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ASYMMETRIC 1,4-ADDITIONS TO 5-ALKOXY-2(5H)-FURANONES. AN EFFICIENT SYNTHESIS OF (R)- AND (S)- 3,4-EPOXY-1-BUTANOL

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Abstract The synthesis of enantiomerically pure 5-menthyloxy-2(5H)-furanones is described as well as the diastereoselective 1,4-addition of thiols to these butenolides to yield new homochiral C4-synthons. Kinetic resolution of 5-methoxy-2(5H)-furanone, with an enantiomeric excess of 13%, was achieved by cinchonidine catalyzed thiophenol addition.
The synthetic utility of the asymmetric thiol additions is illustrated in an efficient route to enantiomerically pure (R)- and (S)-3,4-epoxy-1-butanol.

Optically active 2,3-epoxyalcohols have served as starting materials in the synthesis of numerous complex chiral compounds[1] ever since the discovery, by Katsuki and Sharpless[2], of an efficient method for their preparation by asymmetric epoxidation. Similarly 3,4-epoxyalcohols might be applied as key chiral building blocks in synthesis. These developments have been hampered sofar by limited availability of enantiomerically pure 3,4-epoxyalcohols.

In contrast to the asymmetric epoxidation of allylic alcohols, the titaniumtetraisopropoxide ($Ti(OiPr)_4$), diethyltartrate, t-butylhydroperoxide mediated epoxidation of homoallylic alcohols gives rise to low to medium range enantiomeric excesses (e.e.'s 23-55%)[3] whereas chemical yields are rather low. Similar results were reported for the formation of 3,4-epoxy-1-butanol using $Zr(OiPr)_4$ instead of $Ti(OiPr)_4$ (e.e. 40%)[4]. For substituted homoallylic alcohols e.e.'s up to 77% have been reached[3,4].

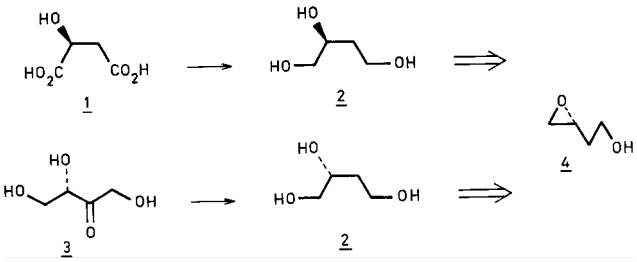
Currently the most frequently applied route to optically active 3,4-epoxyalcohols relies on natural products as chiral starting materials. A convenient, though multistep conversion of S-malic acid (1) into both (R)- and (S)- 3,4-epoxy-1-butanol (4) has been described by several groups[5,6,7] (scheme 1). An efficient enantioselective synthesis of (R)- and (S)-malic acid was developed by Wynberg and Staring[8] based on the cinchonidine catalyzed addition of ketene to chloral.

Vandewalle and coworkers[9] reported a route to 2 and related C4-chiral synthons from (S)-Erythrulose (3) containing the unnatural sugar configuration (scheme 1).

Furthermore asymmetric syntheses of 4 are based on:

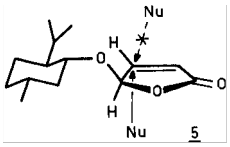
i. kinetic resolution using a lipase catalyzed hydrolysis of esters of epoxyalcohols (e.e. 73% for recovered ester)[10].
ii. asymmetric thiophenol addition to maleic esters mediated by cinchonidine followed by conversion into 4 (e.e. 81%)[7].

SCHEME 1



Extensive synthetic use of simple chiral building blocks such as 4 depends however largely on the availability of both enantiomers in an optically pure form.

The limited success in asymmetric syntheses of 3,4-epoxyalcohols sofar urged us to develop a preparatively useful method for (R)- and (S)-4.
Our methodology is based on 5-alkoxy-2(5H)-furanones (5), a new class of chiral synthons recently described.[11,12,13]
It can be predicted that due to steric shielding of the si-face of 5 addition reactions to the α,β-unsaturated moiety in 5 will preferentially proceed stereoselective to the re-face.

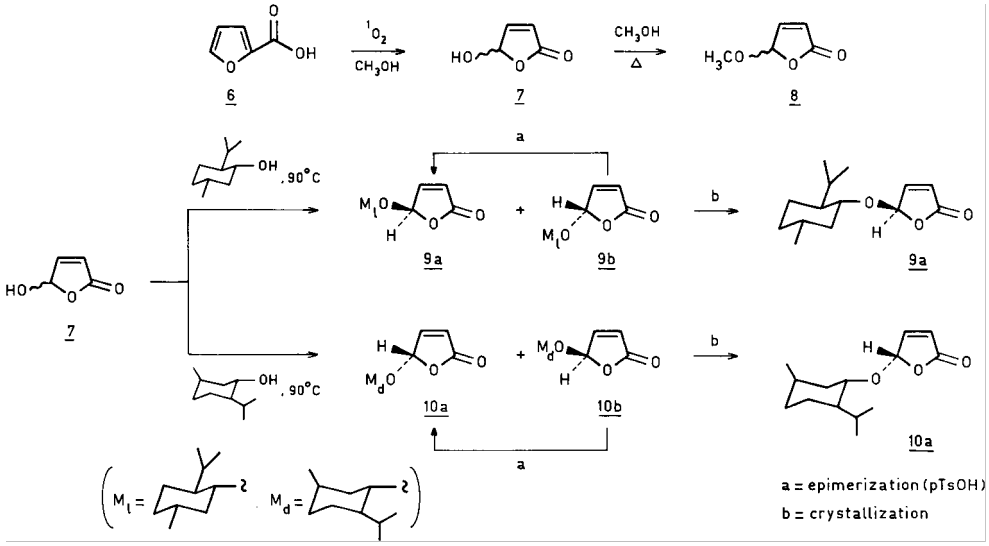


This expectation has been realized in the Diels Alder reactions of a variety of dienes with 5 with diastereoselectivities > 96%.[12]
Furthermore we found that 1,4-additions of amines to 5 provide β-aminolactones with exclusively a trans relationship between amine- and menthyloxy-functionalities. These adducts could be converted to enantiomerically pure aminodiols.[13]
Based on these results we reasoned that new C4-chiral synthons would be accessible by diastereoselective 1,4-additions to 5 using appropriate nucleophiles. We describe herein the asymmetric thiol addition to butenolides such as 5 and the asymmetric synthesis of optically pure (R)- and (S)-3,4-epoxy-1-butanol.

Asymmetric thiol additions.

Racemic 5-methoxy-2(5H)-butenolide 8 was prepared by acetalization of 5-hydroxy-2(5H)-butenolide 7 which was readily obtained by singlet oxygen photooxidation of furfural[14] (scheme 2).
Acetalization of 7 with menthol yielded 5-menthyloxy-2(5H)-butenolides 9 and 10 as mixtures of diastereoisomers (60:40 ratio). Crystallization (twice) from petroleum-ether or n-hexane provided enantiomerically pure 9a and 10a starting with l- or d-menthol respectively (scheme 2).

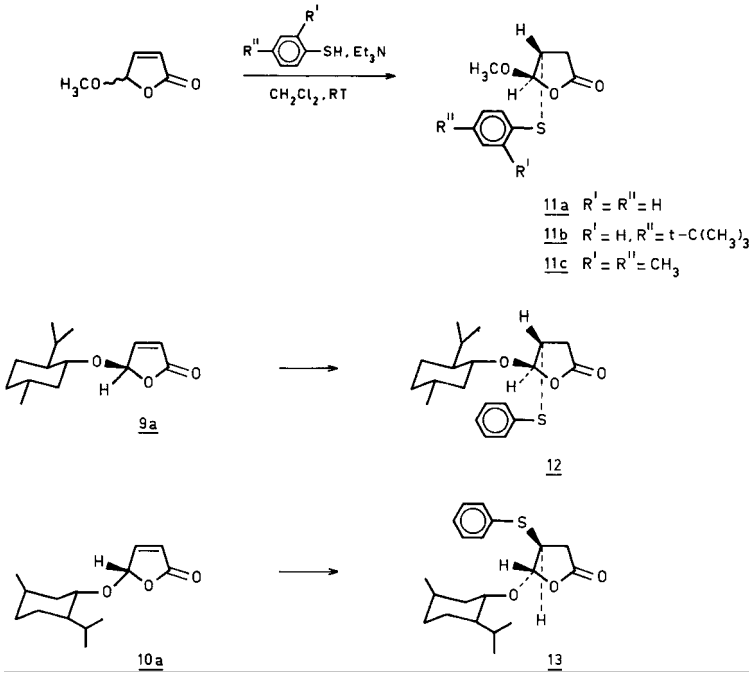
SCHEME 2



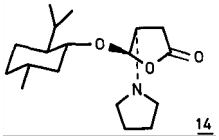
An epimerization of 9b to 9a and 10b to 10a takes place in solution during the crystallization process. This epimerization can be accelerated by treatment with a catalytic amount of p-toluenesulphonic acid. The procedure described here facilitates the formation of multigram quantities of enantiomerically pure synthons 9a and 10a as it makes separation of diastereoisomers unnecessary.

1,4-Addition reactions of thiophenols to 8, 9a and 10a take place at room temperature in the presence of triethylamine to give a quantitative yield of adducts 11a - 11c and 12, 13 (scheme 3).

SCHEME 3



Complete diastereoselective Michael type addition occurred in all cases. Only one diastereoisomer was observed in the ^{1}H- and ^{13}C-NMR spectra of 12 (and 13) whereas starting with a 60:40 mixture of 9a and 9b (or 10a and 10b) a 60:40 mixture of diastereoisomers of 12 (or 13) was found. The trans-relationship between the alkoxy- and thiophenoxy-substituent was deduced from the ^{1}H NMR coupling constant between the hydrogen atoms at the asymmetric centers in the lactone ring. ($J_{H4,H5}$ < 1Hz). Similar results were previously obtained in the additions of amines to 9a.[13] The absolute configuration at the newly formed chiral center is predicted to be R in the adduct 12 obtained from 9a and S in the case of the adduct 13. This assignment is based on the absolute configurations of 9a and 10a[12], the observed trans-diastereoselectivity and the X-ray analysis of the corresponding pyrrolidine adduct 14.[13,15].



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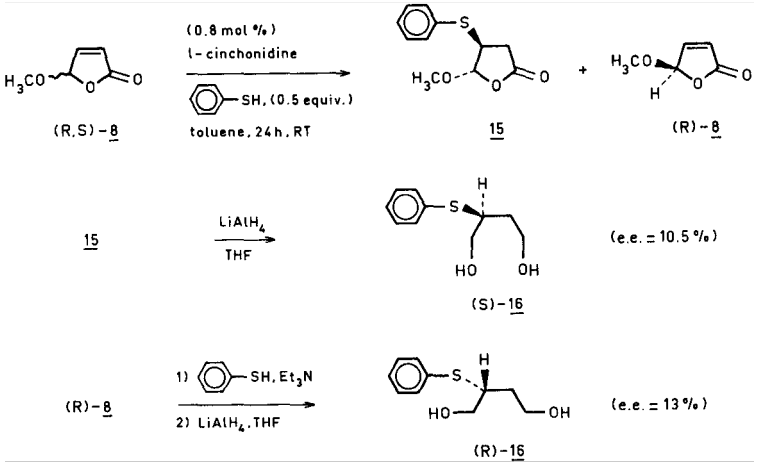
This 1,4-adduct of 9a and pyrrolidine, obtained via an analogous procedure, has the trans relative- and 4R,5R-absolute configuration.[15] In accordance with these assigments we were able to convert 12 and 13 into S- and R- 3,4-epoxy-1-butanol respectively (vide infra). Although thiol additions to butenolides have been extensively investigated, especially in connections with biomimetic studies of the thiol group as Michael donor[16], similar addition reactions to 5-alkoxy-butenolides have only recently been reported by Farina and co-workers.[17] Our results show that asymmetric thiol additions to chiral γ-alkoxy-butenolides yield enantiomerically pure C4-chiral synthons in high yield under mild conditions.

Kinetic resolution of 5-methoxy-2(5H)-furanone.

A number of studies on asymmetric thiol additions to achiral enones have been described.[18] Enantioselective thiol additions to α,β-unsaturated ketones[18] and to maleic esters[7] catalyzed by cinchona-alkaloids have been particularly successful. These reports prompted us to investigate the possible kinetic resolution[19] of racemic γ-alkoxy butenolides 8 by means of asymmetric thiophenol addition (scheme 4).

As the thiol adduct 15 can be easily reconverted into butenolide 8 by treatment with base this approach would in principle allow the formation of both enantiomers of 8 without the use of a chiral auxiliary.

SCHEME 4



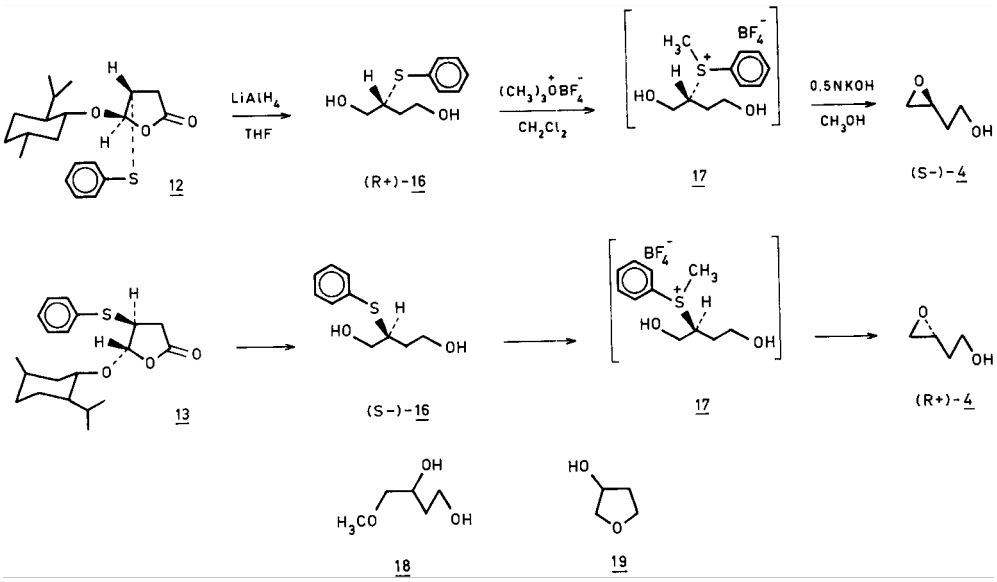
The addition of 0.5 equivalents of thiophenol to racemic 5-methoxy-2(5H)-furanone (8) was performed at room temperature in the presence of a catalytic amount (0.8 mol%) of l-cinchonidine as a chiral base. Separation of the adduct and the remaining starting material by distillation yielded (4S,5S)-15 ($[\alpha]^{D}_{20}$ + 0.7° (c=1.0, $CHCl_3$)) and butenolide (5R)-8 ($[\alpha]^{D}_{20}$ + 9.9° (c=1.0,$CHCl_3$)). The optical purity and absolute configuration at the C_4 chiral center of 15 was determined via its lithiumaluminiumhydride reduction product 16. ($[\alpha]^{D}_{20}$ + 4.1° (c=1.4, CH_3OH)). Comparison with literature data[7] on 16 indicate an optical purity of 10.5%.

The configuration at the acetal chiral center in 8 and the optical purity of 8 was established in the following manner. Addition of thiophenol in the presence of triethylamine followed by reduction with $LiAlH_4$ yielded R-16 ($[\alpha]^{D}_{20}$ - 5.0° (C=1.4,CH_3OH)).

Provided no partial racemization takes place during thiol addition and reduction reactions (see next part) and a linear correlation between enantiomeric excess and optical purity[20] is assumed it can be deduced from these data that the kinetic resolution catalyzed by cinchonidine leads to (+)-butenolide 8 with an enantiomeric excess of 13%. Furthermore the stereoselective trans-addition to 8 and the R-configuration in 16 obtained from (+)-8 means that the (+)-enantiomer of 8 contains the R-configuration at the acetal chiral center (scheme 4).

Although the optical purity of 8 obtained by the procedure described here is rather low it is as far as we know the first time that a cinchona-alkaloid catalyzed 1,4-addition has been applied for kinetic resolution of butenolides. As 8 does not contain a chiral auxiliary alkoxy-group as compared to 9a and 10a we have now available for the first time partial enriched 5-methoxy-2(5H)-furanone, a compound not easily resolved by classical means. This allows a study of potential racemization via the 2-hydroxy-5-alkoxy furan tautomeric form of these promising chiral synthons. Preliminary results indicate that racemization of 8 does not readily takes place under neutral conditions.

SCHEME 5



Synthesis of 3,4-epoxy-1-butanol.

The synthesis of (R)- and (S)-3,4-epoxy-1-butanol from 12 and 13 was performed in a two step procedure (scheme 5). Reduction with $LiAlH_4$ in THF yielded (R)- and (S)-diols 16 respectively in 81% yield. The chiral auxiliary d- or l-menthol was recovered by distillation in 80-90% yield in this step. Subsequent alkylation of 16 with trimethyloxoniumtetrafluoroborate to the sulphoniumsalt 17 was followed by base treatment to provide (S)- ($[\alpha]_D^{20}$ - 30.7° (c=1,CH_2Cl_2)) and (R)-3,4-epoxy-1-butanol ($[\alpha]_D^{20}$ + 31.4° (c=0.5, CH_2Cl_2)).
The intramolecular substitution reaction with elimination of methylphenyl-sulfide proceeds with complete inversion of configuration at the C_2-carbon atom, analogous to reported procedures for the formation of epoxides from α-hydroxy sulfides.[21]

Comparison of the optical rotations of (S)- 4 and (R)-4 obtained in this way with those reported established an optical purity >99%.[5-7] Literature data on optical rotations of 4 are controversial and furthermore the optical rotations of 4 strongly depend on solvent and concentration. For our purpose we used data for (+)- and (-)- 4 for which optical purity was independently determined by G.C.analysis.[6]

In the last steps of our route we followed a slightly modified version of methodology previously used by Yamashita and Mukaiyama[7]; no experimental details were provided by these authors. It has to be noted that for the base treatment of 17 carefully controlled conditions are essential to obtain high yields of 4, as otherwise, depending upon temperature, concentration of base and solvent, various amounts of byproducts are present.
^1H NMR analysis indicates that longer reaction times and higher base concentrations as those reported here, lead to nucleophilic ring opening to yield 18 or cyclisation to give 19.

Following the asymmetric synthesis procedure described here (R)-and (S)-4 are obtained in 58% and 54% overall yields from the chiral synthons 12 and 13 respectively. Several important applications of optically active 3,4-epoxy-1-butanol have been recently described for instance the synthesis of all four stereoisomers of the insect pheromones of Paresvespula vulgaris L.[6] This is further illustrated by the asymmetric synthesis of (-)-γ-amino-β-(R)-hydroxy-butyric acid ((-)-GABOB), an antiepileptic and hypotensive drug, in 49% enantiomeric excess via (R)-4.[3] Both enantiomers of these products are now readily available using the asymmetric synthesis procedures described here.

In conclusion we have synthesized new multifunctional C_4-chiral synthons and have found an efficient route to enantiomerically pure (R)- and (S)-3,4-epoxy-1-butanol.

Experimental

^1H NMR (200 MHz and 300 MHz) and ^{13}C NMR spectra were obtained on Nicolet NT200 and Varian VXR 300 spectrometers in deuterochloroform solution. Chemical shifts are reported as δ values relative to tetramethylsilane (δ=0 ppm). Infrared spectra were recorded on a Unicam SP200 infrared spectrophotometer. Melting points (uncorrected) were determined on a Mettler FP-2 melting point apparatus. High resolution mass spectra (HRMS) were recorded on

a AEI-MS-902 spectrometer. Elemental analyses were performed in the microanalytical department of this laboratory. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl. All other solvents were distilled before use. Et_3N was dried over KOH. d- and l-Menthol were purchased from Janssen Chimica. Optical rotations were measured on a Perkin Elmer 241 Polarimeter. Photooxidations of furfural and the preparation of 7 were performed using rose bengal or methylene blue as sensitizer and a 700 Watt high pressure mercury lamp (Hanau) analogous to procedures described before.[22]

5-Hydroxy-2(5H)-furanone (7)
A solution of freshly distilled furfural (250 g, 2.6 mol) in 1.9 l of methanol containing 0.050 g Rose Bengal was irradiated using a 750W immersion lamp equipped with a water cooled jacket and a Kapton 500H filter. A small stream of oxygen gas was continuously passed through the solution. Irradiation was continued for approximately 26 h, while the conversion was monitored by ^1H NMR. At 8 h intervalls small portions of sensitizer (10 mg) were added. After complete conversion the solvent was removed by rotary evaporation to yield 280 g of crude 7 that solified upon standing. This product was sufficiently pure for use as such in the next step. Recrystallization from CCl_4 yielded white crystalline 7; m.p. 57.3-59.2°C; lit.[25] m.p. 58.0-60.0°C.

5-Methoxy-2(5H)-furanone (8).
A solution of 50 g(0.5 mol) of 5-hydroxy-2(5H)-furanone (7) in methanol (200 ml) was heated at reflux for 3 days. The solvent was removed by rotary evaporation and the residue distilled to give 42 g (74%) of 8 as a colourless oil; b.p. 70-72°C, 2mm; lit.[26] b.p. 45-48°C, 0.1 mm, ^1H NMR ($CDCl_3$) 3.5 (s,3H,CH_3), 5.8 (s,1H,C_4-H), 6.2, 7.2 (ABq,2H,J=6Hz,C_2-H,C_3-H).

5-(l)-Menthyloxy-2(5H)-furanone (9a).
5-Hydroxy-2(5H)-furanone (4.08 g,40.8 mmol) was heated under stirring at 100-110°C with 8.06 g(51.7 mmol) l-menthol for 3 days. The excess menthol was removed by distillation (b.p. 80-90°C, 0.1 mm) and prolonged distillation yielded 5.34 g (55%) of butenolide 9 as a viscous oil; (b.p. 128-132°C (0.1 mm); mixture (60:40 ratio) of 9a and 9b) that solidified upon standing. ^1H NMR ($CDCl_3$) 0.7-2.0 (m,18H,menthyl-H's), 3.60 (m,1H,C(H)O), 5.86 (s,0.4H,C_5-H(9b)), 5.97 (s,0.6H,C_5-H(9a)), 6.10, 7.10 (dd,2H,J=6Hz,C_3-H,C_4-H).
Two crystallizations of 7.25 g of 9 from petroleum ether (40/60) or n-hexane at -18°C yielded 3.12 g (43%) of enantiomerically pure 9a as white needles. The combined mother liquors were evaporated to dryness. The remaining solid was redissolved in benzene and heated at reflux in the presence of a catalytic amount (0.3 mol%) of p-toluenesulphonic acid during 1 hour. The solvent was removed in vacuo and the residue crystallized twice as described above to afford additional 1.2 g of enantiomerically pure 9a (combined yield 60%):
9a: m.p.70.7-71.3°C; $[\alpha]_D^{20}$ - 136.8° (c=1.0,$CHCl_3$);
^1H NMR ($CDCl_3$) 0.65-2.32 (m,18H, menthyl-H's), 3.58 (m, 1H, C(H)O), 5.97 (s, 1H, C_5-H), 6.10 (d, 1H, J=6.0 Hz, C_3-H), 7.08 (d, 1H, J=6.0 Hz, C_4-H); ^{13}C NMR ($CDCl_3$) 15.51 (q), 20.57 (q), 21.93 (q), 22.87 (t), 25.04 (d), 31.17 (d), 33.93 (t), 40.05 (t), 47.46 (d), 78.79 (d), 100.26 (d), 124.36 (d), 150.79 (d), 170.46 (s); HRMS calcd. 238.157, found 238.155. Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.49; H, 9.18.
5-((d)-Menthyloxy-)-2(5H)-furanone (10a).
Prepared as described for 9a using d-menthol:
m.p. 74.2 - 74.4°C; $[\alpha]_D^{20}$ + 139.7° (c 1.0, $CHCl_3$).

Thiophenoladditions to γ-alkoxybutenolides; typical procedure.

To a solution of 1.0 g (4.2 mmol) 5-(l)-menthyloxy -2(5H)-furanone (9a) in 10 ml of CH_2Cl_2 was added 0.46 g (4.2 mmol) of thiophenol. The mixture was cooled to 0°C and triethylamine (0.21 mmol) was added. The solution was subsequently stirred at 0°C for 15 min. and at 20°C for 1 hour. The methylenechloride and triethylamine were removed in vacuo to yield 5-(l)-menthyloxy-4-phenylthiobutyrolactone (12) as a white solid; 1.44 g (100%) m.p. 77.8-78.0°C; $[\alpha]_D^{20}$ - 62.2° (c 1.0,$CHCl_3$); ^1H NMR: 0.65-2.05 (m,18H, menthyl-H's), 2.34-2.41 (dd,1H,J=15Hz, J=3Hz), 3.01-3.08 (dd,1H,J=15Hz, J=8Hz), 3.35-3.45 (m,1H), 3.72-3.80 (m,1H), 5.45 (s,1H,J=8Hz), 7.20-7.39 (m,5H,aryl-H's).
^{13}C NMR: 15.41 (q), 20.66 (q), 21.95 (q), 22.85 (t), 25.29 (d), 31.04 (t), 33.58 (t), 33.99 (d), 39.46 (t), 46.25 (d), 47.43 (d), 77.47 (d), 103.81 (d), 127.67 (d), 129.17 (d), 131.31 (d), 132.32 (s), 174.05 (s).
IR (KBr, cm^{-1}): 3100-2900 (C-H), 1800 (C=O), 1600 (C=C), 800-650 (aryl)
HRMS calcd 348.176, found 348.175.

5-(d)-menthyloxy-4-phenylthiobutyrolactone (13)
m.p. 79.1-79.3°C, $[\alpha]_D^{20}$ + 60.6° (c 1.0, $CHCl_3$); further data as described above.

Kinetic resolution of 5-methoxy-2(5H)-furanone (8).

To a solution of 0.5 g (4.3 mmol) of thiophenol and 0.01 g l-cinchonidine in 5 ml of toluene at 0°C was added 1.0 g (8.7 mmol) of 5-methoxy-2(5H)-furanone. After stirring at room temperature for 24 hours the solvent was removed in vacuo and the residue fractionated by distillation. There was obtained 0.4 g (40%) of (S-)-5-methoxy-2(5H)-furanone(8); b.p. 80-90° C, 0.1 mm, $[\alpha]_D^{20}$ + 9.9° (c 1.0, $CHCl_3$) and 0.3 g (20% based on 8) of 5-methoxy-4-phenylthiobutyrolactone (15); b.p. 140-150°C, 0.1 mm, $[\alpha]_D^{20}$ +0.7° (c 1.0, $CHCl_3$).
Compound 15 (0.3 g) was reduced with $LiAlH_4$ in THF as described below to yield (S)-2-phenylthio-1,4-butanediol (S-16); 0.23 g (90%); $[\alpha]_D^{20}$ - 5.0° (c 1.4, CH_3OH) (optical purity 13%). In all respects (except for rotation) identical with (S)-16 prepared from 13.
The addition of thiophenol to (S)-8 was performed following the typical procedure described above to give (4S),(5R)-15 (100% yield): $[\alpha]_D^{20}$ - 0.80° (c 1.0, $CHCl_3$), ^1H NMR ($CDCl_3$): 2.21-2.48 (dd,1H,J=15Hz,J=3Hz,C_3-H), 2.86-3.18 (dd,1H,J=15Hz,J=8Hz,C_3-H), 3.4 (s, 3H, OCH_3), 3.61-3.79 (m,1H,C_4-H), 5.2 (s,1H, C_5-H), 7.20-7.40 (m,5H,aryl-H's).
Reduction of (4S),(5R)-15 with $LiAlH_4$ in THF as described below yielded (R)-16, $[\alpha]_D^{20}$ + 4.1° (c 3.0, CH_3OH) (optical purity 10.5%).
In all respects (except for rotation) identical with (S)-16 prepared from 13.

2-Phenylthio-1,4-butanediol (16):

To a stirred suspension of 0.27 g (7.0 mmol) of $LiAlH_4$ in tetrahydrofuran under a nitrogen atmosphere at 0°C was added 1.3 g (3.5 mmol) of 5-(l)-menthyloxy-4-phenylthiobutyrolactone (12) dissolved in 20 ml of tetrahydrofuran.

The mixture was stirred at 0°C for 1 hour and subsequently at room temperature for 12 hours. The excess $LiAlH_4$ was destroyed by careful addition of 1 ml of water and 1 ml of 10% aqueous KOH solution. The salts that precipitated were removed by filtration and washed with diethylether (2x50 ml).
The combined organic layers were dried (Na_2SO_4), and the organic solvent removed in vacuo. Distillation of the residue gave 0.49 g l-menthol at 80-100°C (0.1 mm) and subsequently (R)-16 as a colourless oil;
yield 0.56 g (81%), b.p. 160°C, 0.1 mm; $[\alpha]_D^{20}$ + 40.2 (c 3.5, CH_3OH), lit.[7]: $[\alpha]_D^{20}$ + 40.2° (c 3.5, CH_3OH) (100% optical purity).
^1H NMR ($CDCl_3$): 1.65-1.81 (m,2H,C_3-H), 3.15-3.27 (m,1H,C_2-H), 3.38-3.76 (m,4H,C_1-H, C_4-H), 3.95-4.18 (s,br,2H,OH), 7.05-7.32 (m,5H,aryl-H's).
^{13}C NMR: 34.59 (t), 48.73 (d), 59.98 (t), 64.32 (t), 127.28 (d), 128.93 (d), 132.25 (d), 133.47 (s).
IR: 3500-3200 (br,OH), 3100-2900 (C-H), 1200-1000 (C-O).
HRMS calcd. 198.071, found 198.072.

Following the same procedure (S)-16 was obtained; yield 0.58 g (84%), b.p. 160°C (0.1 mm); $[\alpha]_D^{20}$ -41.7° (c 3.5, CH_3OH), lit.[7] $[\alpha]_D^{20}$ - 32.60 (c 3.5, CH_3OH) for (S)-16 with an optical purity of 81%.

3,4-epoxy-1-butanol (4).

To a solution of 0.15 g (0.8 mmol) of (R)-2-phenylthio-1,4-butanediol in 10 ml of dichloromethane was added 0.15 g (1.0 mmol) of freshly prepared[23] trimethyloxoniumtetrafluoroborate. The suspension was stirred at room temperature for 2 hours during which period the major part of the salt dissolved. To the solution was added 10 ml of a 0.5N solution of KOH in methanol. The conversion of 17 was followed in this stage by T.L.C. on silica with n-hexane as an eluens. Complete conversion was reached in 40 min. The reaction mixture was purified by flash chromatography over silica-gel using ether as the eluens.
The ether was removed in vacuo and the residue purified by chromatography (silica-gel, n-hexane, diethylether 80/20, Rf=0.4), to give (S)-3,4-epoxy-1-butanol 4 as a colourless oil: 0.050 g (71%); $[\alpha]_D^{20}$ - 30.7° (c 1.0, CH_2Cl_2) lit.[6] $[\alpha]_D^{20}$ - 30.6° (c 5.1, CH_2Cl_2) for 4 with an e.e. > 99%.
^1H NMR ($CDCl_3$): 1.7-2.0 (m,2H,C_2-H), 2.4 (s,1H,OH), 2.5-2.7 (m,1H,C_4-H), 2.8-3.0 (m,1H,C_4-H), 3.0-3.2 (m,1H,C_3-H), 3.6-4.0 (t,2H,J=6Hz,C_1-H). All further spectral data in accordance with those reported in the literature[5-7] and measured for an independently prepared sample of (R,S)-4.
(R)-3,4-epoxy-1-butanol: prepared following the same procedure from (S)-2-phenylthio-1,4-butanediol in 64% yield: $[\alpha]_D^{20}$ +31.4° (c 0.5, CH_2Cl_2), lit.[6] $[\alpha]_D^{20}$ +29.5° (c 5.1, CH_2Cl_2) for 4 with an e.e. = 93%.
(R,S)-3,4-epoxy-1-butanol:
This compound was synthesized according to the procedure described by Bats et.al.[24] via $LiAlH_4$ reduction of 3-butenoic acid to 3-butene-1-ol (50% yield) followed by epoxidation with metachloroperbenzoicacid (77% yield).
(R,S)-4: b.p. 70°C (12 mm), lit.[24]: b.p. 89°C (25 mm), all spectral data as reported.

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