; N, 9.58. Found: C, 61.41; H, 7.14; N, 9.31.

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