Tetrahedron 66 (2010) 3814–3823

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

# Formation of chiral tertiary homoallylic alcohols via Evans aldol reaction or enzymatic resolution and their influence on the Sharpless asymmetric dihydroxylation

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ARTICLE INFO

*Article history:*
Received 21 December 2009
Received in revised form
8 March 2010
Accepted 15 March 2010
Available online 20 March 2010

*Keywords:*
Asymmetric synthesis
Homoallylic alcohols
Enzymatic resolution
Lipases
Sharpless asymmetric dihydroxylation

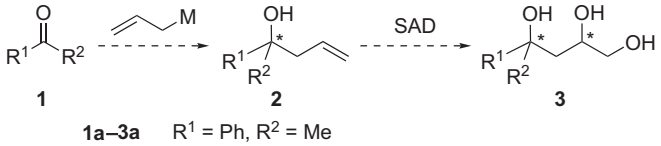
ABSTRACT

Enantioenriched tertiary homoallylic alcohol derivatives (*S*)-**2c** and (*S*)-**2a** were obtained via Evans aldol methodology and enzymatic resolution of racemic tertiary acetate **2e**, respectively. In order to study asymmetric 1,3-induction of the stereogenic center present in **2**, congener (*R*)-**2a** as well as its *O*-protected derivatives (*R*)-**2b**–**d** were submitted to Sharpless asymmetric dihydroxylation to yield the diastereomeric 1,2,4-triol derivatives (2*R*,4*R*)- and (2*S*,4*R*)-**3a**–**d**, revealing that neither the substrate nor the Sharpless catalyst exert any stereocontrol. Similar observations were made for the less bulky alkynyl-substituted derivative **12b**. However, by using a directed dihydroxylation, the *anti* product (2*R*,4*R*)-**3a** was favored.



## 1. Introduction

The area of the asymmetric synthesis of compounds with quaternary stereogenic centers is still a challenging task for organic chemists.[1] In particular enantiomerically pure tertiary homoallylic alcohols **2** constitute valuable building blocks for natural product synthesis as has been recently demonstrated by Sugai,[2] Theodorakis,[3] or Tietze.[4] A variety of methods deal with the asymmetric allylation of ketones such as Nozaki–Hiyama–Kishi reactions by Sigman[5] and Guiry,[6] allylborations by Brown,[7] Shibasaki,[8] Chong,[9] Schaus,[10] Jarvo,[11] Batey,[12] Goodman and Pellegrinet,[13] indium-mediated allylations by Singaram,[14] titanocene-catalyzed Barbier-type allylations by Gansäuer,[15] BINOL–Ti-catalyzed allylations employing tetraallylstannane by Tagliavini[16] and Walsh,[17,18] auxiliary-mediated or catalytic allylsilane transfer by Tietze[4,19] and Shibasaki,[20] respectively, and addition of allyl(bisoxazoline)zinc by Nakamura.[21,22] However, several of these reagents and catalysts are limited, e.g., with regard to the ketone substrates, enantioselectivities or use of highly toxic reagents. In addition, homoallylic alcohols such as **2** can be further functionalized to the corresponding 1,2,4-triols **3** by Sharpless asymmetric dihydroxylation (SAD)[23] (Scheme 1).




**Scheme 1.**

1,2,4-Triols **3** are highly attractive building blocks for natural product syntheses, such as spongistatine,[24] amphidinolide B,[25] L-methylmycaropyranoside,[26] mevalonolactone,[27] vitamin E,[28] and anthracycline antibiotics.[29] Despite a tremendous amount of work on *matched/mismatched* relationships in Sharpless asymmetric dihydroxylations,[30] only a few reports deal with tertiary homoallylic alcohols as substrates.[31–34] For example, Carter observed that shifting of a C=C double bond in the side chain attached to the heterosubstituted quaternary stereocenter reduced the diastereomeric ratio from 86:14 to 50:50.[31] For acyclic precursors Myles reported diastereoselectivities up to 75:25.[32] Brimble obtained diols from spiroacetals with only 28% ee.[33] In contrast, good selectivities were determined by Jefford for sterically congested tricyclic cyclopenteno-1,2,4-trioxanes, employing an iterative dihydroxylation.[34]

We therefore explored the double stereodifferentiation of tertiary homoallylic alcohols in more detail. We were particularly

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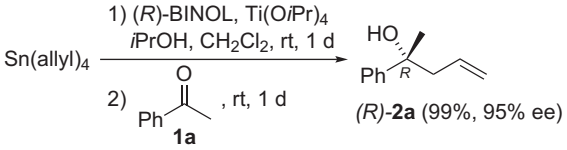
0040-4020/$ – see front matter © 2010 Published by Elsevier Ltd.
doi:10.1016/j.tet.2010.03.048

interested in the effect of the OH-protecting group on the Sharpless asymmetric dihydroxylation. As a suitable model substrate, 2-phenylpent-4-en-2-ol **2a** was chosen. Following the method by Walsh,[17a] i.e., treatment of ketone **1a** with tetraallylstannane in the presence of (*R*)-BINOL and Ti(O*i*-Pr)$_4$ in *i*-PrOH/$CH_2Cl_2$ at room temperature, gave (*R*)-**2a** in 99% yield and 95% ee (Scheme 2).




**Scheme 2.**

However, to avoid the use of stoichiometric amounts of tetraallylstannane we looked for more environmentally benign routes. Evans aldol methodology was chosen[35] because it gives reliable stereoselectivities even on a large scale and the auxiliary is easily recovered.

Biocatalysis is an environmentally benign alternative to chemical synthesis. The enzymatic synthesis of quaternary centers such as tertiary alcohols, however, is hampered by some difficulties. On one hand, the method of choice for the biocatalytic preparation of alcohols would be the enantioselective reduction of prochiral ketones and aldehydes to enantiopure alcohols catalyzed by alcohol dehydrogenases. This is not applicable in the case of tertiary alcohols. On the other hand, the hydrolase-catalyzed kinetic resolution of tertiary alcohols is a difficult task. Very few enzymes are active for this process, and enantioselectivities are usually low. Nevertheless, considerable progress has been made.[36] Tertiary alcohols have been synthesized in excellent optical purity by using epoxide hydrolases,[2,36b] proteases,[36c] and esterases.[36d,e] For the enantioselective synthesis of arylaliphatic tertiary alcohols such as **2**, several potentially selective esterases are available now, including variants of the esterase BS2 from *Bacillus subtilis*[36d] and several wild-type enzymes derived from metagenomic sources.[36e]

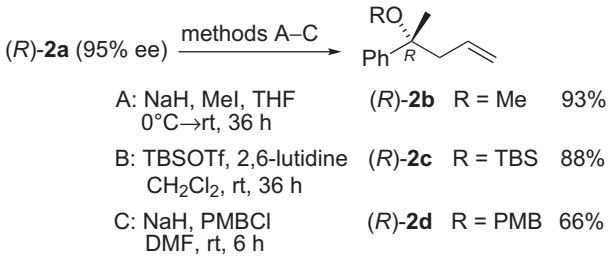
Thus the feasibility of Evans aldol versus biocatalysis followed by SAD for the conversion of acetophenone **1a** into 1,2,4-triol **3a** was investigated and the results are reported below.

## 2. Results and discussion

The Evans route commenced with L-phenylalaninol-derived oxazolidinone **4**,[35a] which was *N*-acetylated with *n*-BuLi, acetyl chloride in THF at −78 °C to give the *N*-acetamide **5** in 82%. Subsequent deprotonation with LiHMDS in THF at −78 °C, followed by addition of acetophenone **1a** at −95 °C and aqueous work-up yielded a diastereomeric mixture (dr 86:14) from which the major diastereomer **6a** was easily isolated in 78% by flash chromatography (Scheme 3).

After TBS protection, the chiral auxiliary was reductively cleaved with $LiBH_4$ (1 M in THF) in MeOH/$Et_2O$ at −10 °C to the primary alcohol **7** in 60%.[37] Dess–Martin periodinane oxidation[38] yielded the aldehyde **8** in 89%, which was then submitted to Wittig methylenation with $Ph_3PMe^+Br^-$ and KO*t*-Bu in THF to give the desired TBS-protected homoallylic alcohol (*S*)-**2c** in 84%. Thus, (*S*)-**2c** is available from **1a** in five steps with 33% overall yield.

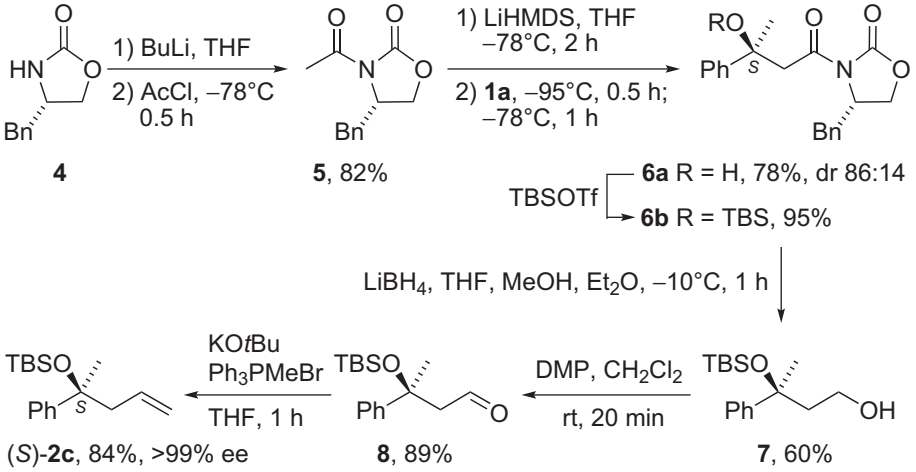
Since the protection experiments were already in progress before the Evans route was established, homoallylic alcohol (*R*)-**2a** from the allylstannane addition was used (Scheme 4). Methylated and PMB-protected derivatives **2b**,**d** were isolated after deprotonation with NaH and quenching with MeI or PMBCl in 93% and 66%, respectively. Treatment of (*R*)-**2a** with TBSOTf in the presence of 2,6-lutidine provided TBS-ether (*R*)-**2c** in 88%.



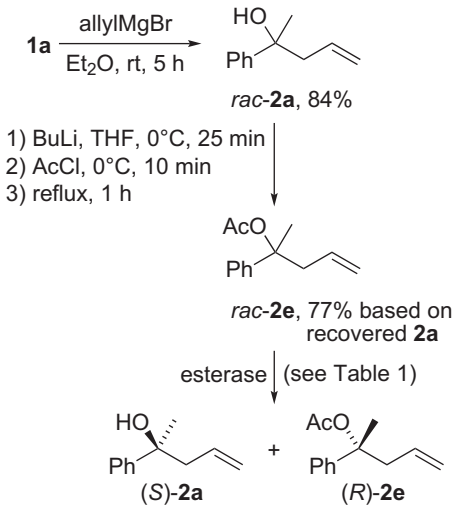

**Scheme 4.**

For analytical purposes and as racemic starting material for the enzymatic resolution, *rac*-**2a** was prepared in 84% by Grignard addition to acetophenone **1a** (Scheme 5). Further treatment with *n*-BuLi in THF and acetyl chloride produced the acetate *rac*-**2e** in 77% yield, based on recovered starting material. Next, enzymatic resolutions of racemic acetate *rac*-**2e** with esterases were investigated (Scheme 5, Table 1). Out of 17 esterases with a verified activity towards tertiary alcohols,[36d,e] only a few showed activity in the hydrolysis of *rac*-**2e**. Several enzyme variants of esterase BS2 from *B. subtilis* were previously shown to be highly enantioselective in the conversion of several compounds very similar to **2e**.[36d]

Surprisingly, the enantioselectivity of the wild-type enzyme towards **2e** was very low; two variants, BS2G105A and BS2 E188W/M198C, did not convert the substrate at all. Most of the remaining enzymes had no or low enantioselectivity. The metagenomic esterase Est8 converted **2e** at room temperature with a moderate *E*




**Scheme 3.**




**Scheme 5.**

**Table 1**
Selected examples of enzymatic kinetic resolution reactions of *rac*-**2e**

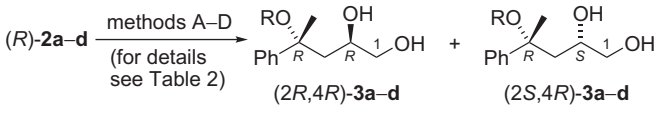
| Enzyme | Time (h) | Chiral analysis | | | |
|---|---|---|---|---|---|
| | | (*S*)-**2a** (ee%)[a] | (*R*)-**2e** (ee%)[b] | Conv. (%) | *E* value |
| BS2 | 4 | 37 | n.d. | 28[a] | 3 |
| BS2G105A | n.d. | n.d. | n.d. | n.c. | n.d. |
| BS2 E188W/M193C | n.d. | n.d. | n.d. | n.c. | n.d. |
| CAL-A | 4 | 28 | n.d. | 25[a] | 2 |
| PestA | 4 | 5 | n.d. | 62 | n.d. |
| Est8 | 1 | 85 | 71 | 46[c] | 26[d] |

n.d. not determined; n.c. no conversion.
[a] Determined by gas chromatography.
[b] Determined by HPLC.
[c] Calculated from (*S*)-**2a** and (*R*)-**2e**.
[d] At 4 °C.

value of $E$=23. Lowering the temperature to 4 °C did not substantially increase the enantioselectivity ($E$=26) (Table 1), neither did cosolvent optimization. The conversion of *rac*-**2e** was repeated on a 120 mg-scale, giving rise to enantiomerically enriched (*R*)-**2e** and (*S*)-**2a** with good yields (34% **2e**, 39% for **2a**) and good optical purities (71% ee for **2e**, 85% ee for **2a**).

Est8 was found to be enantioselective in the hydrolysis of some aliphatic tertiary alcohols while the enantioselectivity of Est8 towards analogues of **2e** bearing an ethynyl substituent is very low.[36d] The analogous butyric ester of **2e** was not converted by Est8. The remaining enzymes had no or only low enantioselectivity with this substrate (data not shown).

Next, enantiomerically enriched homoallylic alcohol derivatives (*R*)-**2a–d** were either submitted to dihydroxylation with $K_2OsO_4$, NMO in acetone/$H_2O$ (method A), AD-mix-α in *t*-BuOH/$H_2O$ (method B), AD-mix-β in *t*-BuOH/$H_2O$ (method C) or $OsO_4$, TMEDA in $CH_2Cl_2$ (method D) to yield the diastereomeric 1,2-diols **3** (Scheme 6, Table 2).




| 2, 3 | R |
|---|---|
| a | H |
| b | Me |
| c | TBS |
| d | PMB |

A: $K_2OsO_4$, NMO, acetone/$H_2O$, 0°C→rt, 12 h
B: AD-mix-α, *t*BuOH/$H_2O$, 0°C, 48 h
C: AD-mix-β, *t*BuOH/$H_2O$, 0°C, 48 h
D: $OsO_4$, TMEDA, $CH_2Cl_2$, -78°C, 1 h

**Scheme 6.**

**Table 2**
Dihydroxylations of homoallylic alcohols (*R*)-**2** under various conditions[a,b]

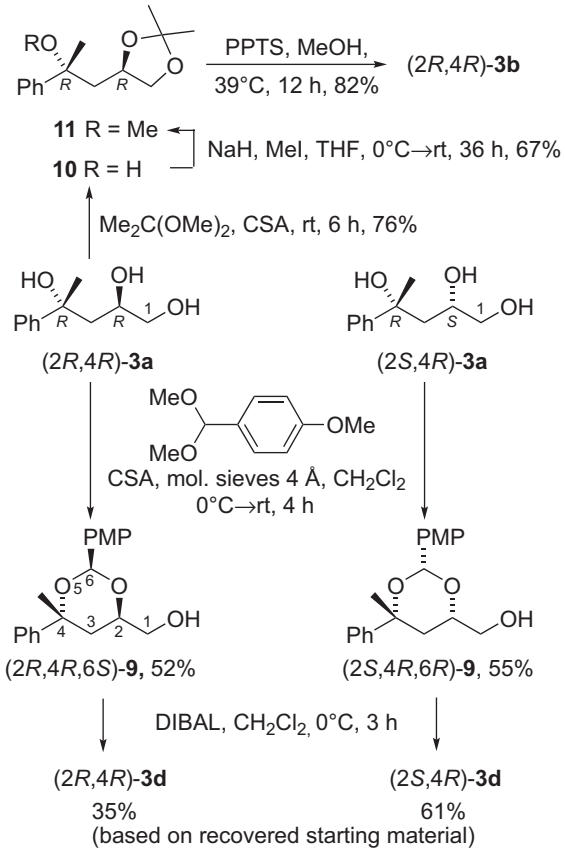
| Entry | Alcohol (*R*)-**2** | R | Method | Product **3** | Yield (%) | Diastereomeric ratio (2*R*,4*R*)/(2*S*,4*R*) |
|---|---|---|---|---|---|---|
| (1) | **2a** | H | A | **3a** | 94 | 46:54[c] |
| (2) | **2a** | H | B | **3a** | 79 | 49:51 |
| (3) | **2a** | H | C | **3a** | 87 | 55:45 |
| (4) | **2b** | Me | A | **3b** | 92 | 49:51 |
| (5) | **2b** | Me | B | **3b** | 92 | 35:65 |
| (6) | **2b** | Me | C | **3b** | 85 | 60:40 |
| (7) | **2c** | TBS | A | **3c** | 91 | 42:58 |
| (8) | **2c** | TBS | B | **3c** | 80 | 54:46 |
| (9) | **2c** | TBS | C | **3c** | 79 | 41:59 |
| (10) | **2d** | PMB | A | **3d** | 99 | 47:53[c] |
| (11) | **2d** | PMB | B | **3d** | 85 | 51:49 |
| (12) | **2d** | PMB | C | **3d** | 77 | 54:46 |
| (13) | **2a** | H | D | **3a** | 87 | 86:14 |

[a] Reactions conditions: see Scheme 6. Method A: $K_2OsO_4$, NMO, acetone/$H_2O$, 0 °C→rt, 12 h; method B: AD-mix-α, *t*-BuOH/$H_2O$, 0 °C, 48 h; method C: AD-mix-β, *t*-BuOH/$H_2O$, 0 °C, 48 h; method D: $OsO_4$, TMEDA, $CH_2Cl_2$, −78 °C, 1 h.
[b] Yields refer to isolated yields. Diastereomeric ratios were determined by $^1$H NMR.
[c] Diastereomeric ratio was determined by gas chromatography.

Surprisingly, regardless of the protecting group R or the dihydroxylation method employed, very poor diastereoselectivities 49:51 up to 35:65 were observed. An illustrative example is the TBS-protected derivative (*R*)-**2c**, which yielded 91% of a (42:58) mixture of (2*R*,4*R*)-**3c** and (2*S*,4*R*)-**3c**, respectively, via method A (entry 7). Treatment of (*R*)-**2c** with AD-mix-α (method B) gave **3c** in 80% (dr 54:46) (entry 8). The diastereomeric ratio was reversed by employing AD-mix-β (method C), yielding 79% of **3c** (dr 41:59) (entry 9). A slightly better situation was observed for the methyl-protected derivative (*R*)-**2b** where the use of AD-mix-α led to a dr 35:65 of **3b** (entry 5) and AD-mix-β to dr 60:40 (entry 6) as compared to the non-selective case via method A (entry 4). The selectivities for the PMB-protected derivative (*R*)-**2d** were again very poor (entries 10–12). We anticipated that the presence of a protecting group at the tertiary alcohol moiety might interfere with the Sharpless catalyst. However, even the unprotected derivative (*R*)-**2a** gave disappointing results (entries 1–3).

Thus, the overall steric bulkiness of the tertiary alcohol moiety in the neighborhood of the C=C double bond seems to minimize the energetic differences between the diastereomorphic transition states of the Sharpless asymmetric dihydroxylation. Even the chirality transfer in the absence of AD-mix-α (or -β) is very poor, resulting in a slight preference of the (2*S*,4*R*)-diastereomer (2*S*,4*R*)-**3** regardless of the R group. The results are somewhat surprising because Carter[31] and Eng[32] observed at least some kind of stereocontrol with steric bulky substrates. However, as mentioned above, Carter already noticed that slight side chain modifications such as a C=C double bond isomerization resulted in complete loss of diastereoselectivity. Finally, we tested Donohoe's hydrogen-bond-directed dihydroxylation using unprotected homoallylic alcohol **2a**, $OsO_4$, and TMEDA (method D),[39,40] which has been reported to give promising diastereoselectivities also for homoallylic alcohols.[41] Gratifyingly, the diastereomeric triols **3a** were isolated in 87% yield with a dr of 86:14 (entry 13). Thus, even in this sterically hindered environment, the tertiary alcohol moiety of **2a** is to some extent able to direct the attack of osmium tetroxide via hydrogen bonding and chelation by TMEDA.

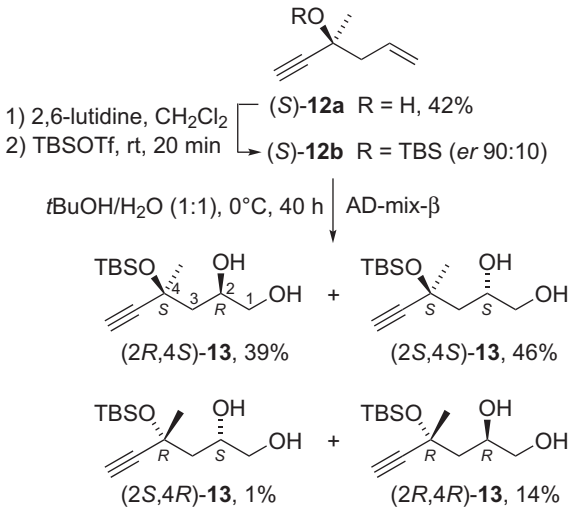
Unfortunately, no single crystals could be grown for diastereomeric triols **3a**. For assignment of the configuration, compounds **3a**, which could be easily separated by flash chromatography were therefore treated with *p*-anisaldehyde dimethyl acetal in $CH_2Cl_2$[42] in the presence of camphorsulfonic acid and molecular sieves. The corresponding PMP-acetals (2*R*,4*R*,6*S*)-**9** and (2*S*,4*R*,6*R*)-**9** were isolated in 52 and 55% yields, respectively (Scheme 7).[43]




**Scheme 7.**

PMP-acetals **9** could be reduced to the corresponding PMB-protected 1,2-diols (2*R*,4*R*)-**3d** and (2*S*,4*R*)-**3d** with DIBAL in $CH_2Cl_2$ at 0 °C (35 and 61% yield, respectively, based on recovered starting material). The configurational assignment of the PMB-protected 1,2-diols **3d** could be correlated with the unprotected triols **3a** via detailed NMR analysis (Supplementary data). The diastereomeric methyl-protected 1,2-diols **3b** could not be separated chromatographically. Therefore, unprotected triol (2*R*,4*R*)-**3a** was converted in three steps to methyl-protected 1,2-diol (2*R*,4*R*)-**3b** in 42% overall yield by acetalization of the 1,2-diol moiety with 2,2-dimethoxypropane in the presence of CSA followed by methylation and subsequent cleavage of the acetal (Scheme 7).

With regard to the Sharpless asymmetric dihydroxylation of homoallylic alcohol **2a** we surmised that the phenyl ring at the tertiary alcohol stereocenter might interfere with the Sharpless catalyst through π–π interactions or steric hindrance, resulting in a complete loss of the stereoselectivity. In order to test this hypothesis, the known (*S*)-3-methyl-5-hexen-1-yn-3-ol (*S*)-**12a**,[7] bearing an almost linear alkynyl moiety at the quaternary stereocenter, was converted to the TBS-ether (*S*)-**12b** (Scheme 8). Due to the incomplete stereocontrol of the Brown allylation with diisopinocampheylborane,[7] the enantiomeric excess of (*S*)-**12b** was only 80%. Treatment of compound (*S*)-**12b** with AD-mix-β under the above described conditions yielded a mixture of four diastereomers **13** (46:39:1:14). Thus, the (*S*)-configured homoallylic alcohol (*S*)-**12b** produced a *mismatched* pair (2*S*,4*S*)-**13** and (2*R*,4*S*)-**13** in 46% and 39%, respectively, whereas the minor enantiomer (*R*)-**12b** yielded a *matched* pair (2*S*,4*R*)-**13** and (2*R*,4*R*)-**13** in 1% and 14%, respectively. Thus, it seems that neither the type of substituents nor the OH-protecting group exerts any positive control on the stereoselectivity of the Sharpless asymmetric dihydroxylation.




**Scheme 8.**

## 3. Conclusion

The Evans aldol addition to acetophenone **1a** was shown to offer an efficient access to enantiopure homoallylic alcohol **2a** by environmentally benign protocols as compared to the allylstannane procedure. Even if some progress has been made, the enzymatic kinetic resolution of tertiary alcohols is still not always straightforward. Taking into account the very low number of hydrolases with activity towards tertiary alcohols, the identification of some hydrolases with activity towards **2e** was a promising result. With Est8, one biocatalyst was identified that produces (*S*)-**2a** with moderate optical purity (85% ee). Together with the easy preparation of the starting compounds, the biocatalytic preparation can be considered as a straightforward, environmentally benign alternative. In addition, a series of differently protected homoallylic alcohols (*R*)-**2**, (*S*)-**12b** was submitted to Sharpless asymmetric dihydroxylation. Regardless of the protecting group, the dihydroxylation catalyst is hardly able to overcome the small chirality transfer of the quaternary stereogenic center towards the (2*S*,4*R*)-diastereomer (2*S*,4*R*)-**3** and (2*S*,4*S*)-**13**. This is probably due to the steric bulkiness of the tertiary alcohol moiety. The observation that the substrate **2** has little intrinsic bias for formation of the *syn* or *anti* product **3** probably reflects a failure of the alkene **2** to adequately dock with the Os/ligand assembly due to steric hindrance. However, this problem can be solved by the use of Donohoe's hydrogen-bond-directed dihydroxylation, which yielded preferably the *anti*-1,2,4-triol (2*R*,4*R*)-**3a**. Unfortunately, none of the methods shown above is able to produce the *syn*-1,2,4-triol with high selectivities. In particular, alternative routes for the missing 1,3-induction in tertiary homoallylic alcohols via Sharpless dihydroxylation are highly desirable, and the scope of directed dihydroxylation must be explored further for acyclic substrates in order to use the current routes towards 1,2,4-triol subunits for natural product synthesis.

## 4. Experimental

### 4.1. General

Melting points (uncorrected) were determined on a Büchi 510 melting point apparatus. Optical rotations were determined with a Perkin–Elmer 241 LC polarimeter. IR spectra: Bruker Vektor 22 FT-IR spectrometer. Mass spectra: Finnigan MAT 95, Varian MAT 711, and Bruker Daltonics micrOTOF_Q spectrometers. NMR spectra: Bruker ARX 300 and Bruker ARX 500 spectrometers. The spectra

were recorded with TMS as an internal standard. $^{13}C$ NMR multiplicities were determined by DEPT135 experiments. Assignments were done by using $^{1}H$–$^{1}H$-COSY, $^{1}H$–$^{13}C$-correlation, and NOESY experiments. Column chromatography: Fluka silica gel 60 (40–63 μm). All syntheses were performed under nitrogen using standard Schlenk technique.

### 4.2. Biocatalytic reactions

Recombinant esterases were produced as described.[36d,e] All metagenomic esterases were provided by B.R.A.I.N. AG (Zwingenberg, Germany) and used as glycerol-stabilized crude cell extracts or lyophilisate.

*4.2.1. General procedure for esterase-catalyzed small-scale resolutions.* To a stirred solution of acetate (25 mM) in phosphate buffer (100 mM, pH 7.5) and the appropriate amount of cosolvent DMSO [10–20% (v/v)], the appropriate amount of esterase solution was added to a total volume of 1 mL. The amount of enzyme in crude extracts was determined according to the activity in hydrolysis of *p*-nitrophenyl butyrate. The reaction mixture was stirred in a thermoshaker (Eppendorf, Hamburg, Germany) at 37 °C for 15 min. Samples were taken every 1, 4, and 24 h. After two times extraction with $CH_2Cl_2$, the organic layer was dried ($Na_2SO_4$) and filtered. Enantioselectivity and conversion were calculated according to Chen.[44] The enantiomeric purity of **2e** was analyzed on a Chiralcel OD-H column by HPLC (hexane/isopropanol 99:1, flow: 0.5 mL min$^{-1}$) with a retention time of 12.0 min (*R*)-**2e** and 12.8 min (*S*)-**2e**. Alcohol **2a** was analyzed with an FS-Hydrodex β-column (Macherey Nagel, Düren, Germany) on a Shimadzu 2010 gas chromatograph (Shimadzu, Japan) at a constant temperature of 90 °C. Retention times: 22.2 min (*R*)-**2a** and 23.5 min (*S*)-**2a**.

*4.2.2. Preparative scale enzyme hydrolysis of (**2e**).* To a stirred solution of the substrate (120 mg, 0.59 mmol) in DMSO (4 mL) was added a solution of the enzyme (320 mg, 185 U) in phosphate buffer (7 mL, 100 mM, pH 7.4). The reaction mixture was stirred at 4 °C for 4 h. After extraction with MTBE, the organic layers were combined and dried ($Na_2SO_4$). The organic solvent was removed under reduced pressure and the residue chromatographed on silica gel with *n*-pentane/EtOAc to give (*R*)-2-phenylpent-4-en-2-yl-acetate (*R*)-**2e** as white powder (41 mg, 0.2 mmol, 34%, 71% ee) and (*S*)-2-phenylpent-4-en-2-ol (*S*)-**2a** as white powder (37.5 mg, 0.23 mmol, 39%, 85% ee).

### 4.3. Synthesis and characterization

*4.3.1. (R)-2-Phenylpent-4-en-2-ol (**2a**).* To a solution of (*R*)-BINOL (803 mg, 2.8 mmol) in $CH_2Cl_2$ (21 mL) were sequentially added Ti(O*i*-Pr)$_4$ (0.84 mL, 0.80 g, 2.8 mmol), *i*-PrOH (14.5 mL, 0.19 mol), and tetraallylstannane (3.36 mL, 3.96 g, 14.0 mmol) and the mixture was stirred at rt for 1 day. Then **1a** (1.07 mL, 1.1 g, 9.2 mmol) was added and the mixture was stirred at rt for a further day. The reaction mixture was diluted with aqueous $NH_4Cl$ solution (10 mL) and extracted with $CH_2Cl_2$ (3×20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residue was dissolved in hexanes, filtered through Celite, and evaporated. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 15:1→10:1) to give **2a** (1.48 g, 99%) as a colorless oil; $R_f$ (hexane/EtOAc 6:1) 0.51; $[\alpha]_D^{20}$ +21.8 (*c* 0.36, $CH_2Cl_2$); $\delta_H$ (300 MHz, $CDCl_3$) 1.55 (s, 3H, $CH_3$), 2.03 (s, 1H, OH), 2.50 (dd, *J*=13.7, 8.2 Hz, 1H, H-3$_a$), 2.70 (dd, *J*=13.7, 6.5 Hz, 1H, H-3$_b$), 5.10–5.18 (m, 2H, H-5), 5.62 (dddd, *J*=17.0, 10.2, 8.3, 6.5 Hz, 1-H, H-4), 7.21–7.27 (m, 1H, *p*-H, Ph), 7.31–7.38 (m, 2H, *m*-H, Ph), 7.42–7.47 (m, 2H, *o*-H, Ph); $\delta_C$ (75 MHz, $CDCl_3$) 29.9 ($CH_3$), 48.5 (C-3), 73.6 (C-2), 119.5 (C-5), 124.8 (2C, Ph), 126.6 (C-$p_{Ph}$), 128.2 (2C, Ph), 133.7 (C-4), 147.6 (C-$i_{Ph}$); HPLC: Chiralcel OJ-H, hexane/isopropanol (98:2), flow rate 1.0 mL min$^{-1}$, $t_{R,major}$=11.26 min and $t_{R,minor}$=13.94 min; ee 95%.

*4.3.2. (S)-3-Acetyl-4-benzyloxazolidin-2-one (**5**).* Following the procedure by Evans[35b,c] compound **5** (2.48 g, 82%) was obtained as a colorless solid; mp 109 °C; $\delta_H$ (500 MHz, $CDCl_3$) 2.56 (s, 3H, $CH_3$), 2.78 (dd, *J*=13.4, 9.5 Hz, 1H, C*H*$_2$Ph), 3.31 (dd, *J*=13.4, 3.5 Hz, 1H, C*H*$_2$Ph), 4.15–4.22 (m, 2H, H-5), 4.67 (dddd, *J*=10.4, 9.5, 7.1, 3.5 Hz, 1H, H-4), 7.20–7.22 (m, 2H, *o*-H, Bn), 7.27–7.30 (m, 1H, *p*-H, Bn), 7.32–7.36 (m, 2H, *m*-H, Bn).

*4.3.3. (S)-4-Benzyl-3-((S)-3-hydroxy-3-phenylbutanoyl)oxazolidin-2-one (**6a**).* A solution of **5** (1.00 g, 4.60 mmol) in dry THF (10 mL) was slowly added at −78 °C to a solution of LiHMDS (5.7 mL, 4.6 mmol, 0.84 M in THF). After 2 h at −78 °C, the solution was cooled to −95 °C and **1a** (365 mg, 360 μL, 3.00 mmol), dissolved in THF (6 mL) was slowly added. The solution was kept for an additional 30 min at −95 °C and then for 45 min at −78 °C. Subsequently, the reaction was stopped by the addition of aqueous 0.5 M HCl (10 mL). The THF layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (3×15 mL). The combined organic layers were dried ($Na_2SO_4$) and the solvent was removed in vacuo. The crude product was purified by column chromatography (silica gel, hexane/EtOAc 4:1→1:1) to obtain **6a** (790 mg, 78%, dr=84:14 by $^{1}H$ NMR) as a colorless solid; mp 101–103 °C. Found: C, 70.74; H, 6.28; N, 4.07. $C_{20}H_{21}NO_4$ requires C, 70.78; H, 6.24; N, 4.13%; $R_{f,major}$ (hexane/EtOAc 2:1) 0.35; $R_{f,minor}$ (hexane/EtOAc 2:1) 0.51; $[\alpha]_D^{20}$+126.2 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3490 (w, br), 3062 (w), 3029 (w), 1964 (m), 1779 (vs), 1681 (s), 1380 (s), 1213 (s), 701 (m) cm$^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.60 (d, *J*=0.9 Hz, 3H, $CH_3$), 2.41 (dd, *J*=13.6, 9.3 Hz, 1H, C*H*$_2$Ph), 2.83 (dd, *J*=13.6, 3.4 Hz, 1H, C*H*$_2$Ph), 3.06 (d, *J*=16.5 Hz, 1H, H-2′$_a$), 4.09 (dd, *J*=9.1, 2.9 Hz, 1H, H-5$_a$), 4.15 (dd, *J*=9.1, 7.8 Hz, 1H, H-5$_b$), 4.21 (d, *J*=16.5 Hz, 1H, H-2′$_b$), 4.57 (d, *J*=0.9 Hz, 1H, OH), 4.59 (dddd, *J*=9.4, 7.8, 3.4, 2.9 Hz, 1H, C*H*Bn), 6.99–7.01 (m, 2H, *o*-H, Bn), 7.22–7.30 (m, 4H, *m*-H, *p*-H, Bn, *p*-H, Ph), 7.34–7.39 (m, 2H, *m*-H, Ph), 7.50–7.53 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 31.1 ($CH_3$), 37.3 (*C*H$_2$Ph), 45.7 (C-2′), 54.8 (C-4), 66.0 (C-5), 73.8 (C-3′), 124.6 (2C, C-$o_{Ph}$), 126.9 (C-$p_{Ph}$), 127.4 (C-$p_{Bn}$), 128.3 (2C, C-$m_{Ph}$), 128.9 (2C, C-$m_{Bn}$), 129.3 (2C, C-$o_{Bn}$), 134.8 (C-$i_{Bn}$), 147.0 (C-$i_{Ph}$), 153.3 (C=O), 172.9 (*C*OCH$_2$); *m*/*z* (ESI) 362 ($M^+$), 322, 216, 190; HRMS (ESI): $MNa^+$, found 362.1363. $C_{20}H_{21}NO_4Na^+$ requires 362.1363.

*4.3.4. (S)-4-Benzyl-3-((S)-3-(tert-butyldimethylsilyloxy)-3-phenylbutanoyl)oxazolidin-2-one (**6b**).* To a solution of **6a** (130 mg, 0.30 mmol) in $CH_2Cl_2$ (2 mL) were added at rt 2,6-lutidine (78 μL, 72 mg, 0.52 mmol) and TBSOTf (133 μL, 153 mg, 0.45 mmol). After the solution was stirred for an additional 30 min, the reaction mixture was quenched by the addition of satd aqueous $NH_4Cl$ solution (2 mL). The organic layer was separated, and the aqueous layer was extracted with $CH_2Cl_2$ (3×10 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 5:1) to give **6b** (129 mg, 95%) as a colorless oil; $R_f$ (hexane/EtOAc 2:1) 0.67; $[\alpha]_D^{20}$+27.5 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 2954 (s), 2929 (s), 2857 (m), 1962 (w), 1728 (vs), 1698 (s), 1358 (s), 1210 (s), 1002 (m), 835 (s) cm$^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) −0.12 (s, 3H, Si–$CH_3$), 0.10 (s, 3H, Si–$CH_3$), 0.94 (s, 9H, C–$CH_3$), 1.88 (s, 3H, $CH_3$), 2.54 (dd, *J*=13.3, 10.2 Hz, 1H, C*H*$_2$Ph), 3.22 (dd, *J*=13.3, 3.4 Hz, 1H, C*H*$_2$Ph), 3.51 (d, *J*=14.3 Hz, 1H, H-2′$_a$), 3.59 (d, *J*=14.3 Hz, 1H, H-2′$_b$), 3.85 (dd, *J*=9.0, 7.8 Hz, 1H, H-5$_a$), 3.97 (dd, *J*=9.0, 2.6 Hz, 1H, H-5$_b$), 4.41 (dddd, *J*=10.2, 7.8, 3.4, 2.6 Hz, 1H, H-4), 7.14–7.17 (m, 2H, *o*-H, Bn), 7.21–7.27 (m, 2H, *p*-H, Bn, *p*-H, Ph), 7.29–7.34 (m, 4H, *m*-H, Bn, *m*-H, Ph), 7.51–7.54 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) −2.6 (Si–*C*H$_3$), −2.0 (Si–*C*H$_3$), 18.4 [Si*C*(CH$_3$)$_3$], 26.0 [SiC(*C*H$_3$)$_3$], 28.6 ($CH_3$), 37.8 (*C*H$_2$Ph), 49.1 (C-2′), 55.4 (C-4), 65.7 (C-5), 76.2 (C-3′), 125.7

(2C, C-$o_{Ph}$), 127.0 (C-$p_{Ph}$), 127.2 (C-$p_{Bn}$), 127.7 (2C, C-$m_{Ph}$), 128.9 (2C, C-$m_{Bn}$), 129.4 (2C, C-$o_{Bn}$), 135.5 (C-$i_{Bn}$), 147.0 (C-$i_{Ph}$), 153.2 (C=O), 169.8 ($COCH_2$); *m*/*z* (ESI) 476 ($MNa^+$), 322, 242, 145; HRMS (ESI): $MNa^+$, found 476.2221. $C_{26}H_{35}NO_4SiNa^+$ requires 476.2228.

*4.3.5. (S)-3-(tert-Butyldimethylsilyloxy)-3-phenylbutan-1-ol (**7**).* To a solution of **6b** (90 mg, 198 μmol) in $Et_2O$ (2 mL) and MeOH (9.6 μL, 7.7 mg, 0.24 mmol) was added $LiBH_4$ (119 μL, 5.17 mg, 238 μmol, 2 M in THF) at −10 °C. After the solution was stirred for 1 h, the mixture was quenched by the addition of aqueous NaOH solution (1 mL, 1 M). The mixture was warmed to 0 °C and stirred for 15 min, subsequently shaken with brine (10 mL) and the organic layer was separated. The aqueous layer was extracted with $Et_2O$ (3×10 mL). The combined organic layers were dried ($Na_2SO_4$), and the solvent was evaporated. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 2:1) to give **7** (34 mg, 60%) as a colorless oil; $R_f$ (hexane/EtOAc 1:1) 0.78; $[\alpha]_D^{20}$ −38.4 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3348 (m, br), 2954 (s), 2929 (s), 2856 (m), 1968 (w), 1472 (m), 1255 (s), 1030 (m), 834 (vs), 774 (vs), 700 (s) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) −0.06 (s, 3H, Si–$CH_3$), 0.12 (s, 3H, Si–$CH_3$), 0.96 (s, 9H, C–$CH_3$), 1.72 (s, 3H, $CH_3$), 1.99 (ddd, *J*=14.2, 6.7, 5.5 Hz, 1H, H-$2_a$), 2.06 (ddd, *J*=14.2, 6.7, 5.4 Hz, 1H, H-$2_b$), 2.42 (br tr, *J*=5.3 Hz, 1H, OH), 3.57–3.67 (m, 2H, H-1), 7.22–7.26 (m, 1H, *p*-H, Ph), 7.31–7.35 (m, 2H, *m*-H, Ph), 7.42–7.45 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) −2.3 (Si–$CH_3$), −1.8 (Si-$CH_3$), 18.4 [SiC$(CH_3)_3$], 26.2 [SiC($CH_3)_3$], 29.6 ($CH_3$), 47.5 (C-2), 59.9 (C-1), 78.4 (C-3), 125.2 (2C, C-$o_{Ph}$), 126.7 (C-$p_{Ph}$), 128.1 (2C, C-$m_{Ph}$), 147.5 (C-$i_{Ph}$); *m*/*z* (ESI) 281 ($MH^+$), 147, 131, 105, 91; HRMS (ESI): $MNa^+$, found 303.1761. $C_{16}H_{28}O_2Si\ Na^+$ requires 303.1751.

*4.3.6. (S)-3-(tert-Butyldimethylsilyloxy)-3-phenylbutanal (**8**).* To a solution of Dess–Martin periodinane (127 mg, 0.3 mmol) in $CH_2Cl_2$ (0.6 mL) was added a solution of alcohol **7** (34 mg, 0.12 mmol) in $CH_2Cl_2$ (0.5 mL) at rt. After the solution was stirred for an additional 20 min at rt, the mixture was diluted by the addition of $CH_2Cl_2$ (3 mL) and aqueous NaOH solution (1 mL, 1 M) and stirred for an additional 10 min. The organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (3×10 mL). The combined organic layers were dried ($Na_2SO_4$), and the solvent was evaporated. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 10:1) to give **8** (30 mg, 89%) as a colorless oil; $R_f$ (hexane/EtOAc 10:1) 0.55; $[\alpha]_D^{20}$ −37.0 (*c* 0.5, $CH_2Cl_2$); $\nu_{max}$ (neat) 2955 (m), 2929 (m), 2856 (m), 1723 (vs), 1463 (w), 1256 (s), 1126 (m), 832 (vs), 774 (vs), 670 (vs) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) −0.06 (s, 3H, Si–$CH_3$), 0.05 (s, 3H, Si–$CH_3$), 0.88 (s, 9H, C–$CH_3$), 1.65 (s, 3H, $CH_3$), 2.61 (dd, *J*=15.3, 3.5 Hz, 1H, H-$2_a$), 2.79 (dd, *J*=15.3, 2.4 Hz, 1H, H-$2_b$), 7.17–7.21 (m, 1H, *p*-H, Ph), 7.26–7.30 (m, 2H, *m*-H, Ph), 7.38–7.41 (m, 2H, *o*-H, Ph), 9.52 (dd, *J*=3.5, 2.4 Hz, 1H, H-1); $\delta_C$ (125 MHz, $CDCl_3$) −2.3 (Si–$CH_3$), −1.9 (Si–$CH_3$), 18.5 [SiC$(CH_3)_3$], 26.0 [SiC($CH_3)_3$], 30.2 ($CH_3$), 57.9 (C-2), 75.8 (C-3), 125.0 (2C, C-$o_{Ph}$), 127.1 (C-$p_{Ph}$), 128.3 (2C, C-$m_{Ph}$), 147.0 (C-$i_{Ph}$), 202.8 (C-1); *m*/*z* (ESI) 279 ($MH^+$), 149, 133, 119; HRMS (ESI): $MNa^+$, found 301.1601. $C_{16}H_{26}O_2Si\ Na^+$ requires 301.1594.

*4.3.7. (S)-tert-Butyldimethyl(2-phenylpent-4-en-2-yloxy)silane [(S)-**2c**].* To a solution of $MePPh_3Br$ (31 mg, 86.0 μmol) in THF (0.3 mL) was added KO*t*-Bu (9.7 mg, 86.0 μmol) at rt and the solution was stirred for 30 min at rt. Subsequently, a solution of **8** (12 mg, 43.0 μmol) in THF (1 mL) was added and stirring was continued for another 30 min. The reaction was quenched by the addition of water (2 mL), the organic layer was separated, and the aqueous layer was extracted with $Et_2O$ (3×10 mL). The combined organic layers were dried ($Na_2SO_4$), and the solvent was removed in vacuo. The crude oil was purified by column chromatography (silica gel, hexane) to give (*S*)-**2c** (10 mg, 84%) as a colorless oil; $R_f$ (hexane) 0.50; $[\alpha]_D^{20}$ −9.8 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 2956 (m), 2929 (m), 2857 (m), 1964 (w, br), 1463 (m), 1255 (s), 1072 (s), 996 (s), 833 (vs), 773 (s), 699 (s) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 0.07 (s, 3H, Si–$CH_3$), 0.08 (s, 3H, Si–$CH_3$), 0.94 (s, 9H, C–$CH_3$), 1.61 (s, 3H, $CH_3$), 2.46 (dd, *J*=13.9, 7.2 Hz, 1H, H-$3_a$), 2.55 (dd, *J*=13.9, 7.0 Hz, 1H, H-$3_b$), 4.90–4.96 (m, 2H, H-5), 5.64 (dddd, *J*=14.2, 10.5, 7.2, 7.0 Hz, 1H, H-4), 7.18–7.22 (m, 1H, *p*-H, Ph), 7.28–7.31 (m, 2H, *m*-H, Ph), 7.40–7.43 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) −2.3 (Si–$CH_3$), −1.9 (Si–$CH_3$), 18.5 [SiC$(CH_3)_3$], 26.1 [SiC($CH_3)_3$], 28.6 ($CH_3$), 50.6 (C-3), 76.7 (C-2), 117.1 (C-5), 125.4 (2C, C-$o_{Ph}$), 126.3 (C-$p_{Ph}$), 127.7 (2C, C-$m_{Ph}$), 134.8 (C-4), 148.3 (C-$i_{Ph}$); *m*/*z* (ESI) 277 ($MH^+$), 261, 235, 219, 145; HRMS (ESI): $MH^+$, found 277.1964. $C_{17}H_{29}OSi^+$ requires 277.1982.

*4.3.8. (R)-(2-Methoxypent-4-en-2-yl)benzene (**2b**).* NaH (35 mg, 4.9 mmol, 60% in mineral oil) was washed with dry THF (2×2.5 mL), suspended in THF (1 mL), and treated sequentially with a solution of homoallylic alcohol **2a** (94 mg, 0.58 mmol) in THF (1 mL) and MeI (108 μL, 247 mg, 1.74 mmol). The ice bath was removed and stirring was continued for 36 h at rt. The reaction mixture was quenched by the addition of satd aqueous $Na_2S_2O_3$ solution (2 mL). The organic layer was separated, and the aqueous layer was extracted with $CH_2Cl_2$ (3×10 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 20:1) to give **2b** (95 mg, 93%) as a colorless oil; $R_f$ (hexane/EtOAc 10:1) 0.62; $[\alpha]_D^{20}$ +13.8 (*c* 0.42, $CH_2Cl_2$); $\nu_{max}$ (neat) 2978 (m), 2932 (m), 1640 (w), 1446 (m), 1161 (m), 1073 (vs), 914 (s), 764 (s), 700 (vs) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.52 (s, 3H, $CH_3$), 2.50 (dd, *J*=13.9, 7.2 Hz, 1H, H-$3_a$), 2.56 (dd, *J*=13.9, 7.2 Hz, 1H, H-$3_b$), 3.08 (s, 3H, $OCH_3$), 4.98–5.01 (m, 1H, H-$5_a$), 5.02–5.03 (m, 1H, H-$5_b$), 5.61–5.70 (m, 1H, H-4), 7.23–7.27 (m, 1H, *p*-H, Ph), 7.32–7.39 (m, 4H, *o*-H, *m*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 22.8 ($CH_3$), 47.3 (C-3), 50.4 ($OCH_3$), 78.7 (C-2), 117.6 (C-5), 126.3 (2C, C-$o_{Ph}$), 126.9 (C-$p_{Ph}$), 128.1 (2C, C-$m_{Ph}$), 134.1 (C-4), 144.7 (C-$i_{Ph}$); *m*/*z* (GC–MS, CI) 177 (3, $MH^+$), 145 (35), 135 (100), 99 (15%); HRMS (CI): $MH^+$, found 177.1263. $C_{12}H_{17}O^+$ requires 177.1274.

*4.3.9. (R)-tert-Butyldimethyl(2-phenylpent-4-en-2-yloxy)silane [(R)-**2c**].* To a solution of **2a** (250 mg, 1.54 mmol) in $CH_2Cl_2$ (1.5 mL) were added at rt 2,6-lutidine (360 μL, 332 mg, 3.10 mmol) and TBSOTf (530 μL, 608 mg, 2.30 mmol). After the solution was stirred for an additional 30 min, the reaction mixture was quenched by the addition of satd aqueous $NH_4Cl$ solution (2 mL). The organic layer was separated, and the aqueous layer was extracted with $CH_2Cl_2$ (3×10 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated. The crude oil was purified by column chromatography (silica gel, hexane) to give (*R*)-**2c** (440 mg, 88%) as a colorless oil; $R_f$ (hexane) 0.50; $[\alpha]_D^{20}$ +8.9 (*c* 1.0, $CH_2Cl_2$); for other analytical data: see (*S*)-**2c**.

*4.3.10. (R)-1-Methoxy-4-((2-phenylpent-4-en-2-yloxy)methyl)-benzene [(R)-**2d**].* To a stirred suspension of NaH (197 mg, 4.9 mmol, 60% in mineral oil) in DMF under nitrogen was added dropwise **2a** (400 mg, 2.5 mmol) in THF (16 mL) and after 30 min a mixture of PMBCl (0.50 mL, 579 mg, 3.7 mmol) and TBAI (91 mg, 0.25 mmol) in 6 mL of THF. After 5 h, the reaction mixture was poured into a mixture of ice and satd aqueous $NH_4Cl$ solution and extracted with $Et_2O$ (3×20 mL). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 20:1→10:1) to give (*R*)-**2d** (0.46 g, 66%) as a colorless oil; $R_f$ (hexane/EtOAc 6:1) 0.65; $[\alpha]_D^{20}$ −25.9 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 2931 (w), 2363 (w), 1613 (w), 1514 (vs), 1248 (vs), 1036 (m), 701 (s) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.61 (s, 3H, $CH_3$), 2.57 (dd, *J*=13.8, 7.2 Hz, 1H, H-$3_a$), 2.66 (dd, *J*=13.8, 7.0 Hz, 1H, H-$3_b$), 3.78 (s, 3H, $OCH_3$), 4.12 (d, *J*=10.8 Hz, 1H, $OCH_2$PMP), 4.24 (d, *J*=10.8 Hz, 1H, $OCH_2$PMP), 5.00–5.04 (m, 2H, H-5), 5.66–5.77 (m, 1H, H-4), 6.85–6.88 (m, 2H, *m*-H, PMP), 7.23–7.28 (m, 3H, *o*-H, PMP, *p*-H, Ph), 7.34–7.38 (m, 2H, *m*-H, Ph), 7.44–7.46 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 23.5 ($CH_3$), 47.6 (C-3), 55.3 ($OCH_3$),

64.3 ($OCH_2PMP$), 78.8 (C-2), 113.7 (2C, C-$m_{PMB}$), 117.6 (C-5), 126.3 (2C, C-$o_{Ph}$), 127.0 (C-$p_{Ph}$), 128.2 (2C, C-$m_{Ph}$), 128.8 (2C, C-$o_{PMB}$), 131.4 (C-$i_{PMB}$), 134.2 (C-4), 145.0 (C-$i_{Ph}$), 158.9 (C-$p_{PMB}$); *m/z* (ESI) 305 ($MNa^+$), 213, 195, 145, 121; HRMS (ESI): $MNa^+$, found 305.1508. $C_{13}H_{16}O_2Na^+$ requires 305.1508.

*4.3.11. 2-Phenylpent-4-en-2-ol (rac-**2a**).* In a three-necked flask equipped with a dropping funnel and a reflux condenser were placed Mg-turnings (3.89 g, 160 mmol), a crystal of iodine, and 70 mL of anhydrous ether. Within 30 min, a solution of allylbromide (10.4 ml, 14.5 g, 120 mmol) in $Et_2O$ (50 mL) was added dropwise at rt in a rate sufficient to maintain a gentle reflux and the solution was stirred at rt for an additional hour. A solution of **1a** (4.68 ml, 4.80 g, 40 mmol) in 40 mL of anhydrous $Et_2O$ was added dropwise within 30 min, and then stirring was continued for an additional 2.5 h at rt. The reaction was quenched with 1 M HCl (70 mL). The organic layer was separated, and the aqueous layer was extracted with $Et_2O$ (3×50 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was removed in vacuo. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 15:1→10:1) to give *rac*-**2a** (5.44 g, 84%) as a colorless oil.

*4.3.12. 2-Phenylpent-4-en-2-yl-acetate (rac-**2e**).* To a solution of homoallylic alcohol *rac*-**2a** (1.00 g, 6.25 mmol) in THF (16 mL) was added at 0 °C *n*-BuLi (4.7 mL, 7.4 mmol, 1.6 M in hexane) over a period of 10 min. After the solution was stirred for additional 15 min, freshly distilled acetyl chloride (0.53 mL, 0.58 g, 7.4 mmol) was added within 10 min and the mixture was heated under reflux for 1 h. Subsequently, the mixture was cooled down to rt and quenched by the addition of water (10 mL). The organic layer was separated, and the aqueous layer was extracted with $Et_2O$ (3×20 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and the solvent was evaporated. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 20:1) to give *rac*-**2e** (505 mg, 2.47 mmol, 77% based on recovered starting material) as a colorless oil. Found: C, 74.4; H, 8.0. $C_{13}H_{16}O_2$ requires C, 74.4; H, 7.9%; $R_f$ (hexane/EtOAc 20:1) 0.30; $\nu_{max}$ (neat) 3063 (w), 2981 (w), 2364 (w), 1738 (vs), 1368 (m), 1239 (vs), 1016 (w), 700 (m) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.80 (s, 3H, $CH_3$), 2.03 (s, 3H, $COCH_3$), 2.74 (dd, *J*=13.9, 7.6 Hz, 1H, H-$3_a$), 2.83 (dd, *J*=13.9, 6.9 Hz, 1H, H-$3_b$), 5.01–5.07 (m, 2H, H-5), 5.56–5.74 (m, 1H, H-4), 7.21–7.25 (m, 1H, *p*-Ph), 7.29–7–34 (m, 4H, *o*-H, *m*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 22.2 ($COCH_3$), 24.9 ($CH_3$), 46.4 (C-3), 83.0 (C-2), 118.6 (C-5), 124.6 (2C, C-$o_{Ph}$), 126.9 (C-$p_{Ph}$), 128.2 (2C, C-$m_{Ph}$), 132.8 (C-4), 144.7 (C-$i_{Ph}$), 169.5 ($COCH_3$); *m/z* (EI, 70 eV) 204 (10, $M^+$), 163 (40), 121 (100%); HRMS (ESI): $MNa^+$, found 227.1044. $C_{13}H_{16}O_2Na^+$ requires 227.1043.

*4.3.13. General procedure for the dihydroxylation of olefins **2** with $K_2OsO_4$ and NMO (method A).* To a solution of **2** (4.9 mmol) in 50 mL of acetone/water (8:1) were added at 0 °C NMO (1.67 g, 12.3 mmol) and $K_2OsO_4 \cdot 2H_2O$ (67 mg, 0.18 mmol). The ice bath was removed and the mixture was stirred overnight at rt before the reaction was quenched by the addition of solid $Na_2SO_3$ (9.50 g). The resulting suspension was stirred for 45 min and extracted with EtOAc (5×15 mL). The combined organic layers were washed with satd aqueous $NaHCO_3$ solution, dried ($MgSO_4$), and the solvent was removed in vacuo. The residue was purified by flash column chromatography (silica gel).

*4.3.14. General procedure for the Sharpless asymmetric dihydroxylation of olefins **2** (methods B and C).* AD-mix-α (method B) or AD-mix-β (method C) (1.44 g, i.e., 0.75 mg, 2 μmol $K_2OsO_4 \cdot 2H_2O$) was dissolved in 7 mL of *t*-BuOH/water (1:1) and cooled to 0 °C. To the resulting mixture was added **2** (0.72 mmol) and stirring at 0 °C was continued for 2 days, before the reaction was quenched by the addition of solid $Na_2SO_3$ (1.1 g). The resulting suspension was stirred for 45 min and extracted with EtOAc (5×7 mL). The combined organic layers were washed with satd aqueous $NaHCO_3$ solution, dried ($MgSO_4$), and the solvent was removed in vacuo. The residue was purified by flash column chromatography (silica gel).

*4.3.15. (2R,4R)- and (2S,4R)-4-Phenylpentane-1,2,4-triol [(2R,4R)-**3a**] and [(2S,4R)-**3a**].* Column chromatography (silica gel, hexane/EtOAc 1:6) gave **3a** as colorless oils; 903 mg (4.6 mmol, 94%), dr 46:54 (GC) via method A; 28 mg (0.14 mmol, 79%), dr 49:51 ($^1H$ NMR) via method B; 24 mg (0.12 mmol, 87%), dr 55:45 ($^1H$ NMR) via method C; separation of diastereoisomers: preparative HPLC: Knauer Eurospher 100-5 Si, hexane/EtOAc (1:6), flow rate 8 mL $min^{-1}$. Compound (2*R*,4*R*)-**3a**: $R_f$ (hexane/EtOAc 1:6) 0.38; $[\alpha]_D^{20}$ +26.2 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3336 (br s), 2928 (m), 1444 (s), 1073 (s), 1054 (s), 700 (vs) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.53 (s, 3H, $CH_3$), 1.89 (dd, *J*=14.6, 2.4 Hz, 1H, H-$3_a$), 1.97 (dd, *J*=14.6, 10.4 Hz, 1H, H-$3_b$), 3.32 (dd, *J*=11.2, 6.8 Hz, 1H, H-$1_a$), 3.42 (dd, *J*=11.2, 3.2 Hz, 1H, H-$1_b$), 3.48 (dddd, *J*=10.4, 6.8, 3.2, 2.4 Hz, 1H, H-2), 7.22–7.25 (m, 1H, *p*-H, Ph), 7.32–7.35 (m, 2H, *m*-H, Ph), 7.39–7.41 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 32.2 ($CH_3$), 44.1 (C-3), 66.7 (C-1), 70.3 (C-2), 75.5 (C-4), 124.8 (2C, C-$o_{Ph}$), 126.5 (C-$p_{Ph}$), 128.3 (2C, C-$m_{Ph}$), 147.0 (C-$i_{Ph}$); *m/z* (ESI) 214 ($MNH_4^+$), 143, 119; HRMS (ESI): $MNa^+$, found 219.0991. $C_{11}H_{16}O_3Na^+$ requires 219.0992. Compound (2*S*,4*R*)-**3a**: $R_f$ (hexane/EtOAc 1:6) 0.31; $[\alpha]_D^{20}$ +32.7 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3334 (br m), 2929 (m), 1446 (s), 1026 (s), 764 (s), 699 (vs) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.64 (s, 3H, $CH_3$), 1.80 (dd, *J*=14.6, 2.7 Hz, 1H, H-$3_a$), 1.99 (dd, *J*=14.6, 9.9 Hz, 1H, H-$3_b$), 3.46 (dd, *J*=10.9, 6.6 Hz, 1H, H-$1_a$), 3.62 (dd, *J*=10.9, 3.6 Hz, 1H, H-$1_b$), 4.15 (dddd, *J*=9.9, 6.6, 3.6, 2.7 Hz, 1H, H-2), 7.23–7.29 (m, 1H, *p*-H, Ph), 7.32–7.39 (m, 2H, *m*-H, Ph), 7.44–7.49 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 28.5 ($CH_3$), 45.0 (C-3), 66.9 (C-1), 70.0 (C-2), 74.6 (C-4), 124.4 (2C, C-$o_{Ph}$), 126.8 (C-$p_{Ph}$), 128.3 (2C, C-$m_{Ph}$), 148.6 (C-$i_{Ph}$); *m/z* (ESI) 214 ($MNH_4^+$), 143, 119; HRMS (ESI): $MNa^+$, found 219.0984. $C_{11}H_{16}O_3Na^+$ requires 219.0992.

*4.3.16. (2R,4R)- and (2S,4R)-4-Methoxy-4-phenylpentane-1,2-diol [(2R,4R)-**3b**] and [(2S,4R)-**3b**].* Column chromatography (silica gel, hexane/EtOAc 1:2) gave **3b** as colorless oils. Compound (2*S*,4*R*)-**3b** was characterized in a mixture of both diastereoisomers; 44 mg (0.21 mmol, 92%), dr 49:51 ($^1H$ NMR) via method A; 70 mg (0.33 mmol, 92%), dr 35:65 ($^1H$ NMR) via method B; 64 mg (0.30 mmol, 85%), dr 60:40 ($^1H$ NMR) via method C. Compound (2*R*,4*R*)-**3b**: $R_f$ (hexane/EtOAc 1:3) 0.24; $[\alpha]_D^{20}$ +59.9 (*c* 0.83, $CH_2Cl_2$); $\nu_{max}$ (neat) 3394 (br m), 2925 (m), 2364 (w), 1445 (m), 1165 (m), 1065 (vs), 1027 (s), 766 (s), 701 (vs) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.62 (dd, *J*=14.5, 2.0 Hz, 1H, H-$3_a$), 1.66 (s, 3H, $CH_3$), 2.11 (dd, *J*=14.5, 10.0 Hz, 1H, H-$3_b$), 3.25 (s, 3H, $OCH_3$), 3.33 (dd, *J*=11.1, 5.7 Hz, 1H, H-$1_a$), 3.44 (dd, *J*=11.1, 3.7 Hz, 1H, H-$1_b$) 3.63 (dddd, *J*=10.0, 5.7, 3.7, 2.0 Hz, 1H, H-2), 7.25–7.30 (m, 1H, *p*-H, Ph), 7.34–7.39 (m, 4H, *m*-H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 24.8 ($CH_3$), 46.3 (C-3), 50.8 ($OCH_3$), 66.8 (C-1), 68.9 (C-2), 80.9 (C-4), 125.9 (2C, C-$o_{Ph}$), 127.1 (C-$p_{Ph}$), 128.5 (2C, C-$m_{Ph}$), 143.1 (C-$i_{Ph}$); *m/z* (CI, $CH_4$) 211 (10, $MH^+$), 179 (40), 135 (75), 119 (100%); HRMS (ESI): $MNa^+$, found 233.1150. $C_{12}H_{18}O_3Na^+$ requires 233.1148. Compound (2*S*,4*R*)-**3b**: $R_f$ (hexane/EtOAc 1:3) 0.24; $\delta_H$ (500 MHz, $CDCl_3$) 1.57 (dd, *J*=14.8, 2.0 Hz, 1H, H-$3_a$), 1.74 (s, 3H, $CH_3$), 2.04 (dd, *J*=14.8, 10.5 Hz, 1H, H-$3_b$), 3.10 (s, 3H, $OCH_3$), 3.42 (dd, *J*=11.1, 6.0 Hz, 1H, H-$1_a$), 3.55 (dd, *J*=11.1, 3.7 Hz, 1H, H-$1_a$) 4.09 (dddd, *J*=10.5, 6.0, 3.7, 2.0 Hz, 1H, H-2), 7.25–7.30 (m, 1H, *p*-H, Ph), 7.34–7.39 (m, 4H, *m*-H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 20.7 ($CH_3$), 46.9 (C-3), 50.5 ($OCH_3$), 67.0 (C-1), 69.4 (C-2), 80.4 (C-4), 125.7 (2C, C-$o_{Ph}$), 127.3 (C-$p_{Ph}$), 128.5 (2C, C-$m_{Ph}$), 144.8 (C-$i_{Ph}$).

*4.3.17. (2R,4R)- and (2S,4R)-4-(tert-Butyldimethylsilyloxy)-4-phenylpentane-1,2-diol [(2R,4R)-**3c**] and [(2S,4R)-**3c**].* Column chromatography (silica gel, hexane/EtOAc 2:1) gave **3c** as colorless oils; separation of diastereoisomers was not possible; 117 mg (0.38 mmol, 91%), dr 42:58 ($^1H$ NMR) via method A; 76 mg (0.24 mmol, 80% based

on recovered starting material), dr 54:46 ($^1$H NMR) via method B; 88 mg (0.28 mmol, 79%), dr 41:59 ($^1$H NMR) via method C; $R_f$ (hexane/EtOAc 1:1) 0.44; $[\alpha]_D^{20}$ +30.0 (*c* 0.58, $CH_2Cl_2$); $\nu_{max}$ (neat) 3396 (br m), 2928 (s), 2856 (m), 2360 (w), 1455 (s), 1126 (s), 1061 (s), 1029 (s), 833 (vs), 773 (vs), 699 (vs) $cm^{-1}$; main isomer following methods A and C: $\delta_H$ (500 MHz, $CDCl_3$) 0.02 (s, 3H, Si–$CH_3$), 0.18 (s, 3H, Si–$CH_3$), 1.00 (s, 9H, C–$CH_3$), 1.72 (dd, *J*=14.3, 2.1 Hz, 1H, H-$3_a$), 1.74 (s, 3H, $CH_3$), 2.06 (dd, *J*=14.3, 10.1 Hz, 1H, H-$3_b$), 2.24 (br s, 1H, OH), 3.26–3.32 (m, 1H, H-$1_a$), 3.38–3.44 (m, 1H, H-$1_b$), 3.53–3.59 (m, 1H, H-2), 4.12 (s, 1H, OH), 7.22–7.27 (m, 1H, *p*-H, Ph), 7.31–7.36 (m, 2H, *m*-H, Ph), 7.39–7.43 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) −2.1 (Si–*C*$H_3$), −1.4 (Si–*C*$H_3$), 18.4 [Si*C*$(CH_3)_3$], 26.2 [SiC(*C*$H_3)_3$], 31.2 ($CH_3$), 47.7 (C-3), 66.8 (C-1), 69.3 (C-2), 79.5 (C-4), 125.1 (2C, C-$o_{Ph}$), 126.8 (C-$p_{Ph}$), 128.1 (2C, C-$m_{Ph}$), 146.3 (C-$i_{Ph}$); minor isomer following methods A and C: $\delta_H$ (500 MHz, $CDCl_3$) −0.23 (s, 3H, Si–$CH_3$), 0.03 (s, 3H, Si–$CH_3$), 0.94 (s, 9H, C–$CH_3$), 1.56 (dd, *J*=14.7, 1.9 Hz, 1H, H-$3_a$), 1.81 (s, 3H, $CH_3$), 2.10 (dd, *J*=14.7, 10.0 Hz, 1H, H-$3_b$), 2.35 (br s, 1H, OH), 3.38–3.43 (m, 1H, H-$1_a$), 3.49–3.54 (m, 1H, H-$1_b$), 3.75 (s, 1H, OH), 4.05–4.10 (m, 1H, H-2), 7.22–7.27 (m, 1H, *p*-H, Ph), 7.31–7.36 (m, 2H, *m*-H, Ph), 7.39–7.43 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) −2.9 (Si–*C*$H_3$), −2.0 (Si–*C*$H_3$), 18.3 [Si*C*$(CH_3)_3$], 26.1 [SiC(*C*$H_3)_3$], 26.9 ($CH_3$), 48.6 (C-3), 67.0 (C-1), 69.5 (C-2), 78.0 (C-4), 125.3 (2C, C-$o_{Ph}$), 127.2 (C-$p_{Ph}$), 128.2 (2C, C-$m_{Ph}$), 147.9 (C-$i_{Ph}$); *m*/*z* (EI, 70 eV) 309 (2, M−H), 295 (10), 235 (75), 195 (25), 143 (45), 117 (100%); HRMS (ESI): $MNa^+$, found 333.1862. $C_{17}H_{30}O_3Si\,Na^+$ requires 333.1856.

*4.3.18. (2R,4R)- and (2S,4R)-4-(4-Methoxybenzyloxy)-4-phenylpentane-1,2-diol [(2R,4R)-**3d**] and [(2S,4R)-**3d**].* Column chromatography (silica gel, hexane/EtOAc 1:3) gave **3d** as colorless oils; 457 mg (1.44 mmol, 99%), dr 47:53 (GC) via method A; 193 mg (0.61 mmol, 85%), dr 51:49 ($^1$H NMR) via method B; 122 mg (0.39 mmol, 77%), dr 54:46 ($^1$H NMR) via method C; separation of diastereoisomers: preparative HPLC: Knauer Eurospher 100-5 Si, hexane/EtOAc (1:3), flow rate 8 mL $min^{-1}$. Compound (2*R*,4*R*)-**3d**: $R_f$ (hexane/EtOAc 1:2) 0.41; $[\alpha]_D^{20}$ −23.4 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3404 (br m), 2923 (s), 1613 (m), 1514 (vs), 1249 (vs), 1033 (vs), 704 (s) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.66 (dd, *J*=14.5, 2.0 Hz, 1H, H-$3_a$), 1.79 (s, 3H, $CH_3$), 2.19 (dd, *J*=14.5, 10.1 Hz, 1H, H-$3_b$), 3.33 (dd, *J*=11.2, 5.7 Hz, 1H, H-$1_a$), 3.43 (dd, *J*=11.2, 3.5 Hz, 1H, H-$1_b$), 3.68 (dddd, *J*=10.1, 5.7, 3.5, 2.0 Hz, 1H, H-2), 3.81 (s, 3H, $OCH_3$), 4.29 (d, *J*=10.5 Hz, 1H, $OCH_2$PMP), 4.45 (d, *J*=10.5 Hz, 1H, $OCH_2$PMP), 6.88–6.92 (m, 2H, *m*-H, PMB), 7.27–7.32 (m, 3H, *o*-H, PMB, *p*-H, Ph), 7.38–7.45 (m, 4H, *m*-H, Ph, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 25.6 ($CH_3$), 46.8 (C-3), 55.3 ($OCH_3$), 65.1 ($OCH_2$PMP), 66.9 (C-1), 68.8 (C-2), 81.2 (C-4), 114.1 (2C, C-$m_{PMB}$), 126.0 (2C, C-$o_{Ph}$), 127.3 (C-$p_{Ph}$), 128.5 (2C, C-$m_{Ph}$), 129.0 (2C, C-$o_{PMB}$), 130.3 (C-$i_{PMB}$), 143.4 (C-$i_{Ph}$), 159.2 (C-$p_{PMB}$); *m*/*z* (ESI) 339 ($MNa^+$), 201, 161, 121; HRMS (ESI): $MNa^+$, found 339,1563. $C_{19}H_{24}O_4Na^+$ requires 339,1567. Compound (2*S*,4*R*)-**3d**: $R_f$ (hexane/EtOAc 1:2) 0.36; $[\alpha]_D^{20}$ −17.6 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3416 (br m), 2922 (m), 1613 (m), 1514 (vs), 1249 (vs), 1031 (vs), 703 (s) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.60 (dd, *J*=14.8, 1.9 Hz, 1H, H-$3_a$), 1.87 (s, 3H, $CH_3$), 2.12 (dd, *J*=14.8, 10.6 Hz, 1H, H-$3_b$), 3.41 (dd, *J*=11.1, 5.9 Hz, 1H, H-$1_a$), 3.55 (dd, *J*=11.1, 3.7 Hz, 1H, H-$1_b$), 3.80 (s, 3H, $OCH_3$), 4.10 (d, *J*=10.4 Hz, 1H, $OCH_2$PMP), 4.14 (dddd, *J*=10.6, 5.9, 3.7, 1.9 Hz, 1H, H-2), 4.30 (d, *J*=10.4 Hz, 1H, $OCH_2$PMP), 6.86–6.89 (m, 2H, *m*-H, PMB), 7.20–7.23 (m, 2H, *o*-H, PMB), 7.28–7.32 (m, 1H, *p*-H, Ph), 7.37–7.41 (m, 2H, *m*-H, Ph), 7.45–7.48 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $CDCl_3$) 21.4 ($CH_3$), 47.2 (C-3), 55.3 ($OCH_3$), 64.9 ($OCH_2$PMP), 67.0 (C-1), 69.4 (C-2), 80.7 (C-4), 114.0 (2C, C-$m_{PMB}$), 125.8 (2C, C-$o_{Ph}$), 127.5 (C-$p_{Ph}$), 128.6 (2C, C-$m_{Ph}$), 129.1 (2C, C-$o_{PMB}$), 130.2 (C-$i_{PMB}$), 145.1 (C-$i_{Ph}$), 159.2 (C-$p_{PMB}$); *m*/*z* (EI, 70 eV) 316 (20, $M^+$), 137 (75), 121 (100%); HRMS (ESI): $MNa^+$, found 339,1568. $C_{19}H_{24}O_4Na^+$ requires 339,1567.

*4.3.19. (2R,4R)- and (2S,4R)-4-Phenylpentane-1,2,4-triol [(2R,4R)-**3a**] and [(2S,4R)-**3a**].* To a −78 °C cold solution of (*R*)-2-phenylpent-4-en-2-ol (14 mg, 86 μmol) and TMEDA (14 μL, 11 mg, 95 μmol) in $CH_2Cl_2$ (1 mL) was added a solution of $OsO_4$ (24 mg, 95 μmol) in $CH_2Cl_2$ (0.5 mL). After 1 h, the reaction mixture was warmed to rt and the solvent was removed in vacuo. The brown residue was dissolved in methanol (2 mL) and two drops of concentrated hydrochloric acid were added. The mixture was stirred at rt for another 1 h before the solvent was removed again. The remaining crude triol was purified by column chromatography (silica gel, hexane/EtOAc 1:6) to give **3a** (15 mg, 87%, dr 86:14 (GC)) as a colorless oil.

*4.3.20. PMP-acetals [(2R,4R,6S)-**9**] and [(2S,4R,6R)-**9**].* For the correct IUPAC name see Ref. 43. Triol **3a** (106 mg, 0.54 mmol) was dissolved in $CH_2Cl_2$ (5 mL). Molecular sieves (4 Å, 1 g), *p*-anisaldehyde dimethyl acetal (93 μL, 99 mg, 0.55 mmol), and camphorsulfonic acid (6 mg, 26.0 μmol) were added at 0 °C. After 10 min, the ice bath was removed and the reaction mixture was stirred for 4 h. The molecular sieves were filtered off and washed with EtOAc (20 mL). Subsequently, the organic layer was washed with satd aqueous $NaHCO_3$ solution and brine. The aqueous layers were extracted with EtOAc (2×20 mL). The combined organic layers were dried ($Na_2SO_4$) and concentrated in vacuo. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 4:1, 1% $NEt_3$) to obtain **9** as colorless oils. Compound (2*R*,4*R*,6*S*)-**9**: 89 mg, 52%; $R_f$ (hexane/EtOAc 1:1) 0.50; $[\alpha]_D^{20}$ +19.1 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3416 (br m), 2928 (m), 2545 (w, br), 2178 (m), 1974 (m), 1518 (vs), 1249 (vs), 1065 (s), 1033 (s) $cm^{-1}$; for detailed NMR analysis: see Tables 3 and 4; *m*/*z* (ESI) 337 ($MNa^+$), 315, 240, 137; HRMS (ESI): $MNa^+$, found 337.1414. $C_{19}H_{22}O_4Na^+$ requires 337.1410. Compound (2*S*,4*R*,6*R*)-**9**: 75 mg, 55%. Found: C, 72.24; H, 7.16. $C_{19}H_{22}O_4$ requires C, 72.59; H, 7.05%; $R_f$ (hexane/EtOAc 1:1) 0.42; $[\alpha]_D^{20}$ +44.2 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3417 (br m), 2925 (s), 1615 (s), 1517 (s), 1248 (vs), 1030 (vs), 829 (s) $cm^{-1}$; for detailed NMR analysis: see Tables 3 and 4; *m*/*z* (EI, 70 eV) 314 (55,

**Table 3**
$^1$H NMR data (500 MHz, $C_6D_6$) of compounds (2*R*,4*R*,6*S*)-**9** and (2*S*,4*R*,6*R*)-**9**

| Position | δ (ppm) for (2*R*,4*R*,6*S*)-**9** | δ (ppm) for (2*S*,4*R*,6*R*)-**9** |
|---|---|---|
| $CH_3$ | 1.47 (s, 3H) | 1.45 (s, 3H) |
| H-$3_{ax}$ | 1.82 (dd, *J*=13.9, 11.9 Hz, 1H) | 1.77 (dd, *J*=13.2,12.1 Hz, 1H) |
| H-$3_{eq}$ | 1.98 (dd, *J*=13.9, 2.2 Hz, 1H) | 1.42 (dd, *J*=13.2, 2.4 Hz, 1H) |
| $OCH_3$ | 3.31 (s, 3H) | 3.34 (s, 3H) |
| $CH_2OH$ (H-1) | 3.49–3.53 (m, 2H) | 3.46–3.47 (m, 1H)<br>3.48–3.49 (m, 1H) |
| H-2 | 3.76 (dddd, *J*=11.8, 5.6, 4.1, 2.1 Hz, 1H) | 3.93 (dddd, *J*=12.1 5.6, 4.3, 2.3 Hz, 1H) |
| *CH*-PMP | 5.63 (s, 1H) | 5.92 (s, 1H) |
| *m*-H, PMP | 6.87–6.92 (m, 2H) | 6.89–6.92 (m, 2H) |
| *p*-H, Ph | 7.12–7.16 (m, 1H) | 7.13–7.17 (m, 1H) |
| *m*-H, Ph | 7.21–7.26 (m, 2H) | 7.24–7.28 (m, 2H) |
| *o*-H, Ph | 7.32–7.35 (m, 2H) | 7.50–7.52 (m, 2H) |
| *o*-H, PMP | 7.59–7.62 (m, 2H) | 7.66–7.69 (m, 2H) |

**Table 4**
$^{13}$C NMR data (125 MHz, $C_6D_6$) of compounds (2*R*,4*R*,6*S*)-**9** and (2*S*,4*R*,6*R*)-**9**

| Position | δ (ppm) for (2*R*,4*R*,6*S*)-**9** | δ (ppm) for (2*S*,4*R*,6*R*)-**9** |
|---|---|---|
| $CH_3$ | 34.5 (qd, *J*=127.8, 3.9 Hz) | 23.5 (qdd, *J*=126.9, 6.2, 1.9 Hz) |
| C-3 | 35.2 | 37.6 |
| $OCH_3$ | 54.8 | 54.8 |
| $CH_2OH$ (C-1) | 65.9 | 66.0 |
| C-2 | 74.3 | 74.0 |
| C-4 | 77.2 | 75.2 |
| C-PMP | 96.5 | 95.2 |
| C-$m_{PMP}$ | 113.8 | 113.8 |
| C-$o_{Ph}$ | 126.4 | 124.3 |
| C-$p_{Ph}$ | 127.2 | 126.9 |
| C-$m_{Ph}$ | 128.1 | 128.3 |
| C-$o_{PMP}$ | 129.1 | 128.4 |
| C-$i_{PMP}$ | 132.1 | 132.3 |
| C-$i_{Ph}$ | 144.5 | 149.4 |
| C-$p_{PMP}$ | 160.5 | 160.5 |

$M^+$), 163 (35), 143 (60), 135 (85), 131 (100%); HRMS (ESI): $MH^+$, found 315.1586. $C_{19}H_{23}O_4^+$ requires 315.1591.

*4.3.21. General procedure for the reductive opening of PMP-acetals **9**.* To a solution of **9** (33 mg, 0.10 mmol) in $CH_2Cl_2$ (2 mL) was added DIBAL (0.3 mL, 0.3 mmol, 1 M solution in hexane) at 0 °C and the reaction mixture was stirred for 3 h at 0 °C. The mixture was cooled down to −78 °C and quenched by the addition of EtOAc (5 mL). The mixture was warmed to rt and shaken with Rochelle salt solution. The organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (3×10 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and the solvent was evaporated. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 1:3) to give the diols **3d** as colorless oils; (2*R*,4*R*)-**3d** (5 mg, 16 μmol, 35%, based on recovered starting material); (2*S*,4*R*)-**3d** (9 mg, 28 μmol, 61%, based on recovered starting material); $R_f$ and $\delta_H$ were identical with the two diols **3d** obtained by dihydroxylation of **2d** (vide supra).

*4.3.22. (R)-1-((R)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2-phenylpropan-2-ol (**10**).* To a solution of triol **3a** (95 mg, 0.48 mmol) in 2,2-dimethoxypropane (3 mL) was added camphorsulfonic acid (1.5 mg, 6.5 μmol) at rt. After the solution was stirred for 6 h, the reaction was quenched by the addition of $NEt_3$ (0.3 mL), evaporated, and the residue was purified by column chromatography (silica gel, hexane/EtOAc 4:1, 1% $NEt_3$) to give **10** (86 mg, 76%) as a colorless oil. Found: C, 71.03; H, 8.62. $C_{14}H_{20}O_3$ requires C, 71.16; H, 8.53%; $R_f$ (hexane/EtOAc 4:1) 0.37; $[\alpha]_D^{20}$ +47.9 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3460 (br m), 2983 (m), 2934 (m), 1447 (m), 1371 (s), 1217 (s), 1050 (vs), 701 (vs) $cm^{-1}$; NMR-assignment according to the corresponding triol **3a**: $\delta_H$ (500 MHz, $C_6D_6$) 1.07 (s, 3H, C-($CH_3$)$_2$), 1.31 (s, 3H, C-(C$H_3$)$_2$), 1.50 (s, 3H, $CH_3$),1.66 (dd, *J*=14.4, 4.5 Hz, 1H, H-3$_a$), 1.86 (dd, *J*=14.4, 10.2 Hz, 1H, H-3$_b$), 3.16 (dd, *J*=8.2, 6.9 Hz, 1H, H-1$_a$), 3.47 (dd, *J*=8.2, 6.1 Hz, 1H, H-1$_b$), 3.75–3.81 (m, 1H, H-2), 4.01 (s, 1H, OH), 7.08–7.12 (m, 1H, *p*-H, Ph), 7.20–7.24 (m, 2H, *m*-H, Ph), 7.43–7.46 (m, 2H, *o*-H, Ph); $\delta_C$ (125 MHz, $C_6D_6$) 25.7 (C-(*C*H$_3$)$_2$), 27.0 (C-(*C*H$_3$)$_2$), 32.2 ($CH_3$), 46.5 (C-3), 69.7 (C-1), 74.1 (C-2), 74.5 (C-4), 109.4 (*C*-(CH$_3$)$_2$), 125.4 (2C, C-$o_{Ph}$), 126.6 (C-$p_{Ph}$), 128.4 (2C, C-$m_{Ph}$), 148.5 (C-$i_{Ph}$); *m*/*z* (EI, 70 eV) 236 (15, $M^+$), 221 (35), 178 (30), 143 (100), 121 (85%); HRMS (ESI): $MNa^+$, found 259.1310. $C_{14}H_{20}O_3Na^+$ requires 259.1305.

*4.3.23. (R)-4-((R)-2-Methoxy-2-phenylpropyl)-2,2-dimethyl-1,3-dioxolane (**11**).* Alcohol **10** (29 mg, 0.12 mmol) was converted into the corresponding methyl ether following the procedure reported for **2b**. The crude product was purified by column chromatography (silica gel, hexane/EtOAc 10:1→4:1) to give **11** (20 mg, 67%) as a colorless oil; $R_f$ (hexane/EtOAc 4:1) 0.66; $[\alpha]_D^{20}$ +5.2 (*c* 0.33, $CH_2Cl_2$); $\nu_{max}$ (neat) 2984 (s), 2934 (m), 1377 (s), 1370 (s), 1225 (s), 1161 (s), 1071 (vs), 1054 (vs), 702 (s) $cm^{-1}$; $\delta_H$ (300 MHz, $C_6D_6$) 1.36 (s, 3H, C–(C$H_3$)$_2$), 1.40 (s, 3H, C–(C$H_3$)$_2$), 1.44 (s, 3H, $CH_3$), 1.90 (dd, *J*=14.4, 6.3 Hz, 1H, H-3$_a$), 2.09 (dd, *J*=14.4, 5.4 Hz, 1H, H-3$_b$), 2.88 (s, 3H, $OCH_3$), 3.33 (dd, *J*=8.1, 8.1 Hz, 1H, H-1$_a$), 3.83 (dd, *J*=8.1, 5.8 Hz, 1H, H-1$_b$), 4.37–4.46 (m, 1H, H-2), 7.04–7.10 (m, 1H, *p*-H, Ph), 7.12–7.19 (m, 2H, *m*-H, Ph), 7.22–7.27 (m, 2H, *o*-H, Ph); $\delta_C$ (75 MHz, $C_6D_6$) 22.8 ($CH_3$), 26.3 (C–(*C*H$_3$)$_2$), 27.3 (C–(*C*H$_3$)$_2$), 48.0 (C-3), 50.1 ($OCH_3$), 70.6 (C-1), 73.1 (C-2), 77.9 (C-4), 108.2 (*C*–(CH$_3$)$_2$), 126.1 (2C, C-$o_{Ph}$), 127.1 (C-$p_{Ph}$), 128.5 (2C, C-$m_{Ph}$), 146.2 (C-$i_{Ph}$); *m*/*z* (CI, $CH_4$) 251 (7, $MH^+$), 219 (30), 175 (15), 163 (30), 143 (45), 135 (100), 101 (70%); HRMS (ESI): $MNa^+$, found 273.1456. $C_{15}H_{22}O_3Na^+$ requires 273.1461.

*4.3.24. (2R,4R)-4-Methoxy-4-phenylpentane-1,2-diol [(2R,4R)-**3b**].* To a solution of **11** (16 mg, 64 μmol) in MeOH (5 mL) was added PPTS (16 mg, 64 μmol). After the solution was stirred overnight at 39 °C, aqueous NaOH (3 mL, 1 M) was added and stirring was continued for an additional hour. The mixture was diluted by the addition of water and EtOAc (2 mL each) and the pH adjusted to 2–3 by the addition of 1 M aqueous HCl. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3×10 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated. The crude oil was purified by column chromatography (silica gel, hexane/EtOAc 1:3) to give (2*R*,4*R*)-**3b** (11 mg, 82%) as a colorless oil; $R_f$ and $\delta_H$ were identical with those of the diol (2*R*,4*R*)-**3b** obtained by dihydroxylation of **2b** (vide supra).

*4.3.25. (S)-3-Methylhex-5-en-1-yn-3-ol [(S)-**12a**].* To a solution of (−)-*B*-allyl-diisopinocampheylborane (7.91 g, 24.2 mmol) in $Et_2O$ (50 mL) was added 3-butyn-2-one (1.9 mL, 1.65 g, 24.2 mmol) at −78 °C. After the solution was stirred for an additional 3 h at −78 °C, it was warmed to rt. Under nitrogen, the precipitated solid was filtered off and the filtrate was treated with ethanolamine (2.2 mL, 2.22 g, 36.6 mmol) at 0 °C. Subsequently, the mixture was warmed to rt and stirred for another 5 h. The solvent was removed and the residue was purified by distillation to give (*S*)-**12a** (1.12 g, 42%) as a colorless liquid; bp 68–70 °C/110 mbar; $\delta_H$ (500 MHz, $CDCl_3$) 1.51 (s, 3H, $CH_3$), 2.13 (s, 1H, OH), 2.36 (dddd, *J*=13.5, 8.1, 1.0, 1.0 Hz, 1H, H-4$_a$), 2.46 (s, 1H, H-1), 2.52 (dddd, *J*=13.5, 6.5, 1.0, 1.0 Hz, 1H, H-4$_b$), 5.18–5.25 (m, 2H, H-6), 5.98 (dddd, *J*=16.9, 10.2, 8.1, 6.5 Hz, 1H, H-5); $\delta_C$ (125 MHz, $CDCl_3$) 29.2 ($CH_3$), 48.0 (C-4), 66.8 (C-3), 71.5 (C-1), 87.2 (C-2), 119.9 (C-6), 133.0 (C-5).

*4.3.26. (S)-tert-Butyldimethyl(3-methylhex-5-en-1-yn-3-yloxy)-silane [(S)-**12b**].* Alcohol **12a** (280 mg, 2.53 mmol) was converted into the corresponding TBS-ether following the procedure reported for **2c**. The crude product was purified by column chromatography (silica gel, pentane) to give **12b** (540 mg, 95%) as a colorless oil; $R_f$ (pentane) 0.86; $[\alpha]_D^{20}$ −4.4 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3311 (m), 3080 (w), 2930 (s), 2194 (w), 1252 (s), 1067 (s), 832 (vs), 774 (vs) $cm^{-1}$; $\delta_H$ (300 MHz, $CDCl_3$) 0.17 (s, 6H, Si–$CH_3$), 0.87 (s, 9H, C–(C$H_3$)$_3$), 1.42 (s, 3H, $CH_3$), 2.38–2.41 (m, 2H, H-4), 2.43 (s, 1H, H-1), 5.05–5.12 (m, 2H, H-6), 5.87 (dddd, *J*=12.9, 11.0, 7.2, 3.8 Hz, 1H, H-5); $\delta_C$ (75 MHz, $CDCl_3$) −2.9 (Si–$CH_3$), −2.9 (Si–$CH_3$), 18.1 (Si–*C*(CH$_3$)$_3$), 25.7 (Si–C(*C*H$_3$)$_3$), 30.5 ($CH_3$), 49.6 (C-4), 68.5 (C-3), 72.2 (C-1), 88.0 (C-2), 117.8 (C-6), 134.0 (C-5); *m*/*z* (CI, $CH_4$) 225 (45, $MH^+$), 209 (30), 183 (80), 167 (100), 132 (25), 93 (30%); HRMS (CI, $CH_4$): $MH^+$, found 225.1659. $C_{13}H_{25}OSi^+$ requires 225.1675; GC: *HRGC Mega 2*, Bondex un-α-CD column (20 m, 0.4 bar $H_2$, on column), temperature program: 40 °C, 3 min isothermal, then 1.5 °C $min^{-1}$ gradient to 90 °C, then 10 °C $min^{-1}$ gradient to 200 °C, $t_{R,minor}$=21.727 min and $t_{R,major}$=22.127 min; ee 80%.

*4.3.27. (2R,4S)- and (2S,4S)-4-(tert-Butyldimethylsilyloxy)-4-methylhex-5-yne-1,2-diol [(2R,4S)-**13**] and [(2S,4S)-**13**].* Following method C, olefin **12b** (0.50 g, 2.22 mmol) was dihydroxylated using AD-mix-β (3.15 g). The crude product was purified by column chromatography (silica gel, hexane/EtOAc 5:2) to give **13** (0.5 g, 88%, dr 40:60 ($^1$H NMR)) as a colorless oil. Compound (2*R*,4*S*)-**13**: Found: C, 60.1; H, 10.0. $C_{13}H_{26}O_3Si$ requires C, 60.4; H, 10.1%; $R_f$ (hexane/EtOAc 5:2) 0.29; $[\alpha]_D^{20}$ −1.8 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3391 (m), 3309 (m), 2930 (s), 2858 (s), 2109 (w), 1740 (w), 1251 (s), 1028 (s), 833 (vs), 775 (vs) $cm^{-1}$; $\delta_H$ (300 MHz, $CDCl_3$) 0.23 (s, 3H, Si–$CH_3$), 0.24 (s, 3H, Si–$CH_3$), 0.87 (s, 9H, C(CH$_3$)$_3$), 1.54 (s, 3H, $CH_3$), 1.68 (dd, *J*=14.4, 1.9 Hz, 1H, H-3$_a$), 1.90 (dd, *J*=14.4, 9.7 Hz, 1H, H-3$_b$), 2.39 (s, 1H, OH), 2.53 (s, 1H, H-6), 3.45–3.52 (m, 1H, H-1$_a$), 3.60–3.68 (m, 1H, H-1$_b$), 3.84 (s, 1H, OH), 4.25 (dddd, *J*=9.7, 5.6, 3.7, 1.9 Hz, 1H, H-2); $\delta_C$ (75 MHz, $CDCl_3$) −3.2 (Si–$CH_3$), −2.7 (Si–$CH_3$), 17.9 (Si–*C*(CH$_3$)$_3$), 25.6 (Si–C(*C*H$_3$)$_3$), 31.8 ($CH_3$), 47.1 (C-3), 66.7 (C-1), 70.2 (C-2), 70.7 (C-4), 73.6 (C-6), 86.4 (C-5); *m*/*z* (CI, $CH_4$) 259 (100, $MH^+$), 243 (10), 183 (30), 143 (15), 117 (50%); GC: *HRGC Mega* 2, Bondex un-β-CD column (20 m, 0.4 bar $H_2$, split), 100 °C isothermal, $t_{R,minor}$=42.692 min and $t_{R,major}$=44.103 min; ee 96%. Compound (2*S*,4*S*)-**13**: $R_f$ (hexane/EtOAc 5:2) 0.21; $[\alpha]_D^{20}$ −9.3 (*c* 1.0, $CH_2Cl_2$); $\nu_{max}$ (neat) 3391 (br m), 3309 (m), 2930 (s), 2858 (s), 2109 (w), 1740 (w), 1251 (s), 1028 (s), 833 (vs), 775

(vs) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 0.21 (s, 3H, Si–$CH_3$), 0.21 (s, 3H, Si–$CH_3$), 0.85 (s, 9H, C($CH_3$)$_3$), 1.23 (s, 1H, OH), 1.54 (s, 3H, $CH_3$), 1.72 (dd, $J$=14.4, 2.6 Hz, 1H, H-3$_a$), 1.97 (dd, $J$=14.4, 9.3 Hz, 1H, H-3$_b$), 2.55 (s, 1H, H-6), 3.45–3.48 (m, 1H, H-1$_a$), 3.58–3.61 (m, 1H, H-1$_b$), 3.64 (s, 1H, OH), 4.08–4.11 (m, 1H, H-2); $\delta_C$ (125 MHz, $CDCl_3$) −3.2 (Si–$CH_3$), −2.8 (Si–$CH_3$), 17.9 (Si–*C*($CH_3$)$_3$), 25.7 (Si–C($CH_3$)$_3$), 30.3 ($CH_3$), 47.2 (C-3), 66.8 (C-1), 68.7 (C-4), 69.1 (C-2), 73.4 (C-6), 87.8 (C-5); $m/z$ (CI, $CH_4$) 259 (100, $MH^+$), 243 (10), 183 (30), 143 (15), 117 (50%); GC: *HRGC Mega 2*, Bondex un-β-CD column (20 m, 0.4 bar $H_2$, split), temperature program: 70 °C, 3 min isothermal, then 1.5 °C $min^{-1}$ gradient to 200 °C, $t_{R,minor}$=40.307 min and $t_{R,major}$=40.740 min; ee 52%.

## Acknowledgements

Generous financial support by the Deutsche Forschungsgemeinschaft, the Ministerium für Wissenschaft, Forschung und Kunst des Landes Baden-Württemberg and the Fonds der Chemischen Industrie is gratefully acknowledged. We would like to thank Dennis Wan Hussin, Katharina Lindermayr and Jakob Belka for skilfull experimental work. The authors are indebted to B.R.A.I.N. AG, Zwingenberg, Germany, for providing the metagenome-derived esterases. R.K. and G.S.N. thank the European Social Funds and the VentureCup M-V (UG09005) for financial support. G.S.N. also thanks the Deutscher Akademischer Austauschdienst (DAAD) (Grant A/07/95194), the Vietnamese Ministry of Education and Training (Grant 3413/QDBGDDT-VP) for financial support.

## Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.03.048.

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43. In order to allow convenient comparison of the NMR data of the triols **3** with those of the PMP-acetals **9**, the numbering scheme indicated in Scheme 7 (and used throughout the text and experimental part) is different from the IUPAC nomenclature. The correct IUPAC numbering and -naming of **9** is: 2-(4-methoxyphenyl)-6-methyl-6-phenyl-1,3-dioxan-4-yl)methanol.
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