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Selectivity enhancement of epoxide hydrolase catalyzed resolution of 2,2-disubstituted oxiranes by substrate modification

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A series of (±)-2,2-disubstituted oxiranes bearing an alkene or alkyne functional group were resolved by bacterial epoxide hydrolases with excellent selectivities. The presence of a carbon–carbon double or triple bond furnished a highly flexible system for substrate modification, which allowed the enantioselectivity to be tuned by rational substrate modification. Thus, a significant selectivity enhancement of more than a ten-fold increase of *E*-values was achieved by appropriate choice of the C–C multiple bond, *i.e.* by (i) choosing an alkene or alkyne moiety or by (ii) variation of the *E*/*Z*-configuration of olefinic substrates. The enantioenriched epoxides and vicinal diols thus obtained may be easily transformed into ω-functionalized building blocks containing a chiral fully substituted carbon atom by oxidative cleavage of the carbon–carbon multiple bond.

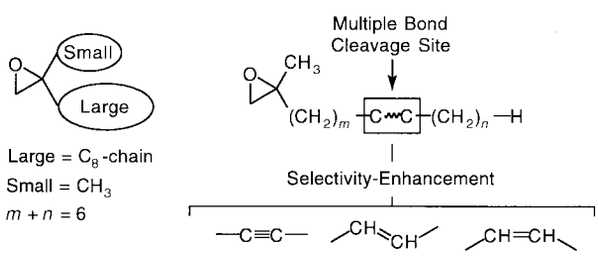
Introduction

Over the past few years, biocatalytic asymmetric hydrolysis of epoxides has been shown to offer a versatile method for the preparation of enantiopure oxiranes and their corresponding vicinal diols.[1] However, the selection of the optimum biocatalyst for a given substrate is still largely empirical requiring tedious trial-and-error experimentation. It was only recently that a crude picture on the different substrate requirements of epoxide hydrolases from various microbial sources was elucidated.[2] Thus, (i) fungal enzymes displayed their best selectivities on styrene oxide type substrates, (ii) red yeasts proved to be capable of resolving 'slim' monosubstituted oxiranes[3] and (iii) bacterial enzymes were the catalysts of choice for sterically more demanding 2,2- and 2,3-disubstituted epoxides.[4,5] Following the general trend to avoid the formation of an undesired enantiomer in kinetic resolution, several 'deracemization' techniques,[6] which lead to the formation of a single enantiomer in 100% theoretical yield were developed. The latter was achieved either by combination of two biocatalysts[7] or by using a bio- and chemo-catalytic step.[8] In contrast, only a single biocatalyst was required for the enantioconvergent hydrolysis of 2,3-disubstituted oxiranes.[4b]

In order to extend the applicability of bacterial epoxide hydrolases, we investigated the possibility of tuning enantioselectivity by rational substrate modification. Based on the fact that bacterial epoxide hydrolases preferably accept hydrophobic substrates, we chose a multiple carbon–carbon bond as the 'medium of change' for the following reasons. (i) The high lipophilicity of the substrates should lead to fast reaction rates.[9] (ii) Modulation of the selectivity by variation of the electron-density is feasible *via* an alkene- or alkyne-moiety. (iii) Geometric variation of a C=C-bond by choice of an *E*- or *Z*-configured alkene offers an additional possibility for selectivity enhancement. The latter technique was successfully employed in lipase catalysed reactions, such as ester hydrolysis and formation.[10] (iv) Oxidative cleavage of the C–C multiple bond[11] furnishes an ω-functionalized epoxide or vicinal diol bearing a fully substituted chiral carbon atom, which allows further synthetic transformations.

Results and discussion

Based on our experience that (for bacterial epoxide hydrolases) best selectivities were obtained with 2,2-disubstituted oxiranes bearing a small and a large group, a methyl and *n*-octyl chain was selected to form the basic scaffold (Scheme 1). The



Scheme 1 Substrate design for selectivity enhancement study.

scissile multiple carbon–carbon bond was introduced in the C_8-chain at an increasing distance from the chirality center to test the flexibility of the system leading to a substrate of type **a**–**c** (Table 1). In addition, the nature of the C–C multiple bond in each position was varied from an alkyne to an *E*- or *Z*-configured alkene moiety (substrate types **1**–**3**).

Racemic substrates were synthesized as follows (Scheme 2). Epoxy-alkyne **1a** was obtained in one step by ethynylation of 2-methylepichlorohydrin (**9**) using the Li derivative of hept-1-yne *via* Payne rearrangement. Substrates **1b** and **1c** were obtained by epoxidation of the corresponding alkenes **11** and **15**, respectively, using *m*-chloroperbenzoic acid. Alkene **11** was synthesized by coupling of 1-lithiohex-1-yne to bromoalkene **10**. In a related fashion, the bromoalkyne **14** was coupled to a Grignard reagent derived from methallyl chloride to give alkene **15**. Bromoalkyne **14** was synthesized from the silyl ether of hex-5-yn-1-ol *via* methylation at the acetylenic position, deprotection of the primary alcohol and bromination *via* the corresponding tosylate.

Substrates of type **2** bearing a *Z*-alkene unit were prepared by partial hydrogenation of the acetylenic moiety of substrates

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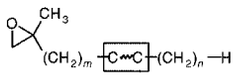
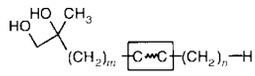
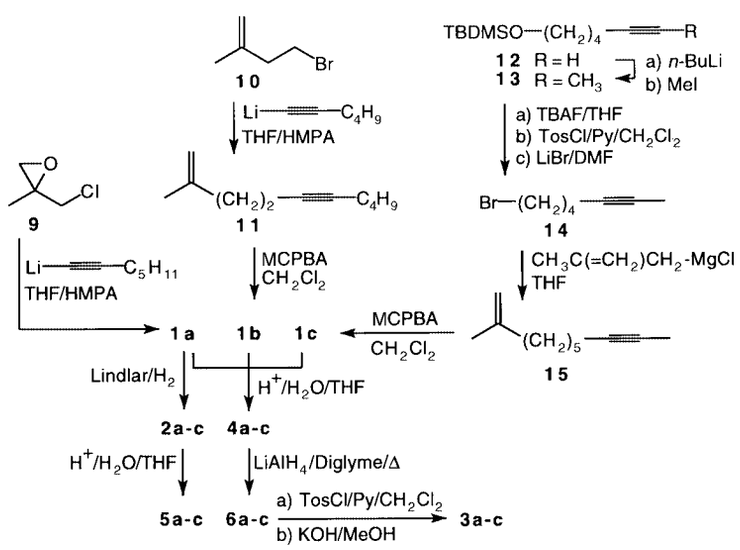
Table 1 2,2-Disubstituted oxiranes used as substrates and vicinal diols obtained as products

Comp.	*m*	Multiple bond	*n*	Comp.	*m*	Multiple bond	*n*
1a	1	–C≡C–	5	**4a**	1	–C≡C–	5
1b	2	–C≡C–	4	**4b**	2	–C≡C–	4
1c	5	–C≡C–	1	**4c**	5	–C≡C–	1
2a	1	*Z*-CH=CH–	5	**5a**	1	*Z*-CH=CH–	5
2b	2	*Z*-CH=CH–	4	**5b**	2	*Z*-CH=CH–	4
2c	5	*Z*-CH=CH–	1	**5c**	5	*Z*-CH=CH–	1
3a	1	*E*-CH=CH–	5	**6a**	1	*E*-CH=CH–	5
3b	2	*E*-CH=CH–	4	**6b**	2	*E*-CH=CH–	4
3c	5	*E*-CH=CH–	1	**6c**	5	*E*-CH=CH–	1
7	1	$-CH_2-CH_2-$	5	**8**	1	$-CH_2-CH_2-$	5

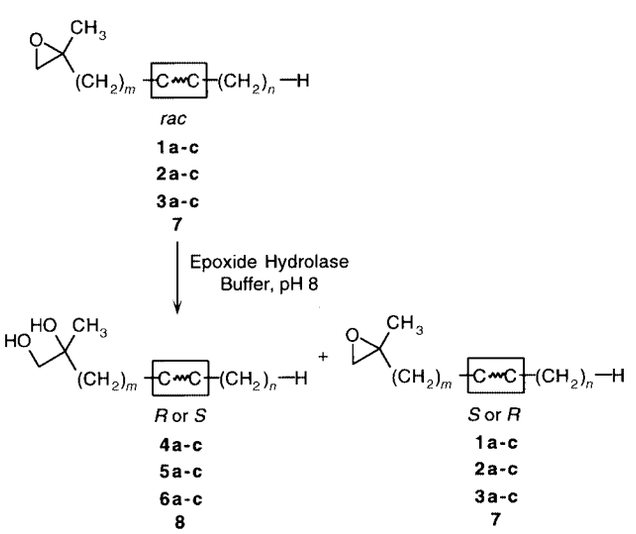


Scheme 2 Synthesis of substrates **1a**–**c** to **3a**–**c** and diols **4a**–**c** to **6a**–**c**.

1a–**c** using a Lindlar catalyst. The corresponding *E*-analogues **3a**–**c** were obtained in three steps *via* (i) hydrolytic opening of the epoxide under acid catalysis to yield diols **4a**–**c**, followed by (ii) reduction using a complex hydride ($LiAlH_4$) and (iii) ring closure of diols **6a**–**c** *via* the tosylate in a one-pot sequence. In order to obtain racemic reference material for the diols **4a**–**c** to **6a**–**c** formed during biohydrolysis, epoxides **1a**–**c** to **3a**–**c** were hydrolyzed under acidic conditions in THF–water. The saturated substrate-analog **7** was obtained from decan-2-one and trimethylsulfoxonium ylide.

Substrates **1a**–**c** to **3a**–**c** and **7** were subjected to a set of lyophilized bacterial cells under optimized conditions (Scheme 3) (Tris buffer pH 8, 30 °C). When a certain degree of conversion was reached, the reaction was quenched by extraction of the organic materials, and products were analyzed for their enantiomeric purity (Table 2). In addition, a blank experiment was run for each substrate to ensure that no spontaneous unspecific hydrolysis was taking place in the absence of biocatalysts.

The absolute configuration of diols **4a**–**c** to **6a**–**c** and **8** formed and the remaining non-hydrolyzed epoxides **1a**–**c** to **3a**–**c** and **7** was elucidated by co-injection with independently synthesized samples on GLC on a chiral stationary phase. Reference materials were obtained as follows (Scheme 4). (*R*)-2-Methylglycidol (**16**) was alkylated to give (*S*)-**4a**,[12] which in turn was methylated at the primary hydroxy moiety to yield (*S*)-**17**. Hydrogenation gave a standard specimen of (*S*)-**18**. Samples of the remaining non-hydrolyzed epoxides (**1b**,**c**, **2b**,**c**, and **3a**–**c**) from the biotransformations were hydrogenated



Scheme 3 Kinetic resolution of substrates (±)-**1a**–**c** to (±)-**3a**–**c** and (±)-**7**.

(Pt on C–H_2–EtOH) and treated with NaOMe to yield **18**. Samples of diols **4a**–**c**, **5a**–**c** and **6a**–**c** were converted to the corresponding epoxides (TsCl–Py–CH_2Cl_2) prior to analysis.

In each case it was verified that the diol formed and the remaining non-hydrolyzed epoxide possessed opposite configuration and that the biohydrolysis was following a single stereochemical pathway *via* attack of [OH^-] at the

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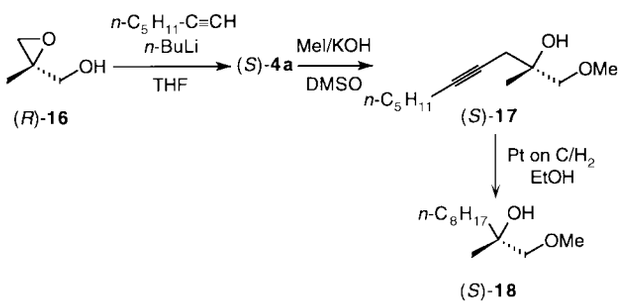
Table 2 Selectivities and enantiopreference of biocatalytic hydrolysis of substrates **1a–c**, **2a–c**, **3a–c** and **7**

		Enantioselectivity (*E* value)/enantiopreference[a]									
Entry	Biocatalyst	**1a**	**2a**	**3a**	**1b**	**2b**	**3b**	**1c**	**2c**	**3c**	**7**
1	*Rhodococcus* sp. NCIMB11216	12/*S*	14/*S*	49/*S*	2.7/*S*	14/*S*	27/*S*	>200/*S*	142/*S*	125/*S*	>200/*S*
2	*Rhodococcus ruber* DSM43338	32/*S*	10/*S*	32/*S*	1.7/*S*	3.9/*S*	8.5/*S*	46/*S*	54/*S*	42/*S*	80/*S*
3	*Rhodococcus ruber* SM1788	1.7/*S*	10/*S*	14/*S*	1.6/*S*	19/*S*	8.4/*S*	171/*S*	48/*S*	75/*S*	95/*S*
4	*Rhodococcus ruber* SM1789	2.3/*S*	12/*S*	16/*S*	1.4/*S*	13/*S*	8.0/*S*	144/*S*	56/*S*	94/*S*	78/*S*
5	*Rhodococcus ruber* SM1790	4.4/*S*	25/*S*	10/*S*	1.5/*S*	5.4/*S*	12/*S*	66/*S*	41/*S*	66/*S*	21/*S*
6	*Mycobacterium paraffinicum* NCIMB10420	17/*S*	30/*S*	2.4/*S*	1.7/*S*	5.3/*S*	9.2/*S*	32/*S*	10/*S*	36/*S*	24/*S*
7	*Rhodococcus equi* IF03730	4.1/*S*	14/*S*	10/*S*	10/*S*	18/*S*	6.3/*S*	28/*S*	29/*S*	17/*S*	20/*S*
8	*Arthrobacter* sp. DSM312	30/*S*	20/*S*	40/*S*	n.d.[b]	7.9/*S*	11/*S*	74/*S*	97/*S*	61/*S*	172/*S*
9	*Rhodococcus* sp. CBS717.73	26/*S*	16/*S*	39/*S*	1.5/*S*	7.1/*S*	10/*S*	111/*S*	99/*S*	74/*S*	124/*S*
10	*Mycoplana rubra* SM73	17/*S*	n.d.[b]	2.8/*S*	n.d.[b]	3.3/*R*	n.d.[b]	5.4/*R*	n.d.[b]	n.d.[b]	3.0/*R*
11	*Methylobacterium* sp. SM1793	66/*S*	25/*S*	n.d.[b]	1.3/*S*	n.d.[b]	n.d.[b]	2.7/*R*	n.d.[b]	n.d.[b]	1.7/*R*

[a] Configuration of faster reacting enantiomer. [b] Not determined due to very slow reaction.



Scheme 4 Determination of absolute configuration.

non-substituted oxirane carbon atom with retention of configuration. As a consequence, the applicability of *E*-values for the description of enantioselectivities is allowed.[13,14] The latter were calculated from ee_P and ee_S,† using the formula of Rakels *et al.*[15] This method is largely independent from errors derived from sample manipulation, such as extraction and evaporation, and it gives more accurate results as compared to calculations using ee_P or ee_S and the conversion.[14]

The data shown in Table 2 depict the following trends. (i) In contrast to substrates bearing rather polar functional groups, such as hydroxy and azide,[16] C–C multiple bonds were well accepted by the majority of strains. Slow reaction rates were only occasionally observed with methylotrophs, such as *Mycoplana rubra* and *Methylobacterium* sp. (entries 10 and 11). Depending on the substrate–biocatalyst combination, the selectivities ranged from low to excellent, occasionally even exceeding the value for the saturated substrate counterpart **7** (entries 4–7 and 11). (ii) The position of the C–C multiple bond within the C_8-alkyl chain with respect to its distance from the chiral oxirane center had a profound influence on the selectivity. Whereas substrates of series **a** and **b** bearing the C–C multiple bond in close proximity to the chiral center (2 and 3 C–C bonds, respectively) exhibited somewhat reduced enantioselectivities when compared to the saturated analog **7**, substrates **1c**–**3c** were resolved with excellent *E*-values. (iii) The enantioselectivity of the reaction could be modulated to a great extent by variation of the nature of the C–C multiple bond. Selectivity enhancement was most prominent for variations of a C≡C-triple to a C=C-double bond, and *E*-values were improved by up to more than one order of magnitude. Compare entry 1: **1b/2b**; entry 3: **1a/ 3a**, **1c/2c**; entry 4: **1a/3a**, **1b/2b**; entry 5: **1a/2a**; entry 7: **1a/2a**; entry 10: **1a/3a**; entry 11: **1a/2a**. Similarly, the *E*/*Z*-geometry of the olefinic bond had a remarkable impact on the selectivity. Compare entry 3: **2b/3b**; entry 5: **2b/3b**; entry 6: **2a/3a**; entry 7: **2b/3b**; entry 9: **2a/3a**. A possible explanation for this phenomenon is the alteration of the substrate binding through π–π-interactions within the active site of the enzyme(s) through variations of the electron density and the stereochemistry of the C–C multiple bond. (iv) The enantiopreference of the strains deserves a special comment. From structurally related (saturated) 2,2-disubstituted oxiranes, it is known that the majority of strains belonging to the *Actinomyces* family, such as *Mycobacterium*, *Arthrobacter* and *Rhodococcus* strains, almost invariably preferred the (*S*)-configured epoxide (entries 1–9),[17] whereas a matching opposite preference for (*R*)-oxiranes was observed for methylotrophs, such as *Mycoplana* and *Methylobacterium* sp. (entries 10, 11). For unsaturated substrates, a complex picture was observed. As expected, (*R*)-preference was observed for the saturated analog **7** and substrates **1c**–**3c**. This may be explained by the long distance of the C–C multiple bond from the oxirane moiety. On the other hand, the enantiopreference became scattered, when the distance was decreased (substrates **1b** and **2b**), and complete reversal to the (*S*)-counterpart took place for substrates **1a**–**3a** bearing a single short CH_2-spacer unit between the epoxy moiety and the unsaturated system. Furthermore, the selectivity for **1a** was much superior as compared to analog **7**.

The development of a general substrate model which should allow a semiquantitative prediction of the enantioselectivity for a given substrate by comparable molecular field analysis (COMFA) based on the data from this study is currently under investigation. The enantioenriched epoxides and vicinal diols thus obtained may be easily transformed into ω-functionalized building blocks containing a chiral fully substituted carbon atom by oxidative cleavage of the C–C multiple bond.[12] The use of these enantiopure synthons for the synthesis of bioactive compounds is currently being studied in our laboratories.

Experimental

General

Reactions were monitored by TLC (Merck silica gel 60 F_{254}), compounds were visualized by spraying with vanillin–conc. H_2SO_4 (5g L^{-1}) or by dipping into an aq. $KMnO_4$ solution. GLC analyses were carried out on a Varian 3800 gas chromatograph equipped with a FID and either an HP 1301 or an HP 1701 capillary column (both 30 m × 0.25 mm, 0.25 μm film, N_2). For chiral analyses *vide infra*. Preparative chromatography was performed on silica gel Merck 60 (40–63 μm).

^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ solution on a Bruker AMX 360 at 360 (^{1}H) and 90 (^{13}C) MHz, respectively. Chemical shifts are reported in δ from TMS ($\delta = 0$) as internal standard, coupling constants (J) are given in Hz.

† Ee_P and ee_S stand for the enantiomeric excess of the substrate and product, respectively.

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Optical rotation values were measured on a Perkin-Elmer polarimeter 341 at 589 nm (Na-line) in a 1 dm cuvette and are given in units of 10^{-1} deg cm^2 g^{-1}.

High resolution mass spectra were recorded on a Kratos Profile Mass Spectrometer with double focussing and EI ionization at +70 eV.

Solvents were dried and freshly distilled by standard techniques. For anhydrous reactions, flasks were dried overnight at 150 °C and flushed with dry argon just before use. Organic extracts were dried over Na_2SO_4, and then the solvent was evaporated under reduced pressure. Lindlar catalyst was purchased from Aldrich [Pd on CaCO3 (5% w/w) poisoned with Pb]. 70% *m*-Chloroperbenzoic acid (MCPBA, Fluka) was used. 60% NaH suspended in mineral oil (Aldrich) was used. Petroleum ether had a boiling point range of 40–60 °C.

For biotransformations, lyophilized bacterial cells were used. 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.[17–20]

Synthesis of substrates and reference materials

2-Methyl-2-(oct-2-ynyl)oxirane (1a). To a stirred solution of hept-1-yne (4.96 g, 51.6 mmol) in dry THF (150 mL) containing HMPA (9 mL) under an argon atmosphere, *n*-BuLi (20.6 mL of a 2.5 M solution in hexane, 51.6 mmol) was added at −20 °C. After 1 hour, a solution of **9** [5.00 g, 46.9 mmol, prepared by epoxidation of methallyl chloride (3-chloro-2-methylpropene)[21]] in dry petroleum ether (5 mL) was added dropwise and the mixture was allowed to warm to rt. After 20 h, the reaction was quenched with semi-saturated NH_4Cl solution (100 mL) and the product was extracted with petroleum ether. The combined organic extracts were dried and concentrated. Flash chromatography (petroleum ether–EtOAc, 40 : 1) followed by distillation through a Vigreux-column gave **1a** as a clear oil; yield: 4.59 g (59%); $bp_{3\ mbar}$: 58–60 °C. ^{1}H-NMR: $\delta = 0.87$ (3H, t, $J = 7$, CH_3-CH$_2$); 1.38 (3H, s, CH$_3$-C$_{quat.}$); 1.21–1.52 (6H, m, 3 × CH$_2$); 2.08–2.17 (2H, m, ≡C-CH_2-CH$_2$); 2.35, 2.49 (1H each, t × d, $J = 17$ and 2.4, ≡C-CH$_2$-C$_{quat.}$); 2.59, 2.75 (1H each, d, $J = 4.9$, CH$_2$-O). ^{13}C-NMR: $\delta = 14.0$ (*C*H$_3$-CH$_2$); 18.7, 20.7, 22.2, 27.4, 28.6, 31.1 (5 CH$_2$, *C*H$_3$-C$_{quat.}$); 53.3 (CH$_2$-O); 55.8 (C$_{quat.}$); 74.9, 82.9 (C≡C). MS: 165.1263 [M − H]$^+$, 165.1279 (calc.).

Preparation of oxiranes 1b and 1c. Oxiranes **1b** and **1c** were prepared from the corresponding alkenes **11** and **15** *via* method A.

Method A. To a stirred solution of alkene (*ca*. 0.07 M) in CH_2Cl_2 *ca*. 2.5 equiv. Na_2HPO_4 and 1.5 equiv. MCPBA were added at 0 °C. The reaction was allowed to warm to rt and stirring was continued for an additional 24 h, after which the white suspension was removed by filtration. The resulting solution was treated with 10% aq. $Na_2S_2O_5$ (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 sat. aqueous $NaHCO_3$ (0.2 × reaction volume). The organic phase was dried and evaporated. Flash chromatography and Kugelrohr distillation afforded pure oxiranes **1b** and **1c**, details and spectroscopic data are given below.

2-Methyl-2-(oct-3-ynyl)oxirane (1b). Method A was employed using crude alkene **11**. Flash chromatography (petroleum ether–EtOAc, 40 : 1) followed by Kugelrohr distillation gave **1b** as a clear oil; yield: 2.17 g (20%, calcd. from **10**); $bp_{6\ mbar}$ (Kugelrohr): 140 °C. ^{1}H-NMR: $\delta = 0.90$ (3H, t, $J = 6.7$, CH_3-CH$_2$); 1.33 (3H, s, CH$_3$-C$_{quat.}$); 1.33–1.45 (4H, m, CH_2-CH_2-CH$_3$); 1.64–1.87 (2H, m, CH$_2$-C$_{quat.}$); 2.11–2.26 (4H, m, 2 × CH$_2$C≡); 2.59, 2.71 (1H each, d, $J = 4.6$, CH$_2$-O). ^{13}C-NMR: $\delta = 13.6$ (*C*H$_3$-CH$_2$); 20.8 (*C*H$_3$-C$_{quat.}$); 14.9, 18.4, 22.0, 31.1, 36.2 (5 × CH$_2$); 53.9 (CH$_2$-O); 56.4 (C$_{quat.}$); 79.1, 80.8 (C≡C).

2-Methyl-2-(oct-6-ynyl)-oxirane (1c). Method A was employed using crude alkene **15**. Flash chromatography (petroleum ether–EtOAc, 40 : 1) followed by Kugelrohr distillation gave **1c** as a clear oil; yield: 2.89 g (51%, calcd. from **14**); $bp_{5\ mbar}$ (Kugelrohr): 140 °C; (*R*)-**1c**: $[a]_D^{22}$ −5.4 ($c = 0.25$, EtOH, 98% ee). ^{1}H-NMR: $\delta = 1.26$ (3H, s, CH$_3$-C$_{quat.}$); 1.34–1.54 (8H, m, 4 × CH$_2$); 1.72 (3H, br s, CH$_3$C≡); 2.05–2.10 (2H, m, CH$_2$C≡); 2.52, 2.56 (1H each, d, $J = 4.6$, CH$_2$-O). ^{13}C-NMR: $\delta = 3.5$ (*C*H$_3$C≡); 20.9 (*C*H$_3$-C$_{quat.}$); 18.7, 24.8, 28.9, 29.0, 36.6 (5 × CH$_2$); 53.9 (CH$_2$-O); 57.0 (C$_{quat.}$); 75.5, 79.2 (C≡C). MS: 165.1270 [M − H]$^+$, 165.1279 (calc.).

2-Methyldec-1-en-5-yne (11). To a stirred solution of hex-1-yne (16.5 g, 201.3 mmol) in dry THF (100 mL) containing HMPA (10 mL) under an argon atmosphere was added *n*-BuLi (80.5 mL of a 2.5 M solution in hexane, 201.3 mmol) at −20 °C. After 2 h, **10** (10.0 g, 67.1 mmol, prepared from 3-methylbut-3-en-1-ol[22]) was added dropwise and the mixture was stirred at rt until the reaction was complete (if necessary, another portion of 1-lithiohex-1-yne was added). Then semi-saturated NH_4Cl solution (200 mL) was added and the product was extracted with CH_2Cl_2. The combined organic extracts were dried and (due to the high volatility of the product) directly epoxidized without further purification. For spectroscopic characterization, a small sample was concentrated and purified by flash chromatography (pentane) followed by Kugelrohr distillation, $bp_{100\ mbar}$ (Kugelrohr): 120 °C. ^{1}H-NMR: $\delta = 0.91$ (3H, t, $J = 7.0$, CH_3-CH$_2$); 1.39–1.46 (4H, m, (CH_2)$_2$-CH$_3$); 1.74 (3H, s, CH$_3$-C=C); 2.13–2.29 (6H, m, (CH_2)$_2$-C≡C-CH_2); 4.72, 4.76 (1H each, s, C=CH$_2$). ^{13}C-NMR: $\delta = 13.6$ (*C*H$_3$-CH$_2$); 17.6, 18.5, 21.9, 31.3, 37.4 (5 × CH$_2$); 22.3 (*C*H$_3$-C=C); 79.6, 80.6 (C≡C); 110.6 (C=*C*H$_2$); 144.6 (*C*=CH$_2$).

7-(*tert*-Butyldimethylsilyloxy)hept-2-yne (13). To a stirred solution of **12** (16.7 g, 78.6 mmol, prepared from hex-5-yne-1-ol[23]) in dry THF (150 mL) under an argon atmosphere was added *n*-BuLi (32 mL of a 2.5 M solution in hexane, 80 mmol) at −50 °C. After 2 h, MeI (9.8 mL, 99.4 mmol) was added dropwise at −10 °C and the mixture was stirred for 20 h at rt. Then semi-saturated NH_4Cl solution (150 mL) was added and the product was extracted with Et_2O. The combined organic extracts were dried and evaporated. Flash chromatography (petroleum ether–EtOAc, 20 : 1) gave **13** as a clear oil; yield: 15.4 g (87%). ^{1}H-NMR: $\delta = 0.02$ [6H, s, Si-(CH$_3$)$_2$]; 0.86 [9H, s, Si-C-(CH$_3$)$_3$]; 1.49–1.58 (4H, m, CH$_2$-(CH_2)$_2$-CH$_2$); 1.74 (3H, t, $J = 2.5$, CH$_3$); 2.12 (2H, m, CH$_2$-C≡); 3.59 (2H, t, $J = 6$, CH$_2$-O). ^{13}C-NMR: $\delta = -5.3$ [Si-(CH$_3$)$_2$]; 3.5 (CH$_3$); 18.4 [Si-*C*-(CH$_3$)$_3$]; 18.6 (*C*H$_2$-C≡); 25.5, 32.1 [-CH$_2$-(*C*H$_2$)$_2$-CH$_2$]; 26.0 [Si-C-(*C*H$_3$)$_3$]; 62.8 (CH$_2$-O); 75.6, 79.1 (C≡C).

7-Bromo-hept-2-yne (14). To a solution of **13** (15.4 g, 68.0 mmol) in THF (200 mL) was added tetrabutylammonium fluoride (25.8 g, 81.6 mmol) and the reaction mixture was stirred at rt for 5 h, after which 300 mL distilled H_2O were added. The product was extracted with CH_2Cl_2 and the organic phase was dried and evaporated. Flash chromatography gave 7.40 g (90%) hept-5-yn-1-ol, which was tosylated (TsCl–Py–CH_2Cl_2) followed by bromination (LiBr–DMF) *via* standard procedures (all intermediate structures were verified by NMR spectroscopy). Kugelrohr distillation gave 7.45 g (65%, over two steps) of **14** as a clear oil; $bp_{20\ mbar}$ (Kugelrohr): 120 °C. NMR-data match those previously reported.[24]

2-Methyldec-1-ene-8-yne (15). To a stirred solution of **14** (6.0 g, 34.3 mmol) in dry THF (50 mL) under an argon atmosphere

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a freshly prepared Grignard reagent of methallyl chloride (102.8 mmol in 100 mL dry THF) was added at rt. The mixture was stirred at rt until the reaction was complete (if necessary, another portion of Grignard reagent was added). Then 5% aq. HCl (200 mL) was added at 0 °C and after 10 min, the product was extracted with CH_2Cl_2. The combined organic extracts were dried and (due to the high volatility of the product) epoxidized without further purification. For spectroscopic characterization a small sample was concentrated and purified by flash chromatography (pentane) followed by Kugelrohr distillation, $bp_{60\ mbar}$ (Kugelrohr) 120 °C. ^{1}H-NMR: $\delta = 1.39$–1.49 (6H, m, CH_2-(CH_2)$_3$-CH_2); 1.71 (3H, s, CH_3-C=C); 1.79 (3H, t, $J = 2.5$, ≡C–CH_3); 2.01 (2H, t, $J = 7$, CH_2-C=C); 2.13 (2H, m, CH_2-C≡); 4.67, 4.69 (1H each, s, C=CH_2). ^{13}C-NMR: $\delta = 3.7$ (CH_3C≡); 18.9, 22.6, 27.4, 28.8, 29.2, 37.8 (5 × CH_2, CH_3-$C_{quat.}$); 75.6, 79.5 (C≡C); 109.9 (C=CH_2); 146.3 (C=CH_2).

Preparation of oxiranes 2a–c. Oxiranes **2a**–**c** were prepared by *cis*-selective reduction (>95% *Z*) of the corresponding epoxy-alkynes **1a**–**c** using Method B. The stereoselective outcome was verified by a decoupling experiment [(*Z*)-H-C=C-H, $J = 11$].

Method B. To a solution of the alkyne (*ca*. 0.5 M) in EtOH were added 1.4 equiv. of freshly distilled quinoline and Lindlar catalyst (40% w/w) and the resulting mixture was vigorously stirred under H_2 for 30 min at ambient pressure. Then the mixture was filtered through a plug of Celite-545 and the solvent was evaporated. Flash chromatography and Kugelrohr distillation afforded pure oxiranes **2a**–**c**, details and spectroscopic data are given below.

(*Z*)-2-Methyl-2-(oct-2-enyl)oxirane (2a). Method B was employed using 1.00 g (6.0 mmol) of alkyne **1a**. Flash chromatography (petroleum ether–EtOAc, 40 : 1) followed by Kugelrohr distillation gave **2a** as a clear oil; yield: 0.89 g (88%); $bp_{5\ mbar}$ (Kugelrohr): 140 °C. ^{1}H-NMR: $\delta = 0.88$ (3H, t, $J = 6.6$, CH_3-CH_2); 1.22–1.42 [7H, m, (CH_2)$_2$-CH_3, CH_3-$C_{quat.}$]; 1.95–2.08 (2H, m, CH_2); 2.15–2.45 (4H, m, 2 × =C–CH_2); 2.56, 2.64 (1H each, d, $J = 5$, CH_2-O); 5.3–5.6 (2H, m, CH=CH). ^{13}C-NMR: $\delta = 14.1$ (CH_3-CH_2); 21.2, 22.6, 27.4, 29.3, 31.5, 34.5 (5 × CH_2, CH_3-$C_{quat.}$); 53.3 (CH_2-O); 56.9 ($C_{quat.}$); 123.7, 133.0 (C=C). MS: 168.1530 $[M]^+$, 168.1514 (calc.).

(*Z*)-2-Methyl-2-(oct-3-enyl)oxirane (2b). Method B was employed using 150 mg (0.9 mmol) of alkyne **1b**. Flash chromatography (petroleum ether–EtOAc, 40 : 1) followed by Kugelrohr distillation gave **2b** as a clear oil; yield: 100 mg (66%); $bp_{7\ mbar}$ (Kugelrohr): 150 °C. ^{1}H-NMR: $\delta = 0.87$ (3H, t, $J = 5.7$, CH_3-CH_2); 1.28–1.32 (7H, m, (CH_2)$_2$-CH_3, CH_3-$C_{quat.}$); 1.53–1.65 (2H, m, CH_2-$C_{quat.}$); 1.99–2.12 (4H, m, 2 × =C–CH_2); 2.55, 2.60 (1H each, d, $J = 4.8$, CH_2-O); 5.33 (2H, m, CH=CH). ^{13}C-NMR: $\delta = 14.0$ (CH_3-CH_2); 21.0 (CH_3-$C_{quat.}$); 22.4, 23.1, 27.0, 31.9, 36.8 (5 × CH_2); 54.0 (CH_2-O); 56.9 ($C_{quat.}$); 128.6, 130.7 (C=C). MS: 168.1513 $[M]^+$, 168.1514 (calc.).

(*Z*)-2-Methyl-2-(oct-6-enyl)oxirane (2c). Method B was employed using 200 mg (1.2 mmol) of alkyne **1c**. Flash chromatography (petroleum ether–EtOAc, 40 : 1) followed by Kugelrohr distillation gave **2c** as a clear oil; yield: 180 mg (89%); $bp_{5\ mbar}$ (Kugelrohr): 130 °C; (*S*)-**2c**: $[a]_D^{20}$ +2.4 ($c = 0.25$, EtOH, 95% ee). ^{1}H-NMR: $\delta = 1.30$ (3H, s, CH_3-C_{quat}); 1.30–1.57 (8H, m, 4 × CH_2); 1.57 (3H, d, $J = 5.9$, CH_3-C=); 2.00–2.06 (2H, m, =C–CH_2); 2.57, 2.60 (1H each, d, $J = 4.9$, CH_2-O); 5.35–5.45 (2H, m, CH=CH). ^{13}C-NMR: $\delta = 12.9$ (CH_3-C=); 21.1 (CH_3-$C_{quat.}$); 25.3, 26.9, 29.5, 29.6, 36.9 (5 × CH_2); 54.1 (CH_2-O); 57.2 ($C_{quat.}$); 124.0, 130.8 (C=C). MS: 168.1525 $[M]^+$, 168.1514 (calc.).

Preparation of oxiranes 3a–c. Oxiranes **3a**–**c** were obtained from diols **4a**–**c** after *trans*-selective reduction (>98% *E*), followed by tosylation and ring closure using Method C. The stereoselective outcome was verified by a decoupling experiment [(*E*)-H-C=C-H, $J = 16$].

Method C. Under an argon atmosphere, the corresponding alkynyl-diol was dissolved in dry diglyme (*ca*. 0.3 M) and the resulting stirred solution was cooled to 0 °C. After the careful addition of $LiAlH_4$ (3 equiv.) the cooling bath was removed and the reaction was refluxed until conversion was complete (if necessary, another portion of $LiAlH_4$ was added). The reaction mixture was cooled to 0 °C and 5% aq. HCl (*ca*. 1 × reaction volume) was carefully added. Then, the product was extracted with CH_2Cl_2 and the organic phase was dried and concentrated. This crude product (containing some diglyme) was used for the next step without further purification. The *E*-alkenyl-diol was dissolved in CH_2Cl_2 (*ca*. 0.3 M) and pyridine (1.5 equiv.) was added. The stirred solution was cooled to 0 °C and toluenesulfonyl chloride (1.3 equiv.) was added in small portions. The reaction was allowed to warm to rt and its progress was monitored by TLC. After the reaction reached completion, water (0.5 × reaction volume) was added and the resulting two-phase system was stirred for several hours to destroy excess tosyl chloride. Then the layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were extracted with 5% aq. HCl followed by extraction with sat. aq. $NaHCO_3$ (0.3 × reaction volume). The organic phase was dried and concentrated. This crude tosylate (*ca*. 0.5 M) was stirred at rt in a 10% solution of KOH in MeOH for *ca*. 30 min. After the addition of water (2 × reaction volume) the product was extracted with petroleum ether. The combined organic extracts were dried and evaporated. Flash chromatography and Kugelrohr distillation afforded pure oxiranes **3a**–**c**, details and spectroscopic data are given below.

(*E*)-2-Methyl-2-(oct-2-enyl)oxirane (3a). Method C was employed using 1.00 g (5.4 mmmol) of diol **4a**. Flash chromatography (petroleum ether–EtOAc, 40 : 1) followed by Kugelrohr distillation gave **3a** as a clear oil; yield: 0.40 g (44%, calcd. from **4a**); $bp_{8\ mbar}$ (Kugelrohr): 130 °C; (*S*)-**3a**: $[a]_D^{20}$ +6.0 ($c = 0.25$, EtOH, 96% ee). ^{1}H-NMR: $\delta = 0.88$ (3H, t, $J = 6.4$, CH_3-CH_2); 1.23–1.39 (7H, m, (CH_2)$_2$-CH_3, CH_3-$C_{quat.}$); 1.92–2.08 (2H, m, CH_2); 2.12–2.35 (4H, m, 2 × =C–CH_2); 2.56, 2.63 (1H each, d, $J = 4.9$, CH_2-O); 5.29–5.59 (2H, m, CH=CH). ^{13}C-NMR: $\delta = 14.1$ (CH_3-CH_2); 21.0, 22.6, 29.1, 31.4, 32.6, 40.6 (5 × CH_2, CH_3-$C_{quat.}$); 53.3 (CH_2-O); 56.9 ($C_{quat.}$); 124.5, 133.4 (C=C).

(*E*)-2-Methyl-2-(oct-3-enyl)oxirane (3b). Method C was employed using 0.46 g (2.5 mmol) of diol **4b**. Flash chromatography (petroleum ether–EtOAc, 40 : 1) followed by Kugelrohr distillation gave **3b** as a clear oil; yield: 0.26 g (61%, calcd. from **4b**); $bp_{4\ mbar}$ (Kugelrohr): 130 °C. ^{1}H-NMR: $\delta = 0.86$ (3H, t, $J = 6.8$, CH_3-CH_2); 1.27 [7H, br s, (CH_2)$_2$-CH_3, CH_3-$C_{quat.}$]; 1.53–1.65 (2H, m, CH_2-$C_{quat.}$); 1.94–2.10 (4H, m, 2 × =C–CH_2); 2.54, 2.59 (1H each, d, $J = 4.9$, CH_2-O); 5.33–5.34 (2H, m, CH=CH). ^{13}C-NMR: $\delta = 14.0$ (CH_3-CH_2); 21.0 (CH_3-$C_{quat.}$); 22.2, 28.4, 31.8, 32.3, 36.8 (5 × CH_2); 54.0 (CH_2-O); 56.8 ($C_{quat.}$); 129.2, 131.1 (C=C). MS: 168.1503 $[M]^+$, 168.1514 (calc.).

(*E*)-2-Methyl-2-(oct-6-enyl)oxirane (3c). Method C was employed using 0.41 g (2.2 mmol) of diol **4c**. Flash chromatography (petroleum ether–EtOAc, 20 : 1) followed by Kugelrohr distillation gave **3c** as a clear oil; yield: 0.24 g (65%); $bp_{5\ mbar}$ (Kugelrohr): 130 °C; (*S*)-**3c**: $[a]_D^{20}$ +0.9 ($c = 0.35$, EtOH, 95% ee). ^{1}H-NMR: $\delta = 1.30$ (3H, s, CH_3-$C_{quat.}$); 1.30–1.61 (8H, m, 4 × CH_2); 1.64 (3H, d, $J = 5.9$, CH_3-C=); 1.92–2.00 (2H, m, =C–CH_2); 2.56, 2.60 (1H each, d, $J = 4.9$, CH_2-O); 5.35–

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5.47 (2H, m, CH=CH). ^{13}C-NMR: δ = 18.1 (CH_3-C=); 21.1 (CH_3-$C_{quat.}$); 25.3, 29.4, 29.7, 32.7, 37.0 (5 × CH_2); 54.1 (CH_2-O); 57.2 ($C_{quat.}$); 125.0, 131.7 (C=C). MS: 168.1502 $[M]^+$, 168.1514 (calc.).

2-Methyl-2-octyloxirane (7). Under an argon atmosphere, a solution of trimethylsulfoxonium iodide (6.33 g, 28.8 mmol) in dry DMSO (60 mL) was added slowly to a stirred suspension of NaH (28.8 mmol) in anhydrous DMSO (12 mL)–THF (18 mL) at 0 °C. After 30 min, decan-2-one (3.0 g, 19.2 mmol), dissolved in dry DMSO (20 mL) was added dropwise. Then, the cooling bath was removed and the reaction mixture was stirred for 20 h at rt, after which semi-saturated NH_4Cl solution (150 mL) was added. The product was extracted with petroleum ether and the combined organic phases were dried and evaporated. Flash chromatography (petroleum ether–EtOAc, 20 : 1) and Kugelrohr distillation gave pure **7**; yield: 2.59 g (79%); $bp_{7\,mbar}$ (Kugelrohr): 130 °C. ^{1}H-NMR: δ = 0.87 (3H, t, J = 6, CH_3-CH_2); 1.22–1.66 (17H, m, 7 × CH_2, CH_3-$C_{quat.}$); 2.56, 2.60 (1H each, d, J = 4.9, CH_2-O). ^{13}C-NMR: δ = 14.1 (CH_3-CH_2); 20.9, 22.7, 25.3, 29.3, 29.6, 29.7, 31.9, 36.8 (7 × CH_2, CH_3-$C_{quat.}$); 54.0 (CH_2-O); 57.1 ($C_{quat.}$).

Preparation of diols 4a–c, 5a–c, 6a–c and 8. Diols **4a**–**c**, **5a**–**c**, **6a**–**c** and **8** were obtained by acid catalyzed hydrolysis of the corresponding racemic oxiranes **1a**–**c**, **2a**–**c**, **3a**–**c** and **7** [0.1 M in H_2O–THF (1 : 1) containing 3–10 drops of 12 M H_2SO_4]. Workup and flash chromatography (petroleum ether–EtOAc, 1 : 1) gave pure diols (55–90%). Their NMR data are listed below.

2-Methyldec-4-yne-1,2-diol (4a). ^{1}H-NMR: δ = 0.90 (3H, t, J = 7, CH_3-CH_2); 1.25 (3H, s, CH_3-$C_{quat.}$); 1.25–1.57 (6H, m, $(CH_2)_3$-CH_3); 2.06–2.52 (6H, m, CH_2-C≡C-CH_2, 2 × OH); 3.48, 3.58 (1H each, dd, J = 11 and 5, CH_2-OH). ^{13}C-NMR: δ = 14.0 (CH_3-CH_2); 18.7, 22.2, 23.6, 28.7, 29.5, 31.1 (5 × CH_2, CH_3-$C_{quat.}$); 69.1 (CH_2-OH); 72.1 ($C_{quat.}$); 75.5, 84.0 (C≡C).

2-Methyldec-5-yne-1,2-diol (4b). ^{1}H-NMR: δ = 0.90 (3H, t, J = 7.2, CH_3-CH_2); 1.19 (3H, s, CH_3-$C_{quat.}$); 1.32–1.50 (4H, m, $(CH_2)_2$-CH_3); 1.65–1.83 (2H, m, CH_2-CH_2-$C_{quat.}$); 2.12–2.16 (2H, m, CH_2C≡); 2.27–2.30 (3H, m, CH_2-C≡, OH); 2.59 (1H, br s, OH); 3.43, 3.51 (1H each, d, J = 11, CH_2-OH). ^{13}C-NMR: δ = 13.5 (CH_3-CH_2); 23.3 (CH_3-$C_{quat.}$); 13.6, 18.4, 22.0, 31.1, 37.3 (5 × CH_2); 69.8 (CH_2-OH); 72.9 ($C_{quat.}$); 80.0, 81.4 (C≡C).

2-Methyldec-8-yne-1,2-diol (4c). ^{1}H-NMR: δ = 1.12 (3H, s, CH_3-$C_{quat.}$); 1.22–1.48 (8H, m, 4 × CH_2); 1.74 (3H, br s, CH_3-C≡); 2.03–2.17 (2H, br s, CH_2-C≡); 2.24, 2.52 (1H each, br s, OH); 3.36, 3.42 (1H each, dd, J = 11 and 6, CH_2-OH). ^{13}C-NMR: δ = 3.5 (CH_3-C≡); 23.2 (CH_3-$C_{quat.}$); 18.7, 23.4, 29.0, 29.5, 38.6 (5 × CH_2); 69.8 (CH_2-OH); 73.1 ($C_{quat.}$); 75.6, 79.3 (C≡C).

(*Z*)-2-Methyldec-4-ene-1,2-diol (5a). ^{1}H-NMR: δ = 0.88 (3H, t, J = 6.6, CH_3-CH_2); 1.16 (3H, s, CH_3-$C_{quat.}$); 1.22–1.38 (6H, m, $(CH_2)_3$-CH_3); 1.99–2.37 (5H, m, 2 × CH_2-C=, OH); 3.40, 2.48 (1H each, d, J = 11, CH_2-OH); 5.36–5.64 (2H, m, CH=CH). ^{13}C-NMR: δ = 14.1 (CH_3-CH_2); 22.6, 23.5, 27.4, 29.3, 31.6, 36.3 (5 × CH_2, CH_3-$C_{quat.}$); 69.6 (CH_2-OH); 73.1 ($C_{quat.}$); 123.5, 134.1 (C=C).

(*Z*)-2-Methyldec-5-ene-1,2-diol (5b). ^{1}H-NMR: δ = 0.87 (3H, t, J = 6.7, CH_3-CH_2); 1.16 (3H, s, CH_3-$C_{quat.}$); 1.24–1.32 (4H, m, $(CH_2)_2$-CH_3); 1.44–1.59 (2H, m, CH_2-$C_{quat.}$); 1.99–2.12 (5H, m, 2 × =C-CH_2, OH); 2.23 (1H, br s, OH); 3.39, 3.45 (1H each, dd, J = 11 and 5.6, CH_2-OH); 5.30–5.40 (2H, m, CH=CH). ^{13}C-NMR: δ = 14.0 (CH_3-CH_2); 23.3 (CH_3-$C_{quat.}$); 21.7, 21.8, 22.4, 27.0, 38.5 (5 × CH_2); 69.8 (CH_2-OH); 73.1 ($C_{quat.}$); 129.3, 130.6 (C=C).

(*Z*)-2-Methyldec-8-ene-1,2-diol (5c). ^{1}H-NMR: δ = 1.56 (3H, s, CH_3-$C_{quat.}$); 1.33–1.48 (8H, m, 4 × CH_2); 1.60 (3H, d, J = 5.1, CH_3-C=); 2.03 (2H, m, =C–CH_2); 3.40, 3.46 (1H each, dd, J = 11 and 5, CH_2-OH); 5.36–5.44 (2H, m, CH=CH). ^{13}C-NMR: δ = 13.0 (CH_3-CH_2); 23.4 (CH_3-$C_{quat.}$); 23.9, 27.0, 29.7, 30.1, 39.0 (5 × CH_2); 70.0 (CH_2-OH); 73.3 ($C_{quat.}$); 124.0, 130.9 (C=C).

(*E*)-2-Methyldec-4-ene-1,2-diol (6a). ^{1}H-NMR: δ = 0.89 (3H, t, J = 6.8, CH_3-CH_2); 1.16 (3H, s, CH_3-$C_{quat.}$); 1.29–1.39 (6H, m, $(CH_2)_3$-CH_3); 1.99–2.2 (6H, m, 2 CH_2-C=, 2 OH); 3.41, 2.47 (1H each, d, J = 11, CH_2-OH); 5.41–5.60 (2H, m, CH=CH). ^{13}C-NMR: δ = 13.0 (CH_3-CH_2); 21.5, 22.6, 28.1, 30.4, 31.6, 41.0 (5 × CH_2, CH_3-$C_{quat.}$); 68.6 (CH_2-OH); 71.5 ($C_{quat.}$); 123.3, 134.6 (C=C). (*S*)-**6a**: $[a]_D^{20}$ −6.8 (*c* = 0.75, EtOH, 96% ee).

(*E*)-2-Methyldec-5-ene-1,2-diol (6b). ^{1}H-NMR: δ = 0.85 (3H, t, J = 7.0, CH_3-CH_2); 1.13 (3H, s, CH_3-$C_{quat.}$); 1.23–1.32 (4H, m, $(CH_2)_2$-CH_3); 1.44–1.59 (2H, m, CH_2-$C_{quat.}$); 1.92–2.12 (4H, m, 2 × =C–CH_2); 2.38, 2.65 (1H each, br s, OH); 3.36, 3.43 (1H each, dd, J = 11 and 5.8, CH_2-OH); 5.33–5.47 (2H, m, CH=CH). ^{13}C-NMR: δ = 14.0 (CH_3-CH_2); 23.3 (CH_3-$C_{quat.}$); 22.2, 27.0, 31.7, 32.3, 38.4 (5 × CH_2); 69.8 (CH_2-OH); 73.1 ($C_{quat.}$); 129.9, 130.0 (C=C).

(*E*)-2-Methyldec-8-ene-1,2-diol (6c). ^{1}H-NMR: δ = 1.12 (3H, s, CH_3-$C_{quat.}$); 1.29–1.44 (8H, m, 4 × CH_2); 1.60 (3H, s, CH_3-C=); 1.94 (2H, s, =C–CH_2); 2.16 (1H, br s, OH); 2.43 (1H, br s, OH); 3.36, 3.43 (1H each, d, J = 11, CH_2-OH); 5.38 (2H, s, CH=CH). ^{13}C-NMR: δ = 17.9 (CH_3-CH_2); 23.2 (CH_3-$C_{quat.}$); 23.7, 29.6, 29.8, 32.5, 38.8 (5 × CH_2); 69.8 (CH_2-OH); 73.1 ($C_{quat.}$); 124.8, 131.5 (C=C).

2-Methyldecane-1,2-diol (8). ^{1}H-NMR: δ = 0.88 (3H, t, J = 6.5, CH_3-CH_2); 1.16 (3H, s, CH_3-$C_{quat.}$); 1.2–1.5 (14H, m, 7 × CH_2); 3.47, 3.39 (1H each, d, J = 11, CH_2-OH). ^{13}C-NMR: δ = 14.1 (CH_3-CH_2); 22.7, 23.3, 23.8, 29.3, 29.6, 30.3, 31.9, 38.8 (7 × CH_2, CH_3-$C_{quat.}$); 69.8 (CH_2-OH); 73.1 ($C_{quat.}$). (*S*)-**8**: $[a]_D^{20}$ −1.4 (*c* = 1.05, EtOH, 98% ee).

Preparation of monomethylated derivatives 17 and 18. Monomethylated derivatives **17** and **18** were obtained either from the corresponding epoxide by refluxing them in NaOMe–MeOH-solution or from the corresponding diol by treatment with KOH–MeI in DMSO *via* standard procedures. Methylation was closely monitored *via* TLC, since prolonged reaction times led to partial dimethylation. NMR data of these compounds are given below.

1-Methoxy-2-methyldec-4-yn-2-ol (17). ^{1}H-NMR: δ = 0.89 (3H, t, J = 7, CH_3-CH_2); 1.24 (3H, s, CH_3-$C_{quat.}$); 1.27–1.52 (6H, m, 3 × CH_2); 2.1–2.2 (2H, m, CH_2-CH_2-C≡); 2.38 (2H, t, J = 2.4, $C_{quat.}$-CH_2-C≡); 2.44 (1H, s, OH); 3.26, 3.38 (1H each, d, J = 9, CH_2-O-CH_3); 3.39 (3H, s, CH_2-O-CH_3). ^{13}C-NMR: δ = 14.0 (CH_3-CH_2); 18.7, 22.2, 23.6, 28.7, 29.8, 31.1 (5 × CH_2, CH_3-$C_{quat.}$); 59.4 (CH_2-O-CH_3); 71.6 ($C_{quat.}$); 76.0, 83.0 (C≡C); 78.5 (CH_2-O-CH_3).

1-Methoxy-2-methyldecan-2-ol (18). ^{1}H-NMR: δ = 0.87 (3H, t, CH_3-CH_2); 1.34 (3H, s, CH_3-$C_{quat.}$); 1.23–1.52 (14H, m, 7 × CH_2); 2.17 (1H, s, OH); 3.18, 3.25 (1H each, d, J = 9, CH_2-O-CH_3); 3.38 (3H, s, CH_2-O-CH_3). ^{13}C-NMR: δ = 14.1 (CH_3-CH_2); 23.7 (CH_3-$C_{quat.}$); 22.7, 23.8, 29.3, 29.6, 30.3, 31.9 (6 × CH_2); 39.2 (CH_2-CH_2-$C_{quat.}$); 59.3 (CH_2-O-CH_3); 72.1 ($C_{quat.}$); 80.0 (CH_3-O-CH_2).

General procedure for the biocatalytic hydrolysis of epoxides

Lyophilized microbial cells (45–50 mg) were rehydrated in Tris-buffer (1 mL, 0.05 M, pH 8.0) for *ca.* 1 hour in an Eppendorf vial on a rotary shaker (130 rpm, rt). Substrate (5 μL) was then added and the mixture was shaken at 30 °C with 130 rpm.

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After 24 h, the mixture was extracted three times with EtOAc (0.5 mL, phase separation was facilitated using centrifugation). At this point, the conversion was found to be within a range of 30–50%. The combined organic layers were dried and the enantiomeric purities of epoxide and diol were determined as described below. The total recovery of materials was ⩾ 80%. Losses occurred during extractive workup due to the solubility of the diols formed in the aqueous phase and during evaporation of organic solvents due to the volatility of remaining non-converted epoxides. No side products were detected.

Determination of absolute configuration

Diol (*S*)-**4a** was independently synthesized *via* the following procedure. To a stirred solution of hep-1-tyne (330 mg, 3.4 mmol) in dry THF (4 mL) under an argon atmosphere *n*-BuLi (1.4 mL of a 2.5 M solution in hexane, 3.4 mmol) was added at −40 °C. After 90 min (*R*)-2-methylglycidol (2-hydroxymethyl-2-methyloxirane) **16** (100 mg, 1.13 mmol) was added and the solution was allowed to warm to rt. After 6 h, the reaction was quenched with semi-saturated NH_4Cl solution (5 mL) and the product was extracted with Et_2O. The combined organic extracts were dried and concentrated. Flash chromatography (petroleum ether–EtOAc, 2 : 1) gave (*S*)-**4a** as a clear oil; yield: 180 mg (90%); $[\alpha]_D^{20}$ −5.4 (*c* = 1.3, EtOH, 99% ee).

For GLC-analysis, a sample of (*S*)-**17** was synthesized as described above. (*S*)-**18** was obtained *via* catalytic hydrogenation of (*S*)-**17** using Pt on C (5%) under H_2 at atmospheric pressure in EtOH. The peaks on the chromatogram were assigned *via* co-injection of racemate with the (*S*)-enantiomer. Samples from biotransformations were converted to **18** for the elucidation of their absolute configuration. Chiral analysis of substrates and products proved that in each case the enzyme-catalyzed reaction proceeded with retention of configuration.

Determination of enantiomeric purities

Enantiomeric purities were analyzed on a Chrompack Chirasil-DEX CB column (column A, 25 m × 0.32 mm, 0.25 μm film), an Astec Chiraldex B-TA (column B, 30 m × 0.25 mm, 0.125 μm film) or an Astec Chiraldex G-PN (column C, 30 m × 0.32 mm, 0.125 μm film). Details are given in Table 3. For substrate **2a**, product and substrate from the biotransformation could be analyzed directly on GLC. For **1a**, epoxide and diol were separated *via* flash chromatography (petroleum ether–EtOAc, 2 : 1) and were transformed to **17** as described above. For **3b**, epoxide and formed diol were hydrogenated [Pt on C (5%), H_2 (atmospheric pressure), EtOH] to yield **7** and **8**, which were separated *via* flash chromatography (petroleum ether–EtOAc, 2 : 1). Epoxide **7** was analyzed and the diol **8** was monomethylated to yield **18** for GLC-analysis. The enantiomeric purities of products using substrate **7** were determined in an analogous fashion. Products obtained from substrates **1b**,**c**, **2b**,**c** and **3a**,**c** were separated *via* flash chromatography (petroleum ether–EtOAc, 2 : 1). Epoxides were analyzed without further derivatization and diols were transformed to the corresponding epoxides prior to analysis as described for Method C.

Table 3 Data from GLC-analyses on a chiral stationary phase

Comp.	Column	Conditions	Retention time t_r/min
1b	B	1 bar H_2, 85 °C	18.4 (*R*)/18.9 (*S*)
1c	A	1 bar He, 85 °C	45.4 (*R*)/47.6 (*S*)
2a	A	1 bar H_2, 80 °C	10.3 (*R*)/10.8 (*S*)
2b	C	0.4 bar H_2, 63 °C	55.4 (*R*)/58.0 (*S*)
2c	A	1 bar He, 85 °C	25.2 (*R*)/26.2 (*S*)
3a	B	1 bar H_2, 85 °C	12.2 (*R*)/12.5 (*S*)
3c	A	1 bar He, 90 °C	26.8 (*R*)/27.7 (*S*)
5a	A	1 bar H_2, 125 °C	11.1 (*R*)/11.8 (*S*)
7	C	0.45 bar H_2, 63 °C	56.5 (*R*)/58.1 (*S*)
17	A	1 bar N_2, 115 °C	10.2 (*R*)/10.7 (*S*)
18	A	1 bar H_2, 105 °C	10.7 (*R*)/11.3 (*S*)

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