# Optically Active Epoxy Diols by Titanium-Catalyzed Oxidation of Enantiomerically Enriched Hydroperoxy and Hydroxy Homoallylic Alcohols

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The Ti-catalyzed epoxidation of optically active (*S*,*S*)-hydroperoxy homoallylic alcohols **2** affords the epoxy diol (*S*,*R*,*S*)-**4** in high diastereoselectivity (d.r. up to 95:5), while the optically active hydroxy homoallylic alcohols (*R*,*R*)-**3** are epoxidized by the β-hydroperoxy alcohol **5** under titanium catalysis to the corresponding epoxy (*R*,*S*,*R*)-diol **4** in a diastereomeric ratio up to > 99:1. This high diastereoselectivity is rationalized in terms of a rigid template for the oxygen transfer, in which the hydroperoxy alcohol **2** or **5** is ligated tridentately and the diol **3** bound bidentately to the titanium metal. Through these oxidative routes, both enantiomeric epoxy diols **4** are conveniently accessible.

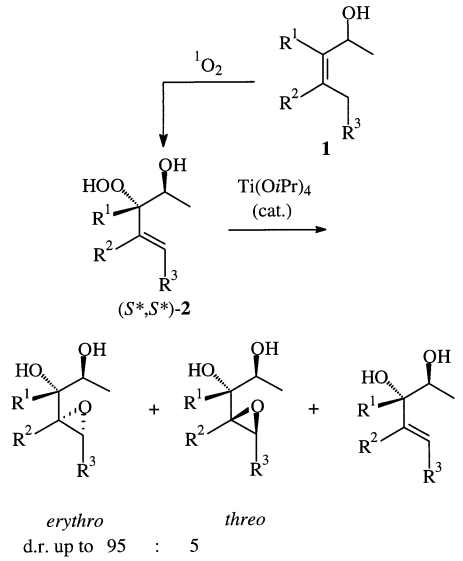
## Introduction

The enormous potential of epoxy alcohols as building blocks in organic synthesis[1] has led to numerous methods for their preparation. Practical routes utilize the metal-catalyzed epoxidations of allylic alcohols with hydroperoxides, among which the enantioselective Sharpless reaction[2] is the most valuable one. With this method, epoxy alcohols of defined configuration are produced, which are especially useful for the synthesis of highly functionalized natural products.[1][3] We have reported on an alternative stereoselective oxyfunctionalization, which starts with the conversion of allylic alcohols **1** to hydroperoxy homoallylic alcohols (alias hydroperoxy alcohols) **2** by photooxygenation. The latter are subsequently transformed under Ti catalysis into the epoxy diols **4** in high *erythro* diastereoselectivity (Scheme 1)[4]. In this epoxy hydroxylation, which may be conducted as a one-pot, two-step synthesis, the actual epoxidized substrate is the hydroxy homoallylic alcohol (alias diol) **3**, which is generated in situ from the hydroperoxy alcohol **2** by oxygen transfer during the Ti-catalyzed epoxidation. Thus, the hydroperoxide **2** plays the double role as oxygen donor and, after oxygen transfer, as oxygen acceptor. By this route, the regio- and diastereoselective introduction of up to three chirality centers in successively adjacent positions to the already existing stereogenic one of the allylic alcohol moiety is realized in predictable stereochemistry.

Another highly stereoselective epoxidation reaction involves the Ti-catalyzed oxidation of diols **3** with β-hydroperoxy alcohols. Also in this case the formation of an *erythro*-epoxy diol **4** (d.r. up to > 95:5) is favored[5].

Recently we showed[6] that optically active hydroperoxy (**2**) and hydroxy (**3**) homoallylic alcohols are readily accessible in preparative amounts by enzymatic kinetic resolution of the racemic hydroperoxy alcohol **2** with horseradish peroxidase (HRP). We now report on the synthesis of both enantiomers of the epoxy diols **4** by employing the enantiomerically enriched substrates **2** and **3** in the above-mentioned Ti-catalyzed, diastereoselective epoxidations.

Scheme 1





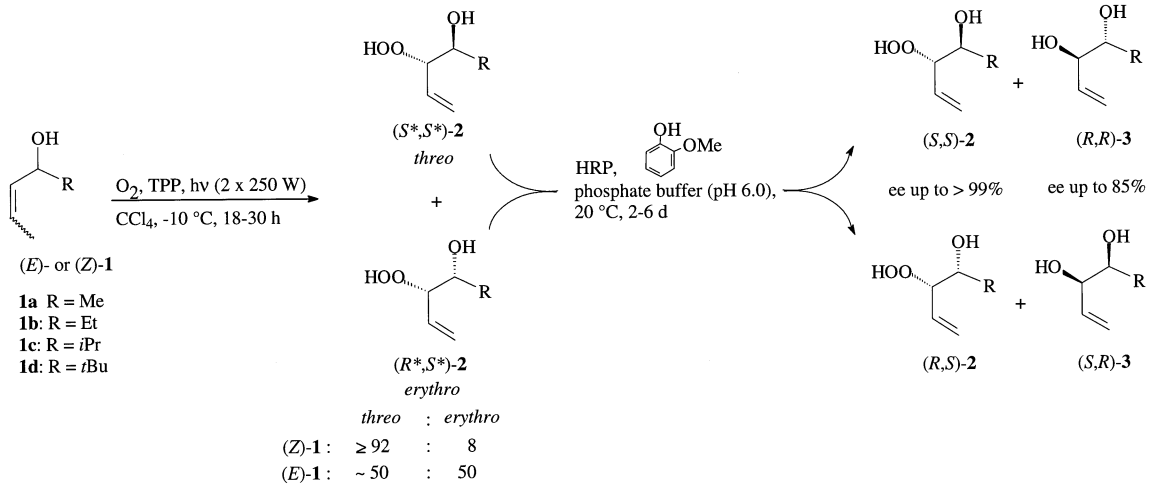
Structures **4**

  1434−193X/98/0505−0907 $ 17.50+.50/0 

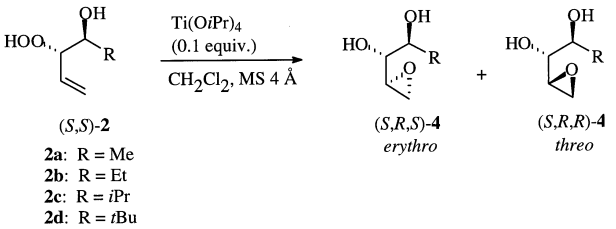
## Results and Discussion

By photooxygenation of the alcohols **1**, the hydroperoxy alcohols **2** were conveniently obtained (Scheme 2). As already described in the literature[7], in this reaction the (*Z*)-allylic alcohols **1** afford the (*S**,*S**)-hydroperoxy alcohols **2** as the main diastereomer in a high *threo* selectivity (d.r. ≥ 92 : 8), whereas the (*E*)-allylic alcohols **1** react totally unselectively. The subsequent enzymatic kinetic resolution of the racemic hydroperoxy alcohols **2** with horseradish peroxidase (HRP) on the preparative scale (Scheme 2) led to the optically active hydroperoxy alcohols **2** in an enantiomeric excess up to > 99% and the diols **3** up to 85%. For the Ti-catalyzed direct epoxidation, the (*S*,*S*)-hydroperoxy homoallylic alcohols **2** were used in a ratio (*S*,*S*)-**2**/(*R*,*S*)-**2** ratio of ≥ 92:8 (Scheme 3).

Scheme 2




Scheme 3




To assess a possible temperature effect on the diatereoselectivity of the oxygen transfer, the epoxidation of the *threo* diastereomer (*S*,*S*)-**2** was carried out between −25 and +20°C. As shown in Table 1, the oxidation of the methyl-substituted hydroperoxy alcohol (*S*,*S*)-**2a** gave at −25°C (entry 2) the same *erythro* selectivity [(*S*,*R*,*S*)-**4a**/(*S*,*R*,*R*)-**4a** = 93:7] for the epoxy diol **4a** as described in literature[4b] for the racemic **4a** (d.r. 91:1, entry 1). When this epoxidation was conducted at 20°C (entry 4), the reaction time for 100% conversion was drastically reduced from four days to only two hours, while the diastereoselectivity slightly decreased to 87:13. Also on the analytical scale (entry 3), the oxidation at 20°C gave a similar selectivity (d.r. 84:16). Larger alkyl groups, namely ethyl, isopropyl, and *tert*-butyl, in the hydroperoxy alcohol (*S*,*S*)-**2b**−**d** also led to high *erythro* selectivities[8] at −25°C (entries 5, 7, and 9), the highest (95:5) one for the isopropyl derivative **2c** (entry 7). Again, at the higher reaction temperature of 20°C (entries 6, 8, and 10), the reaction time decreased dramatically from three days to only about two hours, with no change in the (*S*,*R*,*S*)/(*S*,*R*,*R*)-ratio.

To obtain the *erythro*-configured (*R*,*S*)-4-hydroperoxy-5-hexen-3-ol (**2b**), a 50:50 mixture of the *erythro*/*threo* diastereomers of **2b** was chemically separated by means of Ti-catalyzed epoxidation. Since the *threo* isomer (*S*,*S*)-**2b** reacts much faster to the epoxy diol **4** than the *erythro* one (*R*,*S*)-**2b**, the latter is left behind. Because of the reduced reactivity of the *erythro* diastereomer (*R*,S)-**2b**, a higher reaction temperature (−2°C instead of −25°C) was necessary for its Ti-catalyzed epoxidation (entry 11). After a reaction time of three days, the hydroperoxy alcohol (*R*,*S*)-**2b** was fully converted to afford the epoxy diol **2b**, but in a rather low *erythro* diastereoselectivity, i.e. the (*R*,*R*,*S*)-**2b**/(*R*,*R*,*R*)-**2b** ratio was 62:38.

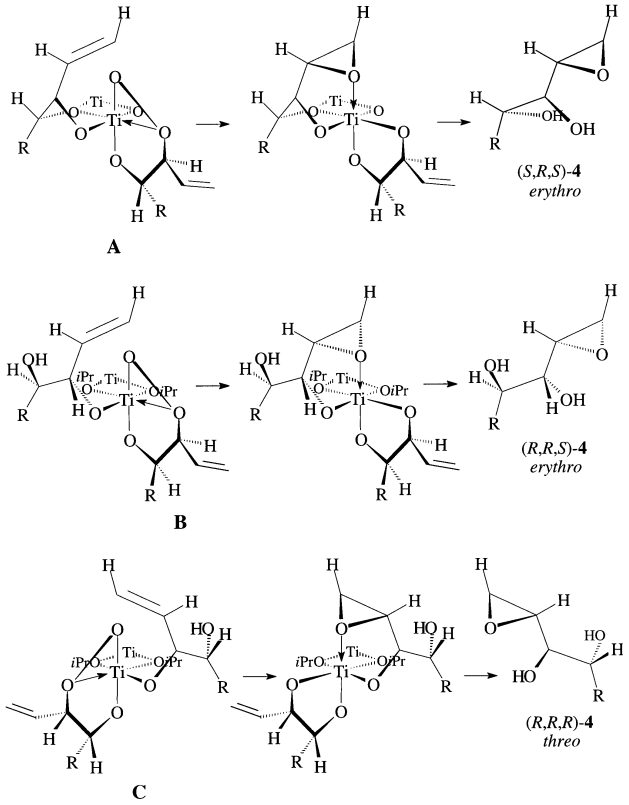
The high stereocontrol for the epoxidation of the hydroperoxy alcohol (*S*,*S*)-**2** is dictated by the rigid template **A** (Figure 1), in which the hydroperoxy alcohol **2** (the oxygen donor) is bound tridentately and the *in-situ*-formed unsaturated *threo* diol (*S*,*S*)-**3** (the oxygen acceptor[9]) is ligated bidentately to the titanium-metal center.[4b] The observed *erythro* selectivity results from the additional bonding of the homoallylic hydroxy group of the *threo* diol (*S*,*S*)-**3** to the titanium metal. This fixes the conformation and the oxygen transfer occurs preferentially from the π face with the allylic oxygen functionality in diol (*S*,*S*)-**3** arranged *syn* to afford mainly the *erythro* epoxide (*S*,*R*,*S*)-**4** (Table 1, entries 1−10). In contrast, the *erythro* diol (*R*,*S*)-**3b** is only monodentately ligated to the titanium metal in the metal templates **B** and **C** (Figure 1) because of unfavorable steric interactions between the ethyl and isoprenyl groups, as shown by the pertinent Newman projections in Figure 2.

Table 1. Reaction conditions and diastereoselectivity of the Ti-catalyzed epoxidation of (*S*,*S*)-**2** and (*R*,*S*)-**2b**

| entry | hydroperoxy alcohol **2** *R* | ee [%] | temperature [° C] | time [h] | yield[a] [%] | epoxy diol **4** *erythro*/*threo*[b] |
|---|---|---|---|---|---|---|
| | (*S*,*S*)-**2** (*threo*) | | | | | |
| 1 | Me (**2a**) | 0 | −25 | 48 | 59 | 91:9[c] |
| 2 | | 64 | −25 | 96 | 35 | 93:7 |
| 3 | | 0 | 20 | 2 | [d] | 84:16 |
| 4 | | 74 | 20 | 2 | 33 | 87:13 |
| 5 | Et (**2b**) | >99 | −25 | 72 | 71 | 91:9 |
| 6 | | >99 | 20 | 2.5 | 52 | 88:12 |
| 7 | *i*Pr (**2c**) | >99 | −25 | 74 | 54 | 95:5 |
| 8 | | >99 | 20 | 1 | 51 | 91:9 |
| 9 | *t*Bu (**2d**) | 89 | −25 | 72 | 58 | 91:9 |
| 10 | | 89 | 20 | 1 | 50 | 91:9 |
| | (*R*,*S*)-**2** (*erythro*) | | | | | |
| 11 | Et (**2b**) | 99 | −2 | 72 | 54 | 62:38 |

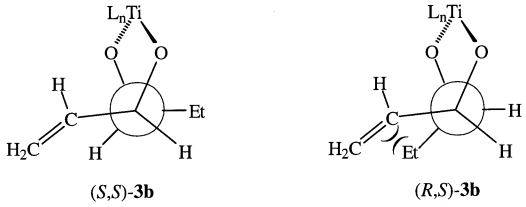
[a] Yield of isolated epoxy diol **4** after silica-gel chromatography, additionally 5−10% of the diol **3** were obtained; conversion in all cases ≥ 95%. − [b] Determined by $^1$H-NMR analysis of the isolated products **4b−d** (600 MHz spectra) or of the crude product mixture of **4a**, error ± 5%. − [c] Value from ref.[4b]. − [d] Reaction on analytical scale in $CDCl_3$.

Figure 1. Bidentate (**A**) and monodentate (**B**, **C**) ligation of the unsaturated diol **3** as the oxygen acceptor in the metal templates for the Ti-catalyzed epoxidation of the hydroperoxy alcohols (*S*,*S*)- and (*R*,*S*)-**2**



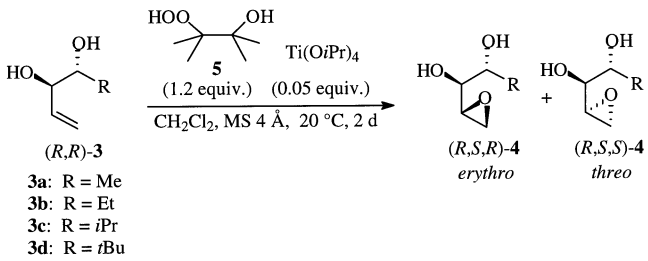

Consequently, unselective oxygen transfer would be expected, since now the epoxidation may occur by way of the template **B** leads to the *erythro* product (*R*,*R*,*S*)-**4b**, Figure 1] and template **C** leads to the *threo* product (*R*,*R*,*R*)-**4b**]. This is confirmed by the (*R*,*R*,*S*)-**4b : (***R*,*R*,*R*)-**4b** ratio of 62 : 38 (Table 1, entry 11).

Figure 2. Steric interactions in the titanium template for the bidentately ligated *erythro* and *threo* diols (*R*,*S*)-**3b** and (*S*,*S*)-**3b**




While the epoxy diols (*S*,*R*,*S*)-**4** are accessible directly by the above highly diastereoselective hydroxy epoxidation of hydroperoxy alcohols (*S*,*S*)-**2,** this method is inadequate for preparing the corresponding (*R*,*S*,*R*)-**4** enantiomer. Fortunately, for the latter the highly diastereoselective epoxidation of the optically active diols (*R*,*R*)-**3** by 3-hydroperoxy-2,3-dimethyl-2-butanol (**5**) has recently become available[5] (Scheme 4).

Scheme 4




This modified Sharpless-type epoxidation may be conducted at 20°C, since the diastereoselectivity does not improve at lower temperatures[5a].

When the methyl-substituted diol (*R*,*R*)-**3a** was epoxidized with the β-hydroperoxy alcohol **5** (Table 2, entry 2), the epoxy diol (*R*,*S*,*R*)-**4a** was obtained in high (d.r. 91:9) *erythro* selectivity. This reaction was repeated with the racemic diol **3a** to confirm the observed diastereoselectivity of the oxygen transfer (Table 2, entry 1). The increase in steric demand of the alkyl groups in (*R*,*R*)-**3** led to a slight raise of the diastereoselectivity for the ethyl-substituted diol (*R*,*R*)-**3b** (d. r. 94:6, Table 2, entry 3) and reached a maximum [d.r. > 99:1, with only traces of the minor diastereomer (*R*,*S*,*S*)-**3c**] for the isopropyl derivative (*R*,*R*)-**3c** (Table 2, entry 4). For the *tert*-butyl-substituted diol (*R*,*R*)-**3d,** the diastereomeric ratio (*R*,*S*,*R*)-**4d**/(*R*,*S*,*S*)-**4d** is marginally reduced to 95:5 (Table 2, entry 5) compared to the isopropyl derivative **4c**.

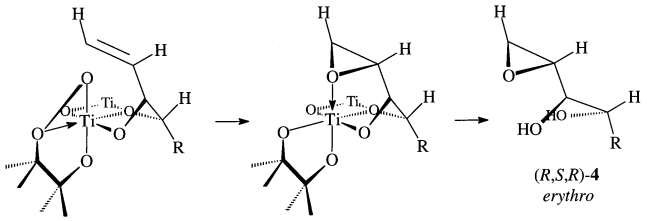
Table 2. Epoxidation of the optically active diols (*R*,*R*)-3 with 3-hydroperoxy-2,3-dimethyl-2-butanol (**5**)

| entry | diol (*R*,*R*)-**3** R | | ee [%] | yield[a] [%] | epoxy diol **4** *erythro*/*threo*[b] |
|---|---|---|---|---|---|
| 1 | Me | (**3a**) | 0 | 50 | 91:9 |
| 2 | Me | (**3a**) | 43 | 51 | 91:9 |
| 3 | Et | (**3b**) | 85 | 57[c] | 94:6 |
| 4 | *i*Pr | (**3c**) | 81 | 61[c] | > 99:1 |
| 5 | *t*Bu | (**3d**) | 54 | 84 | 95:5 |

[a] Yield of isolated epoxy diol **4** after silica-gel chromatography, conversion in all cases ≥ 95%. – [b] Determined by $^1$H-NMR analysis (600 MHz spectra) of the crude product mixture of **4**, error ± 5%. – [c] Epoxy diol **4** was isolated together with small amounts of 2,3-dimethyl-2,3-diol, the reduction product of **5**.

Again, this high *erythro* selectivity is due to the favorable bidentate ligation of the (*R*,*R*)-**3** diol to the titanium center in the metal template (Figure 3). This fixes the conformation in the rigid transition state for oxygen tranfer.

Figure 3. Metal template in the Ti-catalyzed epoxidation of diol (*R*,*R*)-**3** with 2,3-dimethyl-3-hydroperoxy-2-butanol (**5**) as oxygen donor




## Conclusion

The Ti-catalyzed epoxidation of optically active hydroperoxy homoallylic alcohols (*S*,*S*)-**2** and the oxidation of the hydroxy homoallylic alcohols (*R*,*R*)-**3** with the β-hydroperoxy alcohol **5** afford in each case an *erythro* epoxy diol **4** in high diastereoselectivity (d.r. ≥ 90:10). This high *erythro* selectivity derives from the rigid titanium templates for the oxygen transfer in which the oxygen acceptor, the diols **3,** are bidentately bound. In this way, both enantiomeric epoxy diols, namely (*S*,*R*,*S*)-**4** and (*R*,*S*,*R*)-**4**, have been made available in optically active form, which should serve as valuable building blocks in organic synthesis.

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## Experimental Section

*General:* For the epoxidation reactions, all glasware was dried under vacuum (ca. 150°C/0.1 Torr) and all reactions were run under an argon-gas atmosphere. $CH_2Cl_2$ was distilled under an argon-gas atmosphere from calcium hydride. Molecular sieves (4 Å) were activated under vacuum (ca. 200°C/0.1 Torr). Horseradish peroxidase was purchased from Sigma (RZ = 2.0, activity: 190 U/mg) or donated from Boehringer Mannheim (activity: 256 U/mg). The hydroperoxy homoallylic alcohols **2** were synthesized as previoulsly described.[7a]

*Enantiomeric excesses* of the diols **3** were determined by MDGC on a (2,3,6-tri-*O*-methyl)-β-cyclodextrin column in DB 1701 (25 m × 0.25 mm), temperature program 80°C → 1°C/min → 90°C for **3a** and 80°C → 1°C/min → 100°C for **3b–d** with hydrogen as carrier gas. In all cases, the (*S*,*S*)- **3** enantiomer eluted before the (*R*,*R*) one and (*S*,*R*)-**3b** before (*R*,*S*)-**3b**. The hydroperoxy alcohols **2** were reduced with $Ph_3P$ in $CH_2Cl_2$ (20°C, 10 min) to the corresponding diols **3** prior to GC analysis.

IR: FT-IR Perkin-Elmer 1600. – NMR: Bruker AC 200, Bruker AC 250, Bruker DMX 600 (600 MHz). – HPLC: Kontron 322 (pumps), Kontron UVIKON 720 LC micro (detektor). – GC: Fisons HRGC Mega 2 series 8560.

*General Procedure for the Resolution of Hydroperoxy Alcohols* **2** *with HRP:* To 300 ml of a 0.02–0.045 M solution of the racemic hydroperoxy alcohol **2** in 0.1 M phosphate buffer (pH 6.0) was added 1.0 equiv. guaiacol and HRP (3000–5000 U/mmol substrate). After stirring for 2–3 d at room temperature (ca. 20°C), 2–3 ml of the mixture were extracted with ethyl ether (5 × 2 ml), dried over $MgSO_4$, and the solvent was evaporated (20°C/20 Torr). After separation of the hydroperoxy alcohol **2a–c** from the diol **3a–c** by flash chromatographie [silica gel, 1:1 petroleum ether (30–50°C)/ethyl ether] or by preparative HPLC [compounds **2d** and **3d** (LiChrosorb Diol column, 250 × 4 mm, eluent: *n*-hexane/MTB, 80:20, flow: 1.0 ml/min, detection at 205 nm)], the enantiomeric excess of the hydroperoxy alcohols (*S*,*S*)-**2** or (*R*,*S*)-**2b** and the diols (*R*,*R*)-**3** or (*S*,*R*)-**3b** were determined by MDGC as described above. If the ee values for the hydroperoxides **2** were still low, another batch of HRP (4000–5000 U) were added and the ee values determined again after another 1–2 d reaction time. For the work-up, the reaction mixture was extracted with the 2–3 fold volumes of ethyl ether. After the organic phase was centrifugated to remove polymeric guaiacol products, it was dried over $MgSO_4$, and the solvent was evaporated (20°C/20 Torr). The hydroperoxy alcohols **2a–c** and the diols **3a–c** were isolated by flash chromatography [silica gel, started at 1:1 and then 1:2 petroleum ether (30–50°C)/ethyl ether] and **2d** and **3d** by MPLC (2 × 20-cm column, LiChroprep Si 60 silica gel from Merck as adsorbent, 80:20 *n*-hexane/MTB as eluent, at 10 bar pressure). The spectral data match those reported[7a][9], the values of the optical rotations are given in ref.[10].

*(3R,4S)-4-Hydroperoxy-5-hexen-3-ol* (**2b**): To a solution of 195 mg (2.23 mmol) of optically active 4-hydroperoxy-5-hexen-3-ol (**2b**) [50:50 (3*S*,4*S*)-**2b**/(3*R*,4*S*)-**2b** ratio] in 8 ml $CH_2Cl_2$ was added 63.4 mg (22.3 μmol, 65.8 μl) of Ti(O*i*Pr)$_4$ at –25°C. After stirring for 12 h over molecular sieves (4 Å) at –25°C, a 90:10 (3*R*,4*S*)-**2b**/(3*S*,4*S*)-**2b** ratio was determined by $^1$H-NMR analysis of the reaction mixture. For work-up, the Ti catalyst was destroyed by the

addition of 220 µl water and stirred for 1 h at room temperature (ca. 20°C). After removal of the suspended material by filtration und thorough washing of the residue with $CH_2Cl_2$ (5 × 1 ml), the solvent was evaporated (20°C/20 Torr). By flash chromatography [silica gel, 1:1 petroleum ether (30−50°C)/ethyl ether as eluent], the remaining (3*S*,4*S*)-**2b** was separated from the (3*R*,4*S*)-**2b** to yield 49.0 mg (33%) of the hydroperoxy alcohol (3*R*,4*S*)-**2b** (ee 99%) as colorless oil, $[\alpha]_D^{20} = -9$ (*c* = 1.1 in $CHCl_3$, for ee > 99%). − IR (neat): $\tilde{\nu}$ = 3385 $cm^{-1}$ (OH), 2968, 2926, 2884, (CH), 1644 (C=C), 1457, 1425, 1311, 1253, 1123, 1055, 972, 920, 847. − $^1$H NMR ($CDCl_3$, 200 MHz): δ = 0.99 (t, *J* = 7.4 Hz, 3 H, $CH_3$), 1.41 − 1.59 (m, 2 H, $CH_2$), 2.25 (br. s, 1 H, OH), 3.87 (ddd, *J* = 7.4 Hz, *J* = 5.8 Hz, *J* = 3.2 Hz, 1 H, C*H*OH), 4.35 (dd, *J* = 7.9 Hz, *J* = 3.2 Hz, 1 H, C*H*OOH), 5.41 (d, *J* = 11.1 Hz, 1 H, CH=C$H_2$), 5.44 (d, *J* = 16.6 Hz, 1 H, CH=C$H_2$), 5.92 (ddd, *J* = 16.6 Hz, *J* = 11.1 Hz, *J* = 7.9 Hz, 1 H, C*H*=$CH_2$), 8.57 (br. s, 1 H, OOH). − $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 10.1 (q, C-1), 25.4 (t, C-2), 72.7 (d, C-3), 89.5 (d, C-4), 121.9 (t, C-6), 131.6 (d, C-5). − $C_6H_{12}O_3$ (132.2): calcd.C 54.53, H 9.15; found: C 54.14 , H 9.21.

*General Procedure for the Ti-Catalyzed Epoxidation of Hydroperoxy Alcohols* (*S*,*S*)-**2 and** (*R*,*S*)-**2b**: To a solution of 0.112−1.02 mmol of (*S*,*S*)- or (*R*,*S*)-hydroperoxy alcohols **2** in 0.5−2 ml $CH_2Cl_2$ was added 0.1 equiv. of Ti(O*i*Pr)$_4$ at 20 or −25°C [for reactions with (*S*,*S*)-**2**] or −2°C [for the reaction with (*R*,*S*)-**2b**]. After stirring over molecular sieves (4 Å) for the time stated in Table 1, satd. aqueous $NH_4F$ solution (1 ml/mmol Ti) was added and the mixture was worked up as described in the synthesis of (3*R*,4*S*)-4-hydroperoxy-5-hexen-3-ol (**2b**). The epoxy diols **4** were isolated by flash chromatography [silica gel, 1 : 3 petroleum ether (30−50°C)/ ethyl ether as eluent].

*General Procedure for the Epoxidation of the (R,R)-Diols* **3** *with 3-Hydroperoxy-2,3-dimethyl-2-butanol* (**5**): To a solution of 0.111−1.00 mmol of (*R*,*R*)-diol **3** and 1.2 equiv. of 2,3-dimethyl-3-hydroperoy-2-butanol (**5**) in 1−10 ml of $CH_2Cl_2$ was added 0.05 equiv. of Ti(O*i*Pr)$_4$. The mixture was stirred over molecular sieves (4 Å) for 2 d at room temperature (ca. 20°C) and after the addition of satd. aqueous $NH_4F$ solution (1 ml/mmol Ti), worked up and purified as described above.

*Spectral Data of the Epoxy Diols* **4**: The signals of the epoxy diol (*S*,*R*,*R*)-**4** are partially overlapped in the $^1$H-NMR spectrum by those of the diastereomer (*S*,*R*,*S*)-**4**; therefore, only the resolved resonances are given.

*(2S,3R,4S)- and (2S,3R,4R)-4,5-Epoxypentane-2,3-diol* (**4a**): The data match those reported for the racemic epoxy diols **4a** in ref.[4b].

*(3S,4R,5S)- and (3S,4R,5R)-5,6-Epoxyhexane-3,4-diol* (**4b**): Colorless powder, m.p. 47−49°C for a 91:9 (3*S*,4*R*,5*S*)/(3*S*,4*R*,5*R*)-**4b** mixture. − (3*S*,4*R*,5*S*)-**4b**: $^1$H NMR ($CDCl_3$, 600 MHz): δ = 1.01 (t, *J* = 7.5 Hz, 3 H, $CH_3$), 1.56−1.67 (m, 2 H, $CH_2$), 2.13 (d, *J* = 4.8 Hz, 1 H, OH), 2.24 (d, *J* = 4.2 Hz, 1 H, OH), 2.82−2.83 (m, 2 H,CHOC$H_2$), 3.11 (ddd, *J* = 3.8 Hz, *J′* = 3.8 Hz, *J* = 3.1 Hz, 1 H,C*H*OCH$_2$), 3.56−3.61 (m, 2 H, 2 × C*H*OH). − $^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 10.0 (q, C-1), 26.3 (t, C-2), 44.3 (t, C-6), 52.6 (d, C-5), 71.6 (d, C-3), 73.4 (d, C-4).

(3*S*,4*R*,5*R*)-**4b**: $^1$H NMR ($CDCl_3$, 600 MHz): δ = 1.00 (t, *J* = 7.5 Hz, 3 H, $CH_3$), 2.27 (d, *J* = 6.9 Hz, 1 H, OH), 2.79 (dd, *J* = 5.1 Hz, *J* = 2.8 Hz, 1 H, CHOC$H_2$), 3.44 (ddd, *J* = 6.9 Hz, *J* = 4.4 Hz, *J′* = 4.4 Hz, 1 H, C*H*OH), 3.64−3.68 (m, 1 H, $CH_2$C*H*OH). − $^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 10.0 (q, C-1), 26.1 (t, C-2), 44.4 (t, C-6), 53.3 (d, C-5), 72.5 (d, C-3), 74.5 (d, C-4). − IR ($CCl_4$): $\tilde{\nu}$ = 3580 $cm^{-1}$, 3461 (OH), 2967, 2935, 2878, 1464, 1396, 1378, 1309, 1242, 1161, 1130, 1094, 1062, 980, 859. − $C_6H_{12}O_3$ (132.2): calcd.C 54.53, H 9.15; found: C 54.13, H 8.90.

*(3R,4R,5S)- and (3R,4R,5R)-5,6-Epoxyhexane-3,4-diol* (**4b**): Colorless oil. − (3*R*,4*R*,5*S*)-**4b**: $^1$H NMR ($CDCl_3$, 600 MHz): δ = 1.04 [t, *J* = 7.5 Hz, 3 H, $CH_3$], 1.53−1.70 (m, 2 H, $CH_2$), 2.02 (d, *J* = 4.1 Hz, 1 H, OH), 2.10 (d, *J* = 1.9 Hz, 1 H, OH), 2.80 (dd, *J* = 4.8 Hz, *J* = 3.9 Hz, 1 H, CHOC$H_2$), 2.83−2.85 (m, 1 H, CHOC$H_2$), 3.17 (ddd, *J* = 3.9 Hz, *J′* = 3.9 Hz, *J* = 3.0 Hz, 1 H, C*H*OCH$_2$), 3.73 (dtd, *J* = 8.7 Hz, *J* = 4.1 Hz, *J* = 4.0 Hz, 1 H, CH$_2$C*H*OH), 3.77 (ddd, *J* = 3.9 Hz, *J′* = 3.9 Hz, *J* = 1.9 Hz, 1 H, C*H*OH). − $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 10.2 (q, C-1), 25.1 (t, C-2), 43.8 (t, C-6), 51.2 (d, C-5), 71.4 (d, C-3), 74.4 (d, C-4).

(3*R*,4*R*,5*R*)-**4b**: $^1$H NMR($CDCl_3$, 600 MHz): δ = 2.06 (d, *J* = 5.0 Hz, 1 H, OH), 2.26 (d, *J* = 5.8 Hz 1 H, OH), 2.78 (dd, *J* = 5.0 Hz, *J* = 2.9 Hz, 1 H, CHOC$H_2$), 2.83−2.85 (m, 1 H, CHOC$H_2$), 3.23 (ddd, *J* = 4.5 Hz, *J′* = 4.5 Hz, *J* = 2.9 Hz, 1 H, C*H*OCH$_2$), 3.48 (ddd, *J* = 5.8 Hz, *J* = 4.5 Hz, *J′* = 4.5 Hz, 1 H, C*H*OH), 3.68 (dtd, *J* = 9.0 Hz, *J* = 5.0 Hz, *J* = 4.5 Hz, 1 H, CH$_2$C*H*OH). − $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 10.2 (q, C-1), ), 25.6 (t, C-2), 44.9 (t, C-6), 52.0 (d, C-5), 73.2 (d, C-3), 75.1 (d, C-4). − IR ($CCl_4$): $\tilde{\nu}$ = 3601 $cm^{-1}$, 3542 (OH), 2928, 2884, 1549, 1252, 1217, 1084, 1049, 976. − $C_6H_{12}O_3$ (132.2):calcd. C 54.53, H 9.15; found C 54.28, H 9.40.

*(3S,4R,5S)- and (3S,4R,5R)-5,6-Epoxy-2-methylhexane-3,4-diol* (**4c**): Colorless oil. − (3*S*,4*R*,5*S*)-**4c**: $^1$H NMR ($CDCl_3$, 600 MHz): δ = 0.97 [d, *J* = 6.8 Hz, 3 H, CH(C$H_3$)$_2$], 1.01 [d, *J* = 6.8 Hz, 3 H, CH(C$H_3$)$_2$], 1.86−1.94 [m, 1 H, C*H*(CH$_3$)$_2$], 2.15 (d, *J* = 6.1 Hz, 1 H, OH), 2.27 (d, *J* = 4.5 Hz, 1 H, OH), 2.82−2.85 (m, 2 H, CHOC$H_2$), 3.11 (ddd, *J* = 4.0 Hz, *J`* = 4.0 Hz, *J* = 2.9 Hz, 1 H, C*H*OCH$_2$), 3.33 [ddd, *J* = 6.3 Hz, *J* = 6.2 Hz, *J* = 3.7 Hz, 1 H, (CH$_3$)$_2$CHC*H*OH], 3.75 (ddd, *J* = 4.5 Hz, *J* = 4.0 Hz, *J* = 3.7 Hz, 1 H, C*H*OH). − $^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 17.8 (q, C-1), 19.3 (q, C-1), 30.4 (d, C-2), 44.6 (t, C-6), 53.0 (d, C-5), 69.8 (d, C-3), 76.7 (d, C-4).

(3*S*,4*R*,5*R*)-**4c**: $^1$H NMR ($CDCl_3$, 600 MHz): δ = 0.98 [d, *J* = 6.7 Hz, 3 H, CH(C$H_3$)$_2$], 1.00 [d, *J* = 6.7 Hz, 3 H, CH(C$H_3$)$_2$], 2.26 (d, *J* = 4.7 Hz, 1 H, OH), 2.33 (d, *J* = 6.4 Hz, 1 H, OH), 2.78 (dd, *J* = 5.0 Hz, *J* = 2.8 Hz, 1 H, CHOC$H_2$), 2.81 (dd, *J* = 5.0 Hz, *J* = 4.1 Hz, 1 H, CHOC$H_2$), 3.13 (ddd, *J* = 4.2 Hz, *J* = 4.1 Hz, *J* = 2.8 Hz, 1 H, C*H*OCH$_2$), 3.42 (ddd, *J* = 6.0 Hz, *J* = 4.7 Hz, *J* = 4.3 Hz, 1 H, C*H*OH), 3.57 [ddd, *J* = 6.4 Hz, *J* = 4.3 Hz, *J* = 4.2 Hz, 1 H, (CH$_3$)$_2$CHC*H*OH]. − $^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 17.6 (q, C-1), 19.4 (q, C-1), 30.8 (d, C-2), 44.4 (t, C-6), 54.1 (d, C-5), 70.6 (d, C-3). 77.9 (d, C-4). − IR ($CCl_4$): $\tilde{\nu}$ = 3580 $cm^{-1}$ (OH), 2963, 2931, 2906, 2875, 1558, 1471, 1388, 1368, 1263, 1098, 1053, 1025, 1004, 934, 882, 845. − $C_7H_{14}O_3$ (146.2): calcd. C 57.51, H 9.65; found C 57.24, H 9.35.

*(3S,4R,5S)- and (3S,4R,5R)-2,2-Dimethyl-5,6-epoxyhexane-3,4-diol* (**4d**): Colorless powder, m.p. 55−57°C for a 91:9 (3*S*, 4*R*, 5*S*)-/(3*S*, 4*R*, 5*R*)-**4d** mixture. − (3*S*,4*R*,5*S*)-**4d**: $^1$H NMR ($CDCl_3$, 600 MHz): δ = 0.98 [s, 9 H, C(CH$_3$)$_3$], 2.26 (d, *J* = 4.7 Hz, 1 H, OH), 2.30 (d, *J* = 7.5 Hz, 1 H, OH), 2.81 (dd, *J* = 4.7 Hz, *J* = 2.9 Hz, 1 H, CHOC$H_2$), 2.84 (dd, *J* = 4.7 Hz, *J′* = 3.9 Hz, 1 H, CHOC$H_2$), 3.09 (ddd, *J* = 3.9 Hz, *J′* = 3.9 Hz, *J* = 2.9 Hz, 1 H, C*H*OCH$_2$), 3.28 [dd, *J* = 7.5 Hz, *J* = 0.7 Hz, 1 H, (CH$_3$)$_3$CC*H*OH], 3.88 (ddd, *J* = 4.7 Hz, *J* = 3.9 Hz, *J* = 0.7 Hz, 1 H, C*H*OH). − $^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 26.2 (3×q, C-1), 34.9 (s, C-2), 44.8 (t, C-6), 53.9 (d, C-5), 67.5 (d, C-3), 77.3 (d, C-4).

(3*S*,4*R*,5*R*)-**4d**: $^1$H NMR ($CDCl_3$, 600 MHz): δ = 0.98 [s, 9 H, C(CH$_3$)$_3$], 2.36 [d, *J* = 6.8 Hz, 1 H, OH], 2.39 (d, *J* = 6.0 Hz, 1 H, OH), 2.77 (dd, *J* = 5.0 Hz, *J* = 2.7 Hz, 1 H, CHOC$H_2$), 2.79

(dd, $J$ = 5.0 Hz, $J$ = 4.2 Hz, 1 H, CHOC$H_2$), 3.14 (ddd, $J$ = 4.2, $J'$ = 4.2 Hz, $J$ = 2.7 Hz, 1 H, C$H$OC$H_2$), 3.39 (dd, $J$ = 6.0 Hz, $J$ = 1.3 Hz, 1 H, C$H$OH), 3.73 [ddd, $J$ = 6.8 Hz, $J$ = 4.2 Hz, $J$ = 1.3 Hz, 1 H, $(CH_3)_3$CC$H$OH]. – $^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 26.2 (3×q, C-1), 34.8 (s, C-2), 44.7 (t, C-6), 55.6 (d, C-5), 68.5 (d, C-3), 79.1 (d, C-4). – IR ($CCl_4$): $\tilde{\nu}$ = 3564 cm$^{-1}$ (OH), 2959, 2871, 1542, 1480, 1390, 1365, 1289, 1247, 1181, 1114, 1091, 1014, 960, 913, 854. – $C_8H_{16}O_3$ (160.2): calcd. C 59.98, H 10.07; found C 60.10, H 9.67.

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