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# Synthesis of (±) - Thioascorbic Acid

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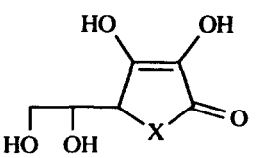
**Key Words:** Thiolactones; reductone ethers; ether cleavage; diastereoselective aldol reaction.

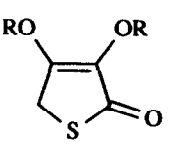
**Abstract:** The synthesis of the hitherto unknown racemic thioanalogue of ascorbic acid **1** was accomplished starting with the reductone derivative **3**. Ether cleavage followed by benzylation furnished thiotetronic acid **10**, which was employed in an aldol-type reaction with *tert*-butyldimethylsilyloxy acetaldehyde giving rise to a mixture of the *threo*- and *erythro*-adducts (±)**11a** and (±)**11b**. Subsequent catalytic hydrogenation of the *threo*-acetal (±)**13** proceeded cleanly to yield racemic thioascorbic acid (±)**14** after deprotection.

Ascorbic acid **1** and its sulphur analogue **2** have different molecular geometries. Therefore it is likely that these two compounds differ in their properties, e.g. the redox potential, the acidity, the propensity for chelation as well as the physiological activity. In order to verify this assumption we have synthesized the hitherto unknown thioascorbic acid as a racemate (scheme 1).

**Scheme 1:**



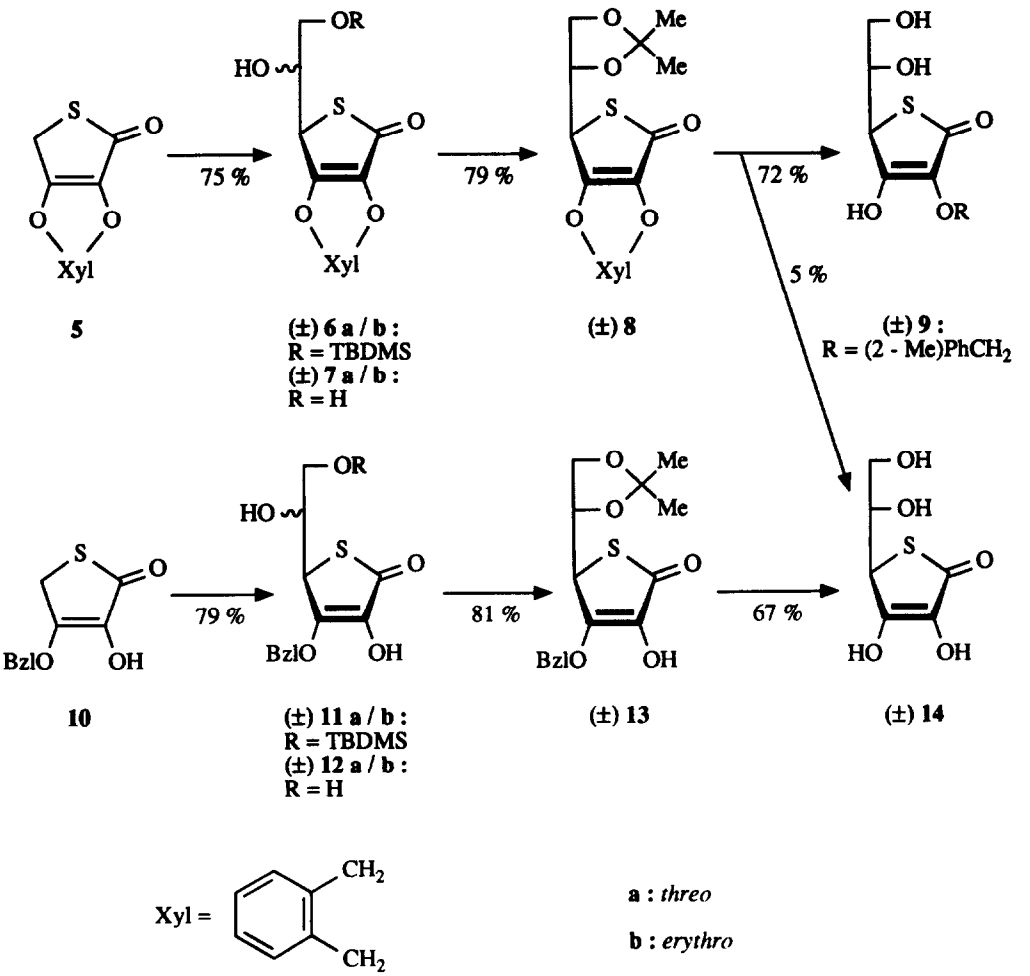

**1** : X = O
**2** : X = S




**3** : R = Me
**4** : R = H

Starting with the thiolactone **3**[2], successive cleavage of the ether groups employing boron tribromide[3] and hydrobromic acid[4] afforded the reductone **4**. The endiol xylylene ether **5**, readily available *via* alkylation of **4** was subjected to an aldol-type reaction with *tert*-butyldimethylsilyloxy acetaldehyde[5] furnishing a mixture of the diastereomeric aldols (±)**6a**/(±)**6b** in a ratio of 85:15, as depicted in scheme 2. After separation by column chromatography the single isomers (±)**6a** and (±)**6b** were desilylated by use of aqueous acetic acid giving rise to the glycols (±)**7a** and (±)**7b**, respectively.

**Scheme 2:**



The $^1$H-NMR spectrum of the major product (±)**7a** displays (with exception of the xylylene peaks) similarity with the spectrum of ascorbic acid, whereas the signal pattern of the minor component (±)**7b** is distinctly different. Accordingly (±)**7a** is considered to be the *threo*-isomer corresponding to the configuration of ascorbic acid (*xylo*-ascorbic acid) and hence (±)**7b** is the *erythro*-stereoisomer analogous to isoascorbic acid (*arabo*-ascorbic acid). This assignment has been confirmed by X-ray diffraction analysis of the acetonide (±)**8**, which was readily obtained from (±)**7a** (figure 1).

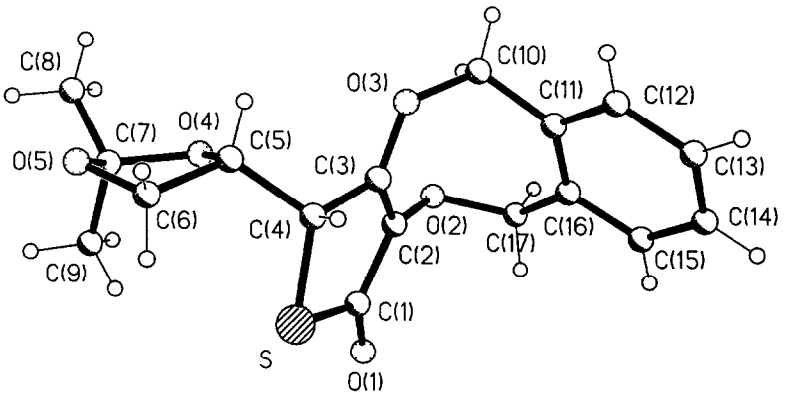


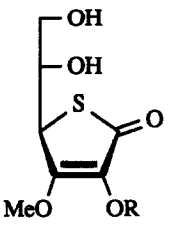

**Figure 1: Crystal structure of (±)8**

In the course of the catalytic debenzylation of (±)**8**, uptake of hydrogen subsided rapidly after consumption of 1.2 equivalents of $H_2$. After deketalization the 3-xylyl ether of thioascorbic acid (±)**9** was isolated as the main product along with modest amounts of thioascorbic acid (±)**14**. In contrast, the corresponding ascorbic acid xylylene ether is reported to undergo hydrogenolytic cleavage to vitamin C fast and completely[6].

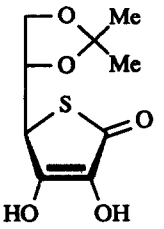
In order to circumvent the difficulties attached to the final debenzylation, the reaction sequence was reiterated with the benzyl ether **10** *in lieu* of the diether **5** (scheme 2). **10** was conveniently prepared from reductone **4** and phenyldiazomethane. Utilizing the aldol-type addition of **10** to *tert*-butyldimethylsilyloxy acetaldehyde a mixture of the diastereomeric isomers (±)**11a**/(±)**11b** in a 6:1 ratio was obtained. These adducts were separated by flash chromatography and thereupon desilylated to the corresponding glycols (±)**12a** and (±)**12b**. The major product (±)**12a** was ketalized to (±)**13** and subjected to hydrogenolysis over Pearlman's catalyst. Following a lively uptake of the theoretical amount of hydrogen the newly obtained acetonide (±)**17** was smoothly hydrolyzed to afford thioascorbic acid, m.p. 173 °C (dec.) in a fairly good yield.

Methylation of (±)**14** with diazomethane proceeded stepwise leading to the monoether (±)**15** and then to the diether (±)**16** (scheme 3).

**Scheme 3:**



(±) **15** : R = H
(±) **16** : R = Me



(±) **17**

For thioascorbic acid $pK_a$ values of 3.90 and 11.50 were measured by potentiometric titration[7] (ascorbic acid $pK_{a1}$ = 4.17; $pK_{a2}$ = 11.57). Thioascorbic acid (±)**14** instantly decolourizes iodine solution as well as Tillman's reagent. A comparison of the cyclovoltammograms[8] of ascorbic acid acetonide and its sulphur analogue (±)**17** suggests the thiocompound is the more powerful reducing agent, but due to the irreversibility of the electrochemical oxidation process no precise data could be deduced from the CV spectra. On oxidimetric titration[9] in a *p*H 4.90 buffer solution an electrode potential E = 0.055 V was measured at the half-equivalence point (ascorbic acid 0.115 V).

## EXPERIMENTAL

Melting points were determined using a Gallenkamp Melting Point Apparatus and are uncorrected. Column chromatography was carried out on silica gel (230 - 400 mesh) from Fa. Merck. $^1$H-NMR spectra were recorded at 400 MHz using $Me_4Si$ as internal standard, $^{13}$C-NMR spectra at 100 MHz on JEOL GSX 400. Mass spectra were obtained with Varian CH7. Infrared spectra were measured as KBr plates using a Perkin-Elmer 710B IR-Spectrometer. UV analysis was performed in methanolic solutions on Uvikon 810 Anakomp 220. Microanalyses were carried out applying an Analysator CHN-O-Rapid of Fa. Heraeus.
Solvents were purified according to standard laboratory techniques.

**3,4-Dihydroxy-2(5H)-thiophenone (4):**

The reductone ether **3** (1.60 g, 10 mmol) was dissolved in anhydrous dichloromethane (100 ml) and cooled to -78 °C under $N_2$. Boron tribromide (7.52 g, 30 mmol) in $CH_2Cl_2$ (30 ml) was added dropwise over 15 min while stirring. Thereupon the mixture was allowed to warm up to -10 °C. On cooling to -78 °C dry diethyl ether (20 ml) was slowly added and stirring continued for another 15 min. After addition of dry methanol (20 ml) the mixture was allowed to reach r.t. The solvents were removed *in vacuo* and the residue was evaporated with dry methanol until the distillate was free of borate. The resultant crystalline mass was dissolved in conc. hydrobromic acid (48% HBr, 50 ml) under $N_2$ and heated to 60 °C for 4 h. After cooling the solution was poured onto ice and saturated with sodium chloride followed by iterative extraction with warm ethyl acetate. The organic phase

was dried over $Na_2SO_4$, filtered and the volatiles stripped off *in vacuo*. The residue was chromatographed using 3% formic acid/diisopropyl ether as eluent to afford **4** as colourless crystals, m.p. 153 °C (benzene/ethyl acetate). Yield 0.79 g (60%). - IR: ν = 3500 - 2200 $cm^{-1}$, 3373, 2968, 2934, 1701, 1620, 1573, 1413. - UV: $\lambda_{max}$(lg ε) = 239 nm (3.777), 283 (3.689). - $^1$H-NMR (d3-acetonitrile): δ = 3.75 (s, 2 H). - Anal. ($C_4H_4O_3S$) Calcd C,36.36; H,3.05; S,24.27; found C,36.37; H,3.04; S,24.20%. - MS: 132 ($M^+$).

**5,10-Dihydrothieno[3.4-c]-[2.5]benzodioxocin-1(3H)-one (5):**

Potassium carbonate (2.90 g, 21 mmol) was added to a solution of endiol **4** (1.32 g, 10 mmol) in freshly distilled DMF (50 ml) under $N_2$ and the mixture heated to 60 °C for 45 min. *o*-Xylylene bromide (2.77 g, 10.5 mmol) in DMF (30 ml) was added in one portion and stirring continued for another 90 min. On cooling the mixture was slowly ($CO_2$↑) diluted with 2N $H_2SO_4$ (100 ml) and extracted thrice with ethyl acetate. The combined organic phases were sequentially washed with water and brine before drying over $Na_2SO_4$. After removal of solvents the residue was chromatographed using 20% ethyl acetate/hexane as eluent affording **5** as colourless needles, m.p. 157 °C (diisopropyl ether). Yield 1.05 g (45%). - IR: ν = 2918 $cm^{-1}$, 1688, 1625, 1497, 1472, 1447. - UV: $\lambda_{max}$(lg ε) = 240 nm (3.817), 266 (3.736). - $^1$H-NMR ($CDCl_3$): δ = 7.39 - 7.11 (m, 5 H), 5.72 (s, 2 H), 5.36 (s, 2 H), 3.53 (s, 2 H). - Anal. ($C_{12}H_{10}O_3S$) Calcd C,61.52; H,4.30; S,13.69; found C,61.28; H,4.53; S,13.80%. - MS: 234 ($M^+$).

**(3R*)-(±)-3-[(1S*)-2-(*tert*-Butyldimethylsilyloxy)-1-hydroxyethyl]-5,10-dihydrothieno[3.4-c]-[2.5]benzodioxocin-1(3H)-one ((±)6a):**
**(3R*)-(±)-3-[(1R*)-2-(*tert*-Butyldimethylsilyloxy)-1-hydroxyethyl]-5,10-dihydrothieno[3.4-c]-[2.5]benzodioxocin-1(3H)-one ((±)6b):**

Diisopropylamine (1.41 ml, 10 mmol) was dissolved in dry THF (50 ml) and cooled to 0 °C under $N_2$. *n*-Butyllithium (6.25 ml of a 1.6 M solution in hexane, 10 mmol) was added dropwise and the mixture left to stir for 30 min. On cooling the solution to -78 °C xylylene ether **5** (2.34 g, 10 mmol) in THF (20 ml) was added slowly *via* syringe. After 15 min *tert*-butyldimethylsilyloxy acetaldehyde (1.74 g, 10 mmol) in THF (10 ml) was added dropwise to the solution and stirring continued for another 15 min. The mixture was quenched by addition of sat. aq. citric acid solution (50 ml). After dilution with ethyl acetate (100 ml) the phases were separated and the aqueous phase was reextracted twice with ethyl acetate (2 x 50 ml). After drying over $Na_2SO_4$ and removal of the solvents *in vacuo* the residue was chromatographed using 20% ethyl acetate/hexane as eluent to give **(±)6a** and **(±)6b**.

**(±)6a**: Colourless needles, m.p. 104 °C (hexane/diisopropyl ether). Yield 2.60 g (64%). - IR: ν = 3402 $cm^{-1}$, 2953, 2928, 2855, 1671, 1610, 1472. - UV: $\lambda_{max}$(lg ε) = 241 nm (3.882), 269 (3.709). - $^1$H-NMR ($CDCl_3$): δ = 7.39 - 7.12 (m, 4 H), 5.82 (d, J = 12 Hz, 1H), 5.65 (d, J = 12 Hz, 1H), 5.37 (d, J = 15 Hz, 1H), 5.33 (d, J = 15 Hz, 1H), 4.10 (m, 2 H), 3.67 (dd, $J_1$ = 4 Hz, $J_2$ = 10 Hz, 1 H), 3.52 (dd, $J_1$ = 6 Hz, $J_2$ = 10 Hz, 1 H), 1.91 (d, J = 8 Hz, 1 H, OH), 0.87 (s, 9 H), 0.04 (s, 6 H). - Anal. ($C_{20}H_{28}O_5SSi$) Calcd C,58.79; H,6.91; S,7.85; found C,58.80; H,6.89; S,7.92%. - MS: 408 ($M^+$).

**(±)6b**: Colourless crystals, m.p. 85 °C (hexane/diisopropyl ether). Yield 0.46 g (11%). - IR: ν = 3467

$cm^{-1}$, 2935, 2854, 1661, 1610, 1459. - UV: $\lambda_{max}$(lg $\epsilon$) = 243 nm (3.944), 269 (3.766). - $^1$H-NMR ($CDCl_3$): $\delta$ = 7.40 - 7.12 (m, 4 H), 5.85 (d, J = 12 Hz, 1 H), 5.62 (d, J = 12 Hz, 1 H), 5.39 (d, J = 15 Hz, 1 H), 5.31 (d, J = 15 Hz, 1 H), 4.28 (d, J = 6 Hz, 1 H), 4.03 (m, 1 H), 3.35 (dd, $J_1$ = 7 Hz, $J_2$ = 10 Hz, 1 H), 3.09 (dd, $J_1$ = 4 Hz, $J_2$ = 10 Hz), 2.83 (d, J = 3 Hz, 1 H, OH), 0.84 (s, 9 H), 0.06 (s, 6 H). - Anal. ($C_{20}H_{28}O_5SSi$) Calcd C,58.79; H,6.91; S,7.85; found C,58.68; H,7.02; S,7.86%. - MS: 408 ($M^+$).

**(3R*)-(±)-3-[(1S*)-1,2-Dihydroxyethyl]-5,10-dihydrothieno[3.4-c]-[2.5]benzodioxocin-1(3H)-one ((±)7a):**

The silylated aldol (±)**6a** (2.05 g, 5 mmol) was dissolved in a mixture of acetic acid (60 ml), THF (20 ml) and water (20 ml) and left at r.t. for 18 h. The volatiles were evaporated *in vacuo* and the residue triturated with diisopropyl ether to afford (±)**7a** as colourless crystals, m.p. 129 °C (diisopropyl ether/acetonitrile). Yield 1.15 g (78%). - IR: $\nu$ = 3415 $cm^{-1}$, 2925, 1688, 1627, 1497, 1448. - UV: $\lambda_{max}$(lg $\epsilon$) = 241 nm (3.904), 268 (3.746). - $^1$H-NMR (d3-acetonitrile): $\delta$ = 7.45 - 7.17 (m, 4 H), 5.87 (d, = 11 Hz, 1 H), 5.59 (d, J = 11 Hz, 1H), 5.33 (d, J = 15 Hz, 1 H), 5.26 (d, J = 15 Hz, 1 H), 4.09 (d, J = 3 Hz, 1 H), 3.98 (m, 1 H), 3.46 (m, after addition of $D_2O$: dd, $J_1$ = 6 Hz, $J_2$ = 11 Hz, 1 H), 3.35 (m, after addition of $D_2O$: dd, $J_1$ = 6 Hz, $J_2$ = 11 Hz, 1 H), 2.94 (t, J = 5 Hz, 1 H, OH), 2.79 (d, J = 6 Hz, 1 H, OH). - Anal. ($C_{14}H_{14}O_5S$) Calcd C,57.13; H,4.79; S,10.89; found C,56.83; H,4.97; S,10.90%. - MS: 294 ($M^+$).

**(3R*)-(±)-3-[(1R*)-1,2-Dihydroxyethyl]-5,10-dihydrothieno[3.4-c]-[2.5]benzodioxocin-1(3H)-one ((±)7b):**

This compound was prepared in the same manner as (±)**7a** using (±)**6b** (2.05 g, 5 mmol); reaction time 24 h. Colourless crystals, m.p. 170 °C (diisopropyl ether/acetonitrile). Yield 1.05 g (71%). - IR: $\nu$ = 3451 $cm^{-1}$, 3327, 2915, 1668, 1619, 1473. - UV: $\lambda_{max}$(lg $\epsilon$) = 243 nm (3.956), 268 (3.784). - $^1$H-NMR (d3-acetonitrile): $\delta$ = 7.44 - 7.13 (m, 4 H), 5.80 (d, J = 12 Hz, 1 H), 5.64 (d, J = 12 Hz, 1 H), 5.32 (d, J = 15 Hz, 1 H), 5.25 (d, J = 15 Hz, 1 H), 4.22 (d, J = 4 Hz, 1 H), 3.94 (m, 1 H), 3.45 (d, J = 4 Hz, 1 H, OH), 3.25 (m, after addition of $D_2O$: dd, $J_1$ = 7 Hz, $J_2$ = 10 Hz, 1 H), 2.81 (m, after addition of $D_2O$: dd, $J_1$ = 4 Hz, $J_2$ = 10 Hz, 1 H), 2.58 (t, $J_1$ = 4 Hz, $J_2$ = 6 Hz, 1 H, OH). - Anal. ($C_{14}H_{14}O_5S$) Calcd C,57.13; H,4.79; S,10.89; found C,56.94; H,4.88; S,10.88%. - MS: 294 ($M^+$).

**(3R*)-(±)-3-[(4S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-5,10-dihydrothieno[3.4-c]-[2.5]benzodioxocin-1(3H)-one ((±)8):**

2,2-Dimethoxypropane (0.7 g, 6.7 mmol) and one crystal of PTS were added to a solution of glycol (±)**7a** (295 mg, 1 mmol) in dry dichloromethane (10 ml). After stirring for 6 h at r.t. the volatiles were removed *in vacuo* and the residue triturated with hexane to give (±)**8** as colourless small rods, m.p. 93 °C (hexane/diisopropyl ether). Yield 265 mg (79%). - IR: $\nu$ = 2990 $cm^{-1}$, 2937, 2889, 1680, 1629, 1497, 1468. - UV: $\lambda_{max}$(lg $\epsilon$) = 241 nm (3.936), 268 (3.746). - $^1$H-NMR (d6-benzene): $\delta$ = 6.93 - 6.46 (m, 4 H), 5.23 (d, J = 11 Hz, 1 H), 5.09 (d, J = 11 Hz, 1 H), 5.06 (dd, J = 14 Hz, 2 H), 3.71 (m, 2 H), 3.56 (m, 1 H), 3.31 (d, J = 7 Hz, 1 H), 1.21 (s, 3 H), 1.10 (s, 3 H). - Anal. ($C_{17}H_{18}O_5S$) Calcd C,61.06; H,5.43; S,9.60; found C,61.12; H,5.37; S,9.73%. - MS: 334 ($M^+$).

**X-Ray Crystallographic Analysis Data.** *Crystal data* $C_{17}H_{18}O_5S$, M = 334.4, transparent colourless crystals of size 0.8 x 0.6 x 0.1 mm. Triclinic space group P1, a = 6.523 (4), b = 10.500 (5), c = 12.914 (6) Å, α = 74.48 (2), β = 78.41 (2), γ = 75.70 (2) °, Z = 2, d = 1.359 g/cm$^3$. *Data Collection* All data were collected on a Siemens R3m/V diffractometer with Ni-filtered $CuK_\alpha$ radiation. 2179 unique reflections were collected, of which 1961 satisfied the criterion $F > 4.0\ \sigma(F)$ and were used in the refinement. *Structure Determination and Refinement* The structure was solved by direct methods using SHELXTL[10] and refined by full matrix least square routines [quantity minimized $\Sigma w(F_O-F_C)$]. The hydrogen atoms were calculated from the positions of the carbons to which they are bound (riding model with fixed isotropic U). Anisotropic refinement cycles converged at wR = 6.92 % (with unit weights). Full crystallographic data are available on request from the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.

**(5R*)-(±)-5-[(1S*)-1,2-Dihydroxyethyl]-4-hydroxy-3-(2-methylbenzyloxy)-2(5H)-thiophenone ((±)9):**

$Pd(OH)_2$/C (20 % Pd, 700 mg) was added to a solution of acetonide (±)**8** (335 mg, 1 mmol) in ethyl acetate (50 ml). The mixture was hydrogenated with $H_2$ under atmospheric pressure, filtered under nitrogen through a small pad of Celite and evaporated under reduced pressure. Deketalization furnished (±)**9** as colourless crystals, m.p. 119 °C (diisopropyl ether/ethyl acetate). Yield 213 mg (72%). Thioascorbic acid (±)**14** was isolated by fractional crystallization of the mother liquor. Yield 10 mg (5%). - IR: ν = 3600 - 2200 cm$^{-1}$, 3292, 2920, 1673, 1608, 1494, 1452. - UV: $\lambda_{max}$(lg ε) = 237 nm (3.670), 298 (3.804). - $^1$H-NMR (d6-DMSO): δ = 11.80 (s, 1 H, OH), 7.40 - 7.17 (m, 4 H), 5.06 (s, 1 H, OH), 4.91 (dd, J = 12 Hz, 2 H), 4.32 (d, J = 3 Hz, 1 H), 4.16 (m, 1 H), 3,47 (dd, $J_1$ = 5 Hz, $J_2$ = 10 Hz), 3.24 (dd, $J_1$ = 7 Hz, $J_2$ = 10 Hz), 2.34 (s, 3 H). - Anal. ($C_{14}H_{16}O_5S$) Calcd C,56.74; H,5.44; S,10.82; found C,56.78; H,5.40; S,11.13%. - MS: 296 ($M^+$).

**4-Benzyloxy-3-hydroxy-2(5H)-thiophenone (10):**

A solution of freshly distilled phenyldiazomethane in hexane was added dropwise to an ice-cold methanolic solution of endiol **4** (132 mg, 1 mmol) until nitrogen evolution ceased. After quenching excessive reagent with acetic acid (1 ml) and removal of the volatiles *in vacuo* the residue was chromatographed using 25% ethyl acetate/hexane as eluent affording **10** as pale yellow needles, m.p. 129 °C (hexane/diisopropyl ether). Yield 178 mg (80%). - IR: ν = 3339 cm$^{-1}$, 2952, 1694, 1602, 1499, 1455. - UV: $\lambda_{max}$(lg ε) = 206 nm (3.929), 242 (3.903), 280 (3.946). - $^1$H-NMR ($CDCl_3$): δ = 7.41 - 7.35 (m, 5 H), 5.50 (s, 2 H), 5.38 (s, 1 H, OH), 3.69 (s, 2 H). - Anal. ($C_{11}H_{10}O_3S$) Calcd C,59.44; H,4.53; S,14.43; found C,59.47; H,4.65; S,14.21%. - MS: 222 ($M^+$).

**4-Benzyloxy-(5R*)-(±)-5-[(1S*)-2-(*tert*-butyldimethylsilyloxy)-1-hydroxyethyl]-3-hydroxy-2(5H)-thiophenone ((±)11a):**
**4-Benzyloxy-(5R*)-(±)-5-[(1R*)-2-(*tert*-butyldimethylsilyloxy)-1-hydroxyethyl]-3-hydroxy-2(5H)-thiophenone ((±)11b):**

These compounds were synthesized in the same manner as (±)**6** employing diisopropylamine

(1.41 ml, 10 mmol), *n*-butyllithium (6.25 ml of a 1.6 M solution in hexane, 10 mmol), benzyl ether **10** (1.11 g, 5 mmol) and *tert*-butyldimethylsilyloxy acetaldehyde (0.87 g, 5 mmol). Chromatographic separation using 20% ethyl acetate/hexane as eluent afforded (±)**11a** and (±)**11b**.

(±)**11a**: Colourless needles, m.p. 133 °C (hexane/diisopropyl ether). Yield 1.34 g (68%). - IR: ν = 3313 $cm^{-1}$, 2928, 2857, 1691, 1605, 1559, 1469. - UV: $\lambda_{max}$(lg ε) = 242 nm (3.961), 284 (3.878). - $^1$H-NMR ($CDCl_3$): δ = 7.42 - 7.36 (m, 5 H), 5.54 (s, 2 H), 5.32 (s, 1 H, OH), 4.27 (m, 1 H), 4.19 (d, J = 2 Hz, 1 H), 3.74 (dd, $J_1$ = 4 Hz, $J_2$ = 10 Hz, 1 H), 3.64 (dd, $J_1$ = 5 Hz, $J_2$ = 10 Hz, 1 H), 2.30 (d, J = 8 Hz, 1 H, OH), 0.87 (s, 9 H), 0.06 (s, 6 H). - Anal. ($C_{19}H_{28}O_5SSi$) Calcd C,57.54; H,7.12; S,8.08; found C,57.37; H,7.18; S,7.76%. - MS: 396 ($M^+$).

(±)**11b**: Colourless needles, m.p. 95 °C (hexane). Yield 0.22 g (11%). - IR: ν = 3379 $cm^{-1}$, 2952, 2925, 2890, 2854, 1685, 1611, 1498, 1468. - UV: $\lambda_{max}$(lg ε) = 243 nm (3.940), 284 (3.842). - $^1$H-NMR ($CDCl_3$): δ = 7.39 - 7.34 (m, 5 H), 5.50 (dd, J = 12 Hz, 2 H), 5.22 (s, 1 H, OH), 4.38 (d, J = 6 Hz, 1 H), 4.19 (m, 1 H), 3.52 (m, 2 H), 2.91 (s, 1 H, OH), 0.87 (s, 9 H), 0.04 (s, 6 H). - Anal. ($C_{19}H_{28}O_5SSi$) Calcd C,57.54; H,7.12; S,8.08; found C,57.72; H,6.93; S,7.81%. - MS: 396 ($M^+$).

**4-Benzyloxy-(5R*)-(±)-5-[(1S*)-1,2-dihydroxyethyl]-3-hydroxy-2(5H)-thiophenone ((±)12a)**:

Desilylation according to the procedure described for (±)**7** employing *threo*-aldol (±)**11a** (400 mg, 1 mmol) gave (±)**12a** as colourless crystals, m.p. 106 °C (diethyl ether). Yield 226 mg (80%). - IR: ν = 3283 $cm^{-1}$, 2938, 1690, 1619, 1500, 1454. - UV: $\lambda_{max}$(lg ε) = 241 nm (3.949), 284 (3.881). - $^1$H-NMR (d3-acetonitrile): δ = 7.46 - 7.36 (m, 5 H), 6.19 (s, 1 H, OH), 5.53 (d, J = 12 Hz, 1 H), 5.46 (d, J = 12 Hz, 1 H), 4.28 (d, J = 2 Hz, 1 H), 4.16 (m, 1 H), 3.56 (dd, $J_1$ = 6 Hz, $J_2$ = 11 Hz, 1 H), 3.43 (dd, $J_1$ = 7 Hz, $J_2$ = 11 Hz, 1 H), 3.03 (s, 1 H, OH). - Anal. ($C_{13}H_{14}O_5S$) Calcd C,55.31; H,5.00; S,11.36; found C,55.23; H,5.09; S,11.08%. - MS: 282 ($M^+$).

**4-Benzyloxy-(5R*)-(±)-5-[(1R*)-1,2-dihydroxyethyl]-3-hydroxy-2(5H)-thiophenone ((±)12b)**:

This compound was prepared in the same manner as (±)**7** from *erythro*-aldol (±)**11b** (400 mg, 1 mmol) affording (±)**12b** as colourless crystals, m.p. 118 °C (diethyl ether). Yield 215 mg (76%). - IR: ν = 3434 $cm^{-1}$, 2876, 1686, 1591, 1499, 1455. - UV: $\lambda_{max}$(lg ε) = 243 nm (3.946), 285 (3.882). - $^1$H-NMR (d3-acetonitrile): δ = 7.45 - 7.36 (m, 5 H), 6.20 (s, 1 H, OH), 5.51 (d, J = 12 Hz, 1 H), 5.44 (d, J = 12 Hz, 1 H), 4.37 (d, J = 4 Hz, 1 H), 4.18 (m, 1 H), 3.54 (m, 2 H), 2.79 (s, 1 H, OH). - Anal. ($C_{13}H_{14}O_5S$) Calcd C,55.31; H,5.00; S,11.36; found C,55.34; H,4.96; S,11.26%. - MS: 282 ($M^+$).

**4-Benzyloxy-(5R*)-(±)-5-[(4S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-hydroxy-2(5H)-thiophenone ((±)13)**:

2,2-Dimethoxypropane (0.7 g, 6.7 mmol) and one crystal of PTS were added to a solution of *threo*-glycol (±)**12a** (282 mg, 1 mmol) in anhydrous dichloromethane (20 ml). After stirring for 1 h at r.t. the volatiles were removed *in vacuo* and the residue was filtered through a small pad of silica gel using 33% ethyl acetate/hexane as eluent to afford (±)**13** as colourless needles, m.p. 87 °C (hexane). Yield 260 mg (81%). - IR: ν = 3361 $cm^{-1}$, 2989, 2872, 1694, 1614, 1499, 1455. - UV: $\lambda_{max}$(lg ε) = 241 nm (3.949), 283 (3.870). - $^1$H-NMR ($CDCl_3$): δ = 7.42 - 7.35 (m, 5 H), 5.53 (d, J = 12 Hz, 1 H), 5.49 (d, J = 12 Hz, 1 H), 5.37 (s, 1 H, OH), 4.19 (m, 1 H), 4.12 (dd, $J_1$ = 7 Hz, $J_2$ = 9 Hz,

1 H), 4.03 (d, $\underline{J}$ = 8 Hz, 1 H), 3.93 (dd, $\underline{J}_1$ = 6 Hz, $\underline{J}_2$ = 9 Hz, 1 H), 1.41 (s, 3 H), 1.33 (s, 3 H). - Anal. ($C_{16}H_{18}O_5S$) Calcd C,59.61; H,5.63; S,9.95; found C,59.61; H,5.63; S,9.83%. - MS: 322 ($M^+$).

**(5R*)-(±)-5-[(1S*)-1,2-Dihydroxyethyl]-3,4-dihydroxy-2(5H)-thiophenone ((±)14):**

2N Hydrochloric acid (0.55 ml, 1.1 mmol) was added under $N_2$ to a solution of endiol (±)**17** (232 mg, 1 mmol) in freshly distilled methanol (10 ml). The mixture was left at r.t. for 12 h, evaporated under reduced pressure and the residue dried at ambient temperature for 2 h under high vacuum. The remaining crystalline mass was washed once with a small amount of ice-cold methanol to give (±)**14** as colourless crystals, m.p. 172 - 173 °C (benzene/methanol, dec.). Yield 154 mg (80%). - IR: ν = 3600 - 2200 $cm^{-1}$, 1705, 1623, 1474, 1452. - UV: $\lambda_{max}$(lg ε) = 240 nm (3.879), 288 (3.717). - $^1$H-NMR (d6-DMSO): δ = 8.41 (s, 1 H, OH), 4.92 (s, 1 H, OH) 4.24 (d, $\underline{J}$ = 2 Hz, 1 H), 4.10 (m, 1 H), 3.47 (dd, $\underline{J}_1$ = 6 Hz, $\underline{J}_2$ = 11 Hz, 1 H), 3.26 (dd, $\underline{J}_1$ = 7 Hz, $\underline{J}_2$ = 11 Hz, 1 H).- $^{13}$C-NMR ($D_2O$): δ = 194.3 (C-2), 161.5 (C-4), 129.8 (C-3), 69.3 (CH), 64.5 ($CH_2$), 47.5 (C-5). - Anal. ($C_6H_8O_5S$) Calcd C,37.50; H,4.20; S,16.68; found C,37.52; H,4.18; S,16.44%. - MS: 192 ($M^+$).

**(5R*)-(±)-5-[(1S*)-1,2-Dihydroxyethyl]-3-hydroxy-4-methoxy-2(5H)-thiophenone ((±)15):**

On cooling a suspension of thioascorbic acid (±)**14** (192 mg, 1 mmol) in a 25% methanol/diethyl ether mixture (20 ml) to -10 °C under $N_2$ etherical diazomethane solution was added dropwise, monitoring the reaction by TLC. The slightly yellow solution was evaporated under reduced pressure and the residue dissolved in a minimum amount of ether. On cooling (±)**15** separated as colourless needles, m.p. 111 °C (diethyl ether/ethyl acetate). Yield 184 mg (89%). - IR: ν = 3377 $cm^{-1}$, 2966, 2929, 1692, 1601, 1458. - UV: $\lambda_{max}$(lg ε) = 243 nm (3.893), 284 (3.776). - $^1$H-NMR (d3-acetonitrile): δ = 6.06 (s, 1 H, OH), 4.35 (d, $\underline{J}$ = 4 Hz, 1 H), 4.15 (m, 1 H), 4.11 (s, 3 H), 3.58 (s, 1 H, OH), 3.46 (m, 2 H), 2.85 (s, 1 H, OH). - Anal. ($C_7H_{10}O_5S$) Calcd C,40.77; H,4.89; S,15.55; found C,40.67; H,4.99; S,15.84%. - MS: 206 ($M^+$).

**(5R*)-(±)-5-[(1S*)-1,2-Dihydroxyethyl]-3,4-dimethoxy-2(5H)-thiophenone ((±)16):**

A slight excess of diazomethane solution was added to a methanolic solution of thioascorbic acid (±)**14** (192 mg, 1 mmol). After 1 h at r.t. the volatiles were evaporated *in vacuo* and the residue was chromatographed using 25% acetonitrile/diisopropyl ether as eluent affording (±)**16** as colourless needles, m.p. 106 °C (ether). Yield 165 mg (75%). - IR: ν = 3396 $cm^{-1}$, 3292, 2942, 2919, 2874, 1671, 1616, 1451. - UV: $\lambda_{max}$(lg ε) = 240 nm (3.986), 269 (3.738). - $^1$H-NMR ($CDCl_3$): δ = 4.25 (d, $\underline{J}$ = 5 Hz, 1 H), 4.18 (s, 3 H), 4.17 (m, 1H), 3.80 (s, 3 H), 3.69 (m, 2 H), 2.37 (d, $\underline{J}$ = 9 Hz, 1 H, OH), 2.04 (s, 1 H, OH). - Anal. ($C_8H_{12}O_5S$) Calcd C,43.63; H,5.49; S,14.56; found C,43.70; H,5.42; S,14.20%. - MS: 220 ($M^+$).

**3,4-Dihydroxy-(5R*)-(±)-5-[(4S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2(5H)-thiophenone ((±)17):**

Benzyl ether (±)**13** (600 mg, 1.86 mmol) in ethyl acetate (100 ml) was added to a pre-reduced suspension of $Pd(OH)_2$/C (20% Pd, 2.0 g) in ethyl acetate (300 ml). The resulting mixture was hydrogenated under atmospheric pressure for 4 h. Filtration through a small pad of Celite under $N_2$ followed by removal of the solvent *in vacuo* yielded (±)**17** as colourless needles, m.p. 155 °C

(diisopropyl ether). Yield 360 mg (83%). - IR: ν = 3322 $cm^{-1}$, 2991, 2935, 2863, 1694, 1609, 1459. - UV: $\lambda_{max}$(lg ε) = 240 nm (3.813), 291 (3.614). - $^1$H-NMR (d3-acetonitrile): δ = 7.24 (s, 1 H, OH), 4.40 (m, 1 H), 4.26 (d, J = 7 Hz, 1 H), 4.23 (dd, $J_1$ = 7 Hz, $J_2$ = 9 Hz, 1 H), 3.91 (dd, $J_1$ = 6 Hz, $J_2$ = 9 Hz, 1 H), 1.42 (s, 3 H), 1.35 (s, 3 H).- $^{13}$C-NMR (d3-acetonitrile): δ = 188.7 (C-2), 155.2 (C-4), 130.2 (C-3), 109.0 (O-C-O), 75.8 (CH), 67.7 ($CH_2$), 46.5 (C-5), 25.4 ($CH_3$), 24.4 ($CH_3$). - Anal. ($C_9H_{12}O_5S$) Calcd C,46.54; H,5.21; S,13.81; found C,46.55; H,5.32; S,13.57%. - MS: 232 ($M^+$).

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9. Experimental conditions: 0.1 N $Ce(SO_4)_2$, $H_2O$, $N_2$, 20 °C, combined redox-electrode Pt *vs.* Ag / AgCl (Fa. Ingold), acetate buffer solution pH 4.90. In an identical manner the electrode potential for the redox pair $Fe^{2+}/Fe^{3+}$ in a half-oxidized solution was estimated to $E_P$ = 0.149 V corresponding to a real potential $E_R$ = 0.653 V.
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