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Preparation of a novel, camphor-derived sulfide and its evaluation as a chiral auxiliary mediator in asymmetric epoxidation via the Corey-Chaykovsky reaction

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Abstract—Sulfonium ylide-mediated asymmetric one-pot synthesis of optically active epoxides from aldehydes and bromides via the Corey–Chaykovsky reaction is described. The optically pure chiral sulfide was readily prepared from natural camphor via thiabutadiene Diels–Alder cycloaddition, followed by $LiAlH_4$ reduction and hydrogenation of the cycloadduct. © 2000 Elsevier Science Ltd. All rights reserved.

Optically active epoxides are useful and versatile synthetic intermediates.¹ Although principal methodologies of asymmetric epoxidation from olefins by oxidation or from aldehydes/ketones by Darzens approach still continue to be a subject of great challenge,² sulfonium vlide-mediated asymmetric epoxidation (Corey-Chaykovsky reaction) of aldehydes or ketones has recently begun to receive much attention.³ This methodology involves the ylide formation via essentially two independent routes, viz.: (i) alkylation of a sulfide, followed by deprotonation of the resulting sulfonium salt and (ii) direct coupling of a sulfide and a carbene (or carbenoid) generated from a diazomethane. Furukawa et al. first reported a pioneering work on asymmetric, sulfur ylide-mediated epoxidation via the salt method using (+)-10-camphorsulfonic acid-derived sulfides, which resulted in the formation of trans-stilbene oxides in moderate enantiomeric excess (up to 47% ee).⁴ Asymmetric epoxidation via a sulfonium salt method was developed thereafter by the groups of Durst,⁵ Solladiè-Cavallo,⁶ and Dai.⁷ Aggarwal et al. made advances in the sulfur ylide-catalyzed, asymmetric epoxidation via the latter (ii) route and reported excellent results when chiral 1,3-oxathianes (monothioacetals) derived from (+)-10-camphorsulfonic acid were employed as the catalyst.⁸ In this case, a disadvantage is suggested to be the instability of the sulfides for use under acidic circumstances.8 Metzner showed that even a simple, C_2 -symmetric chiral sulfide, 2,3-dimethylthiolane, is an efficient mediator for the epoxidation via the salt route.⁹ In very recent reports, efforts have also been made in the synthesis of new chiral sulfonium ylides for the epoxidation to give good to excellent enantioselectivity.^{10–12} Thus, information regarding chiral sulfides and/or sulfonium ylides associated with structure and chemistry in terms of the efficiency on yields and stereoselectivities (de and ee) for the epoxidation is always necessary from the synthetic and mechanistic points of view.¹³ In this letter, we report a facile synthesis of a new chiral cyclic sulfide and its evaluation in the Corey–Chaykovsky epoxidation.

Previously, we reported a hetero Diels-Alder reaction of homochiral thiabutadienes, arylmethylenethiocamphors, with several dienophiles to afford cycloadducts 1 in quantitative yield with high *exo* and complete π -facial selectivities.¹⁴ Unfortunately, some of the obtained optically pure, bornene-fused dihydrothiopyrans 1 or alcohols 2 virtually neither reacted with benzyl bromide to form sulfonium salts nor mediated the epoxidation with aldehydes in the presence of a base. This is probably due to the lower nucleophilicity of the vinyl sulfides. Then, we envisioned that the hydrogenated sulfide 3would act efficiently as a mediator in the epoxidation. The sulfide 3 was obtained optically pure in good yield from 1 (Ar = p-Tol, R¹ = R² = H) by LiAlH₄ reduction to afford alcohol 2 (98%, Ar = p-Tol, $R^1 = R^2 = H$) with good crystallinity, followed by hydrogenation $[H_2/$ Pd-C] (85%) in the presence of a catalytic amount of camphorsulfonic acid in ethanol.

Keywords: asymmetric synthesis; epoxidation; oxiranes; chiral sulfide; bornane.

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With the chiral sulfide 3 in hand, we performed a one-pot reaction of the epoxidation. Gratifyingly, a model reaction of benzaldehyde with benzyl bromide using sulfide 3 (n = 1.0 equiv) in acetonitrile under the conditions furnished the desired epoxide 4 in 72% yield with high diastereoselectivity (*trans:cis* = 96:4) and with moderate enantioselectivity of the trans isomer (56% ee), when K₂CO₃ was used as a base (Table 1). Encouraged by this result, we next screened solvents for better stereoselectivities. The results are summarized in Table 1. Among the solvents used, the best enantiomeric excess of the trans isomer was obtained in the reaction in t-butyl alcohol, although the yield and diastereoselectivity were both decreased. The reaction in tetrahydrofuran or acetone gave only a trace amount of the epoxide. Acetonitrile can be the solvent of choice in

terms of balance of yield and diastereo- and enantioselectivities, whereas water-containing acetonitrile was less effective. Table 2 shows the results on yields and stereoselectivities of epoxides formed by varying the stoichiometry of 3. Obviously, both stereoselectivities were not so markedly decreased by reducing the amounts of 3 added, while the reaction became slow. The electron-withdrawing *p*-nitro substituent of benzaldehyde obviously accelerated the reaction. It was also found that after the reaction, sulfide 3 was recovered optically pure in good yield and could be reused repeatedly. Finally, the reactions of variously substituted aromatic aldehydes and bromides were carried out in the presence of an equimolar amount (n = 1.0) of 3 under the optimized conditions to give fairly satisfactory results (Table 3).

Table 1. Effects of bases and solvents/n = 1.0 (equiv.) ($\mathbf{R} = \mathbf{R'} = \mathbf{Ph}$)

Base ^a	Yield (%) ^c	Trans:cis ^d	Trans ee (%) ^d	Solvent ^b	Yield (%) ^c	Trans:cis ^d	Trans ee (%) ^d
K_2CO_3	72 [>99]	96:4	56 [<i>S</i> , <i>S</i>]	CH ₂ Cl ₂	54 [>99]	94:6	51 [<i>S</i> , <i>S</i>]
$Cs_2CO_3^e$	99	97:3	43 [<i>S</i> , <i>S</i>]	MeCN	72 [>99]	96:4	56 [<i>S</i> , <i>S</i>]
NaH	25 [>99]	92:8	32 [<i>S</i> , <i>S</i>]	MeCN/H ₂ O ^{f,g}	43 [51]	77:23	47 [<i>S</i> , <i>S</i>]
KOH	Trace	-		t-BuOH	30 [>99]	77:23	71 [<i>S</i> , <i>S</i>]

^a MeCN was used as a solvent.

^b K₂CO₃ was used as a base.

^c Percentage conversion in square brackets.

^d Determined by HPLC [Chiralcel OD, *i*-PrOH–hexane (1:100)]. The absolute configuration was assigned by comparison of the sign (-) of specific rotation with the literature data.^{3–9}

^e For 1 day.

f Ratio v/v 9:1.

^g For 1 week.

Table 2. Dependence on stoicniometry of chiral suffice $3/K_2CO_3$	in MeCN
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Run	R R' = Ph	n (equiv.)	Time (days)	Yield [conversion] (%)	Trans:cis ^a	Trans ee (%) ^a
1	Ph	1.0	4	72 [>99]	96:4	56 [S,S]
2		0.5	4	63 [96]	94:6	55 [S,S]
3		0.2	4	36 [45]	94:6	46[S,S]
4		0.1	4	35 [41]	91:9	44[S,S]
5	$p-NO_2C_6H_4$	1.0	1	>99	96:4	57 $[S,S]$
6	1 2 0 4	0.5	1.5	>99	98:2	52 $[S,S]$
7		0.2	3.5	>99	90:10	48[S,S]
8		0.1	6	>99	88:12	48[S,S]

^a Determined by HPLC [Chiralcel OD, *i*-PrOH–hexane (1:100)]. The absolute configuration was assigned by comparison of the sign (-) of specific rotation with the literature data or by assumption.^{3–9}

Table 3. Epoxidation of aromatic aldehydes with arylmethyl bromides and sulfide $3/K_2CO_3$

Run	R	R′	Solvent	Yield [conversion] (%)	Trans:cis ^a	Trans ee (%) ^a
1	Ph	Ph	MeCN	72 [>99]	96:4	56 [S,S]
2	p-MeOC ₆ H ₄	Ph		33 [89]	82:18	61 [S,S]
3	p-Tol	Ph		84 [90]	81:19	75 $[S,S]$
4 ^b	p-ClC ₆ H ₄	Ph		>99	95:5	57 $[S,S]$
5°	$p-NO_2C_6H_4$	Ph		>99	95:5	57 $[S,S]$
6	Ph	p-Tol		58 [69]	80:20	91 $[S,S]$
7	Ph	Ph	t-BuOH	30 [>99]	77:23	71 $[S,S]$
8	p-MeOC ₆ H ₄	Ph		47 [85]	77:23	65[S,S]
9	p-Tol	Ph		51 [>99]	76:24	66 [S,S]
10 ^d	$p-ClC_6H_4$	Ph		>99	79:21	75 $[S,S]$
11	$p-NO_2C_6H_4$	Ph		>99	76:24	76[S,S]

^a Determined by HPLC [Chiralcel OD, *i*-PrOH–hexane (1:30–1:200)]. The absolute configuration was assigned by comparison of the sign (-) of specific rotation with the literature data or by assumption.^{3–9}

° For 1 day.

^d For 3 days.

The present study demonstrates the enantiomeric, onepot synthesis of optically active epoxides via the Corey–Chaykovsky reaction, and makes this process 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 thiane ring to tune up the stereoselectivities by further manipulation.

References

- Bartók, M.; Láng, K. L. In *The Chemistry of Functional Groups*; Patai, S., Ed.; Wiley: New York, 1980; Supplement E, p. 609; Satoh, T. *Chem. Rev.* 1996, 96, 3303.
- Rao, A. S.; Vol. 7, p. 357; Johnson, R. A.; Sharpless, K. B.; Vol. 7, p. 389; and Aube, J.; Vol. 1, p. 819 In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, 1991; Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E. S.; Brauman, J. I. *Science* 1993, 261, 1404.
- Li, A.-H.; Dai, L.-X.; Aggarwal, V. K. Chem. Rev. 1997, 97, 2341; Aggarwal, V. K. Synlett 1998, 329.
- Furukawa, N.; Sugihara, Y.; Fujihara, H. J. Org. Chem. 1989, 54, 4222.
- 5. Durst, T.; Breau, L.; Ben, R. N. *Phosphorus Sulfur Relat. Elem.* **1993**, *74*, 215.

- Solladié-Cavallo, A.; Diep-Vohuule, A.; Sunjic, A.; Vinkovic, V. *Tetrahedron: Asymmetry* 1996, 7, 1783.
- Dai, L.-X.; Lou, B.-L.; Zhang, Y.-Z. J. Am. Chem. Soc. 1988, 110, 5915; Li, A.-H.; Dai, L.-X.; Hou, X.-L.; Huang, Y.-Z.; Li, F.-W. J. Org. Chem. 1996, 61, 489.
- Aggarwal, V. K.; Ford, J. G.; Thompson, A.; Jones, R. V. H.; Standen, M. C. H. J. Am. Chem. Soc. 1996, 118, 704; Aggarwal, V. K.; Ford, J. G.; Fonquerna, S.; Adams, H.; Jones, R. V. H.; Fieldhouse, R. J. Am. Chem. Soc. 1998, 120, 8328; Aggarwal, V. K.; Ford, J. G.; Jones, R. V. H.; Fieldhouse, R. Tetrahedron: Asymmetry 1998, 9, 1801.
- Julienne, K.; Metzner, P.; Henryon, V. J. Chem. Soc., Perkin Trans. 1 1999, 731; Julienne, K.; Metzner, P. J. Org. Chem. 1998, 63, 4532. See also Reference 5.
- 10. Hayakawa, R.; Shimizu, M. Synlett 1999, 1328.
- 11. Imashiro, R.; Yamanaka, T.; Seki, M. Tetrahedron: Asymmetry 1999, 10, 2845.
- Zhou, Y.-G.; Hou, X.-L.; Dai, L.-X.; Xia, L.-J.; Tang, M.-H. J. Chem. Soc., Perkin Trans. 1 1999, 77.
- For theoretical studies, see the following literature: Lindvall, M. K.; Koskinen, A. P. M. J. Org. Chem. 1999, 64, 4596; Kawashima, T.; Ohno, F.; Okazaki, R.; Ikeda, H.; Inagaki, S. J. Am. Chem. Soc. 1996, 118, 12455; Volatron, F.; Eisenstein, O. J. Am. Chem. Soc. 1987, 109, 1.
- Saito, T.; Nishimura, J.; Akiba, D.; Kusuoku, H.; Kobayashi, K. *Tetrahedron Lett.* **1999**, *40*, 8383; Saito, T.; Furuie, H.; Ishigo-oka, Y.; Watanabe, I. *Heterocycles* **2000**, *53*, 1685.

^b For 2 days.