Enantioselective Hydrolysis of Functionalized 2,2-Disubstituted Oxiranes with Bacterial Epoxide Hydrolases

Andreas Steinreiber,*[a] Ingrid Osprian,[a] Sandra F. Mayer,[a] Romano V. A. Orru,[a,b] and Kurt Faber[a]

Keywords: Epoxide hydrolase / Chiral building block / Asymmetric synthesis / Chiral quaternary carbon atoms

The biohydrolysis of 2,2-disubstituted oxiranes bearing various oxygen functional groups was investigated using the epoxide hydrolase activity of 11 bacterial strains. The results show that the activity and the selectivity strongly depend on the substrate structure and the biocatalyst. Whereas substrates possessing free hydroxyl groups were not transformed, their analogs, protected as ethers, were well accepted. This allowed the convenient modulation of the enantioselectivity by proper choice of the ether group according to size and polarity. It was found that the distance of the ether-oxygen to the stereogenic quaternary carbon center of the oxirane ring had a profound influence on the enantioselectivity, and several oxiranes were resolved with good to excellent selectivities. The enantiomerically enriched epoxides and vicinal diols thus obtained contain a useful "synthetic handle" in their side chain, which allows their use as building blocks in asymmetric synthesis.

Introduction

The synthesis of chiral building blocks containing a chiral quaternary carbon center is a considerable challenge for organic synthesis, due to steric inaccessibility. In this context, 2,2-disubstituted oxiranes and their corresponding *vic*-diols constitute highly flexible molecular scaffolds, which have been used for the preparation of enantiopure tertiary alcohols,[1] α-methylamino acids,[2] and α-hydroxy-α-methyl carboxylic acids.[3] Most asymmetric catalytic methods yield 2,2-disubstituted oxiranes and/or *vic*-diols in insufficient optical purity.[4−6] Biocatalytic approaches to the synthesis of compounds possessing a chiral quaternary carbon center are limited.[7] For example, the kinetic resolution of carboxylic esters containing fully substituted chiral centers by proteases and carboxyl esterases is generally impeded by steric repulsion, and is only feasible in special cases. Although asymmetric epoxidation of 2-substituted 1-alkenes using chloroperoxidases[8] furnished 2,2-disubstituted epoxides in good chemical and optical yields, this method is only applicable to a limited range of structurally similar substrates. Furthermore, the scale-up of these reactions is problematic due to the sensitivity of chloroperoxidases towards hydrogen peroxide used as oxidant. Epoxide hydrolases from microbial sources have been shown to be versatile catalysts for the kinetic resolution of structurally different epoxides.[9] For the resolution of sterically demanding (±)-2,2-disubstituted oxiranes in particular, bacterial epoxide hydrolases (BEH) are the catalysts of choice due to their (almost) complete enantioselectivity.[10] In order to overcome the drawbacks of kinetic resolution, deracemization processes based on the combination of bio- and chemo-catalysis were recently developed by us.[11] Due to the easily available biocatalysts by fermentation, these protocols are applicable to multigram-scale reactions, and they yield 2-substituted 1,2-diols in >90% chemical and optical yields from the racemate.

BEH's have been shown to selectively hydrolyze 2,2-disubstituted oxiranes containing synthetically useful functional groups, such as halogens,[11] C=C bonds,[11,12] and aromatic moieties[13] in the side chain. The resulting intermediates have been applied to the asymmetric syntheses of (*S*)-frontalin[12] and (*R*)-mevalonolactone.[14] In order to extend the applicability of this method, we aimed at compounds bearing more polar O- and N-functional groups in the side-chain.

In a preliminary study on the epoxide hydrolase activity of *Rhodococcus* NCIMB 11216, it was demonstrated that polar substituents, such as free hydroxyl groups, are not tolerated.[15] However, it was anticipated that proper masking of the polar group, e.g. as ether, would render the substrates more lipophilic and thus acceptable for BEH. In addition, variation of the protecting group regarding polarity and size allows us to modulate the selectivity of the enzyme. This "substrate-modification technique" has been proven to be a powerful tool for the selectivity enhancement of biocatalyzed reactions, such as lipases, esterases, and proteases.[16]

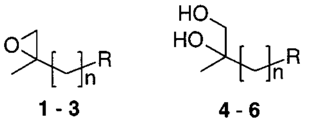
In order to obtain more insight on the relationship between substrate structure and enantioselectivity for BEH, we investigated a range of 2,2-disubstituted oxiranes bearing an ether-functionality in the side chain, with 11 different bacteria for activity and selectivity. The 20 substrates

---

[a] Institute of Chemistry, Organic and Bio-organic Chemistry, University of Graz,
Heinrichstrasse 28, 8010, Graz, Austria
Fax: (internat.) +43-316/3809840
E-mail: kurt.faber@kfunigraz.ac.at
[b] New address: Division of Chemistry, Bio-organic Chemistry, Vrije University,
de Boelelaan 1083, 1081 HV Amsterdam, The Netherlands
Fax: (internat.) +31-20/4447468

1434−193X/00/1122−3703 $ 17.50+.50/0

were chosen along two guidelines: (i) the size and polarity of the ether protecting group was varied, and (ii) the distance of the ether oxygen and the center of chirality on the oxirane moiety was systematically increased by varying the number of carbon atoms from $n = 1$ to $n = 3$ (Scheme 1). In this way, general information on the substrate-selectivity relationship was obtained regarding (i) the acceptance of oxygen atoms in the side chain, and (ii) the impact of the number of carbons separating the ether-oxygen and the stereogenic center on the rate and selectivity of the enzymatic hydrolysis.



1 - 3 **4 - 6**

R =	n = 1	n = 2	n = 3	n = 1	n = 2	n = 3
-OH	**1a**	**2a**	**3a**	**4a**	**5a**	**6a**
-$OCH_2CH=CH_2$	**1b**	**2b**	**3b**	**4b**	**5b**	**6b**
-$OCH_2CH_2CH_3$	**1c**	**2c**	**3c**	**4c**	**5c**	**6c**
-$OCH_2C_6H_5$	**1d**	**2d**	**3d**	**4d**	**5d**	**6d**
-OTBDMS	**1e**	**2e**	**3e**	**4e**	**5e**	**6e**
-$OSiEt_3$	**1f**	-	-	**4f**	-	-
-C≡N	**1g**	-	-	**4g**	-	-
-$OCH_2O(CH_2)_2OCH_3$	-	**2h**	-	-	**5h**	-
-$CH(OCH_2CH_3)_2$	-	**2i**	-	-	**5i**	-
-N_3	-	**2k**	-	-	**5k**	-

Scheme 1

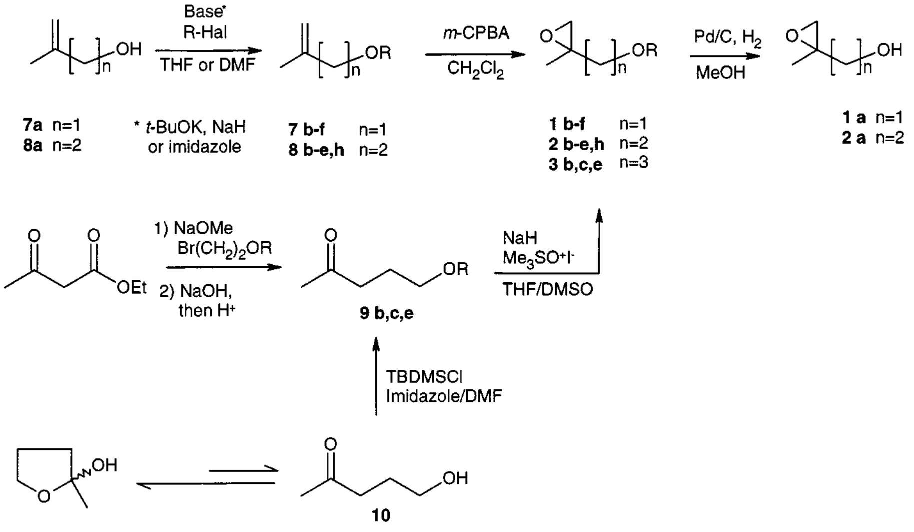
Results and Discussion

Epoxides of type **1** and **2** were prepared from commercially available unsaturated alcohols **7a** and **8a** via the corresponding ethers **7b−f** and **8b−e**,**h** (Scheme 2).

Williamson reactions of **7a** and **8a** using the corresponding organo-halide in refluxing THF in the presence of base afforded alkoxy and benzyloxy ethers **7b−d** and **8b−d**, respectively. Silyl ethers **7e**, **7f**, and **8e** were obtained by treatment of **7a** and **8a** with Et_3SiCl or TBDMSCl in DMF. Subsequent epoxidation using *m*CPBA in CH_2Cl_2 provided oxiranes **1b−f** and **2b−e**, in modest to good yields. Compound **2h** was synthesized according to a known procedure.[17] Hydrogenolysis of benzyloxy oxiranes **1d** and **2d** (Pd/C, H_2, MeOH) afforded the hydroxy oxiranes **1a** and **2a**.

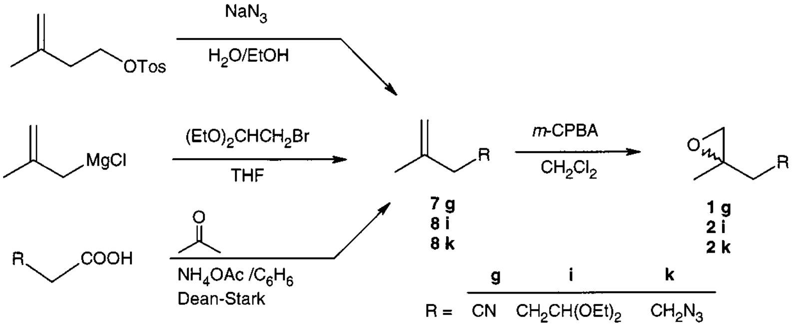
For the synthesis of oxiranes of type **3**, commercially available hydroxy ketone **10** seemed to be a suitable starting material, through O-protection followed by epoxide formation using sulfur ylide chemistry. However, the synthesis of keto-ethers **9b**, **c**, and **e** proved to be difficult, and was only successful for the TBDMS-derivative **9e**, when imidazole was used as base. The formation of ethers **9b**, and **c** requires much stronger bases, such as NaH, which causes the hydroxy ketone-hemiacetal equilibrium to shift towards the cyclic hemiacetal of **10** (Scheme 2). Therefore, another route, by α-alkylation of ethyl acetoacetate, followed by ester hydrolysis and decarboxylation was chosen to obtain keto-ethers **9b**, and **c**.[18] Epoxidation of **9b**, **c**, and **e** using sulfur-ylide chemistry (NaH/Me_3SO^+ I^- in THF/DMSO) afforded epoxides **3b**, **c**, and **e**, respectively.[19]

Substrates **1g** and **2k** contain a nitrile and azide moiety, which can serve as masked amino-groups for further transformations. Nitrile **1g** was obtained from alkene **7g**,[20] the azido-alkene **8k** was synthesized from the corresponding tosylate (Scheme 3). The acetal-protected alkene **8i** was obtained by coupling of bromoacetaldehyde diethylacetal to methallylmagnesium chloride. Epoxidation of alkenes **7g**, **8i**, and **8k** using *m*CPBA furnished substrates **1g**, **2i**, and **2k**, respectively, in fair yields.



	a	b	c	d	e	f	h
R =	H	allyl	*n*-Pr	$CH_2C_6H_5$	TBDMS	$SiEt_3$	$CH_2O(CH_2)_2OCH_3$

Scheme 2. Synthesis of substrates **1a−f**, **2a−e**, **h**, **3b**, **c**, and **e**

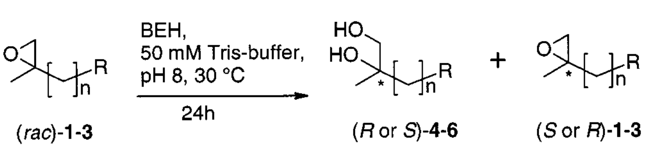


Scheme 3. Synthesis of substrates **1g**, **2i**, and **2k**

The structures of all oxiranes were confirmed by comparison with literature data, when available,[30,31] or by analysis of physical and spectroscopic data, which are described in the Experimental Section.

In order to achieve optimal selectivities, epoxides (±)-**1**−**3** were tested for spontaneous hydrolysis in aqueous buffer in the absence of biocatalyst. Whereas compounds **1** and **2** were sufficiently stable, epoxides **3a**−**c** showed considerable spontaneous hydrolysis. This hydrolytic instability can be explained by the association and activation of a water molecule, as a nucleophile, when bound to the ether oxygen. The other oxirane of this series (**3e**) showed no detectable spontaneous hydrolysis, which is probably due to the sterically demanding side chain. Epoxide **3d** proved to be rather unstable and underwent spontaneous hydrolysis during workup, and could thus not be obtained by either of the methods used.

Oxiranes of type **1** and **2** were used in a screening for activity using a range of bacteria that are known to possess epoxide hydrolase activity. In our experience, the latter is often associated with pigment-producing *Actinomyces* sp.[9a,21] (see Table 1). The screening was performed by using lyophilized cells in Tris-buffer at pH 8 and 30 °C for 24 h (Scheme 4).[13,15,21] In each case, the corresponding diols (**4**−**5**) were the only products that could be detected. Except for **2i**, no side products were observed. The structures of the formed diols were confirmed by comparison with literature data[32] or by spectroscopic methods.



Scheme 4. Biocatalytic hydrolysis of 2,2-disubstituted oxiranes

Oxiranes **1a**, **2a**, and **3a**, bearing a polar hydroxyl group in the side chain showed no biocatalytic hydrolysis at all, which is in agreement with previous observations.[15] In contrast, substrates with a lipophilic side chain were accepted with good rates. Thus, protection of the hydroxyl functionality as allyl-, propyl-, and benzyl-ether led to substrates **1b**−**d** and **2b**−**d**, which showed sufficient conversion within 24 h (Table 1). It should be mentioned that in general, the relative activities of ether-functionalized substrates are lower than that of the corresponding hydrocarbon-analogues of the same chain length.

Sterically demanding silyloxy oxiranes **1e**, **1f**, **2e**, and **3e** proved to be less suited, as they showed no or low conversion. Whereas **1e** and **1f** were not hydrolyzed at all, **2e** (having a longer "spacer" unit between the oxirane moiety and the sterically impeding silyloxy group) was hydrolyzed at a reasonable rate by *Rhodococcus* and *Mycobacterium* sp. In addition, the rather polar oxiranes **2h** and **2k** showed poor to moderate conversion with most of the bacteria.

For substrate **1g** bearing a nitrile group, no products could be detected after biohydrolysis. Based on the fact that

Table 1. Activities from biocatalytic hydrolysis of epoxides **1** and **2**

Conversion [%][a]											
	Rhodococcus sp.						*Mycobacterium*	*Arthrobacter*	*Mycoplana*	*Methylobacterium* sp.	
Substrate	NCIMB 11216	IFO 3730	CBS 717.73	SM 1789	SM 1790	SM 1788	NCIMB 10420	DSM 312	SM 73	SM 1793	DSM 1338
1b	56	38	50	35	>98	50	55	20	14	10	12
1c	17	19	9	24	>98	15	21	13	6	8	10
1d	31	18	32	53	89	42	56	28	3	6	26
2b	26	43	54	54	54	30	15	n.d.	6	< 2	n.d.
2c	71	22	59	>98	>98	88	59	56	50	< 2	n.d.
2d	29	37	25	34	67	45	42	29	< 2	34	n.d.
2e	< 2	16	< 2	20	16	3	16	n.c.	3	n.c.	n.d.
2h	18	13	n.d.	17	n.d.	n.d.	16	n.d.	12	11	n.d.
2k	13	n.d.	n.d.	8	15	10	< 2	n.d.	n.d.	11	n.d.

[a] Conversion values (±5%) were determined by GC analysis. Typical reaction conditions were: 5 µL epoxide, 50 mg lyophilized cells, 1 mL 50 mM Tris-buffer, pH 8, 30 °C, 130 rpm, 24 h. n.c. = no conversion, n.d. = not determined.

most bacteria possessing epoxide hydrolase activity also exhibit nitrile-hydrolyzing activity (via a nitrilase or a nitrile hydratase-amidase pathway), it was concluded that this latter group underwent hydrolysis to furnish the corresponding dihydroxycarboxylic acid, which is difficult to extract from the aqueous phase.[22]

For those substrates, which were hydrolyzed at a reasonable rate, the selectivities were determined (Table 2). In kinetic resolutions, the enantioselectivity is most conveniently described by the Enantiomeric Ratio *E*, since this parameter is independent of the conversion.[23] However, a prerequisite for using *E*-values is that the reaction has to proceed through a single stereochemical pathway with respect to the configuration of the stereogenic center(s). In biohydrolysis, epoxides are opened in a *trans*-specific manner by a formal S_N2-mechanism, and one oxygen from water is incorporated into the product diol. Depending on the substrate structure, hydrolytic opening of the epoxide ring may take place at either oxirane carbon atom by mixed regiochemical pathways, thus precluding the use of *E*-values.[9a,11] On the other hand, *E*-values are allowed for reactions acting by a single stereochemical path.[11] Based on the fact that (for 2,2-disubstituted oxiranes) it was demonstrated that BEH-catalyzed hydrolysis proceeds by attack at the less substituted oxirane-carbon atom, with absolute regioselectivity, leading to complete *retention* of configuration at the stereogenic center,[24] *E*-values are applicable and have been used throughout this study. In addition, it was experimentally verified that *E*-values remained constant during the course of the enzymatic hydrolysis of substrates used in this study.

Table 2. Selectivities from biocatalytic hydrolysis of epoxides **1** and **2**

Enantiomeric ratio *E*[a] (enantiopreference)[b]	*Rhodococcus* sp.						*Mycobacterium*	*Arthrobacter*	*Mycoplana*	*Methylobacterium*	
Substrate	NCIMB 11216	IFO 3730	CBS 717.73	SM 1789	SM 1790	SM 1788	NCIMB 10420	DSM 312	SM 73	SM 1793	DSM 1338
1b	36	14	27	11	<1	25	32	7	3	2	1
	(*S*)	(*S*)	(*S*)	(*S*)	n.d.	(*S*)	(*S*)	(*S*)	(*R*)	(*R*)	(*R*)
1c	10	9	12	9	<1	10	10	10	4	3	1
	(*S*)	(*S*)	(*S*)	(*S*)	n.d.	(*S*)	(*S*)	(*S*)	(*R*)	(*R*)	(*R*)
1d	>200	4	55	108	<1	45	18	5	2	2	3.5
	(*S*)	(*S*)	(*S*)	(*S*)	n.d.	(*S*)	(*S*)	(*S*)	(*R*)	(*S*)	(*R*)
2b	5	5	n.d.	3	3	3	4	n.d.	2	<1	n.d.
	(*S*)	(*S*)	–	(*S*)	(*S*)	(*S*)	(*S*)	–	(*R*)	n.d.	–
2c	5	3	2	>1	>1	1	16	3	8	<1	n.d.
	(*S*)	(*S*)	(*S*)	n.d.	n.d.	(*S*)	(*S*)	(*S*)	(*R*)	n.d.	–
2d	9	2	1	1	1	1	3	2	n.d.	2	n.d.
	(*S*)	(*S*)	(*S*)	(*S*)	(*S*)	(*S*)	(*S*)	(*S*)	–	(*R*)	–
2e	n.d.	8	n.d.	34	28	n.d.	13	n.d.	n.d.	n.d.	n.d.
2h	3	2	n.d.	3	n.d.	n.d.	3	n.d.	<1	<1	n.d.
2k	13	n.d.	n.d.	5	7	5	<1	n.d.	n.d.	2	n.d.

[a] Enantiomeric ratio: $E = (k_{cat}/K_M)_{(R)}/(k_{cat}/K_M)_{(S)}$; calculated from ee_p, ee_s and/or conversion (c) according to Rakels et al.[23a] or Sih et al.[23b,23c] – [b] Absolute configuration of preferably hydrolyzed epoxide enantiomer; n.d. = not determined.

The absolute configurations of diols **4b–d** and **5b–e** formed during biohydrolysis, as well as that of remaining epoxides **1b–d** and **2b–e** were determined on chiral GC or HPLC, by co-injection with independently synthesized material. The latter was obtained from (*R*)-2-methylglycidol for compounds **1a–d** and **4a–d**. The absolute configuration of **5d** was elucidated by comparison of its optical rotation value with literature data, samples of analogs **5b**, **c**, and **e** were synthesized from **5d**. For details see the Experimental Section.

The enantiopreference of bacterial cells showed a previously observed behaviour: Whereas *Rhodococcus, Mycobacterium*, and *Arthrobacter* sp. preferentially afforded (*S*)-diols from (*S*)-epoxides, leaving (*R*)-oxiranes behind, methylotrophs, such as *Mycoplana* and *Methylobacterium* sp. showed the opposite enantiopreference.[25] It has to be emphasized that for substrates **1b–d**, hydrolysis of (*S*)-epoxides with *retention* yields (*R*)-diols and vice versa (i.e. they are homochiral) due to a switch in sequence rules according to Cahn–Ingold–Prelog.

The enantioselectivity data in Table 2 show three general trends: (i) With the exception of substrate **1d**,[9a,13] the introduction of (polar) functional groups into 2,2-disubstituted oxiranes led to a general decrease of enantioselectivity to a certain extent, when compared to the corresponding aliphatic (non-functionalized) counterparts, where the ether-oxygen is replaced by a CH_2-unit.[9a] (ii) The selectivity could be efficiently modulated by variation of the O-protecting group, and by this means, low selectivities could be significantly enhanced. (iii) Selectivities of substrates bearing a short spacer (**1a–d**, $-CH_2-$) between the quaternary oxirane carbon atom gave better selectivities than those bearing a $-CH_2-CH_2-$ spacer (**2b–d**).

Within the $n = 1$ series (**1b–d**), good to excellent *E*-values were obtained. In particular, synthetically useful substrates bearing an allyl- or benzyl protecting group (**1b, 1d**), were resolved by *Rhodococcus* NCIMB 11216 with $E = 36$ and >200, respectively. Other *Rhodococci* and *Mycobacterium* sp. showed good selectivities. It is noteworthy that introduction of π-electrons at the 4,5-position (substrates **1b**, **1d**) relative to the quaternary carbon atom seems to partly compensate (as in **1b**) or completely annihilate (as in **1d**) the negative effect of the ether-oxygen on the selectivity.

The reduction of selectivity by the polar functional groups was found to be most significant within the $n = 2$

oxiranes (**2b−d**), which are too low for preparative purposes, best results were obtained with *Mycobacterium* sp. and compound **2c** ($E = 16$). On the other hand, low selectivities could be effectively compensated by introduction of a sterically demanding silyloxy group. Substrate **2e** was well resolved by *Rhodococcus* sp. (*E*-values up to 34). Substrates bearing more polar functional groups, such as $-O(CH_2)O(CH_2)_2OCH_3$ (**2h**), $-OCH(OCH_2CH_3)_2$ (**2i**) and $-N_3$ (**2k**) gave insufficient selectivities.

Conclusion

A series of 2,2-disubstituted epoxides bearing (polar) functional groups were resolved by using bacterial epoxide hydrolases. It was found that free hydroxyl groups were not tolerated, but when these were protected as more lipophilic ether moieties, the oxiranes are hydrolyzed with good to excellent activity. Three general rules could be defined for the construction of substrates: (i) An increase in the polarity of the functional group led to a decrease in the reaction rate and enantioselectivity, (ii) Low selectivities could be dramatically enhanced by variation of the ether-protecting group and (iii) The number of carbon atoms separating the stereogenic oxirane center and the ether-oxygen has a profound influence on the selectivity, i.e. substrates bearing a short spacer (i.e. $-CH_2-$) gave higher selectivities than those bearing a longer $-CH_2-CH_2-$ unit. The use of the benzyl derivative 1d (which is not easily prepared by conventional methodology[26]) in the asymmetric synthesis of bioactive compounds[27] is currently being exploited in a subsequent study. The data obtained during this study will be used for the development of an active-site model of bacterial epoxide hydrolases based on comparative molecular field analysis (COMFA).

Experimental Section

General Remarks: NMR spectra were recorded in $CDCl_3$ using a Bruker AMX 360 at 360 (^{1}H) and 90 (^{13}C) MHz. Chemical shifts are reported relative to TMS ($\delta = 0.00$) with $CHCl_3$ as internal standard [$\delta = 7.23$ (^{1}H) and 76.90 (^{13}C)], coupling constants (*J*) are given in Hz. ^{13}C NMR multiplicities were determined by using a DEPT pulse sequence. IR spectra were recorded on a Perkin−Elmer 298 spectrometer.

TLC plates were run on silica gel Merck 60 (F_{254}) and compounds were visualized by standard techniques. Compounds were purified either by flash chromatography on silica gel Merck 60 (230−400 mesh) or, for volatile substances, by kugelrohr distillation. Petroleum ether (p.e.) with a boiling range of 60−90 °C was used, unless otherwise noted. GC analyses were carried out on a Varian 3800 gas chromatograph equipped with FID and either a HP1301 or a HP1701 capillary column (both 30 m, 0.25 mm, 0.25 µm film, N_2). For chiral analyses vide infra.

Solvents were dried and freshly distilled by common practice. For anhydrous reactions, flasks were dried at 150 °C and flushed with dry argon just before use. Hydroxy-alkenes **7a** and **8a** were purchased from Aldrich and distilled before use. For biotransformations lyophilized bacterial cells were used. The bacteria were obtained from culture collections. SM strain numbers refer to the culture collection of the Institute of Biotechnology, Graz University of Technology. All strains were grown as previously described.[12,13,21,25]

Substrates and Reference Materials

Racemic Oxiranes 1−3

Oxiranes **1b−g**, **2b−e**, and **2h−k** were prepared from the corresponding alkenes **7b−g**, **8b−e**, and **8h−k**, respectively, and *m*-chloroperbenzoic acid (*m*CPBA) following method A (vide infra). The physical and/or spectroscopic data of all the isolated alkenes were identical to those reported previously.[28]

Oxiranes **3b**, **c**, and **e** were prepared from the corresponding ketones **9b**, **c**, and **e**,[29] respectively, and trimethylsulfoxonium iodide following method B (vide infra). Ketones were prepared according to a known procedure[18] and purified by kugelrohr distillation prior to epoxidation.

Method A: To a vigorously stirred solution of alkene (ca. 0.07 M) in dry CH_2Cl_2 was added ca. 2.6 equiv. of K_2CO_3. After the mixture was stirred for 1 h at room temp., it was cooled to 0 °C and *m*CPBA (1.3 equiv.) was added slowly. The reaction was allowed to warm to room temp. and stirred for additional 20 h, after which the white suspension was filtered. The resulting solution was treated with 10% aqueous $Na_2S_2O_5$ (0.5 reaction volume) to destroy excess peracid. The resulting two-phase system was stirred for 30 min, the layers were separated and the organic phase was washed with saturated aqueous $NaHCO_3$ (0.2 reaction volume). The organic phase was dried and evaporated. Flash chromatography or kugelrohr distillation afforded pure oxiranes **1b−g**, **2b−e**, **h−k**. Spectroscopic data for **1b**, **d**, **e**, **g**, and **2d**, and **e**, were identical to those previously reported.[30] Details and spectroscopic data for oxiranes **1c** and **f** and **2b**, **c**, **h**, **i**, and **k** are given below.

2-Methyl-3-(propyloxy)-1-propene Oxide (1c): Method A was employed by using crude propyloxy alkene **7c** (0.60 g). Workup and flash chromatography (pentane/MeOAc, 100:1) gave 0.33 g (68%, calcd. from **7a**) of **1c**, R_f (petroleum ether/EtOAc, 5:1) = 0.58. − ^{1}H NMR: $\delta = 0.90$ (3 H, t, J=7.5), 1.35 (3 H, s), 1.57−1.62 (2 H, m), 2.61 (1 H, d, J=5.0), 2.72 (1 H, d, J=5.0), 3.37−3.52 (4 H, m). − ^{13}C NMR: $\delta = 10.5$ (q), 18.4 (q), 22.9 (t), 51.6 (t), 56.1 (s), 73.2 (t), 74.1 (t).

2-Methyl-3-(triethylsilyl)oxy-1-propene Oxide (1f): Method A was employed by using 1.32 g (7.1 mmol) triethylsilyloxy alkene **7f**. Workup and kugelrohr distillation afforded 0.91 g (61%) of **1f**, bp 105−110 °C (8 mbar); R_f (petroleum ether/EtOAc, 5:1) = 0.68. − ^{1}H NMR: $\delta = 0.61$ (6 H, m), 0.96 (9 H, m), 1.35 (3 H, s), 2.60 (1 H, d, $J = 5.0$), 2.75 (1 H, d, $J = 5.0$), 3.60 (1 H, d, $J = 11.2$), 3.65 (1 H, d, $J = 11.2$). − ^{13}C NMR: $\delta = 4.4$ (3q), 6.7 (3t), 18.1 (q), 51.7 (t), 57.1 (s), 66.4 (t).

4-Allyloxy-2-methyl-1-butene Oxide (2b): Method A was employed by using crude allyloxy alkene **7d** (4.75 g). Workup and kugelrohr distillation afforded 2.15 g (40%, calcd. from **8a**) of **2b**, bp 130 °C (30 mbar); R_f (p.e./EtOAc, 5:1) = 0.49. − ^{1}H NMR: $\delta = 1.32$ (3 H, s), 1.71−1.97 (2 H, m), 2.56 (1 H, d, $J = 4.9$), 2.66 (1 H, d, $J = 4.9$), 3.50 (2 H, dt, $J = 6$, $J = 1.5$), 3.93 (2 H, d, $J = 5.5$), 5.11−5.29 (2 H, m), 5.78−5.98 (1 H, m). − ^{13}C NMR: $\delta = 21.6$ (q), 36.6 (t), 54.0 (t), 55.4 (s), 66.6 (t), 71.9 (t), 116.9 (t), 134.8 (d).

2-Methyl-4-propyloxy-1-butene Oxide (2c): Method A was employed by using crude propyloxy alkene **8c** (1.50 g). Workup and flash chromatography (pentane) afforded 0.77 g (15%, calcd. from **8a**) of **2c**, R_f (petroleum ether/EtOAc, 1:1) = 0.78. − ^{1}H NMR: δ = 0.86 (3 H, t, J = 7.9), 1.32 (3 H, s), 1.48−1.70 (2 H, m), 1.72−1.98 (2 H, m), 2.58 (1 H, d, J = 5.1), 2.66 (1 H, d, J = 5.1), 3.34 (2 H, t, J = 6.8), 3.48 (2 H, t, J = 6.5) . − ^{13}C NMR: δ = 10.6 (q), 21.6 (q), 22.9 (t), 36.6 (t), 54.0 (t), 55.5 (s), 67.0 (t), 72.7 (t).

2-Methyl-4-(2-methoxyethoxymethyl)oxy-1-butene Oxide (2h): Method A was employed by using 2.00 g (11.6 mmol) (2-methoxyethoxymethyl)oxy alkene **8h**. Workup and flash chromatography (petroleum ether/EtOAc, 5:1) yielded 0.68 g (31%) of **2h**, bp 220 °C (20 mbar); R_f (EtOAc) = 0.68. − ^{1}H NMR: δ = 1.31 (3 H, s), 1.61−1.97 (2 H, m), 2.54 (1 H, d, J = 4.8), 2.64 (1 H, d, J = 4.8), 3.35 (3 H, s) 3.50−3.68 (6 H, m), 4.66 (2 H, s). − ^{13}C NMR: δ = 21.4 (q), 36.6 (t), 53.9 (t), 55.3 (s), 59.03 (q), 64.2 (t), 66.9 (t), 71.7 (t), 95.5 (t).

5,5-Diethoxy-2-methyl-1-pentene Oxide (2i): Method A was employed by using 1.1 g (6.4 mmol) diethoxy alkene **8i**. Workup and flash chromatography (pentane) yielded 0.45 g (38%) of R_f (petroleum ether/EtOAc, 5:1) = 0.40. − ^{1}H NMR: δ = 1.15−1.24 (6 H, m), 1.27 (3 H, s), 1.58−1.64 (4 H, m), 2.51−2.59 (2 H, m), 3.40−3.63 (4 H, m), 4.43 (1 H, t, J = 4.8). − ^{13}C NMR: δ = 15.3 (2q), 21.0 (q), 29.3 (t), 31.7 (t), 53.7 (t), 56.6 (s), 61.1 (t), 61.3 (t), 102.6 (d).

4-Azido-2-methyl-1-butene Oxide (2k): Method A was employed by using crude azido alkene **8k** (0.57 g). Workup and flash chromatography (gradient of pentane to pentane/MeOAc, 20:1) yielded 0.35 g (33%, calcd. from the tosylate of **8a**) of **2k**, R_f (petroleum ether/EtOAc, 2:1) = 0.57. − IR(KBr): $\tilde{\nu}$ = 2100 cm^{-1}. − ^{1}H NMR: δ = 1.33 (3 H, s), 1.83 (2 H, dt, J = 7, J = 2.5), 2.60 (1 H, d, J = 4.6), 2.66 (1 H, d, J = 4.6), 3.37 (2 H, t, J = 7.0). − ^{13}C NMR: δ = 21.1 (q), 35.5 (t), 47.6 (t), 53.7 (t), 54.9 (t).

Method B: A solution of the corresponding ketones **9b**, **c**, and **e** (ca. 1 M) in dry DMSO was added slowly to a stirred suspension of NaH (ca. 1.3 equiv., 0.35 M) and trimethylsulfoxonium iodide (ca. 1.3 equiv., 0.35 M) in dry DMSO/THF (2:3), at 0 °C. The mixture was stirred at 0 °C for 2 h and then allowed to warm to room temp. After completion of the reaction (12−20 h), petroleum ether (0.3 × reaction volume) and saturated aqueous NH_4Cl solution (1 × reaction volume) were added and the mixture was stirred for additional 30 min. Then, the two-phases were separated and the water layer was extracted with petroleum ether. The combined organic phases were dried and evaporated. Kugelrohr distillation afforded the pure oxiranes **3b**, **c**, and **e**. Details and characteristic data follow below.

5-Allyloxy-2-methyl-1-pentene Oxide (3b): Method B was employed by using 1.6 g (11.4 mmol) allyloxy ketone **9b**. Workup and kugelrohr distillation afforded 0.88 g (50%) of **3b**, bp 120−121 °C (15 mbar); R_f (petroleum ether/EtOAc, 10:1) = 0.33. − ^{1}H NMR: δ = 1.29 (3 H, s), 1.56−1.77 (4 H, m), 2.54 (1 H, d, J = 4.9), 2.59 (1 H, d, J = 4.9), 3.42 (2 H, t, J = 6.5), 3.93 (2 H, d, J = 5.5), 5.11−5.28 (2 H, m), 5.76−6.01 (1 H, m). − ^{13}C NMR: δ = 20.9 (q), 25.5 (t), 33.4 (t), 53.8 (t), 56.7 (s), 70.0 (t), 71.8 (t), 116.8 (t), 134.9 (d).

2-Methyl-5-propyloxy-1-pentene Oxide (3c): Method B was employed by using 1.2 g (8.3 mmol) propyloxy ketone **9c**. Workup and kugelrohr distillation afforded 0.44 g (34%) of **3c**, bp 117−119 °C (15 mbar); R_f (p.e./EtOAc, 10:1) = 0.30. − ^{1}H NMR: δ = 0.88 (3 H, t, J = 7.3), 1.29 (3 H, s), 1.50−1.64 (6 H, m), 2.54 (1 H, d, J = 4.8), 2.59 (1 H, d, J = 4.8), 3.30−3.40 (4 H, m, J = 6.5). − ^{13}C NMR: δ = 12.5 (q), 22.9 (q), 24.8 (t), 27.5 (t), 35.3 (t), 55.8 (t), 58.7 (s), 72.4 (t), 74.5 (t).

2-Methyl-5-(*tert*-butyldimethylsilyl)oxy-1-pentene Oxide (3e): Method B was employed by using 0.97 g (4.5 mmol) *tert*-butylsilyloxy ketone **9e**. Workup and kugelrohr distillation afforded 0.46 g (45%) of **3e**, bp 160−161 °C (18 mbar); R_f (petroleum ether/EtOAc, 1:1) = 0.84. − ^{1}H NMR: δ = 0.03 (6 H, s), 0.87 (9 H, s), 1.30 (3 H, s), 1.58−1.61 (4 H, m), 2.54−2.60 (2 H, m), 3.58−3.61 (2 H, m). − ^{13}C NMR: δ = −5.3 (2q), 18.1 (s), 21.0 (q), 26.0 (3q), 28.6 (t), 33.2 (t), 53.9 (t), 57.1 (s), 62.9 (t).

6-Benzyloxy-2-methyl-1-hexene Oxide: Method B was employed by using 0.39 g (1.88 mmol) of the corresponding benzyloxy ketone. Workup and kugelrohr distillation afforded 0.24 g (58%), bp 194−196 °C (3 mbar); R_f (petroleum ether/EtOAc, 1:1) = 0.80. − ^{1}H NMR: δ = 1.31 (3 H, s), 1.45−1.68 (6 H, m), 2.55−2.62 (2 H, m), 3.47 (2 H, d, J = 6.2), 4.51 (2 H, s), 7.29−7.36 (5 H, m). − ^{13}C NMR: δ = 20.9 (q), 22.1 (t), 29.8 (t), 36.6 (t), 53.9 (t), 57.0 (s), 70.2 (t), 73.0 (t), 127.6 (d), 127.9 (2d), 128.4 (2d), 138.6 (s).

Oxiranes **1a** and **2a** were prepared by hydrogenolysis of benzyloxy oxiranes **1d** and **2d**, respectively: To a stirred solution of benzyloxy oxirane (3.5 g, 18−20 mmol) in 60 mL dry MeOH/CH_2Cl_2 (1:1) was added a catalytic amount of Pd/C (5%). The reaction mixture was placed under a H_2 atmosphere. After completion (20 h), the mixture was filtered through Celite-545 and the filter cake was washed with three 15-mL portions of Et_2O. Water (80 mL), NaCl (2 g), and Et_2O (50 mL) were added to the filtrate, the phases were separated, and the water layer was extracted with three 20-mL portions of Et_2O. The combined organic layers were dried and evaporated. Kugelrohr distillation afforded pure hydroxy oxiranes **1a** and **2a**. Physical and spectroscopic data for **1a** and **2a** were identical to those reported previously.[31]

Racemic Diols 4−6

Diols **4a−d**, **5a**, **c**, **d**, and **6b−c** were obtained by hydrolysis of the corresponding racemic oxiranes (0.2 M in water/THF 1:1) under acidic conditions (6 N H_2SO_4, 3−4 drops). Diols **4e**, **f**, and **5e** were prepared by dihydroxylation of the corresponding silyloxy alkenes (0.17 M in acetone) using *N*-methylmorpholine *N*-oxide (0.17 M) and a catalytic amount of OsO_4. Finally, diols **4g** and **5b**, **h−k** were obtained by alkaline hydrolysis (KOH, 5.4 mmol) of the corresponding oxiranes (0.5 mmol) in THF (1.5 mL). Compounds **4a**, **d**, **e**, and **5a**, and **d** have been characterized before.[32] The characteristic data of **4b**, **c**, **f**, **g**, **5b**, **c**, **e**, **h**, **i**, **6b**, **c**, and **h** are listed below.

3-Allyloxy-2-methyl-1,2-propanediol (4b): Yield after flash chromatography (petroleum ether/EtOAc, 2:1) 44%; R_f (EtOAc) = 0.45. − ^{1}H NMR: δ = 1.08 (3 H, s), 2.38 (1 H, br s), 2.47 (1 H, br s), 3.37 (2 H, s), 3.68 (2 H, s), 3.95 (2 H,dd, J = 1.6, 6.1), 5.14−5.25 (2 H, m), 5.72−5.95 (1 H, m). − ^{13}C NMR: δ = 21.4 (q), 66.7 (t), 71.8 (s), 72.6 (t), 76.3 (t), 117.5 (t), 134.2 (d).

2-Methyl-3-propyloxy-1,2-propanediol (4c): Yield after flash chromatography (petroleum ether/EtOAc, 2:1) 62%; R_f (petroleum ether/EtOAc, 2:1) = 0.35. − ^{1}H NMR: δ = 0.88 (3 H, t, J = 7.3), 1.10 (3 H, s), 1.55 (2 H, m), 3.08 (2 H, br s), 3.30−3.68 (6 H, m). − ^{13}C NMR: δ = 10.5 (q), 21.3 (q), 22.7 (t), 68.1 (t), 71.9 (s), 73.5 (t), 76.8 (t).

2-Methyl-3-(triethylsilyl)oxy-1,2-propanediol (4f): Yield after flash chromatography (petroleum ether/EtOAc, 5:1) 30%; R_f (p.e./EtOAc, 5:1) = 0.12. − ^{1}H NMR: δ = 0.60 (6 H, q, J = 7.9), 0.96 (9 H, t, J = 7.8), 1.10 (3 H, s) 2.53 (1 H, br s), 2.88 (1 H, br s), 3.47−3.65 (4 H, m). − ^{13}C NMR: δ = 4.3 (3t), 6.7 (3q), 21.0 (q), 68.5 (t), 68.9 (t), 72.0 (s).

4-Azido-2-methyl-1,2-butanediol (4g): Yield after flash chromatography (petroleum ether/EtOAc, 2:1) 53%; R_f (EtOAc) = 0.56. − ^{1}H NMR: δ = 1.18 (3 H, s), 1.62−1.92 (2 H, m), 2.93 (2 H, m), 3.43−3.53 (4 H, m). − ^{13}C NMR: δ = 23.6 (q), 36.8 (t), 47.2 (t), 69.9 (t), 72.1 (s).

4-Allyloxy-2-methyl-1,2-butanediol (5b): Yield after flash chromatography (petroleum ether/EtOAc, 2:1) 75%; R_f (EtOAc) = 0.35. − ^{1}H NMR: δ = 1.15 (3 H, s), 1.60−1.96 (2 H, m), 3.16 (1 H, t, *J* = 6.4), 3.37−3.43 (3 H, m), 3.51−3.72 (2 H, m), 3.96 (2 H, dt, *J* = 1.3, *J* = 5.7), 5.13−5.28 (2 H, m), 5.76−5.95 (1 H, m). − ^{13}C NMR: δ = 24.3 (q), 37.9 (t), 66.8 (t), 70.0 (t), 71.2 (t), 72.4 (s), 117.6 (t), 134.0 (d).

2-Methyl-4-propyloxy-1,2-butanediol (5c): Yield after flash chromatography (pentane/MeOAc, 1:1) 52%; R_f (petroleum ether/EtOAc, 1:1) = 0.21. − ^{1}H NMR: δ = 0.89 (3 H, t, *J* = 7.5), 1.16 (3 H, s), 1.54−1.68 (3 H, m), 1.86−1.94 (1 H, m), 2.03 (1 H, s), 3.35−3.45 (3 H, m), 3.55−3.57 (1 H, m), 3.65−3.68 (2 H, m). − ^{13}C NMR: δ = 10.6 (q), 22.8 (q), 24.4 (t), 38.0 (t), 67.3 (t), 70.1 (t), 72.5 (s), 73.2 (t).

2-Methyl-4-(*tert*-butyldimethylsilyl)oxy-1,2-butanediol (5e): Yield after flash chromatography (petroleum ether/EtOAc, 5:1) 66%; R_f (EtOAc) = 0.69. − ^{1}H NMR: δ = 0.07 (6 H, s), 0.88 (9 H, s), 1.17 (3 H, s), 1.50−1.90 (2 H, m), 3.05 (1 H, t, *J* = 7), 3.32−3.46 (2 H, m), 3.75 (1 H, br s), 3.77−3.96 (2 H, m). − ^{13}C NMR: δ = −5.58 (q), 18.1 (s), 24.4 (q), 25.8 (3q), 39.9 (t), 60.1 (t), 70.1 (t), 72.6 (s).

2-Methyl-4-(2-methoxyethoxymethyl)oxy-1,2-butanediol (5h): Yield after flash chromatography (EtOAc) 54%; R_f (EtOAc) = 0.16. − ^{1}H NMR: δ = 1.17 (3 H, s), 1.62−1.88 (2 H, m), 2.94 (1 H, br s), 3.23 (1 H, br s), 3.34 (3 H, s), 3.39−3.79 (8 H, m), 4.69 (2 H, s). − ^{13}C NMR: δ = 24.0 (q), 37.6 (t), 59.0 (t), 64.5 (t), 67.2 (q), 70.02 (t), 71.7 (t), 72.4 (s), 95.6 (t).

5,5-Diethoxy-2-methyl-1,2-pentanediol (5i): Yield after flash chromatography (petroleum ether/EtOAc, 1:1) 83%; R_f (EtOAc) = 0.27. − ^{1}H NMR: δ = 1.12−1.22 (6 H, m), 1.17 (3 H, s), 1.42−1.74 (4 H, m), 2.59 (1 H, br s), 2.76 (1 H, br s), 3.38−3.69 (6 H, m), 4.46 (1 H, t, *J* = 4.4). − ^{13}C NMR: δ = 15.3 (2q), 23.4 (q), 27.9 (t), 33.0 (t), 61.4 (t), 61.6 (t), 69.9 (t), 72.3 (s), 103.3 (d).

5-Allyloxy-2-methyl-1,2-pentanediol (6b): Yield after flash chromatography (petroleum/EtOAc, 5:1) 36%; R_f (petroleum ether/EtOAc, 5:1) = 0.12. − ^{1}H NMR: δ = 1.16 (3 H, s), 1.57−1.72 (4 H, m), 2.75 (2 H, br s), 3.38−3.49 (4 H, m), 3.99 (2 H, d, *J* = 5.6), 5.18−5.30 (2 H, m), 5.87−5.95 (1 H, m). − ^{13}C NMR: δ = 23.4 (q), 24.0 (t), 35.8 (t), 70.0 (t), 70.9 (t), 72.0 (t), 72.4 (s), 117.4 (t), 134.4 (d).

2-Methyl-5-propyloxy-1,2-pentanediol (6c): Yield after flash chromatography (petroleum ether/EtOAc, 1:1) 26%; R_f (petroleum ether/EtOAc, 1:1) = 0.19. − ^{1}H NMR: δ = 0.92 (3 H, t, *J* = 7.5), 1.16 (3 H, s), 1.57−174 (6 H, m), 2.50 (2 H, br s), 3.38−3.47 (6 H, m). − ^{13}C NMR: δ = 10.6 (q), 22.8 (t), 23.5 (q), 24.0 (t), 36.1 (t), 70.1 (t), 71.5 (t), 72.2 (s), 72.9 (t).

6-Benzyloxy-2-methyl-1,2-hexanediol: Yield after flash chromatography (petroleum ether/EtOAc, 3:1) 69%; R_f (petroleum ether/EtOAc, 1:1) = 0.23. − ^{1}H NMR: δ = 1.14 (3 H, s), 1.34−1.69 (6 H, m), 2.24 (1 H, br s), 2.51 (1 H, br s), 3.39 (2 H, br s), 3.49 (2 H, t, *J* = 6.0), 4.50 (2 H, s), 7.30−7.34 (5 H, m). − ^{13}C NMR: δ = 20.4 (q), 23.1 (t), 30.1 (t), 38.3 (t), 69.6 (t), 70.1 (t), 72.8 (t), 72.9 (s), 127.5 (d), 127.6 (2d), 128.3 (2d), 138.4 (s).

General Procedure for the Biocatalytic Hydrolysis of (±)-1−3: Racemic epoxides **1−3** (5 µL) were hydrolyzed using rehydrated lyophilized cells (50 mg) in Tris-buffer (1 mL, 0.05 M, pH 8.0) by shaking the mixture at 30 °C and 130 rpm. The reactions were monitored by TLC and GC, and after 24 h the mixtures were extracted with two 1 mL portions of EtOAc. To facilitate phase separation, the cells were removed by centrifugation. The combined organic layers were dried and analyzed.

Chiral Analysis: See Table 3. Enantiomeric purities were determined by analysis on a Varian 3800 gas chromatograph equipped with FID, using a CP-Chirasil-DEX CB column (column A, 25 m, 0.32 mm, 0.25 µm film), an Astec Chiraldex B-TA capillary column (column B, 30 m, 0.25 mm) or Astec Chiraldex G-PN (column C, 30 m, 0.25 mm). Hydrogen was used as a carrier gas unless otherwise noted. Chiral HPLC analyses were performed on a JASCO system containing a PU-980 pump equipped with a DAICEL CHIRALPAK AD column (column D) connected to a MD-910 multi-wavelength detector.

Oxiranes were either hydrolyzed (aqueous KOH, 60 °C) to the corresponding *vic*-1,2-diols (**4** or **5**) or transformed into the corresponding 2-hydroxy-1-methoxy-2-methyl ethers by treatment with NaOMe prior to analysis. Epoxide **2e** (TBAF, THF) as well as diol **5e** (TsCl/pyridine, followed by KOH/MeOH and then TBAF/THF) were transformed into 4-hydroxy epoxide **2a** prior to analysis. Finally, diol **5d** was transformed into the corresponding 2-hydroxy-1-methoxy-2-methyl benzyl ether by treatment with MeI and KOH in DMSO prior to analysis. The other diols could be analyzed directly.

Determination of Absolute Configurations: The absolute configuration was only determined for those compounds that were obtained in a significant optical enrichment from the biotransformation.

Absolute configurations of the biotransformation products **1b**, **1c**, **4b**, and **4c** were determined by co-injection on chiral GC with reference material. This was independently synthesized as follows: Treatment of commercially available (*R*)-2-methylglycidol with allyl bromide in the presence of a strong base (*t*BuOK) in dry ether afforded optically pure (*R*)-**1b**. Subsequent hydrolysis under basic conditions (aqueous KOH, 60 °C) gave enantiopure dihydroxy-allyl ether (*S*)-**4b**. Treatment of this with Pd/C (5%) in dry EtOH under a H_2 atmosphere gave optically pure dihydroxypropyl ether (*S*)-**4c**. Epoxides **1b** and **1c** were hydrolyzed under basic conditions (aqueous KOH, 60 °C) prior to co-injection on chiral GC.

The absolute configuration of the biotransformation products **1d** and **4d** were elucidated as follows: Diol **4d** (*ee* > 98%) was transformed into the corresponding acetonide (2,2-dimethoxypropane, cat. ion exchange resin IR 120 H^+-form, room temp.). Hydrogenolysis of the obtained material, using Pd/C (5%) in dry MeOH/CH_2Cl_2 under an H_2 atmosphere, afforded 4-hydroxymethyl-2,2,4-trimethyl-1,3-dioxolane (*ee* > 98%). The absolute configuration of the latter was determined by co-injection on GC with an independently synthesized enantiopure sample. This was obtained by the procedure of Wirz et al.[32a] Epoxide **1d** was hydrolyzed under basic conditions (KOH, 60 °C), and then treated as described for **6b**.

Absolute configurations of the biotransformation products **2b−d** and **5b−d** were determined by co-injection on chiral GC with reference material, which was obtained as described below. Dihydroxybenzyl ether (*R*)-**5d**[3b] was transformed into the corresponding acetonide (2,2-dimethoxypropane, cat. ion exchange resin IR 120 H^+-

Table 3. Chiral GC/HPLC data

Compound	Method	Chiral column[a]	Conditions	Retention time [min] (absolute config.)
1d[b]	GC	A	0.8 bar, 125 °C (iso)	9.6 (*R*), 10.2 (*S*)
1e[b]	GC	A	1 bar, 80 °C (iso)	10.4, 12.0 (n.d.)
2a[c]	GC	C	0.28 bar, 75 °C (iso)	29.5 (*R*), 31.9 (*S*)
2d[b]	HPLC	D	heptane/*i*PrOH 98:2 0.7 mL/min	27.3 (*R*), 30.6 (*S*)
4b	GC	B	1 bar (N_2), 90 °C (iso)	9.8 (*R*), 10.5 (*S*)
4c	GC	A	1 bar, 100 °C (iso)	5.1 (*R*), 5.6 (*S*)
4d	GC	A	0.8 bar, 130 °C (iso)	16.9 (*R*), 17.4 (*S*)
5b	GC	A	1 bar (He), 125 °C (iso)	7.9 (*S*), 8.3 (*R*)
5c	GC	A	0.35 bar, 110 °C (iso)	15.2 (*S*), 16.0 (*R*)
5d[b]	HPLC	C	heptane/*i*PrOH 98:2 0.7 mL/min	27.3 (*R*), 30.6 (*S*)
5g	GC	A	1 bar, 130 °C (iso)	13.7, 14.3 (n.d.)
5i	GC	A	1 bar (N_2), 125 °C (iso)	13.6, 14.5 (n.d.)
6b[b]	GC	A	0.6 bar, 90 °C (iso)	19.9, 20.9 (n.d.)
6h	GC	A	1 bar, 100 °C (iso)	4.8, 5.3 (n.d.)

[a] For details see below. − [b] Analyzed as the corresponding 1-methoxy derivative. − [c] Compounds **2e** and **5e** were transformed into **2a** prior to analysis. n.d. = not determined.

form, room temp.). Subsequent hydrogenolysis (Pd/C, H_2, MeOH, room temp.), Williamson reaction (allyl bromide, *t*BuOK, dry ether, room temp.), and then acidic hydrolysis (water/THF, cat. ion exchange resin IR 120, H^+-form, room temp.) afforded dihydroxyallyl ether (*R*)-**5b**. Hydrogenation of the latter with Pd/C (5%) in dry EtOH under a hydrogen atmosphere gave optically pure dihydroxypropyl ether (*R*)-**5c**. Epoxides **2b−d** were hydrolyzed under basic conditions (aqueous KOH, 60 °C) prior to co-injection on chiral GC.

Acknowledgments

This research was performed within the Spezialforschungsbereich Biokatalyse (SFB-A4, project no. F-104) and was financed by the Fonds zur Förderung der wissenschaflichen Forschung and the Austrian Ministry of Science.

---

[1] [1a] C. Wattenbach, M. Maurer, H. Frauenrath, *Synlett* **1999**, 303−306. − [1b] P. I. Dosa, G. C. Fu, *J. Am. Chem. Soc.* **1998**, *120*, 445−446. − [1c] R. Barner, J. Hübscher, *Helv. Chim. Acta* **1983**, *66*, 880−891.

[2] [2a] F. J. Lakner, L. P. Hager, *Tetrahedron: Asymmetry* **1997**, *8*, 3547−3550. − [2b] R. L. Parsons, C. H. Heathcock, *J. Org. Chem.* **1994**, *59*, 4733−4734. − [2c] R. J. Boyce, G. Pattendon, *Synlett* **1994**, 587−588.

[3] [3a] G. M. Coppola, H. F. Schuster, *α-Hydroxy Acids in Enantioselective Syntheses*, 1st ed. VCH, Weinheim, **1997**. − [3a] F. A. Davis, G. V. Reddy, B.-C. Chen, A. Kumar, M. S. Haque, *J. Org. Chem.* **1995**, *60*, 6148−6153.

[4] [4a] R. A. Johnson, K. B. Sharpless, *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), VCH, New York, **1993**, pp. 103−159. − [4b] E. N. Jacobsen, *Comprehensive Organometallic Chemistry II* (Eds. F. G. A. Stone, E. W. Abel, L. S. Hegedus), Pergamon, New York, **1995**, *12*, chapter 11.1.

[5] H. C. Kolb, M. S. van Nieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483−2547.

[6] H. Lebel, E. N. Jacobsen, *Tetrahedron Lett.* **1999**, *40*, 7303−7306.

[7] M. Pogorevc, K. Faber, *J. Mol. Catal. B: Enzymatic*, in press.

[8] [8a] F. J. Lakner, K. P. Cain, L. P. Hager, *J. Am. Chem. Soc.* **1997**, *119*, 443−444. − [8b] F. J. Lakner, L. P. Hager, *J. Org. Chem.* **1996**, *61*, 3923−3925.

[9] [9a] R. V. A. Orru, A. Archelas, R. Furstoss, K. Faber, *Adv. Biochem. Eng. Biotechnol.* **1999**, *63*, 145−167; and references cited therein. − [9b] I. V. J.Archer, *Tetrahedron* **1997**, *53*, 15617−15661.

[10] R. V. A. Orru, K. Faber, *Curr. Opin. Chem. Biol.* **1999**, *3*, 16−21.

[11] R. V. A. Orru, S. F. Mayer, W. Kroutil, K. Faber, *Tetrahedron* **1998**, *54*, 859−874 and references therein.

[12] W. Kroutil, I. Osprian, M. Mischitz, K. Faber, *Synthesis* **1997**, 156−158.

[13] I. Osprian, W. Kroutil, M. Mischitz, K. Faber, *Tetrahedron: Asymmetry* **1997**, *8*, 65−71.

[14] R. V. A. Orru, I. Osprian, W. Kroutil, K. Faber, *Synthesis* **1998**, 1259−1263.

[15] M. Mischitz, Ph. D. Dissertation, Technische Universität Graz, **1996**.

[16] K. Faber, *Biotransformations in Organic Chemistry*, 4th edn. pp. 85−87, **2000**, Springer, Heidelberg.

[17] T. W. Green, *Protective Groups in Organic Synthesis*, 2nd edn. p. 27, **1991**, John Wiley & Sons, New York.

[18] For a useful procedure, see: J. Hasserodt, K. D. Janda, R. A. Lerner, *J. Am. Chem. Soc.* **1997**, *119*, 5993−5998.

[19] M. M. Baizer, J. R. Clark, J. Swidinski, *J. Org. Chem.* **1957**, *22*, 1595−1599.

[20] C. M. Marson, U. Grabowska, A. Fallah, *J. Org. Chem.* **1994**, *59*, 291−296.

[21] M. Mischitz, W. Kroutil, U. Wandel, K. Faber, *Tetrahedron: Asymmetry* **1995**, *6*, 1261−1272.

[22] I. Osprian, C. Jarret, U. Strauss, W. Kroutil, R. V. A. Orru, U. Felfer, A. J. Willetts, K. Faber, *J. Mol. Catal. B: Enzymatic* **1999**, *6*, 555−560.

[23] [23a] J. L. L. Rakels, A. J. J. Straathof, J. J. Heijnen, *Enzyme Microb. Technol.* **1993**, *15*, 1051−1056. − [23b] C. J. Sih, S.-H. Wu, *Topics Stereochem.* **1989**, *19*, 63−125. − [23c] C.-S. Chen, Y. Fujimoto, G. Girdaukas, C. J. Sih, *J. Am. Chem. Soc.* **1982**, *104*, 7294−7299.

[24] M. Mischitz, C. Mirtl, R. Saf, K. Faber, *Tetrahedron: Asymmetry* **1996**, *7*, 2041−2046.

[25] See also: W. Krenn, I. Osprian, W. Kroutil, G. Braunegg, K. Faber, *Biotechnol. Lett.* **1999**, *21*, 687−690.

[26] For example see: L. F. Tietze, J. Görlitzer, *Synthesis* **1998**, 873.

[27] A. Steinreiber, S. F. Mayer, R. V. A. Orru, K. Faber, manuscript in preparation, see also ref.[4]

[28] [28a] **7e**: R. Bourhis, E. Frainnet, F. Moulines, *J. Organomet. Chem.* **1977**, *141*, 157−171. − [28b] **7f**: K. Burgess, W. A. van der Donk, S. A. Westcott, T. B. Marder, R. T. Baker, J. C. Calabrese, *J. Am. Chem. Soc.* **1992**, *114*, 9350−9359. − [28c] **8d**: S. Suzuki, M. Shiono, Y. Fujita, *Synthesis* **1983**, 804−806. − [28d] **8e**: C. G. Knudsen, R. A. S. Chandraratna, L. P. Walkeapaeae, Y. S. Chauhan, S. C. Carey, *J. Am. Chem. Soc.* **1983**, *105*, 1626−1631. − [28e] **8f**: D. A. C. Compton, W. F. Murphy, H. H. Mantsch, *Spectrochim. Acta* **1981**, *37A*, 453−455. − [28f] **9f**: R. W. Hoffmann, T. Sander, *Liebigs Ann. Chem.* **1993**, 1185−1191. − [28g] **12**: B. H. Lipschutz, R. Crow, S. H. Dimock, E. L. Ellsworth, R. A. Smith, J. R. Behling, *J. Am. Chem. Soc.* **1990**, *112*, 4063−4064.

[29] [29a] **9b**: G. A. Molander, J. A. McKie, *J. Org. Chem.* **1994**, *59*, 3186−3192. − [29b] **9c**: J. B. Jiang, M. J. Urbanski, Z. G. Hajos, *J. Org. Chem.* **1983**, *48*, 2001−2005. − [29c] **9e**: J. Chiarello, M. M. Joullie, *Tetrahedron* **1988**, *44*, 41−48.

[30] [30a] **1b**: F. C. Frostick, J. B. Phillips, P. S. Starcher, *J. Am. Chem. Soc.* **1959**, *81*, 3350−3356. − [30b] **1d**: M. Ihara, Y. Tanaka, N. Takahashi, Y. Tokunaga, K. Fukumoto, *J. Chem. Soc., Perkin Trans. 1* **1997**, 3043−3052. − [30c] **1e**: P. S. Savle, R. A. Medhekar, E. L. Kelley, J. G. May, S. F. Watkins, F. R. Fronczek, D. M. Quinn, R. D. Gandour, *Chem. Res. Toxicol.* **1998**, *11*, 19−25. − [30d] **2d**: M. Muehlbacher, C. D. Poulter, *J. Org. Chem.* **1988**, *53*, 1026−1030. − [30e] **2e**: J. A. Marshall, C. A. Sehon, *J. Org. Chem.* **1997**, *62*, 4313−4320. − [30f] **2h**: M. Larcheveque, P. Perriot, Y. Petit, *Synthesis* **1983**, 297−300.

[31] [31a] **1a**: D. C. Dittmer, Y. Zhang, R. P. Discordia, *J. Org. Chem.* **1994**, *59*, 1004−1010. − [31b] **2a**: A. Bongini, G. Cardillo, M. Orena, G. Porzi, S. Sandri, *J. Org. Chem.* **1982**, *47*, 4626−4633.

[32] [32a] **4a**: B. Wirz, R. Barner, J. Hübscher, *J. Org. Chem.* **1993**, *58*, 3980−3984. − [32b] **4d** and **4e**: D. Tanner, P. Somfai, *Tetrahedron* **1986**, *42*, 5985−5990. − [32c] **5a** and **5d**: M. Gill, A. F. Smrdel, *Tetrahedron: Asymmetry* **1990**, *1*, 453−464. − [32d] **6a**: K. Mori, *Tetrahedron* **1975**, *31*, 1381−1384.

Received March 23, 2000
[O00148]