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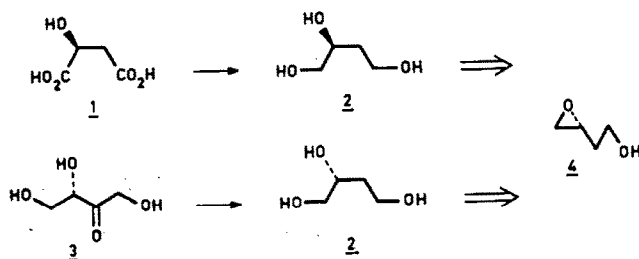
Extensive synthetic use of simple chiral building blocks such as **4** depends however largely on the availability of both enantiomers in an optically pure form.

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.
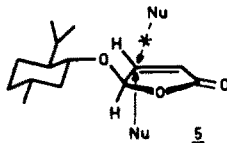
This expectation has been realized in the Diels Alder reactions of a variety of dienes with **5** with diastereoselectivities > 96%.[12]
Furthermore we found that 1,4-additions of amines to **5** provide β-aminolactones with exclusively a trans relationship between amine- and menthyloxy-functionalities. These adducts could be converted to enantio-merically 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 nucleo-philes. 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 acetaliza-tion 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
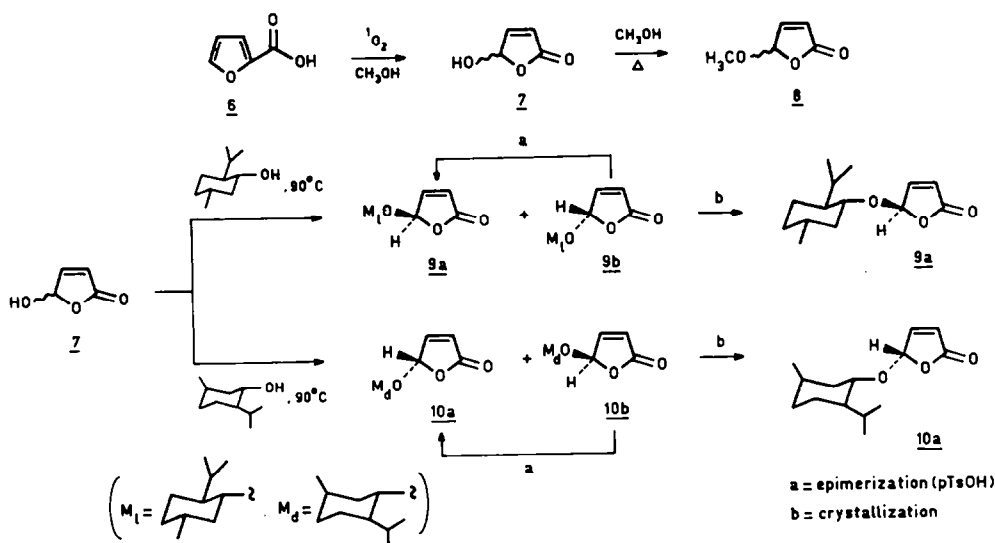
An epimerization of **9b** to **9a** and **10b** to **10a** takes place in solution during the crystallization process. This epimerization can be accelerated by treatment with a catalytic amount of p-toluenesulphonic acid. The procedure described here facilitates the formation of multigram quantities 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

11a R' = R'' = H
11b R' = H, R'' = t-C(CH₃)₃
11c R' = R'' = CH₃
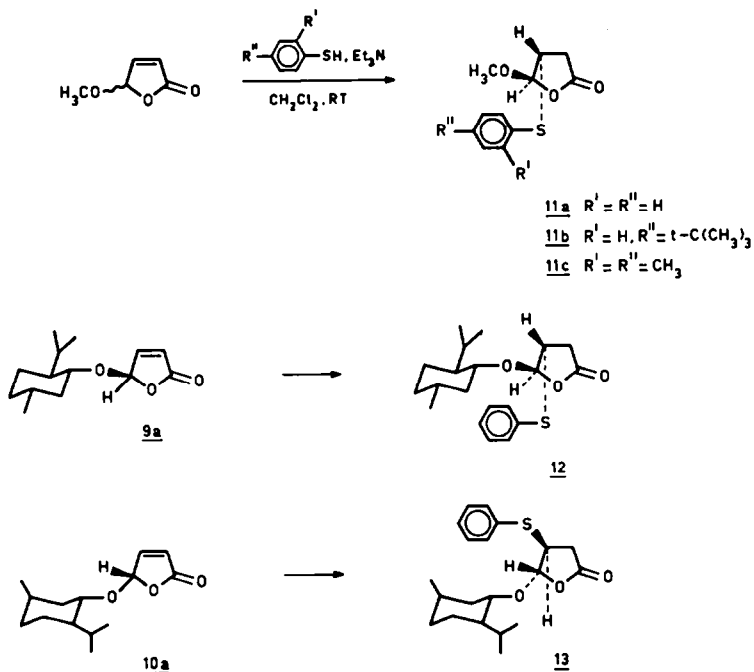
Complete diastereoselective Michael type addition occurred in all cases. Only
one diastereoisomer was observed in the ¹H- and ¹³C-NMR spectra of 12 (and 13)
whereas starting with a 60:40 mixture of 9a and 9b (or 10a and 10b) a 60:40
mixture of diastereoisomers of 12 (or 13) was found. The trans-relationship
between the alkoxy- and thiophenoxy-substituent was deduced from the ¹H 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]


14
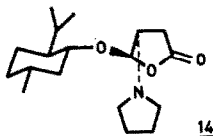
This 1,4-adduct of 9a and pyrrolidine, obtained via an analogous procedure,
has the trans relative- and 4R,5R-absolute configuration.[15] In accordance
with these assignments we were able to convert 12 and 13 into S- and R- 3,4-
epoxy-1-butanol respectively (vide infra). Although thiol additions to
butenolides have been extensively investigated, especially in connections
with biomimetic studies of the thiol group as Michael donor[16], similar ad-
dition 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.
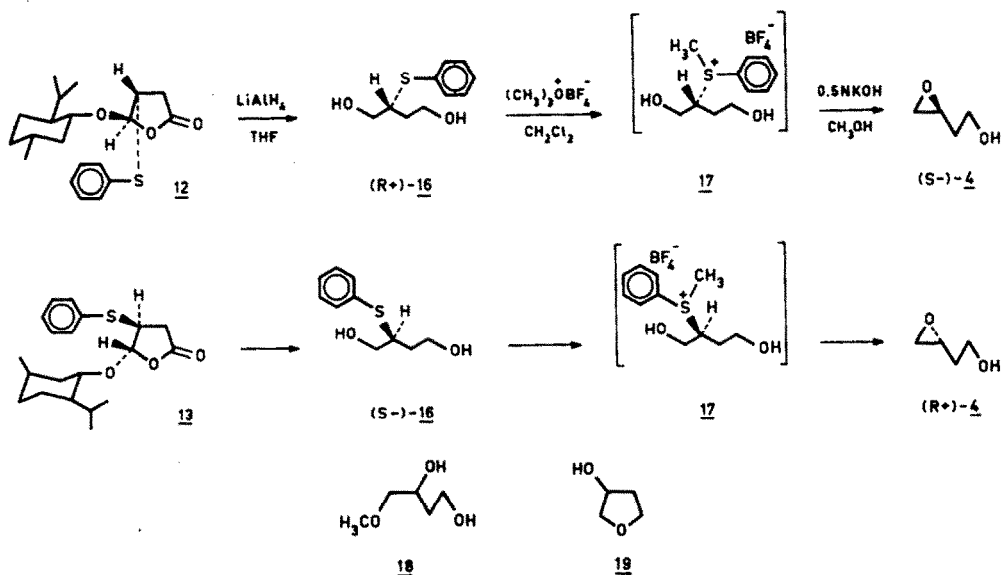
SCHEME 4
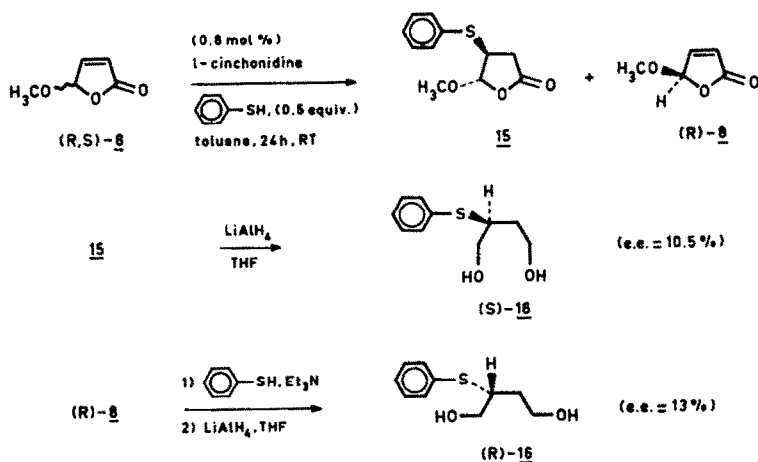
The addition of 0.5 equivalents of thiophenol to racemic 5-methoxy-2(5H)-furanone (8) was performed at room temperature in the presence of a catalytic amount (0.8 mol%) of l-cinchonidine as a chiral base. Separation of the adduct and the remaining starting material by distillation yielded (4S,5S)-15 ([α]²⁰ₒ + 0.7° (c=1.0, CHCl₃)) and butenolide (5R)-8 ([α]²⁰ₒ + 9.9° (c=1.0,CHCl₃)). The optical purity and absolute configuration at the C₄ chiral center of 15 was determined via its lithiumaluminiumhydride reduction product 16. ([α]²⁰ₒ + 4.1° (c=1.4, CH₃OH)). 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 LiAlH₄ yielded R-16 ([α]²⁰ₒ - 5.0° (C=1.4,CH₃OH)).

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 <u>12</u> and <u>13</u> was
performed in a two step procedure (scheme 5). Reduction with LiAlH₄ in THF
yielded (R)- and (S)-diols <u>16</u> 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 <u>16</u> with trimethyloxoniumtetrafluoroborate to the
sulphoniumsalt <u>17</u> was followed by base treatment to provide (S)- ([α]$_8^0$
- 30.7° (c=1,CH₂Cl₂)) and (R)-3,4-epoxy-1-butanol ([α]$_8^0$ + 31.4° (c=0.5,
CH₂Cl₂)).
The intramolecular substitution reaction with elimination of methylphenyl-
sulfide proceeds with complete inversion of configuration at the C₂-carbon
atom, analogous to reported procedures for the formation of epoxides from α-
hydroxy sulfides.[21]

Comparison of the optical rotations of (S)- <u>4</u> and (R)-<u>4</u> obtained in this
way with those reported established an optical purity >99%.[3-7] Literature data
on optical rotations of <u>4</u> are controversial and furthermore the optical
rotations of <u>4</u> strongly depend on solvent and concentration. For our purpose
we used data for (+)- and (-)- <u>4</u> 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 <u>17</u> carefully controlled conditions are essential to obtain high
yields of <u>4</u>, 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 con-
centrations as those reported here, lead to nucleophilic ring opening to
yield <u>18</u> or cyclisation to give <u>19</u>.

Following the asymmetric synthesis procedure described here (R)-and (S)-<u>4</u>
are obtained in 58% and 54% overall yields from the chiral synthons <u>12</u> and <u>13</u>
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)-<u>4</u>.[3] Both enantiomers of these products are now
readily available using the asymmetric synthesis procedures described here.

In conclusion we have synthesized new multifunctional C₄-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 ¹³C 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 spectro-
photometer. 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 micro-
analytical department of this laboratory. Diethyl ether (Et₂O) and tetra-
hydrofuran (THF) were distilled from sodium benzophenone ketyl. All other
solvents were distilled before use. Et₃N 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 intervals 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 CCl₄ 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 (CDCl₃) 3.5
(s,3H,CH₃), 5.8 (s,1H,C₄-H), 6.2, 7.2 (ABq,2H,J=6Hz,C₂-H,C₃-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
(CDCl₃) 0.7-2.0 (m,18H,menthyl-H's), 3.60 (m,1H,C(H)O), 5.86 (s,0.4H,C₅-
H(9b)), 5.97 (s,0.6H,C₅-H(9a)), 6.10, 7.10 (dd,2H,J=6Hz,C₃-H,C₄-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 cata-
lytic 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; [α]$_D^{20}$ - 136.8° (c=1.0,CHCl₃);
¹H NMR (CDCl₃) 0.65-2.32 (m,18H, menthyl-H's), 3.58 (m, 1H, C(H)O), 5.97 (s,
1H, C₅-H), 6.10 (d, 1H, J=6.0 Hz, C₃-H), 7.08 (d, 1H, J=6.0 Hz, C₄-H); ¹³C
NMR (CDCl₃) 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
C₁₄H₂₂O₃: 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; [α]$_D^{20}$ + 139.7° (c 1.0, CHCl₃).

Thiophenoladditions to γ-alkoxybutenolides; typical procedure.

To a solution of 1.0 g (4.2 mmol) 5-(1)-menthyloxy -2(5H)-furanone (9a) in 10
ml of CH$_2$Cl$_2$ 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-(1)-
menthyloxy-4-phenylthiobutyrolactone (12) as a white solid; 1.44 g (100%)
m.p. 77.8-78.0°C; [α]$_D^{20}$ - 62.2° (c 1.0,CHCl$_3$); ^{1}H 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, [α]$_D^{20}$ + 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 1-
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, [α]$_D^{20}$ + 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, [α]$_D^{20}$ +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%); [α]$_D^{20}$ - 5.0° (c
1.4, CH$_3$OH) (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): [α]$_D^{20}$ - 0.80° (c
1.0, CHCl$_3$), ^{1}H 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, [α]$_D^{20}$ + 4.1° (c 3.0, CH$_3$OH) (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-(1)-
menthyloxy-4-phenylthiobutyrolactone (12) dissolved in 20 ml of tetra-
hydrofuran.

The mixture was stirred at 0°C for 1 hour and subsequently at room temperature for 12 hours. The excess LiAlH₄ 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 (Na₂SO₄), 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, CH₃OH), lit.[7]: $[\alpha]_D^{20}$ + 40.2° (c 3.5, CH₃OH) (100% optical purity).

¹H NMR (CDCl₃): 1.65-1.81 (m,2H,C₃-H), 3.15-3.27 (m,1H,C₂-H), 3.38-3.76 (m,4H,C₁-H, C₄-H), 3.95-4.18 (s,br,2H,OH), 7.05-7.32 (m,5H,aryl-H's).

¹³C 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, CH₃OH), lit.[7] $[\alpha]_D^{20}$ - 32.6° (c 3.5, CH₃OH) 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, CH₂Cl₂) lit.[6] $[\alpha]_D^{20}$ - 30.6° (c 5.1, CH₂Cl₂) for 4 with an e.e. > 99%.

¹H NMR (CDCl₃): 1.7-2.0 (m,2H,C₂-H), 2.4 (s,1H,OH), 2.5-2.7 (m,1H,C₄-H), 2.8-3.0 (m,1H,C₄-H), 3.0-3.2 (m,1H,C₃-H), 3.6-4.0 (t,2H,J=6Hz,C₁-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, CH₂Cl₂), lit.[6] $[\alpha]_D^{20}$ +29.5° (c 5.1, CH₂Cl₂) 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 LiAlH₄ 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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