Stereoselective Reduction of Chiral 3-(*p*-Tolylsulfinyl)-2-thienyl Ketones. A Facile Entry to Optically Active Thienylcarbinols

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Stereoselective reduction of chiral 3-(*p*-tolylsulfinyl)-2-thienyl ketones with diisobutylaluminum hydride (DIBAL) or lithium tri-*sec*-butylborohydride (L-Selectride) has been achieved. Reduction of the ketones with DIBAL in the presence of a Lewis acid or with L-Selectride afforded predominantly the thienyl carbinols, while the reduction with DIBAL alone gave the other diastereoisomeric alcohols as the major product. This method has been successfully applied to an efficient route to chiral thienyl alcohols.

Key words 3-(*p*-tolylsulfinyl)-2-thienyl ketone; stereoselective reduction; diisobutylaluminum hydride; lithium tri-*sec*-butylborohydride; diastereoselectivity; Lewis acid

Various diastereoselective reductions of the carbonyl group in optically active β-ketosulfoxides **1** using $LiAlH_4$ or diisobutylaluminum hydride (DIBAL) with or without a Lewis acid have been reported.[1–4] These high levels of asymmetric induction obtained in the presence of a Lewis acid might originate from a conformationally rigid six-membered transition state involving chelation of the Lewis acid metal with the sulfinyl oxygen and the carbonyl group (the "chelate model"[2] A), giving a sulfinyl alcohol **2** (Chart 1). On the other hand, the reversal in diastereoselectivity (the diastereoisomer **2'** is produced predominantly) by the use of DIBAL alone can be accommodated by the "dipole model"[3] B or the cyclic model[3] C, where the conformation of the ketosulfoxides is different from that in the chelate model A. However, there has been no report concerning the reduction of ketosulfoxides where the sulfinyl group is located remotely from the reaction site, *i.e.*, γ-ketosulfoxides **3** (R≠H).

In conjunction with our studies on remote asymmetric induction using chiral sulfoxides as a chiral auxiliary, we previously reported a Lewis acid-mediated diastereoselective allylation of sulfinyl thienyl aldehydes **3** (R=H),[5] which were derived from the sulfinyl thiophene **4**. The results demonstrated that a proper choice of a Lewis acid in stereoselective addition using sulfinyl carbonyl compounds **3** (R=H) can afford a high level of stereocontrol. Consequently we were interested in the use of γ-ketosulfoxides **3** (R=aryl, alkyl) for stereoselective reduction with or without a Lewis acid. We detail here a highly stereoselective reduction of the ketones **3a—d** and a facile route to optically active thienylcarbinols by easy removal of the sulfinyl moiety in the resulting alcohols.

Although sulfinyl thienylcarbinols **5** and **6** can be obtained by lithiation of **4** followed by addition of an appropriate aldehyde, the diastereoselectivity is poor, resulting in essentially equal amounts of two diastereoisomeric alcohols (Chart 2). Similar results were observed in the reaction of the sulfinyl furan analog with aldehyde.[6] We thus examined the reduction of the ketones **3**, which were obtained by oxidation of **5** or **6** with PCC (pyridinium chlorochromate). The results of reduction of **3** with DIBAL are summarized in Table 1. As shown in Table 1, in the absence of a Lewis acid, the diastereoselectivities in reduction are generally moderate (entries 1—4), and the diastereoisomers **5** were predominantly produced. The best result in the reduction with DIBAL alone was observed in the reduction of the phenyl ketone **3b**, giving the benzyl alcohol **5b** with 80% de (diastereoisomeric excess),

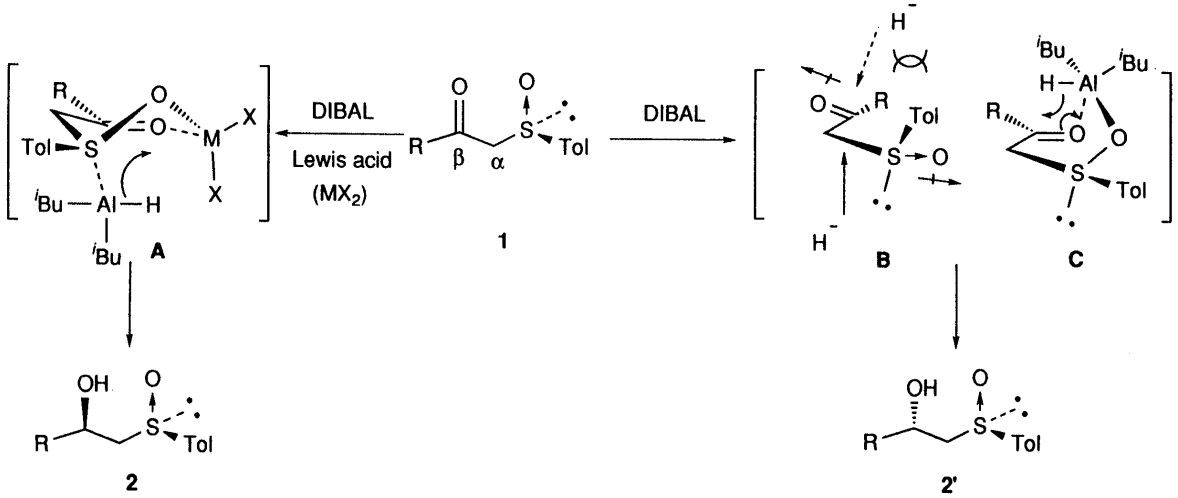

Chart 1

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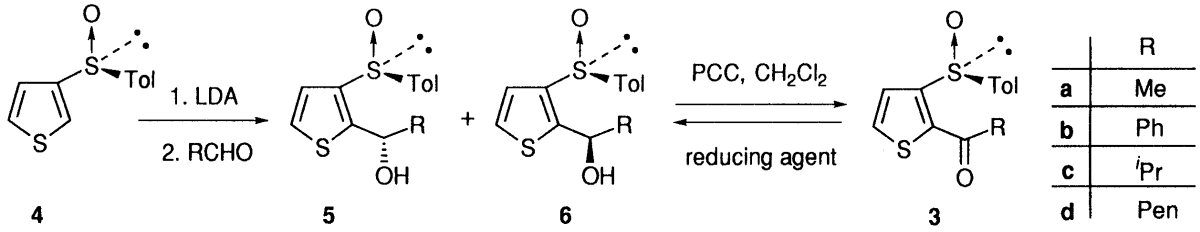

Chart 2

Table 1. DIBAL Reduction of **3** with or without a Lewis Acid

Entry	Ketone **3** (R)	Lewis acid	(eq)	Reaction conditions		Product ratio **5**:**6**	de/%	Isolated total Yield/%
				Time/h	Temp./°C			
1	Me	None		2	−78	3.3:1	54	90
2	Ph	None		3	−78	8.9:1	80	61
3	iso-Pr	None		3	−78	2.3:1	39	37
4	Pen	None		3	−78	3.9:1	59	50
5	Me	$Yb(OTf)_3$	2.0	2	−30	1:8.3	78	88
6	Me	$ZnCl_2$	1.2	1	−78	1:5.2	68	35
7	Me	LiBr	2.0	2	−30	1:5.4	69	89

Table 2. Reduction of **3** with Lithium Tri-*sec*-butylborohydride (L-Selectride) with or without a Lewis Acid

Entry	Ketone **3** (R)	Lewis acid	(eq)	Reaction conditions		Product ratio **5**:**6**	de/%	Isolated total Yield/%
				Time/h	Temp./°C			
1	Me	None		2	−78	1:17.1	89	85
2	Ph	None		3	−78	1:3.6	56	85
3	iso-Pr	None		3	−78	1:3.2	52	92
4	Pen	None		3	−78	1:7.2	76	99
5	Me	$Yb(OTf)_3$	2.0	2	−30	1:41.6	95	99
6	Ph	$ZnCl_2$	1.2	1	−78	1:2.4	41	93
7	iso-Pr	$ZnCl_2$	1.2	2	−78	1:2.5	43	89
8	Pen	$ZnCl_2$	1.2	2	−30	1:7.5	76	99

in 61% yield.

In contrast, the use of a Lewis acid in the reduction afforded the other diastereoisomer **6** as the major product (entries 5—7). The reduction of **3a** conducted in the presence of $Yb(OTf)_3$ gives the highest diastereoselectivity, affording **6a** with up to 78% de. Unfortunately the reduction of **3b—d** in the presence of $Yb(OTf)_3$ did not proceed smoothly.

Much greater stereocontrol was observed in the reduction with a sterically hindered reducing agent, lithium tri-*sec*-butylborohydride (L-Selectride™) with or without a Lewis acid, and the results are given in Table 2. It was found that in both cases, the yields are generally high compared to those of DIBAL reduction, and the diastereoisomers **6** are predominantly produced. The highest stereocontrol (95% de) was achieved in the reduction of **3a** in the presence of $Yb(OTf)_3$, albeit the reductions of **3b—d** under the same conditions were unsuccessful.

The stereochemistry of the newly formed chiral center in **6a** was unequivocally determined as *R* by a single crystal X-ray analysis (Fig. 1); therefore, the stereochemistry of **5a** was assigned as *S*. The relative stereochemistries of other products **5b—d** and **6b—d** were tentatively assigned, and some of them were finally confirmed by transformation of the products into known chiral alcohols **7** (*vide infra*).

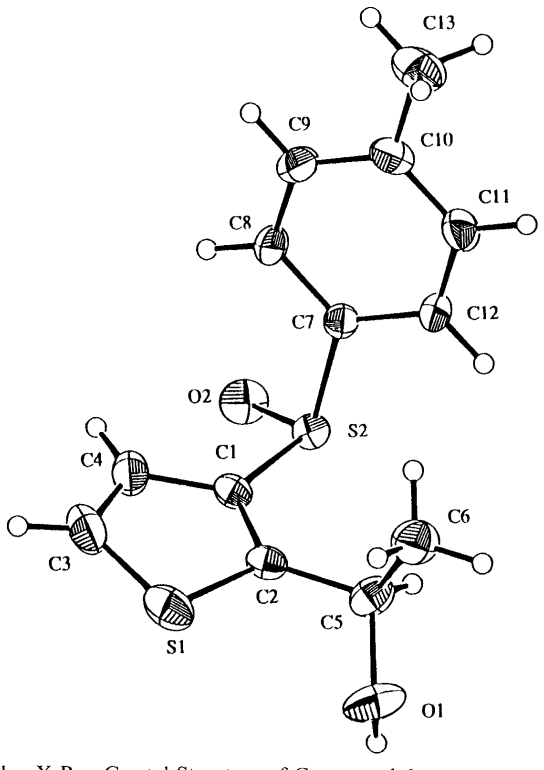

Fig. 1. X-Ray Crystal Structure of Compound **6a**

To elucidate the stereochemical outcome of these selective reductions, further study will be required. However, the predominant production of **6** in both the DIBAL reduction in the presence of a Lewis acid and the L-Selectride reduction may be due to the favorable formation of a seven-membered cyclic chelate (Chart 3). In the presence of the Lewis acid DIBAL reduction should proceed *via* the transition state D due to a stereoelectronic effect[4] (conjugation of the vacant *d* orbital of aluminum with the lone-pair electrons of the sulfur atom) to give rise to **6**. For the reduction with L-Selectride, the hydride would attack from the less hindered lone-pair site *via* the transition state E (M = Li), thereby resulting in the production of the same alcohol **6**.

Alternatively, the products **5** that predominate in the reduction with DIBAL alone would correspond to the transition state F or G (Chart 4), similar to that involved in reduction of β-ketosulfoxides[3]: probably the aluminum metal in DIBAL would coordinate with the sulfinyl oxygen, which has stronger basicity than the carbonyl oxygen. The preferred conformation can be considered as not F but G due to a dipole–dipole interaction, and the sulfur–*p*-tolyl bond would be coplanar with the thiophene ring. As a result, intramolecular delivery of the hydride in DIBAL in G should take place from the *Re* face of the carbonyl which chelates to the aluminum metal, yielding the alcohol **5**.

The usefulness of these stereoselective reductions was exemplified by a facile entry to the optically active thienyl alcohol **7**. To date, chiral thienyl alcohols have been synthesized by kinetic resolution utilizing the Sharpless oxidation procedure,[7] baker's yeast[8] or fungi[9] and by asymmetric reaction[10]; however, the optical purities of the products obtained were frequently unsatisfactory. We prepared optically active **7** by reaction of the sulfinyl carbinol **5** or **6** with an organometallic reagent: desulfinylation[11] of **6b** proceeded smoothly on treatment with butyllithium (4—5 eq) in tetrahydrofuran at −78 °C,

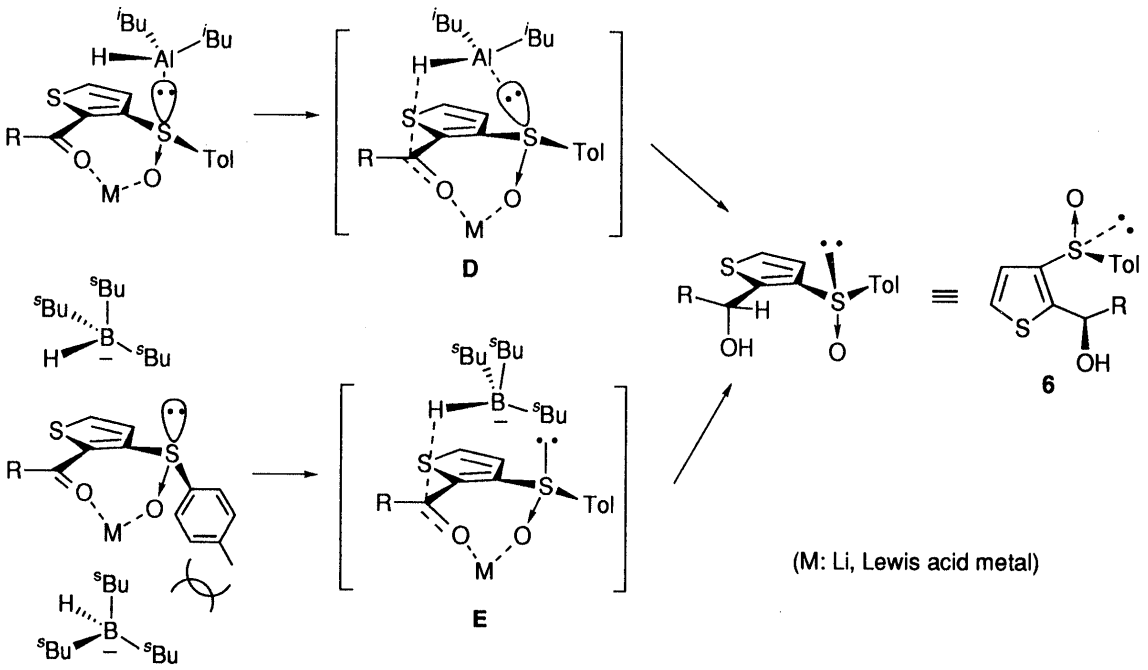

Chart 3

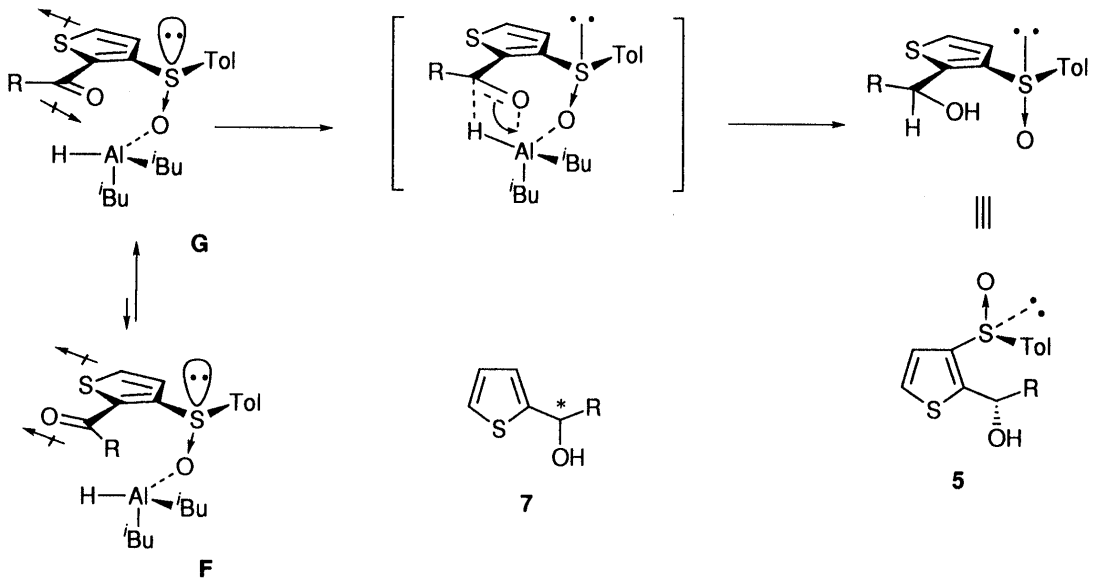

Chart 4

affording (*R*)-**7b**[7] of high optical purity in good yield. Other optically active thienyl alcohols [(*R*)-**7a**, (*S*)-**7c**, (*S*)-**7d**] were also obtained by a similar reaction sequence.

Experimental

Melting points were taken with a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were measured as films or in $CHCl_3$ solution on a JASCO IRA-1 spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-GX270 (270 MHz) spectrometer with $CDCl_3$ as the solvent; *J* values are in hertz (Hz). Tetramethylsilane was used as an internal standard. Mass spectra were recorded with a JEOL JMS D-300 spectrometer. Optical rotations were measured on a JASCO DIP-360 digital polarimeter. All organometallic and low-temperature reactions were carried out in oven-dried glassware under a slight positive pressure of argon. All solvents were distilled prior to use. Extracts were dried over anhydrous $MgSO_4$ before evaporation of the solvents in a rotary evaporator. Flash column chromatography was performed with Merck 230—400 mesh silica gel. Analytical HPLC was performed on a Develosil™ 60 column. Chiral HPLC analyses were carried out with a Shimadzu LC-6A pump and a chiral column, Chiralcel OJ™, with monitoring at 254 nm. Peak ratios on HPLC were measured with a Shimadzu integrator (Chromatopac C-R6A). The symbol S_s indicates that the absolute configuration of the sulfinyl center is *S*.

Typical Procedure for the Preparation of 5 and 6 3-(*p*-Tolylsulfinyl)thiophene **4**[5] (1.8 g, 8.1 mmol) in dry tetrahydrofuran (THF) (10 ml) was added to a solution of lithium diisopropylamide [prepared from BuLi (5.4 ml, 8.9 mmol; 1.64 mol dm^{-3} in hexane) and diisopropylamine (0.8 ml, 8.9 mmol)] in dry THF (3 ml) at 0 °C. The mixture was stirred for 5 min, acetaldehyde (4.5 ml, 81 mmol) was added and the whole was stirred at room temperature for 18 h. It was then treated with 3% HCl (20 ml) and the aqueous layer was extracted with AcOEt (20 ml × 3). The combined extracts were washed with saturated brine (20 ml), dried, and concentrated under reduced pressure. The crude product was passed through a short column of silica gel with AcOEt, giving a mixture of **5a** and **6a** (1.8 g, 83%) in a ratio of 1 : 1. These products were separated by flash chromatography on silica gel with hexane–AcOEt (7 : 1→1 : 1).

(1*S*,*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]-1-ethanol (5a) 40% yield. mp 150—151 °C (from hexane–AcOEt). $[\alpha]_D^{22}$ −133.2° (*c* = 1.8, EtOH). IR ($CHCl_3$): 3360, 3020, 1490, 1210, 1080, 1035, 1010 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 1.60 (3H, d, *J* = 6.4, Me), 2.40 (3H, s, Me), 4.11 (1H, d, *J* = 3.9, OH), 5.28 (1H, dq, *J* = 6.4, 3.9, H-1), 7.10 (1H, d, *J* = 5.4, thiophene), 7.23 (1H, d, *J* = 5.4, thiophene), 7.29 (2H, d, *J* = 8.2, Tol), 7.52 (2H, d, *J* = 8.2, Tol). *Anal.* Calcd for $C_{13}H_{14}O_2S_2$: C, 58.62; H, 5.30. Found: C, 58.99; H, 5.22.

X-Ray Crystal Structure Determination of Compound 6a Crystal Data $C_{13}H_{14}O_2S_2$, *M* = 266.37, orthorhombic, space group $P2_12_12_1$ (#19), *a* = 11.245(2), *b* = 15.349(2), *c* = 7.692(2) Å, *V* = 1327.7(4) Å^3, *Z* = 4, D_c = 1.333 g·cm^{-3}, Cu*Kα* (*λ* = 1.54178 Å). Data were measured on a Rigaku AFC7R diffractometer with nickel-filtered Cu*Kα* radiation using *ω*–2*θ* scans for 1187 reflections, of which 1125 reflections had [$I > 3.00\sigma(I)$]. Atomic coordinates, bond lengths and angles and thermal parameters will be deposited at the Cambridge Crystallographic Data Centre.

(1*R*,*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]-1-ethanol (6a) 41% yield. mp 157—159 °C (from hexane–AcOEt). $[\alpha]_D^{19}$ −108.9° (*c* = 1.3, EtOH). IR ($CHCl_3$): 3360, 3020, 1490, 1400, 1080, 1035, 1010 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 1.61 (3H, d, *J* = 6.3, Me), 2.40 (3H, s, Me), 4.31 (1H, d, *J* = 3.6, OH), 5.53 (1H, dq, *J* = 6.3, 3.6, H-1), 6.74 (1H, d, *J* = 5.4, thiophene), 7.14 (1H, d, *J* = 5.4, thiophene), 7.30 (2H, d, *J* = 8.2, Tol), 7.52 (2H, d, *J* = 8.2, Tol). *Anal.* Calcd for $C_{13}H_{14}O_2S_2$: C, 58.62; H, 5.30. Found: C, 58.35; H, 5.22.

The reaction of **4** with benzaldehyde, 2-methylpropanal, or hexanal was carried out in a manner similar to that described above to give the corresponding compounds **5b—d** and **6b—d**.

(1*S*,*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]benzyl Alcohol (5b) 25% yield. An oil. $[\alpha]_D^{23}$ +246.4° (*c* = 0.6, EtOH). IR (neat): 3300, 1490, 1150, 1080, 1020, 810 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 2.41 (3H, s, Me), 4.58 (1H, br, OH), 6.20 (1H, d, *J* = 3.7, H-1), 7.10 (1H, d, *J* = 5.4, thiophene), 7.20 (1H, d, *J* = 5.4, thiophene), 7.30 (2H, d, *J* = 8.2, Tol), 7.32—7.41 (5H, m, ArH), 7.54 (2H, d, *J* = 8.2, Tol). HR-MS *m/z*: Calcd for $C_{18}H_{14}OS_2$ ($M^+ - H_2O$): 310.0486. Found: 310.0461.

(1*S*,*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]-2-methylpropan-1-ol (5c) 35% yield. mp 120—121 °C (from hexane–AcOEt). $[\alpha]_D^{22}$ −191.1° (*c* = 2.3, EtOH). IR ($CHCl_3$): 3360, 2980, 1490, 1470, 1080, 1030, 1010 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.88 (3H, d, *J* = 6.7, Me), 1.10 (3H, d, *J* = 6.7, Me), 2.12 (1H, m, H-2), 2.38 (3H, s, Me), 3.52 (1H, br, OH), 4.93 (1H, dd, *J* = 7.7, 5.0, H-1), 6.94 (1H, d, *J* = 5.3, thiophene), 7.21 (1H, d, *J* = 5.3, thiophene), 7.27 (2H, d, *J* = 8.3, Tol), 7.51 (2H, d, *J* = 8.3, Tol). *Anal.* Calcd for $C_{15}H_{18}O_2S_2$: C, 61.19; H, 6.16. Found: C, 60.94; H, 6.25.

(1*S*,*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]hexan-1-ol (5d) 32% yield. An oil. $[\alpha]_D^{22}$ −139.9° (*c* = 1.6, EtOH). IR (neat): 3360, 2960, 1480, 1080, 1030, 1010 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.88 (3H, br t, *J* = 6.8, Me), 1.2—1.4 (5H, m), 1.4—1.5 (1H, m), 1.7—2.1 (2H, m), 2.38 (3H, s, Me), 3.82 (1H, br, OH), 5.15 (1H, m, H-1), 7.02 (1H, d, *J* = 5.4, thiophene), 7.21 (1H, d, *J* = 5.4, thiophene), 7.27 (2H, d, *J* = 8.2, Tol), 7.51 (2H, d, *J* = 8.2, Tol). HR-MS *m/z*: Calcd for $C_{17}H_{20}OS_2$ ($M^+ - H_2O$): 304.0955. Found: 304.0966.

(1*R*,*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]benzyl Alcohol (6b) 25% yield. mp 106—108 °C (from hexane–AcOEt). $[\alpha]_D^{22}$ −304.4° (*c* = 1.5, EtOH). IR ($CHCl_3$): 3320, 3020, 1490, 1150, 1080, 1030, 1010, 800 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 2.35 (3H, s, Me), 4.73 (1H, br, OH), 6.47 (1H, d, *J* = 3.4, H-1), 6.79 (1H, d, *J* = 5.4, thiophene), 7.14 (1H, d, *J* = 5.4, thiophene), 7.17—7.36 (7H, m, ArH + Tol), 7.45 (2H, d, *J* = 7.6, Tol). *Anal.* Calcd for $C_{18}H_{16}O_2S_2$: C, 65.82; H, 4.91. Found: C, 65.54; H, 4.98.

(1*R*,*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]-2-methylpropan-1-ol (6c) 34% yield. An oil. $[\alpha]_D^{21}$ +129.0° (*c* = 1.2, EtOH). IR ($CHCl_3$): 3340, 3010, 1490, 1470, 1080, 1030, 1010 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.86 (3H, d, *J* = 6.7, Me), 1.13 (3H, d, *J* = 6.7, Me), 2.07 (1H, m, H-2), 2.39 (3H, s, Me), 3.97 (1H, br, OH), 5.07 (1H, dd, *J* = 7.7, 3.8, H-1), 6.79 (1H, d, *J* = 5.4, thiophene), 7.16 (1H, d, *J* = 5.4, thiophene), 7.28 (2H, d, *J* = 8.3, Tol), 7.49 (2H, d, *J* = 8.3, Tol). HR-MS *m/z*: Calcd for $C_{15}H_{16}OS_2$ ($M^+ - H_2O$): 276.0643. Found: 276.0657.

(1*R*,*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]hexan-1-ol (6d) 38% yield. An oil. $[\alpha]_D^{22}$ −129.4° (*c* = 0.7, EtOH). IR ($CHCl_3$): 3380, 2950, 1470, 1080, 1030, 1010 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.88 (3H, br t, *J* = 5.9, Me), 1.2—1.5 (6H, m), 1.7—2.0 (2H, m), 2.39 (3H, s, Me), 3.98 (1H, br, OH), 5.29—5.35 (1H, m, H-1), 6.78 (1H, d, *J* = 5.4, thiophene), 7.15 (1H, d, *J* = 5.4, thiophene), 7.29 (2H, d, *J* = 8.2, Tol), 7.51 (2H, d, *J* = 8.2, Tol). HR-MS *m/z*: Calcd for $C_{17}H_{20}OS_2$ ($M^+ - H_2O$): 304.0955. Found: 304.0942.

Typical Procedure for PCC Oxidation of Thienyl Carbinols A solution of **5a** and **6a** (2.2 g, 8.3 mmol, 1 : 1 mixture) in dry CH_2Cl_2 (15 ml) was added in one portion to a suspension of PCC (3.6 g, 16.5 mmol) and molecular sieves 4A (powder, 356 mg) in dry CH_2Cl_2 (5 ml) was added at room temperature, and the mixture was stirred vigorously for 4 h. After having been diluted with Et_2O (30 ml), the reaction mixture was filtered with the aid of a short pad of Florisil. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel with hexane–AcOEt (1 : 1) to give **3a** (1.6 g, 73%).

(*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]ethanone (3a) mp 157—158 °C (from hexane–AcOEt). $[\alpha]_D^{18}$ −410.6° (*c* = 1.4, EtOH). IR ($CHCl_3$): 3010, 1680, 1490, 1400, 1240, 1030 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 2.35 (3 H, s, Me), 2.51 (3H, s, Me), 7.23 (2H, d, *J* = 8.2, Tol), 7.63 (1H, d, *J* = 5.1, thiophene), 7.72 (2H, d, *J* = 8.2, Tol), 7.83 (1H, d, *J* = 5.1, thiophene). *Anal.* Calcd for $C_{13}H_{12}O_2S_2$: C, 59.06; H, 4.58. Found: C, 58.87; H, 4.56.

Oxidation of other sulfinyl alcohols, obtained from the condensation of **4**, with PCC was carried out in a manner similar to that described above, affording the ketones **3b—d**.

(*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-benzoyl]thiophene (3b) 53% yield. mp 91—94 °C (from hexane–AcOEt). $[\alpha]_D^{24}$ −390.0° (*c* = 1.4, EtOH). IR ($CHCl_3$): 3010, 1640, 1490, 1400, 1270, 1030, 930 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 2.36 (3H, s, Me), 7.26 (2H, d, *J* = 7.8, Tol), 7.51 (2H, d, *J* = 7.8, Tol), 7.70 (1H, d, *J* = 5.1, thiophene), 7.45—7.95 (6H, m, ArH + thiophene). *Anal.* Calcd for $C_{18}H_{14}O_2S_2$: C, 66.23; H, 4.32. Found: C, 65.96; H, 4.35.

(*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]-2-methylpropan-1-one (3c) 42% yield. An oil. $[\alpha]_D^{28}$ −295.1° (*c* = 1.6, EtOH). IR (neat): 3400, 2980, 1680, 1490, 1400, 1210, 1040 cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 1.14 (3H, d, *J* = 6.8, Me), 1.24 (3H, d, *J* = 6.8, Me), 2.34 (3H, s, Me), 3.14 (1H, septet, *J* = 6.8, H-2), 7.22 (2H, d, *J* = 8.1, Tol), 7.61 (1H, d, *J* = 5.1, thiophene), 7.73 (2H, d, *J* = 8.1, Tol), 7.81 (1H, d, *J* = 5.1, thiophene). HR-MS *m/z*: Calcd for $C_{15}H_{16}O_2S_2$ (M^+): 292.0592. Found: 276.0605.

(*S*$_s$)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]hexan-1-one (3d) 81% yield. An oil. $[\alpha]_D^{24}$ −176.6° (*c* = 1.9, EtOH). IR (neat): 3420, 3090, 2980, 1680,

1490, 1400, 1080, 1040, 1010 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, br t, J=6.8, Me), 1.2—1.4 (4H, m), 1.6—1.8 (2H, m), 2.34 (3H, s, Me), 2.7—2.9 (2H, m), 7.21 (2H, d, J=8.2, Tol), 7.60 (1H, d, J=5.3, thiophene), 7.72 (2H, d, J=8.2, Tol), 7.81 (1H, d, J=5.3, thiophene). HR-MS m/z: Calcd for $C_{17}H_{20}O_2S_2$ (M^+): 320.0904. Found: 320.0884.

Typical Procedure for DIBAL Reduction of 3 in the Presence of a Lewis Acid A mixture of **3a** (50 mg, 0.19 mmol) and $Yb(OTf)_3$ (235 mg, 0.38 mmol) in THF (1 ml) was stirred at −30 °C for 0.5 h. Diisobutylaluminum hydride (0.37 ml, 0.38 mmol, 1.02 mol dm^{-3} in toluene) was then added dropwise to the solution and the mixture was stirred for 2 h. The reaction was quenched with cold 3% HCl (5 ml) and the whole was stirred at room temperature for 0.5 h, then extracted with AcOEt (10 ml × 3). The organic solution was washed with saturated brine (10 ml), dried, and concentrated *in vacuo*. The residue was passed through a short plug of silica gel with AcOEt to give a mixture of **5a** and **6a** (45 mg, 88%), which was identical with that prepared from the above-mentioned reaction. The product ratio (**5a**:**6a**=1:8.3) was estimated by HPLC analysis.

Reduction of the other ketones **3b—d** with DIBAL or L-Selectride in the presence or absence of a Lewis acid was carried out in a similar manner. The results are summarized in Tables 1 and 2.

Typical Procedure for Desulfinylation of Sulfinyl Thienyl Carbinols with BuLi A stirred solution of **6b** (60 mg, 0.18 mmol) in dry THF (3 ml) at −78 °C was treated with BuLi (0.47 ml, 0.73 mmol; 1.57 mol·dm^{-3} in hexane; injected *via* a syringe). The mixture was stirred for 1.5 h, then the reaction was quenched by adding H_2O (5 ml) and the whole was extracted with AcOEt (10 ml × 3). The extracts were washed with saturated brine (10 ml), dried, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with hexane–AcOEt (7:1→1:1) to give (*R*)-**7b** (25 mg, 72%), whose spectral data were in good agreement with those reported previously.[7] The enantiomeric excess and the absolute configuration of (*R*)-**7b** thus obtained were confirmed by use of a chiral column, Chiralcel OJ, with hexane–2-propanol (98:2) (flow rate 1 ml/min; t_R (*R*)-**7b** 93.6 min; t_R (*S*)-**7b** 80.7 min). (*R*)-**7b**: mp 57—58 °C (lit.[7] mp 60.0—60.5 °C). $[\alpha]_D^{20}$ −7.3° (c=0.7, $CHCl_3$) for ≥99% ee [lit.[7] $[\alpha]_D^{25}$ −9.8° (c=0.98, $CHCl_3$) for ≥95% ee].

The reactions of **5c**, **5d** and **6a** conducted under similar conditions (reaction time 4 h for **5c**; 3 h for **5d**; 6 h for **6a**) afforded (*S*)-**7c**, (*S*)-**7d** and (*R*)-**7a**, respectively, in 71—73% yields.

(*R*)-**7a**: $[\alpha]_D^{18}$ +21.5° (c=0.8, $CHCl_3$) for 93% ee. Chiral HPLC (hexane–2-propanol, 100:1, t_R (*R*)-**7a** 58.3 min; t_R (*S*)-**7a** 50.4 min). [lit.[9b] $[\alpha]_D^{25}$ +24.2° (c=5, $CHCl_3$) for 100% ee].

(*S*)-**7c**: $[\alpha]_D^{22}$ −23.8° (c=1.2, $CHCl_3$) for 92% ee. Chiral HPLC (hexane–2-propanol, 200:1, t_R (*R*)-**7c** 26.6 min; t_R (*S*)-**7c** 24.3 min). [lit.[7] *R* enantiomer, $[\alpha]_D^{25}$ +14.2° (c=1.02, $CHCl_3$) for ≥91% ee].

(*S*)-**7d**: $[\alpha]_D^{22}$ −19.7° (c=0.9, $CHCl_3$) for 93% ee. Chiral HPLC (hexane–2-propanol, 200:1, t_R (*R*)-**7d** 28.6 min; t_R (*S*)-**7d** 24.6 min). (±)-**7d** was synthesized by the literature method reported previously.[12]

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References

1) Annunziata R., Cinquini M., Cozzi F., *J. Chem. Soc., Perkin Trans. 1*, **1979**, 1687—1690; Solladié G., Greck C., Demailly G., Solladié-Cavallo A., *Tetrahedron Lett.*, **23**, 5047—5050 (1982); Ogura K., Fujita M., Inaba T., Takahashi K., Iida H., *ibid.*, **24**, 503—506 (1983); Guanti G., Narisano E., Banfi L., Scolastico C., *ibid.*, **24**, 817—818 (1983); Solladié G., Demailly G., Greck C., *ibid.*, **26**, 435—438 (1985); *idem*, *J. Org. Chem.*, **50**, 1552—1554 (1985).
2) Kosugi H., Konta H., Uda H., *J. Chem. Soc., Chem. Commun.*, **1985**, 211—213.
3) Solladié-Cavallo A., Suffert J., Adib A., Solladié G., *Tetrahedron Lett.*, **31**, 6649—6652 (1990).
4) García Ruano J. L., Lorente A., Rodríguez J. H., *Tetrahedron Lett.*, **33**, 5637—5640 (1992); García Ruano J. L., Carmen Maestro M., Sánchez-Sancho F., *Tetrahedron: Asymmetry*, **6**, 2299—2312 (1995).
5) Arai Y., Suzuki A., Masuda T., Masaki Y., Shiro M., *J. Chem. Soc., Perkin Trans. 1*, **1995**, 2913—2917.
6) Arai Y., Masuda T., Masaki Y., Abstracts of Papers, 68th Autumn Annual Meeting of the Chemical Society of Japan, Nagoya, October 1994, p. 71; Girodier L. D., Rouessac F. P., *Tetrahedron: Asymmetry*, **5**, 1203—1206 (1994).
7) Kitano Y., Kusakabe M., Kobayashi Y., Sato F., *J. Org. Chem.*, **54**, 994—996 (1989).
8) Takeshita M., Terada K., Akutsu N., Yoshida S., Sato T., *Heterocycles*, **26**, 3051—3054 (1987); Fantin G., Fogagnolo M., Medici A., Pedrini P., Poli S., *Tetrahedron Lett.*, **34**, 883—884 (1993); Fantin G., Fogagnolo M., Guerzoni M. E., Medici A., Pedrini P., Poli S., *J. Org. Chem.*, **59**, 924—925 (1994); Kang S.-K., Jeon J.-H., Yamaguchi T., Kim J.-S., Ko B.-S., *Tetrahedron: Asymmetry*, **6**, 2139—2142 (1995).
9) *a*) Holland H. L., Bergen E. J., Chenchaiah P. C., Khan S. H., Munoz B., Ninniss R. W., Richards D., *Can. J. Chem.*, **65**, 502—507 (1987); *b*) Fantin G., Fogagnolo M., Medici A., Pedrini P., Poli S., Gardini F., *Tetrahedron: Asymmetry*, **4**, 1607—1612 (1993).
10) Brown H. C., Cho B. T., Park W. S., *J. Org. Chem.*, **53**, 1231—1238 (1988); Brunner H., Kuerzinger A., *J. Organomet. Chem.*, **346**, 413—424 (1988); Hayashi M., Kaneko T., Oguni N., *J. Chem. Soc., Perkin Trans. 1*, **1991**, 25—28; Nishibayashi Y., Singh J. D., Segawa K., Fukuzawa S., Uemura S., *J. Chem. Soc., Chem. Commun.*, **1994**, 1375—1376.
11) Lockard J. P., Schroeck C. W., Johnson C. R., *Synthesis*, **1973**, 485—486; Durst T., LeBelle M. J., Van den Elzen R., Tin K.-C., *Can. J. Chem.*, **52**, 761—766 (1974); Ogura K., Arai K., Tsuchihashi G., *Bull. Chem. Soc. Jpn.*, **55**, 3669—3670 (1982); Satoh T., Kaneko Y., Yamakawa K., *Tetrahedron Lett.*, **27**, 2379—2382 (1986).
12) Van Zyl G., Langenberg R. J., Tan H. H., *J. Am. Chem. Soc.*, **78**, 1955—1958 (1956).