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Control of enantioselectivity through a hydrogen-bonded template in the vanadium(V)-catalyzed epoxidation of allylic alcohols by optically active hydroperoxides

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Abstract—The vanadium(V)-catalyzed asymmetric epoxidation of primary allylic alcohols by the optically active TADDOL-derived hydroperoxide as the asymmetric controller provides the corresponding (*R*)-epoxides in up to 72% ee. From this mechanistic study we conclude that this novel enantioselective oxygen transfer takes place via a hydrogen-bonded template, held together by the vanadium metal.

1. Introduction

Asymmetric metal catalysis remains a current focus of chemical research with significant progress being achieved over recent years.[1] In particular, for the epoxidation of allylic alcohols, high enantiomeric excesses have been obtained by Ti-catalyzed Sharpless–Katsuki epoxidations.[2] Chiral vanadium(V) complexes have also been used as catalysts for such asymmetric epoxidations;[3] the initially employed $VO(acac)_2$, optically active hydroxamic acid, and TBHP as oxygen donor afforded epoxy alcohols in up to 80% ee.[4] Recently, a remarkable improvement in the vanadium-based asymmetric epoxidation was achieved (up to 96% ee) with an optically active binaphthyl-modified hydroxamic acid ligand.[5] In all of these vanadium-mediated epoxidations, the asymmetric induction results from the optically active hydroxamic acid ligands as chirality sources. The question arises as to whether optically active hydroperoxides may also effect asymmetric induction, besides their usual function as the oxygen-atom source. Mechanistically significant, such a study with these enantiomerically pure peroxides should be instrumental in elucidating the details of the oxygen-transfer in vanadium-catalyzed asymmetric oxidations.

To date, the use of chiral hydroperoxides for enantioselective oxidations is still quite rare. The first examples of the asymmetric epoxidation of allylic alcohols under titanium catalysis employed optically active sugar-derived[6] or simple secondary hydroperoxides,[7] which provided ee values of up to 50%. Recently we have utilized such hydroperoxides in the asymmetric Weitz–Scheffer epoxidation of α,β-enones and obtained ee values of up to 90%.[8] Highest enantioselectivities (up to 98% ee) were achieved with the sterically more demanding, optically active, TADDOL-derived hydroperoxide TADOOH as the chirality source in the Weitz–Scheffer epoxidation, the Baeyer–Villiger oxidation and sulfoxidation.[9a] Very recently, we have successfully used the hydroperoxide TADOOH as a chiral oxygen source in the catalytic asymmetric epoxidation of allylic alcohols by an oxovanadium-substituted polyoxometalate.[9b] Herein, we report our mechanistic study on the catalytic asymmetric epoxidation of allylic alcohols **1** by an achiral vanadium complex, but with optically active hydroperoxides **3** as the chiral oxygen donor. The enantiomerically pure hydroperoxides **3a**,**b** employed in this study were obtained by enzymatic kinetic resolution,[10] whereas the enantiomerically pure TADOOH **3c** was readily prepared from H_2O_2 and a TADDOL derivative.[9]

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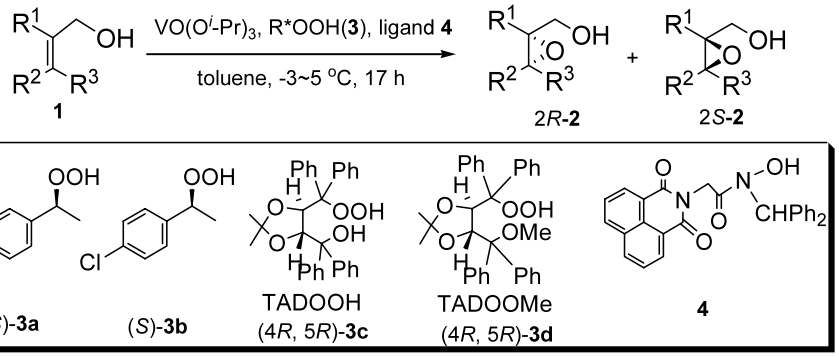
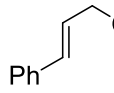
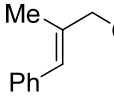
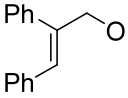
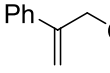
2. Results and discussion

In preliminary experiments, an extensive screening of a variety of catalytically active vanadium complexes revealed that the catalyst generated in situ from $VO(O^iPr)_3$ with the achiral hydroxamic acid **4** suits best the purpose of asymmetric epoxidation by optically active hydroperoxides. In the epoxidation of the test substrate cinnamyl alcohol **1a** with the hydroperoxides **3a**–**c** (Table 1) as chiral oxygen donors, good conversions of **1a** to the respective epoxide were achieved (>83%) within 17 h under mild conditions (entries 1–3); no enone (allylic oxidation) was observed. In every case, the (2*S*,3*S*)-(−)-**2a** enantiomer was favored, but the enantioselectivity was low; for example, for the hydroperoxide (*S*)-**3a** an ee value of only 35% was obtained (entry 1). Whereas the epoxidation of the allylic alcohol **1a** with the structurally related (*S*)-**3b** did not improve the enantioselectivity (entry 2), a substantial increase in asymmetric induction was achieved by the hydroxy-bearing hydroperoxide TADOOH, (4*R*,5*R*)-**3c**) as the chiral oxygen donor, for which the ee value of 52% (entry 3) is the highest that has so far been found in the vanadium-catalyzed epoxidation of substrate **1a** with optically active hydroperoxides. It should be emphasized that after reaction, the optically

Table 1. Vanadium-catalyzed epoxidation of allylic alcohols **1** with optically active hydroperoxides **3**[a]



entry	allylic alcohol **1**	R*OOH **3**	convn (%)[b]	ee (%)[c]	confign
1[d]	 **1a**	(*S*)-**3a**	83	35	(2*S*, 3*S*)-(-)
2[d]		(*S*)-**3b**	> 95	30	(2*S*, 3*S*)-(-)
3		(4*R*, 5*R*)-**3c**	89	52	(2*S*, 3*S*)-(-)
4	 **1b**	(4*R*, 5*R*)-**3c**	73	67	(2*R*, 3*R*)-(+)
5	 **1c**	(4*R*, 5*R*)-**3c**	> 95 (70)[e]	72 (73)[e]	(2*R*, 3*R*)-(-)
6		(4*R*, 5*R*)-**3d**	18	20	(2*R*, 3*R*)-(-)
7	 **1d**	(4*R*, 5*R*)-**3c**	30	41	(2*R*, 3*S*)-(+)
8	 **1e**	(4*R*, 5*R*)-**3c**	94	44	(2*R*)-(+)

[a] All reactions were carried out at 5 °C with 0.15-0.70 mmol of allylic alcohols, 1.5 equiv. of hydroperoxide **3** and 5 mol% of vanadium catalyst, prepared in situ by mixing $VO(O^i\text{-}Pr)_3$ and ligand **4** in a molar ratio of 1:1.5; reaction time 17 h.
[b] Conversion of the allylic alcohol **1** was determined by ^{1}H-NMR analysis of the crude reaction mixture with dimethyl isophtalate as internal standard (error ± 5% of the stated values), material balances > 95%. [c] Determined by HPLC analysis of the isolated, purified epoxides on a chiral column (Chiralcel OD); averaged values of several runs. [d] At -3 °C. [e] Isolated material (see Experimental Section).

active TADDOL was completely recovered without loss of enantiomeric purity, which provides the opportunity to regenerate this chiral oxygen source after use.

The highest ee values (up to 72% ee) were obtained for substrates **1b**,**c** (entries 4 and 5); in the case of substrate **1c**, the epoxidation was conducted on a larger scale (158 mg, 0.751 mmol) and the epoxide **2c** was isolated in 70% yield with an enantiomeric excess of 73%. Evidently, the additional substituent at the C-2 position of the allylic alcohols **1b** and **1c** enhances the enantioselectivity. Not only were the ee values higher compared to substrate **1a**, more significantly, inversion of the configuration had occured. Evidently, the steric effect of the R^1 substituent at the C-2 position dominates that of the R^2 group in the control of the enantioselectivity. It is mechanistically significant to note that when the hydroxy-protected derivative TADOOMe [(4*R*,5*R*)-**3d**] was used instead of TADOOH in the epoxidation of allylic alochol **1c**, the enantioselectivity as well as the reactivity dropped drastically, i.e. only 18% conversion of **1a** was observed and the epoxide **2c** was obtained with an ee value of only 20% (entry 6). Also, the hydroperoxides **3a**,**b** (no hydroxy functionality) exhibited low enantioselectivities (up to 34% ee) in the epoxidations of substrates **1b** and **1c** (data not shown in Table 1).

The allylic alcohol **1d** (entry 7), which is known to display little reactivity and moderate enantioselectivity (65% ee) under Sharpless conditions,[2] was epoxidized under the present conditions in low conversion (30%) and also in low enantiomeric excess [41% in favor of the (2*R*,3*S*)-**2d** enantiomer]. Analogous to substrate **1d**, a similar enantiomeric excess of only 44% was observed also for the allylic alcohol **1e** with only one substituent at the position C-2 (entry 8).

Based on earlier studies,[11] clearly, the appreciable changes in the ee values as a function of the structural variations of hydroperoxide **3** and the allylic alcohol **1** express the pertinent steric interactions between the hydroperoxide, the allylic alcohol, and the hydroxamic acid ligand in the template, held together by the central vanadium metal. For high selectivity, steric interactions alone are usually not sufficient for enantiomeric control, and a highly ordered, rigid transition structure with restricted degrees of freedom through template formation is beneficial. In view of the fact that similar to TADDOLs, the hydroperoxy derivative TADOOH tends to form inclusion compounds with H-bonding acceptors,[9] we propose the formation of a conformationally restricted template through hydrogen bonding between the hydroxy group of the TADOOH and the oxo functionality of the vanadium complex (Fig. 1). Experimental evidence for such a hydrogen-bonded template is provided by the results of the methyl ether **3d** of TADOOH (the hydroxy group is protected through methylation), in which a drastically lower enantioselectivity is exhibited in the epoxidation of **1c** compared to that of TADOOH (Table 1, entry 6).

To rationalize mechanistically the observed enantioselectivities (Table 1), in particular for the TADOOH, we propose the two diastereomeric transition structures **I** and **II** (Fig. 1, top). Of these TS **I** is favored, because in this template the steric repulsions with the hydroperoxide are minimized. Note that one of the phenyl groups of the TADOOH in TS **II** is proximate to the V=O···HO hydrogen bond.

A prerequisite for an effective oxygen transfer along the S_N2 trajectory is that the allylic substrate is positioned in such a way that the midpoint of the CC double bond is in line along the O–O bond axis. This allows two

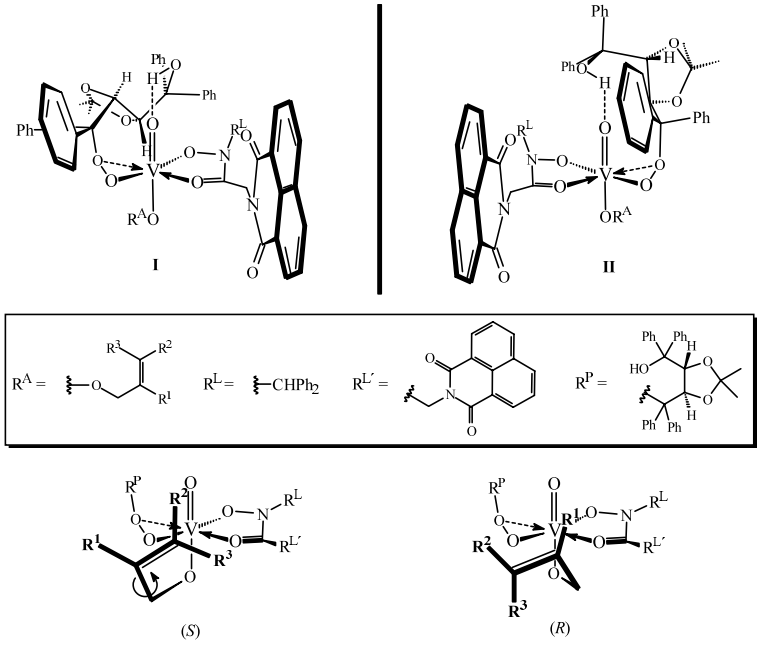
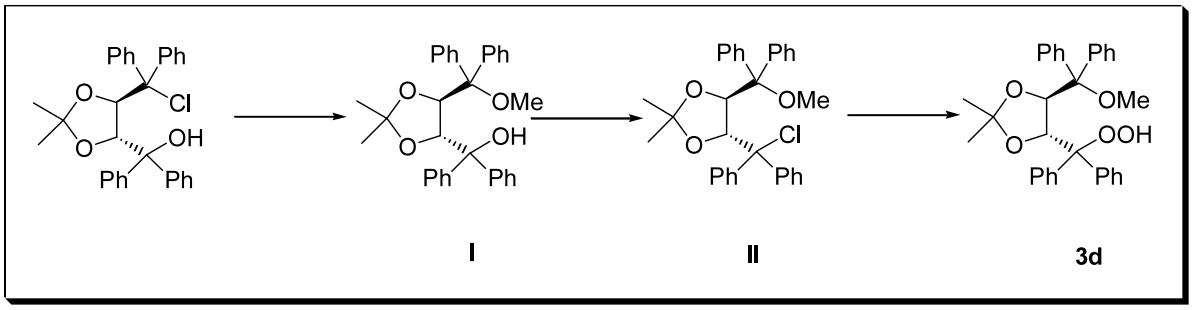


Figure 1. Proposed diastereomeric transition structures **I** and **II** (top) and allylic alcohol arrangements (bottom).



geometrical arrangements for each of the transition structures **I** and **II** to accommodate the allylic alcohol (Fig. 1, bottom), namely the (*S*) and (*R*) enantiomers [(*S*) means the transition state (TS) leads to the (2*S*)-epoxide enantiomer and (*R*) to the (2*R*) one]. Thus, for each allylic substrate four different transition states must be considered, of which two [**I**(*R*), **II**(*R*)] lead to the (2*R*)-configured and the other two [**I**(*S*), **II**(*S*)] to the (2*S*)-configured epoxide enantiomer **2**. With the help of these proposed transition structures, we may adequately account for the observed enantioselectivities in terms of a consistent mechanistic concept for the oxygen transfer. For instance, in the case of substrates **1b** and **1c**, the strong interaction of the hydroperoxide phenyl group with the R^1 group (Me in **1b**, Ph in **1c**) in TS **I**(*S*) makes this template unlikely. Also TS **II**(*S*) is an unfavorable transition structure because the R^1 and R^2 groups are in close proximity to one of the hydroperoxide phenyl groups. Furthermore, the TS **II**(*R*) is unfavorable because of the steric interactions between the R^2 group (Ph) and the TADOOH phenyl group. Therefore, for the allylic alcohols **1b** and **1c**, the transition structure **I**(*R*), which leads to the (2*R*,3*R*)-epoxide enantiomers, is preferred in view of the minimized steric interactions. This is consistent with the highest ee values (67% ee for **1b** and 72% ee for substrate **1c**), observed in this catalytic system (Table 1).

3. Conclusion

In the vanadium(V)-catalyzed asymmetric epoxidation of allylic alcohols by an optically active hydroperoxide, the highest ee values (up to 72%) may be achieved with a hydroxy-functionalized sterically demanding TADDOL-type hydroperoxide as asymmetric inductor. For the first time, it has been demonstrated that a hydrogen-bonded template effects enantiofacial control in the vanadium-catalyzed epoxidation by a chiral hydroperoxide, in combination with an achiral hydroxamic acid ligand. This novel concept should stimulate the development of more effective hydroxy-functionalized hydroperoxides for vanadium-catalyzed asymmetric epoxidation.

4. Experimental

4.1. General

The ^{1}H NMR spectra were recorded on a Bruker AC 200 or 400 spectrometer (200 or 400 MHz) and the ^{13}C NMR spectra on a Bruker AC 250 instrument (63 MHz). Data are reported as follows: Chemical shift, multiplicity, coupling constants, number of H atoms, assignment. The chemical shifts are relative to the solvent used [^{1}H: $CDCl_3$ (δ 7.26), d_8-toluene (δ 2.09), d_6-DMSO (δ 2.50); ^{13}C: $CDCl_3$ (δ 77.0), d_6-DMSO (δ 39.5)]. IR spectra were determined on a FT/IR Perkin-Elmer 410 infrared spectrophotometer. Mass spectra were carried out on a Finnigan MAT8200 or MAT TSQ 7000 (ESI) spectrometer, exact mass on a Finnigan MAT90. Melting points were determined on a Büchi B545 and are uncorrected. The enantiomeric excess of the hydroperoxides (*S*)-(−)-**3a**,**b** and the epoxides **2a**–**e** was measured on the isolated product by high-performance liquid chromatography (HPLC) on chiral columns, UV detection at 220 nm: Hydroperoxide **3a** [Daicel Chiralcel OD column (250×4.6 mm), flow rate of 0.6 mL/min, 9:1 mixture of *n*-hexane: isopropanol as eluent], hydroperoxide **3b** [Daicel Chiralcel OB-H column, (250×4.6 mm), flow rate of 0.5 mL/min, 4:1 mixture of *n*-hexane:isopropanol as eluent]; epoxides **2a**–**e** [Daicel Chiralcel OD column (250×4.6 mm), flow rate of 0.8 mL/min, 9:1 mixture of *n*-hexane:isopropanol as eluent]. Absolute configurations of the epoxides **2a**–**e** were assigned by direct comparison of the literature values with the specific rotation determined on a polarimetric Chiralyser or on a polarimeter.[12,13]

Commercially available reagents, unless otherwise stated, were used without further purification. Horseradish peroxidase was a generous gift sample from Boehringer Mannheim. $VO(O\textit{i}\text{-}Pr)_3$ was stored in a glovebox under a nitrogen-gas atmosphere. CH_2Cl_2 was distilled from calcium hydride under an argon-gas atmosphere; d_8-toluene, for the asymmetric epoxidation reactions, was distilled under an argon-gas atmosphere from sodium hydride, degassed, and stored over molecular sieves (4 Å) under an argon-gas atmosphere. UHP is the urea/hydrogen peroxide adduct. Et_3N was distilled over CaH_2. The hydroperoxides (*S*)-**3a**,**b**[10] and (4*R*,5*R*)-**3c**,[9] α-methylcinnamyl alcohol **1b**,[12,14] α-phenylcinnamylalcohol (**1c**),[12,15] (*Z*)-3-phenyl-2-propen-1-ol **1d**,[12,16] and 2-phenyl-2-propen-1-ol **1e**[12,17] were prepared according to literature procedures. All following reactions, except the preparation of 1,3-dioxo-1*H*-benz[*de*]isoquinoline-2(3*H*)-acetic acid, were carried out under an argon-gas atmosphere.

4.2. Preparation of the hydroxamic acid, 4

4.2.1. 1,3-Dioxo-1*H*-benz[*de*]isoquinoline-2(3*H*)-acetic acid[18]. A solution of 2.97 g (15.0 mmol) of naphthalene-

1,8-dicarboxylic anhydride and 1.13 g (15.0 mmol) of glycine in 30 mL DMF was stirred for 4 h at 100°C. The reaction mixture was cooled to room temperature (ca. 20°C), diluted with 30 mL of ethyl acetate, and washed with water (2×15 mL). The organic phase was dried over $MgSO_4$ and the solvent removed (50°C, 8 torr). The crude product was recrystallized from ethyl acetate to give 2.65 g (10.4 mmol, 69% yield) of the desired carboxylic acid as colorless powder; mp 272–273°C (lit.:[18] 250°C); ^{1}H NMR (200 MHz, d_6-DMSO) δ 4.73 (s, 2H, CH_2), 7.86 (t, $J=8$ Hz, 2H, H arom.), 8.49–8.54 (m, 4H, H arom.); ^{13}C NMR (63 MHz, d_6-DMSO) δ 41.2 (t, CH_2), 121.4 (2×s, C arom.), 127.3 (2×d, C arom.), 127.3 (s, C arom.), 131.1 (2×d, C arom.), 131.3 (s, C arom.), 134.8 (2×d, C arom.), 163.1 (2×s, C(O)–N), 169.3 (s, CO_2H).

4.2.2. 1,3-Dioxo-1*H*-benz[*de*]isoquinoline-2(3*H*)-acetyl chloride. To a suspension of 1.25 g (4.88 mmol) of 1,3-dioxo-1*H*-benz[*de*]isoquinoline-2(3*H*)-acetic acid in 35 mL CH_2Cl_2 and three drops of DMF was added a fivefold excess of oxalic chloride (2.15 mL, 3.17 g, 25.0 mmol) at ca. 20°C. The mixture was stirred for 4 h, the solvent and excess oxalic chloride were removed (20°C at 20 torr) and the solid, green residue was recrystallized from CH_2Cl_2/petroleum ether (30–50°C). The product was obtained as light brown powder in 92% yield (1.23 g, 4.50 mmol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.32 (s, 2H, CH_2), 7.77 (t, $J=8.0$ Hz, 2H, H arom.), 8.25 (dd, $J=8.0$ Hz, $J=0.6$ Hz, 2H, H arom.), 8.60 (dd, $J=8.0$ Hz, $J=0.6$ Hz, 2H, H arom.); ^{13}C NMR (63 MHz, d_6-DMSO) $\delta=41.2$ (CH_2), 121.4 (2×s, C arom.), 129.0 (2×d, C arom.), 129.0 (s, C arom.), 131.1 (2×d, C arom.), 131.3 (s, C arom.), 134.8 (2×d, C arom.), 164.7 (2×s, C(O)–N), 169.3 (s, C(O)-Cl); IR (KBr) 2994, 2954, 1803 [C(O)Cl], 1725 and 1702 (–CO–N–CO–), 1660, 1386, 1237, 968 cm^{-1}. Anal. calcd for $C_{14}H_8ClNO_3$ (273.7): C, 61.44; H, 2.95; N, 5.12. Found C, 61.77; H, 3.24; N, 5.16.

4.2.3. *N*-Hydroxy-α-phenylbenzenemethanamine[19]. A mixture of 2.96 g (15.0 mmol) benzophenone oxime and 5.05 mL (4.65 g, 50 mmol) of the pyridine–borane complex in 25 mL of ethanol was kept below 5°C. To this solution was added dropwise 10% aqueous hydrochloric acid (50 mL) and the mixture was stirred for 15 min at room temperature (ca. 20°C). The solution was made alkaline with sodium carbonate while cooling in an ice-bath, and extracted with $CHCl_3$ (3×120 mL). The combined extracts were dried over $MgSO_4$, and after evaporation of the solvent (40°C at 110 torr), the crude product was purified by silica-gel chromatography with a 1:2 mixture of EtOAc and petroleum ether (30–50°C) as eluent (TLC, $R_f=0.48$), to afford *N*-hydroxy-α-phenylbenzenemethanamine as colorless powder (1.37 g, 6.87 mmol, 46% yield); mp 77–78°C (lit.:[19b] 80–81°C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.23 (s, 1H, C*H*Ph_2), 5.52 (s, br, 2H, NH and OH), 7.21–7.42 (m, 10H, H arom.); ^{13}C NMR (63 MHz, $CDCl_3$) δ 70.8 (NCH), 127.7 (2×d, C arom.), 127.9 (4×d, C arom.), 128.7 (4×d, C arom.), 140.7 (2×s, C arom.).

4.2.4. *N*-(Diphenylmethyl)-*N*-hydroxy-1,3-dioxo-1*H*-benz[*de*]isoquinoline-2(3*H*)-acetamide, 4. To a suspension of 593 mg (2.97 mmol) of the *N*-hydroxy-α-phenylbenzenemethanamine in 30 mL CH_2Cl_2 was added dropwise a solution of 812 mg (2.97 mmol) of 1,3-dioxo-1*H*-benz[*de*]isoquinoline-2(3*H*)-acetyl chloride in 34 mL CH_2Cl_2 at room temperature (ca. 20°C). The mixture was stirred for 1 h, the colorless precipitate was collected by filtration and recrystallized from hot acetone. The product was dried (20°C at 1 torr) to afford 503 mg (1.15 mmol, 39% yield) of the hydroxamic acid **4** as colorless powder; mp 184–185°C; ^{1}H NMR (200 MHz, d_6-DMSO) δ 5.11 (s, 2H, CH_2), 6.70 (s, 1H, *C*HPh_2), 7.27–7.43 (m, 10H, 2×Ph), 7.86–7.94 (m, 2H, H arom.), 8.49–8.54 (m, 4H, H arom.); ^{13}C NMR (63 MHz, d_6-DMSO) δ 41.4 (t, CH_2), 62.5 (d, *C*HPh_2), 121.7 (2×s, C arom.), 127.3 (2×d, C arom.), 127.3 (s, C arom.), 127.4 (2×d, C arom.), 128.3 (4×d, C arom.), 128.8 (4×d, C arom.), 131.0 (2×d, C arom.), 131.4 (s, C arom.), 134.7 (2×d, C arom.), 138.9 (2×s, C arom.), 163.3 [2×s, *C*(O)-N-*C*(O)], 167.5 (s, C=O); IR (KBr) 3143 (OH), 2885, 1699 [–C(O)–N–C(O)–], 1663 [–C(O)–N–], 1615, 1454, 1380, 1239 cm^{-1}; MS [*m*/*z*] (rel. intensity in%): 418 (M^+-H_2O, 7), 238 (19), 221 (25), 211 (20), 210 (55), 208 (58), 182 (100), 180 (32), 167 (37), 77 (27). $C_{27}H_{18}N_2O_3$ (418.1) $[M-H_2O]^+$, HRMS (EI): Anal. calcd 418.1317; found: 418.1319.

4.3. Preparation of the hydroxy-protected hydroperoxide TADOOMe, (4*R*,5*R*)-3d

4.3.1. [(4*R*,5*R*)-5-(Methoxydiphenylmethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]diphenyl-methanol (I). A suspension of the TADDOL monochloride[20] (3.86 g, 7.96 mmol) in MeOH (60 mL) was treated with Et_3N (1.20 mL, 8.61 mmol) and heated under reflux for 1.5 h. After cooling to ca. 20°C, the suspension was filtered to yield analytically pure **I** (3.16 g, 83%) as white solid. Mp 165–166°C, (lit.[20b]169.8–170.4°C); $[\alpha]_D^{rt}=-30.1$ (*c* 1.35, $CHCl_3$), (lit.:[20b] $[\alpha]_D^{rt}=-27.0$ (*c* 1.00, $CHCl_3$); IR ($CHCl_3$) 3321, 3059, 2941, 1957, 1817, 1600, 1495, 1447*s*, 1381, 1372, 1168, 1087, 1048, 882, 641; ^{1}H NMR (300 MHz, $CDCl_3$): 0.93 (*s*, Me), 1.03 (*s*, Me), 2.97 (*s*, OMe), 4.25 (*d*, $J=8.1$, CH), 4.59 (*d*, $J=8.1$, CH), 6.35 (*s*, OH), 7.20–7.50 (*m*, 18 arom. H), 7.62–7.65 (*m*, 2 arom. H); ^{13}C NMR (75 MHz, $CDCl_3$): 26.85, 27.06, 52.41 (Me); 77.24 (C); 79.30, 81.51 (CH); 84.75, 108.87 (C); 126.91, 127.07, 127.20, 127.64, 127.70, 127.88, 128.40, 128.66, 129.98 (CH); 137.11, 138.86, 143.85, 146.43 (C). MALDI-FT-ICR-MS: 503.2 (72, $[M+Na]^+$), 413.2 (20, $[M-OMe-OCMe_2-1+Na]^+$), 273.0 (100). HRMS calcd for $[M+Na]^+$ ($C_{32}H_{32}O_4Na$): 503.2193; found: 503.2191. Anal. calcd for $C_{32}H_{32}O_4$ (480.6): C 79.97, H 6.71; found: C, 79.94; H, 6.63.

4.3.2. (4*R*,5*R*)-4-(Chlorodiphenylmethyl)-5-(methoxydiphenylmethyl)-2,2-dimethyl-1,3-dioxolane II. A solution of **I** (2.50 g, 5.20 mmol) in CH_2Cl_2 (25 mL) was treated with Et_3N (1.10 mL, 7.80 mmol) and $SOCl_2$ (0.50 mL, 6.87 mmol). The mixture was heated at reflux under stirring for 1.5 h, whereby the color of the

reaction mixture changed from yellow to black. After cooling to ca. 20°C, the mixture was carefully poured into saturated $NaHCO_3$ solution (100 mL) and stirred for 5 min. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were washed with H_2O, saturated NaCl solution and dried over Na_2SO_4. The solvent was removed under reduced pressure (40°C, 100 torr) to yield **II** (2.78 g, quantitative) as a brown solid, which was used for the subsequent reaction without further purification. For analytical purposes, a sample was purified by fractional crystallization (pentane/Et_2O); white powder; mp 115–117°C; $[\alpha]_D^{rt}=+50.9$ (*c* 1.07, $CHCl_3$). IR ($CHCl_3$): 3059, 3007, 2936, 2827, 1598, 1492, 1445, 1380, 1370, 1318, 1166, 1093, 1034, 980, 893, 865; ^{1}H NMR (300 MHz, $CDCl_3$): 0.97 (*s*, Me); 1.29 (*s*, Me); 2.30 (*s*, OMe); 4.85 (*d*, $J=6.6$, CH); 5.16 (*d*, $J=6.9$, CH); 7.18–7.50 (*m*, 20 arom. H); ^{13}C NMR (75 MHz, $CDCl_3$): 27.69, 27.80, 51.71 (Me), 79.52 (C); 80.83, 82.50 (CH), 83.80, 109.87 (C), 126.93, 127.10, 127.30, 127.41, 127.44, 127.52, 127.59, 128.79, 129.47, 130.02, 130.63 (CH), 139.32, 140.87, 144.01, 144.80 (C). FAB-MS: 431 (4, $[M-OMe-Cl-1]^+$), 318 (32), 237 (70), 197 (100), 167 (49), 136 (38), 105 (65).

4.3.3. (4*R*,5*R*)-[5-(Methoxydiphenylmethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]diphenylmethyl hydroperoxide 3d. According to the reported procedure,[9] a suspension of **II** (3.00 g, 6.00 mmol), UHP (8.77 g, 93.19 mmol) and DMF (30 mL) were stirred for 24 h at 50°C under an argon-gas atmosphere. The resulting solution was cooled to ca. 20°C, the white precipitate was separated by filtration, and washed with H_2O (100 mL) and pentane (100 mL). The crude product was dissolved in CH_2Cl_2 (25 mL), the organic phase was washed with H_2O (5×25 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure (40°C, 100 torr) and the resulting residue (2.7 g) was purified by fractional crystallization (CH_2Cl_2) to yield a white solid foam (2.02 g). Tritration with hexane (30 mL) at ca. 20°C yielded **3d** (1.41 g, 47%) as white powder, mp 143–144°C. $[\alpha]_D^{rt}=-174.7$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3238, 3091, 3007, 2942, 2840, 1956, 1812, 1602, 1496, 1447, 1382, 1371, 1322, 1166, 1076, 1052, 1034, 1006, 973, 880, 646; ^{1}H NMR (400 MHz, $CDCl_3$): 0.38 (s, Me), 0.96 (s, Me), 3.23 (s, OMe), 4.92 (d, $J=7.1$, CH), 5.33 (d, $J=7.1$, CH), 7.25–7.53 (m, 20 arom. H), 11.52 (s, OOH); ^{13}C NMR (100 MHz, $CDCl_3$): 26.82, 27.07 (Me); 53.40 (OMe), 77.22, 79.20 (CH); 86.20, 89.72 110.74 (C); 127.10, 127.16, 127.45, 127.60, 127.67, 127.78, 127.89, 128.18, 128.43, 129.35 129.45, 130.29 (CH), 139.97, 140.49, 140.70, 144.45 (C). ESI-MS: 1015 (26, $[2M+Na]^+$), 1010.4 (48, $[2M+NH_4]^+$), 556.2 (35), 514.2 (100, $[M+NH_4]^+$). Anal. calcd for $C_{32}H_{32}O_5$ (496.6): C 77.40, H 6.49; found: C 77.33, H 6.69.

4.4. General procedure for the epoxidation of the allylic alcohols 1a–e with the optically active hydroperoxides (*S*)-3a,b and (4*R*,5*R*)-3c,d in the presence of $VO(O^iPr)_3$ and the hydroxamic acid ligand 4

A Schlenk tube was charged with dimethyl isophthalate as internal standard, $VO(O^iPr)_3$ (2 μL, 8.42 μmol, 5–6 mol%), and ligand **4** [12.5 μmol, 1.5 equiv. (relative to $VO(O^iPr)_3$)]. Then a solution of the particular allylic alcohol **1** (ca. 0.15 mmol) in 0.7 mL d_8-toluene was added, the mixture stirred for 1 h, and before addition of the hydroperoxide, the molar ratio of substrate to internal standard was determined by ^{1}H NMR analysis. The reaction mixture was cooled to −3°C [to 5°C for the epoxidations with hydroperoxide (4*R*,5*R*)-**3c** as oxygen donor] and 225 μmol (1.5 equiv.) of the specific enantiomerically pure hydroperoxide **3** was added at that temperature. The resulting mixture was stirred 17 h at −3°C (5°C). Material balances and conversions (Table 1, main text) were determined by ^{1}H NMR analysis directly on the crude reaction mixture. The epoxides **2a**–**e** are all known and have been identified by comparison of their characteristic NMR signals with the literature reported data.[2,7,12] The enantiomeric excess of the epoxides **2a**–**e** was determined by HPLC analysis of the isolated, purified [by silica gel chromatography with a mixture of ethyl ether and petroleum ether (30–50°C) as eluent] epoxides on a chiral column (Chiralcel OD).

The epoxidation of the allylic alcohol **1c** with hydroperoxide (4*R*,5*R*)-**3c** and the catalytic system $VO(O^iPr)_3$/ligand **4** was repeated on a larger scale, analogously to the method described above (17 h at 5°C), by employing 158 mg (751 μmol) of **1c**, 10 μL of $VO(O^iPr)_3$, 27.6 mg (63.3 μmol) of ligand **4**, and 544 mg (1.13 mmol) of hydroperoxide **3c**. Silica-gel chromatography of the crude mixture afforded the epoxide **2c** in 70% yield (119 mg, 526 μmol) and 8% (13.0 mg, 61.8 μmol) of the unreacted starting material **1c** were recovered; the enantiomeric excess of the (2*R*,3*R*)-(−)-**2c** enantiomer was 73%.

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