Diastereoselective allylation of chiral sulfinyl-substituted thiophenecarbaldehydes with a Lewis acid

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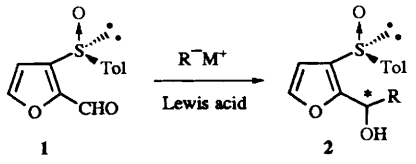
Diastereoselective allylation of the optically active sulfinyl-substituted thiophenecarbaldehydes **3**–**5** with allyltriphenylstannane in the presence of a Lewis acid has been examined. Allylation of compounds **4** and **5** in the presence of titanium(IV) tetrachloride produced the addition products **11** and **13**, respectively, with good diastereoisomeric excesses (de's), whereas in the presence of tin(IV) tetrachloride the corresponding diastereoisomers **12** and **14**, respectively, were obtained. Allylation of compound **5** mediated by ytterbium triflate occurred with excellent diastereoselectivity (96% de) under conventional conditions.

The value of chiral sulfoxides as chiral auxiliary in asymmetric syntheses owes much to the steric and stereoelectronic factors of the three ligands (*i.e.* normally, *p*-tolyl, lone-paired electrons and oxygen) at the sulfur centre.[1] In particular, highly asymmetric, nucleophilic additions and reductions to the carbonyl group in sulfinyl-carbonyl compounds by organometallic reagents have been investigated.[2] The advantages of the use of chiral sulfoxides in these asymmetric reactions are, however, limited by the reactions using α-sulfinylcarbonyl compounds, while the additions using β-sulfinylcarbonyl compounds appear to have been ignored. A principal reason for this is the belief that the conformationally rigid, six-membered cyclic transition state formed by chelation of the α-sulfinylcarbonyl group with the metal atom (a Lewis acid, an alkali metal reagent, and an organometallic species) exerts a high level of stereocontrol (1,3-asymmetric induction from the α-sulfinylcarbonyl).

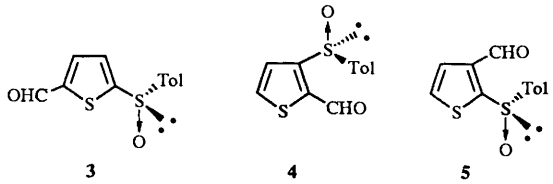
To date, a considerable number of asymmetric allylations of aldehydes with Lewis acids has been reported.[3] While excellent asymmetric inductions have been realized, these reactions have dealt with the use of allylmetal compounds bearing chiral ligands,[4] chiral aldehydes,[5] and chiral Lewis acids or Lewis bases.[6] As part of our own efforts to develop asymmetric reactions using chiral sulfoxides as a chiral auxiliary, we recently reported that a chiral, β-sulfinylcarbonyl compound, *i.e.* 3-sulfinylfurfural **1**, is useful for the asymmetric addition of an allyl metal compound (RM = allyltriphenyltin) mediated by a Lewis acid.[7] It has also appeared that alkylation of the furfural **1** with phenylmagnesium bromide in the presence of zinc bromide yields diastereoselectively the furylmethanol **2** (R = Ph).[8]



1 **2**

Scheme 1

Our interest in asymmetric synthesis using chiral β-sulfinylcarbonyl compounds led us to an extensive investigation of the diastereoselective additions of the other class of aldehydes. In this connection we have now envisaged the reaction of the sulfinyl-substituted thienylaldehydes and allyltriphenyltin. We describe here the synthesis and diastereoselective additions of the aldehydes **3**–**5**.



3 **4** **5**

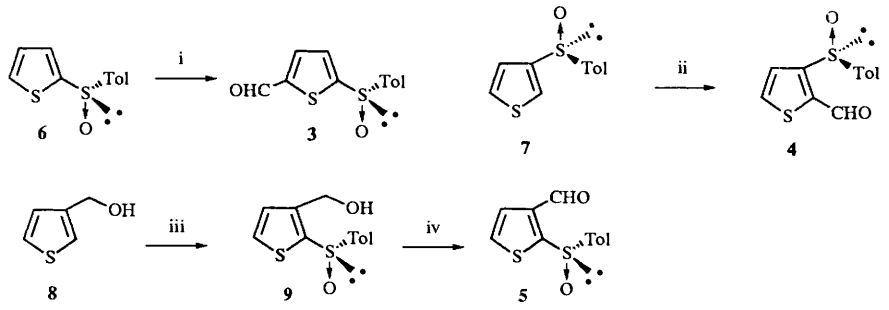
Results and discussion

Synthesis of the sulfinyl-substituted thiophenecarbaldehydes 3–5

The required thiophenecarbaldehydes **3**–**5** were obtained by modifications to the reaction reported previously for the preparation of the furfural derivatives (Scheme 1).[7] The 5-lithiation of 2-(*p*-tolylsulfinyl)thiophene **6**[9] with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) followed by treatment with dimethylformamide (DMF) proceeded smoothly to give 2-*p*-tolylsulfinylthiophene-5-carbaldehyde **3** as crystals {mp 99–101 °C, $[\alpha]_D^{18}$ +319.9 (*c* 1.7, EtOH)} in 44% yield. (The use of an organometallic base such as butyllithium gave unsatisfactory yields, resulting from nucleophilic attack at the sulfinyl centre by the base.) In a similar manner, 3-(*p*-tolylsulfinyl)thiophene-2-carbaldehyde **4** {mp 82–83.5 °C, $[\alpha]_D^{24}$ −224.2 (*c* 1.6, EtOH)} was obtained as a crystalline product by treatment of 3-(*p*-tolylsulfinyl)-thiophene **7**[9] with DMF and LDA in 82% yield, exclusively. The regioselective introduction of the formyl group in **4** was confirmed by its ^{1}H NMR spectrum which showed two protons of the thiophene moiety with a characteristic coupling constant (*J* 5.1 Hz). 2-*p*-Tolylsulfinylthiophene-3-carbaldehyde **5** {mp 89–90 °C, $[\alpha]_D^{21}$ −56 (*c* 1.7, EtOH)} was synthesized in 82% yield by treatment of 3-thienylmethanol **8** with (−)-(*S*)-menthyl toluene-*p*-sulfinate and BuLi (2 equiv.)/$MgBr_2$[9] followed by oxidation of the resulting alcohol **9** with pyridinium chlorochromate (PCC) (Scheme 2).

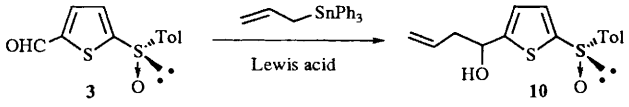
Allylation of compounds 3–5 with allyltriphenyltin in the presence of a Lewis acid

Having the sulfinyl-substituted aldehydes to hand, we evaluated the degree of diastereoselectivity by allylation of **3** in the presence of a Lewis acid (Table 1). The treatment of **3** with allyltriphenyltin[10] in the presence of $TiCl_4$ and $SnCl_4$ afforded almost equal amounts of the two diastereoisomers of the homoallylic alcohol **10** the ratio of which was determined by HPLC analysis.



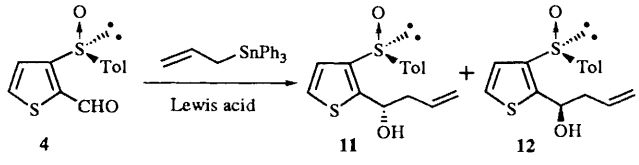
Scheme 2 *Reagents and conditions:* i, LDA, THF, room temp. (30 min), then DMF, 0 °C (10 min) (44%); ii, LDA, 0 °C → room temp. (30 min), then DMF, 0 °C (10 min) (82%); iii, BuLi (2 equiv.), −20 °C (1.5 h); $MgBr_2$, Et_2O, −20 °C (2 h); (−)-menthyl toluene-*p*-sulfinate, THF, −20 °C (1 h) ⟶ room temp. (98%); iv, PCC, molecular sieves 4 Å (powder), CH_2Cl_2, room temp. (3 h) (84%)

Table 1 Allylation of the thiophenecarbaldehyde **3** with allyltriphenyltin in the presence of a Lewis acid



Entry	Lewis acid (equiv.)	Allyltriphenyltin (equiv.)	Reaction conditions: Time (t h)	Reaction conditions: Temp. (T °C)	Diastereoisomeric ratio of **10**	De (%)	Isolated yield (%)
1	$SnCl_4$ (2.0)	2.0	2	−80	1.3:1	13	70
2	$TiCl_4$ (2.0)	2.0	3	−80	1:1.2	9	68

Table 2 Allylation of the thiophenecarbaldehyde **4** with allyltriphenyltin in the presence of a Lewis acid



Entry	Lewis acid (2 equiv.)	Allyltriphenyltin (equiv.)	Reaction conditions: Time (t h)	Reaction conditions: Temp. (T °C)	Diastereoisomeric ratio of **11**:**12**	De (%)	Isolated yield (%)
1	$SnCl_4$	2.0	3	−80	1:5.7	70	83
2	$SnCl_4$	3.0	3	−80	1:5.2	68	87
3	$TiCl_4$	2.0	3	−80	9:1	80	69
4	$TiCl_4$	2.0	3	−20	4.6:1	64	60
5	$TiCl_4$	2.0	1.5	0	2.9:1	49	12

As described for the furan analogue previously reported,[7] the reaction site (aldehyde carbonyl) of **3** is sufficiently distant from the sulfinyl group for the latter not to effect the asymmetric induction.

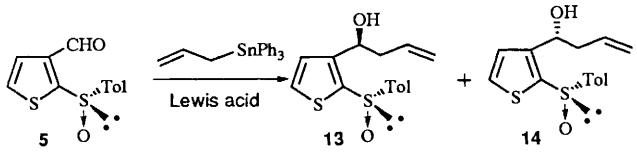
Attempts to develop highly diastereoselective allylation for **3** by the use of other Lewis acids were unsuccessful, resulting only in mass recovery of starting material. We thus undertook the reaction of compound **4** with the allylmetal in the presence of a Lewis acid. The results are indicated in Table 2.

Treatment of **4** with allyltriphenyltin (2 equiv.) in the presence of $SnCl_4$ (2 equiv.) afforded the homoallylic alcohol **12** as the major product (up to 70% de). The use of less Lewis acid and allyltriphenyltin failed to improve the yields. On the other hand treatment of **4** with $TiCl_4$ as a reaction promotor under the same conditions produced the other diastereoisomeric alcohol **11** as the major product (up to 80% de). The stereochemistry of **11** and **12** was tentatively assigned by analogy with the result of the corresponding furan analogues **1**.[7] The diastereoisomeric ratio was determined by HPLC analysis.

Although the previous result for the allylation of **1** had demonstrated that the Lewis acid-mediated reaction with allyltriphenyltin proceeded in a highly diastereoselective manner (up to 90% de), the thiophene analogue **4** showed only moderate selectivity.

We finally undertook to investigate the allylation of 2-sulfinylthiophene-3-carbaldehyde **5**; the results are summarised in Table 3. In a manner similar to that described above for the thiophenecarbaldehyde **4**, treatment of **5** with allyltriphenyltin in the presence of $SnCl_4$ gave predominantly the diastereoisomer **14** along with a small amount of the other diastereoisomer **13**. Under the same conditions but with $TiCl_4$, **13** was obtained with a high degree of diastereoselectivity (90% de). The structure of **13** was finally determined by an X-ray crystal-

Table 3 Allylation of the thiophenecarbaldehyde **5** with allyltriphenyltin in the presence of a Lewis acid



Entry	Lewis acid, equiv. amount	Allyltriphenyltin (equiv.)	Reaction conditions: Solvent	Time (t/h)	Temp. (T/°C)	Diastereoisomeric ratio of **13**:**14**	De (%)	Isolated yield (%)
1	$SnCl_4$, 2.0	1.5	CH_2Cl_2	2	−85	1:7.5	77	91
2	$SnCl_4$, 2.0	2.0	CH_2Cl_2	2	−80	1:7.5	77	97
3	$TiCl_4$, 2.0	1.5	CH_2Cl_2	3	−85	18.9:1	90	74
4	$TiCl_4$, 2.0	2.0	CH_2Cl_2	3	−85	20.5:1	91	87
5	$TiCl_4$, 2.0	2.0	CH_2Cl_2	2	−20	9.0:1	80	100
6	$Sm(OTf)_3$,[a] 2.0	2.0	THF	4	25	6.4:1	73	77
7	$Yb(OTf)_3$, 3.0	2.0	THF	5	25	50:1	96	84
8	$Yb(OTf)_3$, 2.0	2.0	THF	20	0	19:1	90	43
9	$Nd(OTf)_3$, 3.0	2.0	THF	3	25	3.4:1	54	77

[a] Tf = SO_2CF_3.

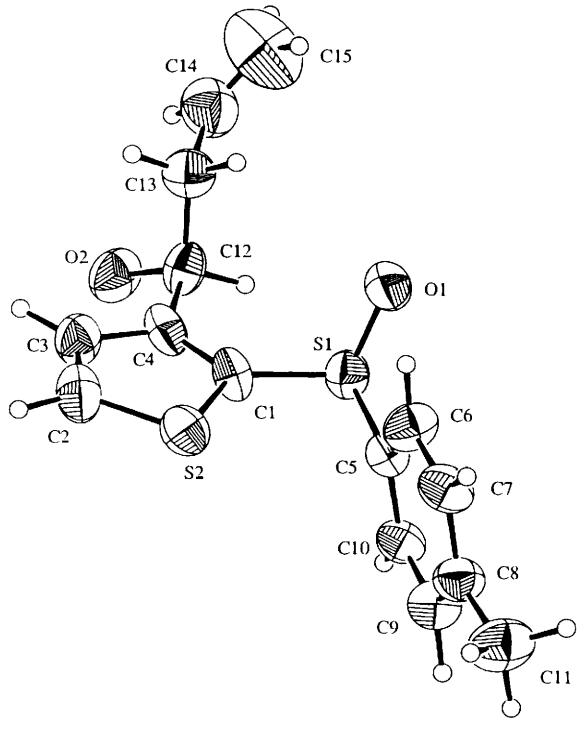


Fig. 1 Molecular structure of compound **13**

structure analysis (Fig. 1),† with the structure of **14** then being deduced from this result.

In order to develop more conventional conditions for the reaction of **5**, the use of lanthanoids as a chelating agent[11] was envisaged (entries 6–9). Surprisingly, of the lanthanoids that have been screened, the reaction using $Yb(OTf)_3$[12] in THF proceeded smoothly at ambient temperature to give the product **13** with excellent diastereoselectivity (96% de). Other lanthanoids {$Sm(OTf)_3$ and $Nd(OTf)_3$} gave lower diastereoselectivity.

† Since the absolute configuration of the *p*-tolylsulfinyl moiety in **13** is known to be of *S* configuration, the other asymmetric centre in **13** is automatically established by X-ray analysis. The absolute configuration determined as described above might be achieved by the inclusion of an enantiomorph-defining parameter (Flack parameter),[13] which subsequently refined to 0.14(2) supporting the correct configuration, although the parameter is not significantly equal to zero.

Since the substrates **3**–**5** have two coordinating groups (*i.e.* aldehyde carbonyl and sulfinyl oxygen) with a Lewis acid, it seems that the allylations should proceed in a chelation-controlled manner. Furthermore, in a Lewis acid-mediated allylation, the choice of the Lewis acid is crucial for the diastereoselectivity. The complexation with a bidentate ligand such as titanium(IV) tetrachloride and tin(IV) tetrachloride might be different from that with a monodentate ligand such as boron trifluoride. The effect of the diastereoselectivities on these additions has been observed by Keck *et al.*[13] However, it is worth noting that in our system the use of tin(IV) tetrachloride gave the reverse diastereoselectivity to that observed on allylation mediated by titanium(IV) tetrachloride. The mechanistic origin of the observed effect remains obscure and is now under investigation.

Experimental

Melting points were taken with a Yanagimoto micro melting-point apparatus and are uncorrected. Boiling points are also uncorrected. IR spectra were measured as films or in $CHCl_3$ solution on a JASCO IRA-1 spectrophotometer. ^1H NMR spectra were recorded on a JEOL JNM-GX270 (270 NHz) spectrometer with $CDCl_3$ as solvent; J values in Hz. Tetramethylsilane was used as internal standard. Mass spectra were recorded with a JEOL JMS D-300 spectrometer. Optical rotations were measured on a JASCO DIP-360 digital polarimeter in $CHCl_3$ solution and are recorded in units of 10^{-1} deg cm^2 g^{-1}. 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 anhyd. $MgSO_4$ before evaporation of solvents on a rotary evaporator. Flash column chromatography was performed with Merck 230–400 mesh silica gel. Analytical high-performance liquid chromatography (HPLC) were performed on a Develosil column (4.6 mm × 250 mm). Chiral HPLC analyses were carried out on a Shimadzu LC-6A pump using a chiral column, Chiralcel OJ (Daicel Chemical Industries Ltd) and monitoring 254 nm. Peak ratios on HPLC were measured with a Shimadzu integrator (Chromatopac C-R3A). The symbol S_S in this text expresses the absolute configuration of the sulfinyl centre as *S*.

(S_S)-5-(*p*-Tolylsulfinyl)thiophene-2-carbaldehyde 3

To a stirred solution of LDA, prepared from butyllithium (1.64 mol dm^{-3} in hexane; 1.96 mmol, 1.2 cm^3) and diisopropylamine

(0.17 cm^3, 1.96 mmol) in dry THF (1 cm^3) at 0 °C was added (S_S)-2-(*p*-tolylsulfinyl)thiophene[9] (396 mg, 1.78 mmol, $[\alpha]_D^{21}$ + 110.7 (*c* 2.5, acetone), >99% ee) in dry THF (2 cm^3), and the mixture was stirred for 10 min. DMF (0.41 cm^3, 5.34 mmol) was added to the mixture *via* a syringe which was then stirred at 0 °C for 10 min, before being quenched with dilute hydrochloric acid (5 cm^3 of 1 mol dm^{-3}). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 5 cm^3). The combined layer and extracts were washed with satd. brine (5 cm^3), dried and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica with hexane–ethyl acetate (5:1→1:1) to give *compound* **3** as a yellow solid (195 mg, 44%) after recrystallisation from hexane–ethyl acetate, mp. 99–101 °C (Found: C, 57.5; H, 4.1. $C_{12}H_{10}S_2O_2$ requires C, 57.6; H, 4.0%); $[\alpha]_D^{18}$ +319.9 (*c* 1.7, EtOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3020, 2830, 1670, 1420 and 1050; δ_H 2.42 (3 H, s, Me), 7.34 (2 H, d, *J* 7.9, ArH), 7.55 (1 H, d, *J* 3.9, thiophene), 7.63 (2 H, d, *J* 7.9, ArH), 7.70 (1 H, d, *J* 3.9, thiophene) and 9.89 (1 H, s, CHO).

(S_S)-3-(*p*-Tolylsulfinyl)thiophene-2-carbaldehyde 4

To a stirred solution of LDA, prepared from butyllithium (1.64 mol dm^{-3} in hexane; 1.81 mmol, 1.1 cm^3) and diisopropylamine (0.15 cm^3, 1.73 mmol) in dry THF (1 cm^3) at 0 °C was added (S_S)-3-(*p*-tolylsulfinyl)thiophene[9] (0.35 g, 1.57 mmol, $[\alpha]_D^{23}$ +21.8 (*c* 1.5, EtOH), >99% ee) in dry THF (1 cm^3). After being stirred for 5 min, the mixture was treated dropwise with DMF (0.37 cm^3, 4.72 mmol) and stirred for 10 min. It was then quenched with 3% hydrochloric acid (5 cm^3) and extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with satd. brine (5 cm^3), dried and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica with hexane–ethyl acetate (5:1→3:1) to give *compound* **4** (324 mg, 82%) as a solid, mp 82–83.5 °C (Found: C, 57.3; H, 4.0. $C_{12}H_{10}S_2O_2$ requires C, 57.6; H, 4.0%); $[\alpha]_D^{18}$ −224.2 (*c* 1.6, EtOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3020, 2850, 1670, 1490, 1410 and 1040; δ_H 2.39 (3 H, s, Me), 7.30 (2 H, d, *J* 8.1, ArH), 7.45 (1 H, d, *J* 5.1, thiophene), 7.62 (2 H, d, *J* 8.1, ArH), 7.74 (1 H, dd, *J* 5.1, 0.7, thiophene) and 10.29 (1 H, d, *J* 0.7, CHO).

(S_S)-2-(*p*-Tolylsulfinyl)-3-thienylmethanol 9

Butyllithium (1.71 mol dm^{-3} in hexane; 0.064 mmol, 37.2 cm^3) was added to a stirred solution of 3-thienylmethanol (3.59 g, 0.31 mmol) in dry THF (20 cm^3) at −20 °C. After being stirred for 1.5 h, the mixture was treated with magnesium bromide–diethyl ether (11.7 g, 0.045 mmol) in dry diethyl ether (30 cm^3). The mixture was stirred at −20 °C for 2 h and then treated with (−)-(*S*)-menthyltoluene-*p*-sulfinate (2.50 g, 8.5 mmol) in dry THF (15 cm^3). After the mixture had been stirred for 1 h it was allowed to warm to room temperature overnight and then poured onto cold 3% hydrochloric acid (10 cm^3). The organic layer was separated and the aqeuous layer was extracted with diethyl ether (3 × 10 cm^3). The combined extracts were washed with satd. brine (10 cm^3), dried and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica with hexane–ethyl acetate (3:1→0:1) to give *compound* **9** (2.10 g, 98%) as a solid, mp 107.5–109 °C (Found: C, 56.9; H, 4.9. $C_{12}H_{12}S_2O_2$ requires C, 57.1; H, 4.8%); $[\alpha]_D^{20}$ +4.5 (*c* 1.8, EtOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3400, 3030 and 1035; δ_H 2.39 (3 H, s, Me), 4.1 (1 H, br s, OH), 4.78 (2 H, ABq, *J* 14.2, $\Delta\nu$ = 14.4, CH_2), 7.07 (1 H, d, *J* 5, thiophene), 7.28 (2 H, d, *J* 8.1, ArH), 7.45 (1 H, d, *J* 5, thiophene) and 7.58 (2 H, d, *J* 8.1, ArH).

The enantiomeric excess of (±)-**9** was estimated as >99% as judged by the Mosher's ester derivative[14] of compound **9**. Compound (±)-**9** was prepared from the treatment of 3-thienylmethanol with butyllithium and ditolyl disulfide followed by oxidation with *m*-chloroperoxybenzoic acid. Compound (±)-**9** (50 mg, 0.2 mmol) in chloroform (1.5 cm^3) was then added to a solution of (*S*)-methoxy-(trifluoromethyl)phenylacetyl chloride (MTPACl) in chloroform (1.5 cm^3), prepared from MTPA (0.07 cm^3) and oxalyl chloride (0.1 cm^3) in DMF (0.03 cm^3). After being stirred for 1 h, the mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica with hexane–ethyl acetate (5:1→1:1) to give the MTPA ester (90 mg, 97%). The Mosher's ester of (±)-**9** was resolved to a pair of doublets (*J* 5.1 Hz) which gave signals at δ 6.99 and 7.05 in its ^1H NMR spectrum, whereas the Mosher's ester of (+)-**9** resonated at δ 7.05.

(S_S)-2-(*p*-Tolylsulfinyl)thiophene-3-carbaldehyde 5

To a vigorously stirred mixture of pyridinium chlorochromate (1.71 g, 7.93 mmol) and molecular sieves 4 Å[15] (powder, 0.17 g) in dry dichloromethane (15 cm^3) was added in one portion the alcohol **9** (1.0 g, 3.96 mmol) in dry dichloromethane (5 cm^3). The mixture was stirred at room temperature for 3 h, after which it was diluted with diethyl ether (30 cm^3) and passed through a short plug of Florisil. The solid filter was washed with diethyl ether (2 × 50 cm^3) and the combined filtrate and washings were concentrated under reduced pressure. The residue was filtered through a short pad of silica with hexane-ethyl acetate (3:1) as eluent to give *compound* **5** (831.5 mg, 84%) as a solid, mp 89–90 °C (Found: C, 57.6; H, 4.1. $C_{12}H_{10}S_2O_2$ requires C, 57.6; H, 4.0%); $[\alpha]_D^{21}$ −55.9 (*c* 1.7, EtOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3050, 2850, 1670, 1500, 1390 and 1040; δ_H 2.38 (3 H, s, Me), 7.29 (2 H, d, *J* 8.1, ArH), 7.49 (1 H, d, *J* 5.4, thiophene), 7.59 (1 H, d, *J* 5.4, thiophene), 7.73 (2 H, d, *J* 8.1, ArH) and 10.08 (1 H, s, CHO).

Typical procedure for the diastereoselective addition of allyltriphenyltin to the thiophenecarbaldehyde 4 (Table 2, entry 3)

To a stirred solution of compound **4** (50 mg, 0.2 mmol) in dry dichloromethane (50 cm^3) at −80 °C was added dropwise titanium tetrachloride (0.5 mol dm^{-3} in dichloromethane; 0.4 mmol, 0.8 cm^3) *via* a syringe. After being stirred for 10 min, the mixture was treated with allyltriphenyltin (156 mg, 0.4 mmol) in dry dichloromethane (2 cm^3) and stirred at −80 °C for 3 h. The reaction mixture was then quenched with satd. sodium hydrogen carbonate (5 cm^3) and stirred for 1 h at room temperature. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 × 5 cm^3). The combined layer and extracts were dried and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica with hexane–ethyl acetate (1:2) to give compounds **11** and **12** (40 mg, 69%) as a diastereoisomeric mixture in a ratio of 9:1. The major diastereoisomer **11** was separated from **12** by preparative TLC {hexane–ethyl acetate (1:2)}.

In a similar manner, the addition of **4** (50 mg, 0.2 mmol) and allyltriphenyltin (234 mg, 0.6 mmol) in the presence of tin tetrachloride (0.5 mol dm^{-3}; in dichloromethane 0.4 mmol, 0.8 cm^3) under the same conditions yielded a mixture of **11** and **12** (52 mg, 87%) in a ratio of 1:5.2. The major diastereoisomer **12** was also separated from **11** by preparative TLC [hexane–ethyl acetate (1:1)]. (1*R*,*S*,S_S)-1-[5-(*p*-Tolylsulfinyl)-2-thienyl]but-3-en-1-ol **10**. This compound was an oil, $[\alpha]_D^{16}$ +83.0 (*c* 1.8, $CHCl_3$) (a diastereoisomeric mixture of 2:3) (Found: M^+, 292.0614. $C_{15}H_{14}OS_2$ requires *M*, 292.0592); ν_{max}(neat)/cm^{-1} 3360, 3020, 1490, 1035, 995 and 920; δ_H 2.40 (3 H, s, Me), 2.5 (2 H, m, CH_2), 3.25, 3.44 (total 1 H, each br s, diastereoisomeric OH), 4.9 (1 H, m, C*H*OH), 5.1–5.2 (2 H, m, 2 × CH=), 5.8 (1 H, m, CH=), 5.84 (1 H, m, CH=), 6.86 (1 H, m, thiophene), 7.29 (2 H, d, *J* 8.1, ArH), 7.38, 7.39

(total 1 H, each d, *J* 4.1, 3.7, thiophene) and 7.54 (2 H, d, *J* 8.1, ArH).

(1*S*,S_S)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]but-3-en-1-ol **11**. This compound was an oil, $[\alpha]_D^{22}$ −52.2 (*c* 0.66, $CHCl_3$) (Found: $M^+ - H_2O$, 274.0468. $C_{15}H_{14}OS_2$ requires $M - H_2O$, 274.0486); ν_{max}(neat)/cm^{-1} 3340, 3070, 1430, 1020, 990 and 915; δ_H 2.39 (3 H, s, Me), 2.66 (2 H, m, CH_2), 3.79 (1 H, br, OH), 5.1–5.2 (2 H, m, CH= and C*H*OH), 5.25 (1 H, m, CH=), 5.84 (1 H, m, CH=), 6.99 (1 H, d, *J* 5.3, thiophene), 7.22 (1 H, d, *J* 5.2, thiophene), 7.27 (2 H, d, *J* 8.5, ArH) and 7.52 (2 H, d, *J* 8.5, ArH).

(1*R*,S_S)-1-[3-(*p*-Tolylsulfinyl)-2-thienyl]but-3-en-1-ol **12**. This compound was an oil, $[\alpha]_D^{22}$ −35.5 (*c* 0.76, $CHCl_3$) (Found: $M^+ - H_2O$, 274.0477. $C_{15}H_{14}OS_2$ requires $M - H_2O$, 274.0486); ν_{max}(neat)/cm^{-1} 3340, 3075, 1430, 1020, 990 and 915; δ_H 2.40 (3 H, s, Me), 2.5–2.8 (2 H, m, CH_2), 3.7 (1 H, br s, OH), 5.1–5.2 (2 H, m, CH= and C*H*OH), 5.4 (1 H, m, CH=), 5.8 (1 H, m, CH=), 6.84 (1 H, d, *J* 5.3, thiophene), 7.20 (1 H, d, *J* 5.3, thiophene), 7.30 (2 H, d, *J* 8.1 ArH) and 7.52 (2 H, d, *J* 8.1, ArH).

Typical procedure for the diastereoselective addition of allyltriphenyltin to the thiophenecarbaldehyde 5 (Table 3, entry 7)

To a stirred solution of compound **5** (50 mg, 0.2 mmol) in dry THF (2 cm^3) was added ytterbium triflate[12] (372 mg, 0.6 mmol) in dry THF (1 cm^3). After being stirred for 10 min, the mixture was treated with allyltriphenyltin (156 mg, 0.4 mmol) in dry THF (2 cm^3) and stirred at room temperature for 3 h. It was then quenched with dil. hydrochloric acid (1 mol dm^{-3}; 5 cm^3) and heated at 40 °C for 5 h in a water-bath to decompose the lanthanoid complex. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 × 10 cm^3). The combined layer and extracts were dried and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica with hexane–ethyl acetate (1:1) to give compounds **13** and **14** (49 mg, 84%) as a diastereoisomeric mixture in a ratio of 50:1. The major diastereoisomer **13** was separated from **14** by simple recrystallisation of the original mixture from hexane–ethyl acetate.

In a manner similar to the reaction of **4** in the presence of a Lewis acid, the addition of **5** (50 mg, 0.2 mmol) and allyltriphenyltin (234 mg, 0.6 mmol) in the presence of titanium tetrachloride (0.5 mol dm^{-3} in dichloromethane; 0.4 mmol, 0.8 cm^3) yielded a mixture of **13** and **14** (57 mg, 97%) in a ratio of 1:7.5. The major diastereoisomer **14** was isolated pure by preparative TLC [hexane–ethyl acetate (1:2)].

(1*S*,S_S)-1-[2-(*p*-Tolylsulfinyl)-3-thienyl]but-3-en-1-ol **13**. Mp 90–92 °C (from hexane–ethyl acetate) (Found: C, 61.6; H, 5.5. $C_{15}H_{16}O_2S_2$ requires C, 61.6; H, 5.5%); $[\alpha]_D^{20}$ −38.1 (*c* 1.5, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3360, 3010, 1490, 1035 and 920; δ_H 2.41 (3 H, s, Me), 2.4–2.7 (2 H, m, CH_2), 2.86 (1 H, br s, OH), 5.1–5.2 (3 H, m, C*H*OH and 2CH=), 5.8–5.9 (1 H, m, CH=), 7.10 (1 H, d, *J* 5.2, thiophene), 7.31 (2 H, d, *J* 8.2, ArH), 7.49 (1 H, d, *J* 5.2, thiophene) and 7.61 (2 H, d, *J* 8.2, ArH).

(1*R*,S_S)-1-[2-(*p*-Tolylsulfinyl)-3-thienyl]but-3-en-1-ol **14**. This compound was an oil (Found: $M^+ - H_2O$, 274.0497. $C_{15}H_{14}OS_2$ requires $M - H_2O$, 274.0487); $[\alpha]_D^{20}$ +20.5 (*c* 1.0, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3360, 3080, 1490, 1030 and 915; δ_H 2.41 (3 H, s, Me), 2.5–2.7 (2 H, m, CH_2), 3.50 (1 H, br s, OH), 5.1–5.2 (3 H, m, C*H*OH and 2CH=), 5.8–5.9 (1 H, m, CH=), 7.11 (1 H, d, *J* 5.2, thiophene), 7.30 (2 H, d, *J* 8.2, ArH), 7.48 (1 H, d, *J* 5.2, thiophene) and 7.60 (2 H, d, *J* 8.2, ArH).

X-Ray structure determination of compound 13

Crystal data. $C_{15}H_{16}O_2S_2$, M = 292.41, orthohombic, space group $P2_12_12_1$, a = 10.911(4), b = 23.642(4), c = 5.963(3) Å, V = 1538.2(9) Å^3, Z = 4, D_c = 1.263 g cm^{-3}, μ(CuKα) = 30.96 cm^{-1}. Data were measured on a Rigaku AFC 7R radiation diffractometer with graphite-monochromated CuKα (λ = 1.541 78 Å) radiation using ω-2θ scans for 1383 reflections with 750 reflections having ($I > 3.00\ \sigma(I)$]. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.‡

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‡ For details of the Supplementary Publications Scheme, see *Instructions for Authors (1995)*, *J. Chem. Soc., Perkin Trans. 1*, 1995 Issue 1.

References

1 G. H. Posner, in *The Chemistry of Sulphones and Sulphoxides*, ed. S. Patai, Z. Rappoport and C. J. M. Stirling, Wiley, Chichester, 1988, p. 823.
2 For reviews, see: G. Solladié, *Synthesis*, 1981, 185; G. H. Posner, *Acc. Chem. Res.*, 1987, **20**, 72.
3 For a recent review, see: Y. Nishigaichi, A. Takuwa, Y. Naruta and K. Maruyama, *Tetrahedron*, 1993, **49**, 7395.
4 H. C. Brown and P. K. Jadhav, *J. Am. Chem. Soc.*, 1983, **105**, 2092; E. J. Corey, C.-M. Yu and S. S. Kim, *J. Am. Chem. Soc.*, 1989, **111**, 5495; M. Riediker and R. O. Duthaler, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 494; W. R. Roush, L. K. Hoong, M. A. J. Palmer and J. C. Park, *J. Org. Chem.*, 1990, **55**, 4109; A. Hafner, R. O. Duthaler, R. Marti, G. Rihs, P. Rothe-Streit and F. Schwarzenbach, *J. Am. Chem. Soc.*, 1992, **114**, 2321; J. D. Buynak, B. Geng, S. Uang and J. B. Strickland, *Tetrahedron Lett.*, 1994, **35**, 985.
5 M. T. Reetz, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 556; G. Guanti, L. Banfi and E. Narisano, *Tetrahedron Lett.*, 1991, **32**, 6939.
6 For a review, see: K. Narasaka, *Synthesis*, 1991, 1; A. L. Costa, M. G. Piazza, E. Tagliavini, C. Trombini and A. Umani-Ronchi, *J. Am. Chem. Soc.*, 1993, **115**, 7001; S. E. Denmark, D. M. Coe, N. E. Pratt and B. D. Griedel, *J. Org. Chem.*, 1994, **59**, 6161.
7 Y. Arai, T. Masuda, Y. Masaki and T. Koizumi, *Heterocycles*, 1994, **38**, 1751.
8 L. D. Girodier and F. P. Rouessac, *Tetrahedron Asymmetry*, 1994, **5**, 1203.
9 L. Girodier, C. Maignan and F. P. Rouessac, *Tetrahedron Asymmetry*, 1992, **3**, 857.
10 H. Gilman and J. Eisch, *J. Org. Chem.*, 1955, **20**, 763.
11 S. Kobayashi, *Chem. Lett.*, 1991, 2187; S. Kobayashi and I. Hachiya, *J. Org. Chem.*, 1994, **59**, 3590.
12 J. H. Forsberg, V. T. Spaziano, T. M. Balasubramanian, G. K. Liû, S. A. Kinsley, C. A. Duckworth, J. J. Poteruca, P. S. Brown and J. L. Miller, *J. Org. Chem.*, 1987, **52**, 1017.
13 G. E. Keck, in *Selectivities in Lewis Acid Promoted Reactions*, ed. D. Schinzer, Kluwer Academic Publishers, Dordrecht, 1989, p. 73.
14 D. E. Ward and C. K. Rhee, *Tetrahedron Lett.*, 1991, **32**, 7165.
15 J. Herscovici, M.-J. Egron and K. Antonakis, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1967.

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