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# Stereoselective $VO(acac)_2$ catalyzed epoxidation of acyclic homoallylic diols. Complementary preparation of C2-*syn*-3,4-epoxy alcohols

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ABSTRACT

A substrate-controlled stereoselective epoxidation of free and monoprotected homoallylic diols was developed. This second-generation approach is based on the incorporation of a primary hydroxy directing group at the C2 methyl carbon, which changes the nature of the vanadium ester intermediate providing a new diastereoselectivity manifold for the preparation of 3,4-epoxy alcohols. This modification favored the formation of the challenging C2-*syn* epoxy alcohol product not previously available using the standard homoallylic alcohol substrates. These new epoxy alcohol diastereomers expand the scope and generality for the utilization of 3,4-epoxy alcohols as precursors for stereoselective polypropionate synthesis.



## 1. Introduction

The 3,4-epoxy alcohol moiety is a useful synthetic precursor that has been extensively used for the preparation of 1,3 diols,[1] oxetanes,[2] furans,[3] and polypropionate fragments[4] (Fig. 1). This functionality is usually prepared from the epoxidation of acyclic homoallylic alcohols using transition metal catalyzed oxidations,[5] iodocarbonation methodologies[6] or peroxy acid conditions.[7] These substrate-controlled approaches have shown good to excellent *syn*/*anti* diastereoselectivities, depending on the cis/trans double bond geometry, the directing influence of the C1 hydroxy and the stereochemical disposition of the C2 methyl group.

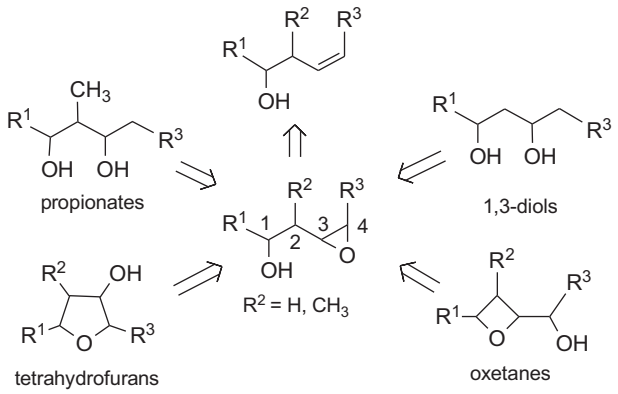
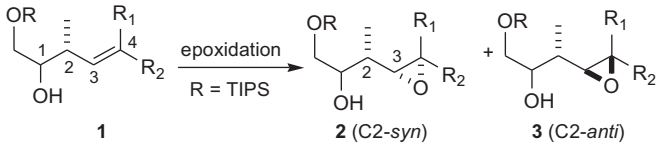



**Fig. 1.** Preparation and common transformations of 3,4-epoxy alcohols.

In contrast to the epoxidation of allylic alcohols, the enantioselective epoxidation of acyclic homoallylic alcohols to produce chiral 3,4-epoxy alcohols has been more difficult. Methods employing metal catalysts[8] and organocatalysis[9] have been explored. Despite the advances in this field, there are no truly general methods for the efficient enantioselective epoxidation of homoallylic alcohols. Moreover, homoallylic alcohols that contain chiral centers are susceptible to kinetic resolution, as found for the vanadium-catalyzed asymmetric epoxidation conditions.[8a,b] This feature, which has been used as an advantage, entails the inherent limitation of a 50% maximum product yield. Therefore, substrate-controlled methodologies for the stereoselective epoxidation of homoallylic alcohols continue to be a practical approach for the preparation of chiral 3,4-epoxy alcohols (Scheme 1).[10]




**Scheme 1.** Substrate-controlled C2-*syn*/*anti* selectivity in the epoxidation of 2-methyl homoallylic alcohols.

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The vanadium-catalyzed epoxidation reaction ($VO(acac)_2$/*tert*-butyl hydroperoxide) has become a very popular procedure for the stereoselective epoxidation of acyclic homoallylic alcohols.[5] This reaction works well for *cis* and terminal homoallylic alcohols, favoring the C2-*anti* epoxide **3** (1,2-relative asymmetric induction), whereas poor stereoselectivities are observed with *trans* alkenols. The improved diastereoselectivity obtained for *cis* homoallylic alcohols is rationalized by the vanadium 'chair-like' cyclic transition state model proposed by Mihelich that minimizes the *syn*-pentane repulsion between the C2 and allylic methyl groups. The poor selectivity observed for the trans systems is due to the formation of a competing boat-like transition state.[5,11]

Different from the C2-*anti* pathway, the stereoselective C2-*syn* epoxidation of *cis*- or *trans*-2-methyl-1-homoallylic alcohols has been more challenging and fewer practical methods have been reported. Yamagushi and co-workers obtained 1,2-*syn*-selectivity for *cis* homoallylic alkenols after protecting the secondary alcohol with a bulky non-coordinating TIPS group using a tungsten-based epoxidizing complex.[5c] Guanti and co-workers reported the C2-*syn* epoxidation of chemoenzymatically generated chiral *cis* homoallylic diols using *m*-CPBA or $VO(acac)_2$/TBHP.[5b,11b] Since both hydroxy groups were primary, the application of a 3–4 steps protecting group manipulation protocol was required prior to the epoxidation reaction. In both studies, *trans* alkenols showed to be poor substrates. To circumvent this limitation, Sato and collaborators introduced a removable TMS group at the C3 epoxide carbon to generate a trisubstituted *Z*-alkene substrate. This modification provided high 1,2-*syn* selectivity in the $VO(acac)_2$/TBHP epoxidation, that after the removal of the TMS group gave rise to the elusive *trans* epoxy alcohols.[4d]

Recently, in studies related to the development of an epoxide-based methodology for polypropionate synthesis, we applied the $VO(acac)_2$ catalyzed epoxidation reaction to a series of hindered *cis*- and *trans*-2-methyl-3-alkenols using a microwave assisted procedure (MW).[5a] In this study the reaction time for the epoxidation was dramatically reduced compared to the use of conventional heating (CH). Similar to the standard conditions, under MW irradiation, the *cis* homoallylic alkenols provided excellent C2-*anti* selectivities, while the trans systems showed a small C2-*syn* preference. This approach provided a series of diastereomeric 2-methyl-3,4-epoxy alcohols, where the C2-*anti*,*cis*-epoxides **3a**-*anti* and **3c**-*anti* were obtained as the only diastereomer, while both *trans* homoallylic alcohols produced the C2-*syn* epoxide **2d**-*syn* and C2-*anti* epoxide **3b**-*anti* with moderate diastereoselectivity (Fig. 2). 2-Methyl-3,4-epoxy alcohols are useful precursors for polypropionate synthesis as their regioselective cleavage produces configurationally defined

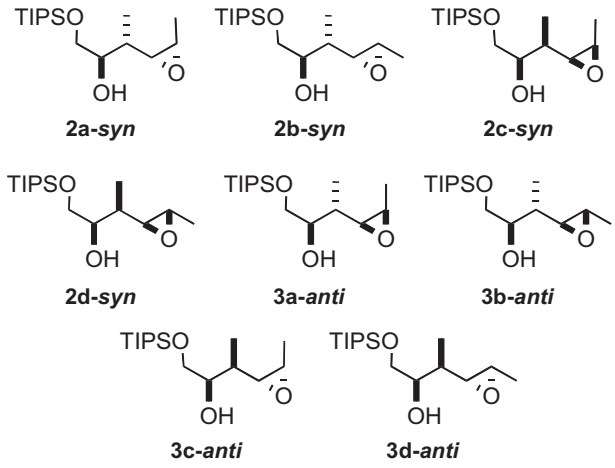


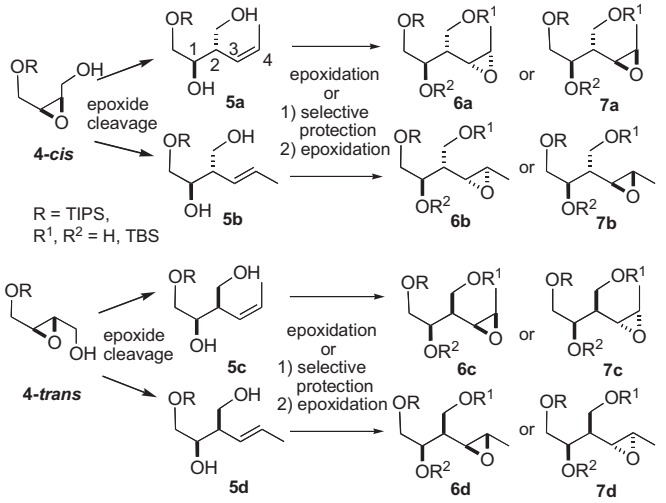

**Fig. 2.** All possible diastereomeric C2-*syn* and C2-*anti* 2-methyl-3,4-epoxy alcohols.

stereotetrads.[4c,6a,12] In fact, this methodology was successfully used in the synthesis of the *all-anti* C5–C10 fragment of streptovaricin U, starting from **3a**-*anti*.[4a] Unfortunately, this approach is not suitable for the stereoselective preparation of the complementary C2-*syn* epoxides **2a**–**c**-*syn* and the *anti* epoxide **3d**-*anti*.

Herein, we present a second-generation approach for the diastereoselective preparation of *syn*-3,4-epoxy diols. This approach consists on the introduction of a primary hydroxy group at the 2-methyl carbon, providing a competing directing effect relative to the standard secondary C1 hydroxy group. Consequently, the diastereoselectivity of the vanadium-catalyzed epoxidation reaction is modified to achieve C2-*syn* diastereoselectivities, not previously attainable with the standard homoallylic alcohols.

## 2. Results and discussion

The approach for the preparation of the second-generation C2-*syn*-3,4-epoxy diols **6a**–**d** and their C2-*anti* counterparts **7a**–**d** involved a sequence similar to that used for the preparation of epoxy alcohols **2** and **3**,[5a] except for the use of epoxides **4**-*cis* and **4**-*trans* as staring materials (Scheme 2). Having an additional directing hydroxy group at the C2 methyl group adds flexibility to the vanadium-catalyzed epoxidation reaction. This primary hydroxy group is also homoallylic but chemically differentiable from the sterically hindered secondary alcohol at the C1 position. It was expected that the primary hydroxy group in alkene diols **5a**–**d** should preferentially form the vanadate ester epoxidizing intermediate, instead of the secondary C1 hydroxy, thus altering the normal diastereoselectivity of the epoxidation reaction. This concept could be further expanded by the selective protection of the primary or secondary alcohols in **5a**–**d**.



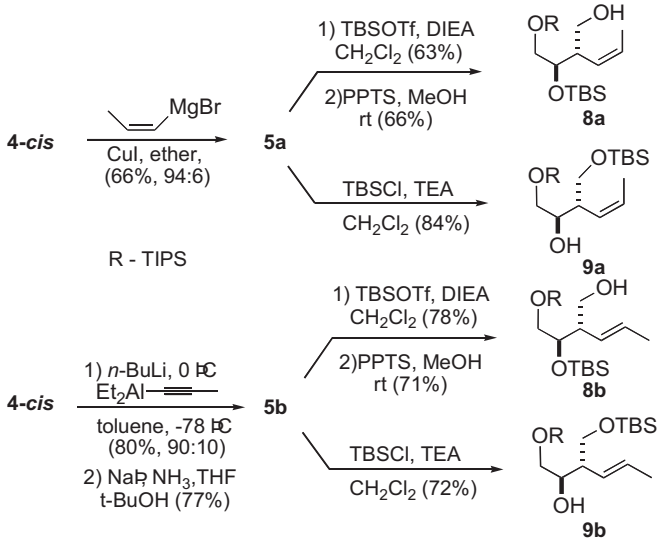

**Scheme 2.** Second-generation epoxy diol-based approach for *syn*- and *anti*-3,4-epoxy alcohols.

Protection of the C1 secondary alcohol would further enhance the diastereoselectivity provided by the primary alcohol. Conversely, selective protection of the primary alcohol should improve the natural diastereoselectivity of the secondary C1 alcohol by introducing additional steric factors. These modifications should provide access to complementary diastereoselectivities to yield C2-*syn* **6a**–**d** or C2-*anti* **7a**–**d** epoxides, some of which have not been stereoselectively available by earlier methodologies.

The starting epoxy alcohol **4**-*cis* was prepared from the TIPS monoprotection of commercially available *cis*-buten-1,4-diol, followed by epoxidation of the resulting allylic alcohol with *m*-CPBA. Similarly, **4**-*trans* was prepared from commercially available 2-

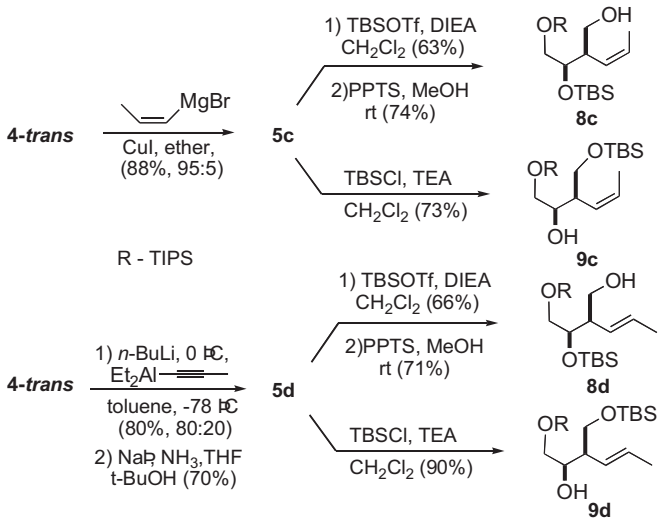
butynyl-1,4-diol via its monoprotection, reduction with Red-Al and *m*-CPBA epoxidation. Epoxides **4**-*cis* and **4**-*trans* were also enantioselectively prepared using the Sharpless asymmetric epoxidation. Epoxide **4**-*cis* and **4**-*trans* were obtained in 81% (76% ee) and 73% (94% ee), respectively.

The *anti*,*cis* diol **5a** was obtained in 66% yield from the regioselective cleavage of epoxy alcohol **4**-*cis* using a copper-catalyzed *cis*-propenyl Grignard reaction, previously developed by our group.[12] The corresponding *anti*,*trans* homoallylic diol **5b** was prepared in 77% yield by the regioselective epoxide ring opening of **4**-*cis* using the diethylpropynylalanate conditions developed by Miyashita[13] followed by the sodium/ammonia reduction of the resulting alkynol (Scheme 3). The synthesis of the free primary homoallylic alcohols **8a** and **8b** was achieved by the diprotection of **5a** and **5b** as the TBS ethers, followed by selective deprotection of the primary TBS group. The selective TBS protection of the primary hydroxyl group in **5a** and **5b** produced **9a** and **9b**, correspondingly.




**Scheme 3.** Synthesis of alkenols **5a**,**b**, **8a**,**b**, and **9a**,**b**.

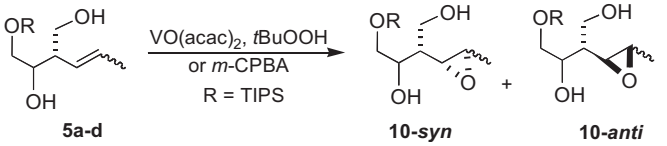
The application of the copper-catalyzed Grignard conditions on **4**-*trans* produced the *syn*,*cis* homoallylic alcohol **5c** in 88% yield. Propynyl alane cleavage of **4**-*trans*, followed by trans reduction produced the *syn*,*trans* homoallylic alcohol **5d** in 70% yield (Scheme 4). The TBS diprotection–deprotection sequence on **5c** and **5d** produced the free primary homoallylic alcohols **8c** and **8d** in 73% and 90% yield, respectively. The selective TBS protection of the primary alcohol in **5c** and **5d** produced alkenols **9c** and **9d** in 74% and 66% yield, correspondingly.




**Scheme 4.** Synthesis of alkenols **5c**,**d**, **8c**,**d**, and **9c**,**d**.

Having the *cis*- and *trans*-homoallylic bis-diols **5a**–**d** on hand, a study on their epoxidation was undertaken. Although it is known that *trans* alkenols do not provide good diastereoselectivity for this reaction, being the *trans* diols **5b** and **5d** atypical substrates, they were also included in the study. To assess the best conditions in terms of reaction time, yield and diastereoselectivity, diols **5a**–**d** were submitted to the $VO(acac)_2$ catalyzed epoxidation reaction at rt, with conventional heating (CH) and the microwave (MW) assisted conditions. While it was expected that the reaction would proceed faster with heating, we were also interested in exploring differences in diastereoselectivity under the rt conditions. In general, the diastereoselectivities were not affected by the conditions, even though the reaction at rt required longer reaction times (36 h–7 days) and produced lower yields. Under the CH and MW conditions, the reaction time was significantly reduced to less than 30 min in most cases. The MW assisted conditions gave the shortest reaction completion times, thus these were the conditions of choice. The epoxidation of the *anti*,*cis*-alkene diol **5a** gave moderate diastereoselectivity favoring the C2-*syn* epoxide **10a**-*syn* (Table 1, entry 1). Epoxidation of the *syn*,*cis*-diol **5c** provided the *syn*,*syn*,*cis*-epoxide **10c**-*syn* with the best C2-*syn* selectivity (84:16), although in a disappointingly low yield (entry 3). Whereas, the *anti*,*trans*-alkene diol **5b** showed no selectivity (entry 5), the *syn*,*trans*-diol **5d** showed a moderate 65:35C2-*syn* selectivity favoring epoxide **10d**-*syn* in 10 min (entry 7). This result is comparable to the first generation-methodology, which provided the structurally related epoxy alcohols **2d**-*syn* in 3 h with a similar stereoselectivity. Even

**Table 1**
Diastereoselectivity of the epoxidation of homoallylic 1,3-diols **5a**–**d**




| Entry | Alkenol | Conditions[a] | C2-*syn* product R=TIPS | C2-*syn*/*anti* selectivity[b] | Yield (%) |
|---|---|---|---|---|---|
| 1 | **5a** | $VO(acac)_2$ | **10a-*syn*** | 59:41 | 65 |
| 2 | **5a** | *m*-CPBA | | 30:70 | 88[c] |
| 3 | **5c** | $VO(acac)_2$ | **10c-*syn*** | 84:16 | 25 |
| 4 | **5c** | *m*-CPBA | | 34:66 | 100[c] |
| 5 | **5b** | $VO(acac)_2$ | **10b-*syn*** | 52:48 | 60[d] |
| 6 | **5b** | *m*-CPBA | | 63:37 | 88 |
| 7 | **5d** | $VO(acac)_2$ | **10d-*syn*** | 65:35 | 68 |

[a] $VO(acac)_2$ (1.4 mol %) in a 0.08 M alkenol soln in toluene under MW or *m*-CPBA, $NaHCO_3$ in DCM at rt.
[b] Determined by $^1H$ NMR spectroscopy.
[c] Crude yield.
[d] Furan product (14%) was also obtained.

though the $VO(acac)_2$ catalyzed epoxidation of the free diols **5a**–**d** provided variable diastereoselectivities, it is remarkable that the C2-*syn* selectivity was favored in all cases, regardless of the alkene geometry or the relative configuration of the C1 and C2 carbons. In these exploratory studies, epoxides **10a**-*syn*, **10c**-*syn*, and **10d**-*syn* were obtained as the mayor products. These 3,4-epoxy alcohols cannot be prepared diastereoselectively by the standard first-generation homoallylic alcohol substrates.

Having prepared the free epoxy diols **5a**–**d**, it gave us the opportunity to also explore the reaction of these second-generation homoallylic alkene diol with *m*-CPBA. Although this epoxidation reagent usually gives poor to moderate *anti* diastereoselectivities on aliphatic epoxy alcohols, it has shown excellent C2-*anti* selectivity in some sterically hindered systems.[5b,7d,e,11] Thus, the epoxidation of **5a** and **5c** with *m*-CPBA provided an approximately 2:1C2-*anti*:C2-*syn* selectivity (entries 2 and 4). Interestingly, a 63:37C2-*syn* selectivity was observed for epoxy alcohol **5b** (entry 6).

To gain insight into the discrimination of the vanadium catalyst between the primary and secondary homoallylic alcohols in the relatively hindered diols **5a**–**d**, we performed a semi-empirical calculation on the exchange reaction between the epoxy alcohols and the vanadium catalyst (Table 2).[14] The formation of a vanadate ester is well precedented and represents the first step in the mechanism of the vanadium epoxidation proposed by Sharpless.[15] For the four systems, the vanadium complex formed from the primary homoallylic alcohol is energetically favored over the secondary hydroxy, ranging from 4.5 kcal/mol for system **5c** to 20.8 kcal/mol in **5b**. These energy differences confirm that the initial vanadate ester complex is formed with the primary alcohol, discarding competition from the secondary alcohols. These results imply that the free primary alcohol solely controls the diastereoselectivity of the epoxidation reaction producing the inverted C2-*syn* selectivity.

**Table 2**
Differences in calculated $\Delta H_f$ between the primary and secondary vanadium ester complexes

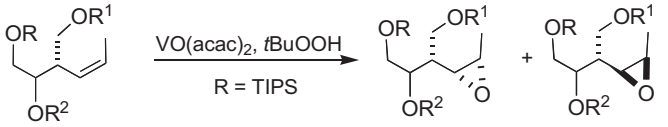
| Entry | Alkene diol | $\Delta E$ (kcal/mol)[a,b] |
|---|---|---|
| 1 | **5a** | 11.0 |
| 2 | **5b** | 20.8 |
| 3 | **5c** | 4.5 |
| 4 | **5d** | 12.6 |

[a] Semi-empirical PM3 method (Ref. 14).
[b] The primary vanadate ester was more stable in all cases.

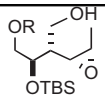
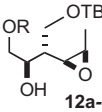
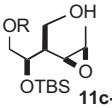
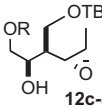
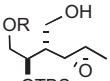
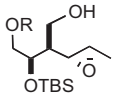
After exploring the reactivity and diastereoselectivity of the $VO(acac)_2$ catalyzed epoxidation of the unprotected homoallylic alkene diols and establishing a bias toward the elusive C2-*syn* selectivity, we turned to the TBS monoprotected homoallylic alcohol derivatives employing the MW conditions (Table 3). The monoprotected alkenols **8a**–**d**, which have a free primary alcohol, were subjected to the $VO(acac)_2$ catalyzed epoxidation conditions. These systems showed somewhat shorter reaction times and overall better yields than the free diols **5**. This time, the *cis* homoallylic alkenols showed excellent diastereoselectivities. Thus, *cis* alkenols **8a** and **8c** exclusively produced epoxides **11a**-*syn* and **11c**-*syn* (entries 1 and 3). Interestingly, the epoxidation of *trans* alkenol **8b** favored epoxide **11b**-*syn* in a much better 70:30 *syn*/*anti* ratio and 90% yield (entry 5), when compared to the free alkene diol **5b** (Table 1, entry 5). Epoxides **11a**-*syn*, **11b**-*syn*, and **11c**-*syn* correspond to the C2-*syn* diastereoisomers not accessible by the first-generation $VO(acac)_2$ catalyzed epoxidations. As an exception, and different from the free diol precursor **5d**, the *trans* alkenol **8d** showed a lack of diastereoselectivity (entry 7). This is the only free primary alcohol system that does not favor the C2-*syn* selectivity.

Because the *trans* alkene diol **5b** showed a 63:37 preference for the C2-*syn* epoxide product under the *m*-CPBA conditions (Table 1, entry 6), we subjected its monoprotected derivative **8b** to the same procedure. Gratifyingly, a 90:10 diastereoselectivity was obtained favoring **11b**-*syn*, in a 68% yield (entry 6). This is a significant outcome as we have efficiently generated a C2-*syn* epoxide product starting from a *trans* alkenol using the *m*-CPBA conditions that typically favor the *anti* products. Compound **11b**-*syn* has the required C1–C4 and C12–C15 configuration of the lankanolide polypropionate chain.[16]

**Table 3**
Stereoselectivity of epoxidation of monoprotected homoallylic 1,3-diols **8** and **9**




**8a,c** $R^1$ = H, $R^2$ = TBS
**9a,c** $R^1$ = TBS, $R^2$ = H
**11-*syn*** **12-*syn***
**11-*anti*** **12-*anti***

| Entry | Alkenol[a] | Major product R=TIPS | C2-*syn*/*anti* selectivity[b] | Yield[c] (%) |
|---|---|---|---|---|
| 1 | **8a** |  **11a-*syn*** | >95:5[d] | 55[e] |
| 2 | **9a** |  **12a-*anti*** | <5:95[d] | 80 |
| 3 | **8c** |  **11c-*syn*** | >95:5[d] | 72[f] |
| 4 | **9c** |  **12c-*anti*** | 17:83 | 57 |
| 5 | **8b** |  | 70:30 | 90 |
| 6 | **8b**[g] | **11b-*syn*** | 90:10 | 68[h] |
| 7 | **8d** |  **11d-*anti*** | 58:42 | 89 |

[a] $VO(acac)_2$ (1.4 mol %) in a 0.08 M alkenol soln in toluene under MW (except for entry 6).
[b] Determined by $^1H$ NMR spectroscopy.
[c] % Isolated product.
[d] Only one isomer was observed by NMR analysis.
[e] Oxetane product (13%) was obtained.
[f] CH heating, 27% of an oxetane product was obtained.
[g] *m*-CPBA, $NaHCO_3$ in DCM at rt.
[h] Oxetane product (6%) was obtained.

Homoallylic alkenols **9a**–**d**, which have a free secondary alcohol at C1, analogous to our first-generation alkenol substrates **1**,[5a] were also studied. As expected, these secondary alcohols exhibited diastereoselectivities very similar to those previously obtained for the first-generation alkenols **1**. The epoxidation of the *cis* homoallylic alcohols **9a** and **9c** produced the expected C2-*anti* epoxides **12a**-

*anti* and **12c**-*anti* (entries 2 and 4) with excellent and good diastereoselectivities (>95:5 and 81:17), respectively. The *trans* alkenols **9b** and **9d** provided the C2-*anti* epoxides **12b**-*anti* and **12d**-*anti* in an approximately 2:1 ratio, similar to the epoxides **3b**-*anti* and **3d**-*anti* (see Supplementary data). These monoprotected homoallylic alkene diols do not present an advantage for the vanadium-catalyzed epoxidation reaction when compared to the first-generation alkenols **1**.

The *syn*/*anti* stereoselectivity of the epoxy alcohols products was established by $^{13}C$ NMR following the tendencies found on the previously reported characterization data for the first-generation epoxides **2** and **3**, using the diagnostic C3 and C4 epoxide carbons.[5a] For the *trans*-2-alkoxymethyl-3,4-epoxy alcohols, when an *anti* 2-alkoxymethyl-3,4-epoxy relationship is present (C2-*anti*), the epoxide C3 and C4 carbons show signals near 59 and 53 ppm (Δ ~5.0 ppm), while a C2-*syn* relationship displays slightly higher chemical shifts near 59 and 55 ppm (Δ ~3.4 ppm). For the *cis* epoxides, a C2-*syn*, relationship showed signals around 56 ppm and 53 ppm (Δ ~3.0 ppm), while the epoxides with an *anti* relationship show signals near 56 ppm and 52 ppm (Δ ~3.5 ppm). While these differences seem to be small, they show consistency for the studied diastereomeric series.

In addition to providing access to new 3,4-epoxy alcohol diastereomers, the new primary hydroxy offers a new dimension in terms of potential usefulness and flexibility, as it can be used for further synthetic manipulations or even become part of the target molecule. For example, the hydroxy group can control the regioselectivity of the epoxide cleavage by assisting the entering organometallic nucleophile.[12] The hydroxy group can also become part of the target molecule. For example, the streptovaricin D ansa chain has a functionalized methyl group at C10[17] and scytophycin E has a hydroxymethyl group at C26.[18] Finally, if the hydroxy group is not further required after exploiting its function, as in the lankanolide polypropionate chain,[16] it can be removed at any step by tosylation-hydride reduction.[4c] These targets are part of our current synthetic interests.

## 3. Conclusion

The $VO(acac)_2$ catalyzed epoxidation of free and monoprotected homoallylic 1,3-diols was conducted in order to determine the C2-*syn*/C2-*anti* diastereoselectivity. This second-generation approach provided preparative access to the 3,4-epoxy alcohol **10a**-*syn*, **10b**-*syn*, **10c**-*syn* **11a**-*syn*, **11b**-*syn*, **11c**-*syn* in moderate to excellent diastereoselectivities from *cis* and *trans* alkene diols. The *trans* epoxide **11b**-*syn* was also obtained with high diastereoselectivity using *m*-CPBA. These epoxy alcohol configurations were previously unattainable by standard homoallylic alcohol epoxidation procedures, opening the door for the elaboration of new target molecules, not accessible by the first-generation approach. This expansion converts our epoxide-based approach into a general preparative method for polypropionate synthesis regardless of the stereochemical requirements.

## 4. Experimental

### 4.1. General experimental details

All reactions were carried out under nitrogen. All solvents were dried and purified in an automated solvent purification system before use. All commercially available compounds were used as received. All reactions under MW irradiation were performed in a laboratory microwave system (115 °C, 150W max) equipped with an IR sensor. Compound **5c** was prepared by a published procedure.[1] Unless otherwise noted, all products were purified by silica gel column chromatography and fully characterized by 1D and 2D (standard COSY and HMQC) NMR. $^1H$ NMR (300 or 500 MHz) and $^{13}C$ NMR (75 or 125 MHz) spectra were obtained as solutions in deuterochloroform. NMR chemical shifts ($\delta$) are given in parts per million relative to TMS and coupling constants ($J$) in hertz. Elemental analyses were done by a commercial analytical laboratory.

### 4.2. General procedure for the $VO(acac)_2$ catalyzed epoxidation reaction

$VO(acac)_2$ (0.014 equiv) was added to a reaction flask followed by toluene (≈0.08 M solution), the alkenol (0.24 mmol), and TBHP (1.1 equiv, 3.80 M in toluene). The reaction was carried out at rt, CH (reflux) or MW irradiation (113 °C, 150 W max). The reaction was followed by TLC. Saturated aqueous $Na_2S_2O_3$ was added and the mixture was extracted with hexane (3×). The combined organic phase was dried over anhyd $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (2:1 or 50:3 hexane/ethyl acetate).

*4.2.1. (±)-(2S*,3R*)-2-((2R*,3S*)-3-Methyloxiran-2-yl)-4-(triisopropylsilyloxy)butane-1,3-diol (**10a**-syn and **10a**-anti).* $^1H$ NMR $\delta$ 3.95 (m, $J$=12.0, 9.2 Hz, 1H), 3.94 (m, $J$=10.0, 7.6, 3.7 Hz, 1H), 3.90 (dd, $J$=12.0, 6.0 Hz, 1H), 3.78 (dd, $J$=9.5, 3.0 Hz, 1H), 3.71 (dd, $J$=9.5, 7.6 Hz, 1H), 3.21 (dd, $J$=9.6, 3.6 Hz, 1H), 3.16 (dq, $J$=4.6, 3.6 Hz, 1H), 2.77 (s, 1H), 2.41 (s, 1H), 1.66 (dddd, $J$=10.0, 9.6, 9.2, 6.0 Hz, 1H), 1.31 (d, $J$=5.4 Hz, 3H), 1.07 (m, 21H). $^{13}C$ NMR $\delta$ 72.2, 65.3, 63.4, 56.1, 53.2, 40.5, 17.9, 13.9, 11.8. Anal. Calcd for $C_{16}H_{34}O_4Si$: C, 60.33; H, 10.76. Found: C, 59.98; H, 10.80. Spectral data for the minor isomer (±)-(2S*,3R*)-2-((2S*,3R*)-3-*methyloxiran*-2-*yl*)-4-(*triisopropylsilyloxy*)*butane*-1,3-*diol* (**10a**-*anti*): $^1H$ NMR $\delta$ 4.12 (ddd, $J$=9.0, 4.5, 3.7 Hz, 1H), 3.93 (dd, $J$=10.3, 9.0 Hz, 1H), 3.87 (dd, $J$=11.4, 1.0 Hz, 1H), 3.81 (dd, $J$=11.4, 1.7 Hz, 1H), 3.78 (dd, $J$=10.3, 3.7 Hz, 1H), 3.21 (dd, $J$=9.1, 3.9 Hz, 1H), 3.11 (dq, $J$=5.4, 3.9 Hz, 1H), 3.02 (s, 1H), 2.86 (s, 1H), 1.55 (dddd, $J$=9.1, 4.5, 1.7, 1.0 Hz, 1H), 1.31 (d, $J$=5.4 Hz, 3H), 1.07 (m, 21H). $^{13}C$ NMR $\delta$ 74.2, 65.7, 62.7, 54.6, 51.9, 41.7, 17.9, 13.5, 11.9.

*4.2.2. (±)-(2S*,3R*)-2-((2R*,3R*)-3-Methyloxiran-2-yl)-4-(triisopropylsilyloxy)butane-1,3-diol (**10b**-syn and **10b**-anti).* $^1H$ NMR $\delta$ 3.97 (ddd, $J$=7.3, 5.0, 5.0 Hz, 1H), 3.85 (d, $J$=10.0 Hz, 2H), 3.78 (dd, $J$=10.0, 5.0 Hz, 1H), 3.73 (dd, $J$=10.0, 7.3 Hz, 1H), 2.98 (dd, $J$=7.4, 2.2 Hz, 1H), 2.93 (dq, $J$=5.2, 2.2 Hz, 1H), 1.58 (dddd, $J$=7.4, 6.5, 5.0, 2.5 Hz, 1H), 1.33 (d, $J$=5.2 Hz, 3H), 1.07 (m, 21H). $^{13}C$ NMR $\delta$ 72.4, 65.4, 62.6, 58.3, 54.7, 44.7, 17.9, 17.5, 11.8. Anal. Calcd for $C_{16}H_{34}O_4Si$: C, 60.33; H, 10.76. Found: C, 60.30; H, 10.74. Spectral data for the minor isomer (±)-(2S*,3R*)-2-((2S*,3S*)-3-*methyloxiran*-2-*yl*)-4-(*triisopropylsilyloxy*)*butane*-1,3-*diol* (**10a**-*anti*): $^1H$ NMR $\delta$ 3.97 (m 1H), 3.85 (m, 2H), 3.85 (m, 2H), 2.99 (dd, $J$=7.3, 2.2 Hz, 1H), 2.92 (m, 1H), 1.48 (m, 1H), 1.33 (d, $J$=5.2 Hz, 3H), 1.08 (m, 21H). $^{13}C$ NMR $\delta$ 73.4, 65.7, 62.9, 57.9, 53.4, 45.6, 17.9, 17.5, 11.8. Anal. Calcd for $C_{16}H_{34}O_4Si$: C, 60.33; H, 10.76. Found: C, 60.13; H, 10.66.

*4.2.3. (±)-(2R*,3R*)-2-((2S*,3R*)-3-Methyloxiran-2-yl)-4-(triisopropylsilyloxy)butane-1,3-diol (**10c**-syn and **10c**-anti).* $^1H$ NMR $\delta$ 4.04 (dd, $J$=11.8, 3.5 Hz, 1H), 3.95 (dd, $J$=11.8, 5.0 Hz, 1H), 3.87 (ddd, $J$=8.7, 6.0, 4.1 Hz, 1H), 3.79 (dd, $J$=9.9, 4.1 Hz, 1H), 3.66 (dd, $J$=9.9, 8.7 Hz, 1H), 3.14 (dq, $J$=5.5, 4.0 Hz, 1H), 3.04 (dd, $J$=9.7, 4.0 Hz, 1H), 3.01 (d, $J$=3.22 Hz, 1H), 1.59 (dddd, $J$=9.7, 6.0, 5.0, 3.5 Hz, 1H), 1.30 (d, $J$=5.5 Hz, 3H), 1.07 (m, 21H). $^{13}C$ NMR $\delta$ 72.9, 65.8, 62.6, 53.1, 53.0, 40.6, 17.9, 13.7, 11.9. Spectral data for the minor isomer (±)-(2R*,3R*)-2-((2R*,3S*)-3-*methyloxiran*-2-*yl*)-4-(*triisopropylsilyloxy*)*butane*-1,3-*diol* (**10c**-*anti*): $^1H$ NMR $\delta$ 4.04 (ddd, $J$=8.8, 5.0, 4.0 Hz, 1H), 3.97 (dd, $J$=10.2, 4.0 Hz, 1H), 3.83 (dd, $J$=10.0, 4.0 Hz, 1H), 3.82 (dd, $J$=10.2, 3.0 Hz, 1H), 3.69 (dd, $J$=10.0, 8.8 Hz, 1H), 3.10 (d, $J$=3.6 Hz, 1H), 3.04 (dq, $J$=5.5, 4.0 Hz, 1H), 3.93 (dd, $J$=9.5, 4.0 Hz, 1H),

1.55 (dddd, *J*=9.5, 5.0, 4.0, 3.0 Hz, 1H), 1.32 (d, *J*=5.5 Hz, 3H), 1.07 (m, 21H). $^{13}$C NMR $\delta$ 74.6, 66.0, 62.4, 55.7, 52.3, 41.8, 17.9, 13.5, 11.9.

*4.2.4. (±)-(2R*,3R*)-2-((2S*,3S*)-3-Methyloxiran-2-yl)-4-(triisopropylsilyloxy)butane-1,3-diol (**10d**-syn and **10d**-anti).* $^1$H NMR $\delta$ 3.96 (dd, *J*=11.0, 3.7 Hz, 2H), 3.88 (ddd, *J*=7.8, 5.0, 4.0 Hz, 1H), 3.84 (dd, *J*=11.0, 6.0 Hz, 1H), 3.82 (dd, *J*=10.0, 4.0 Hz, 1H), 3.69 (dd, *J*=10.0, 7.8 Hz, 1H), 2.92 (dq, *J*=5.1, 2.0 Hz, 1H), 2.76 (dd, *J*=5.2, 2.0 Hz, 1H), 1.56 (dddd, *J*=6.0, 5.2, 5.0, 3.7 Hz, 1H), 1.32 (dd, *J*=5.1, 1.3 Hz, 3H), 1.08 (m, 21H). $^{13}$C NMR $\delta$ 72.2, 65.8, 62.0, 58.5, 54.3, 44.8, 17.9, 17.5, 11.8. Anal. Calcd for $C_{16}H_{34}O_4Si$: C, 60.33; H, 10.76. Spectral data for the minor isomer (±)-(2*R**,3*R**)-2-((2*R**,3*R**)-3-*methyloxiran*-2-yl)-4-(*triisopropylsilyloxy*)*butane*-1,3-*diol* (**10d**-*anti*): $^1$H NMR $\delta$ 3.95 (m, 2H), 3.88–3.80 (m, 3H), 2.92 (m, 1H), 2.75 (m, 1H), 1.45 (m, 1H), 1.29 (d, *J*=5.0 Hz, 3H), 1.08 (m, 21H). $^{13}$C NMR $\delta$ 73.6, 66.0, 62.1, 58.9, 53.8, 45.8, 17.9, 17.5, 11.8.

*4.2.5. (±)-(2R*,3R*)-2-((2R,3S)-3-Methyloxiran-2-yl)-3-(tert-butyldimethylsilyloxy)-4-(triisopropylsilyloxy)butan-1-ol (**11a**-syn).* $^1$H NMR $\delta$ 4.02 (ddd, *J*=10.6, 6.3, 3.4 Hz, 1H), 3.87 (ddd, *J*=8.5, 4.2, 4.0 Hz, 1H), 3.80 (ddd, *J*=10.0, 5.5, 4.2 Hz, 1H), 3.69 (dd, *J*=10.0, 4.2 Hz, 1H), 3.62 (dd, *J*=10.0, 8.6 Hz, 1H), 3.17 (dd, *J*=9.5, 4.3 Hz, 1H), 3.11 (dq, *J*=5.7, 4.3 Hz, 1H), 2.62 (dd, *J*=3.4, 4.2 Hz, 1H), 1.91 (dddd, *J*=9.5, 6.5, 5.5, 4.0 Hz, 1H), 1.34 (dd, *J*=5.4, 1.1 Hz, 3H), 1.07 (m, 21H) 0.9 (s, 9H), 0.09 (s, 6H). $^{13}$C NMR $\delta$ 72.9, 65.6, 63.8, 56.7, 53.0, 41.6, 25.8, 18.0, 14.0, 11.9, −4.9. Anal. Calcd for $C_{22}H_{48}O_4Si_2$: C, 61.05; H, 11.18. Found: C, 61.08; H, 11.34.

*4.2.6. (+)-(2R,3R)-2-((2R,3R)-3-Methyloxiran-2-yl)-3-(tert-butyldimethylsilyloxy)-4-(triisopropylsilyloxy)butan-1-ol (**11b**-syn).* $^1$H NMR $\delta$ 3.96 (dd, *J*=7.0, 6.2 Hz, 1H), 3.93 (ddd, *J*=8.7, 5.5, 5.0 Hz, 1H), 3.77 (dd, *J*=7.0, 3.6 Hz, 1H), 3.72 (dd, *J*=9.8, 5.0 Hz, 1H), 3.60 (dd, *J*=9.8, 8.7 Hz, 1H), 2.91 (dq, *J*=5.2, 2.1 Hz, 1H), 2.83 (dd, *J*=8.5, 2.1 Hz, 1H), 2.34 (q, *J*=3.8 Hz, 1H), 1.73 (dddd, *J*=8.5, 6.2, 5.5, 3.6 Hz, 1H), 1.32 (d, *J*=5.3 Hz, 3H), 1.05 (m, 21H), 0.89 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H). $^{13}$C NMR $\delta$ 72.4, 65.2, 63.3, 58.6, 54.3, 46.2, 25.9, 17.9, 17.5, 11.9, −4.3, −5.0. Anal. Calcd for $C_{22}H_{48}O_4Si_2$: C, 61.05; H, 11.18. Found: C, 61.27; H, 11.27. $[\alpha]_D^{20}$ +17.0, *c* 1.00, $CHCl_3$.

*4.2.7. (+)-(2R,3R)-2-((2R,3R)-3-Methyloxiran-2-yl)-3-(tert-butyldimethylsilyloxy)-4-(triisopropylsilyloxy)butan-1-ol (**11b**-anti).* $^1$H NMR $\delta$ 3.97 (m, 1H), 3.78 (m, 1H), 3.76 (m, 1H), 3.73 (dd, *J*=13.0, 6.2 Hz, 1H), 3.66 (dd, *J*=13.0, 7.2 Hz, 1H), 2.98 (dq, *J*=5.2, 2.3 Hz, 1H), 2.89 (dd, *J*=6.9, 2.4 Hz, 1H), 2.70 (q, *J*=4.21 Hz, 1H), 1.96 (m, 1H), 1.31 (d, *J*=5.2 Hz, 3H), 1.06 (m, 21H) 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). $^{13}$C NMR $\delta$ 73.2, 65.5, 61.4, 58.2, 53.0, 46.1, 25.8, 17.9, 17.6, 11.9, −4.3, −5.1. Anal. Calcd for $C_{22}H_{48}O_4Si_2$: C, 61.05; H, 11.18. Found: C, 60.77; H, 11.00.

*4.2.8. (±)-(2S*,3R*)-2-((2S*,3R*)-3-Methyloxiran-2-yl)-3-(tert-butyldimethylsilyloxy)-4-(triisopropylsilyloxy)butan-1-ol (**11c**-syn).* $^1$H NMR $\delta$ 4.09 (dd, *J*=10.3, 3.6 Hz, 1H), 3.92 (ddd, *J*=8.6, 5.4, 2.5 Hz, 1H), 3.89 (dd, *J*=10.3, 2.5 Hz, 1H), 3.73 (dd, *J*=9.9, 8.6 Hz, 1H), 3.69 (dd, *J*=9.9, 5.4 Hz, 1H), 3.29 (dd, *J*=9.7, 4.2 Hz, 1H), 3.14 (dq, *J*=5.5, 4.2 Hz, 1H), 2.90 (d, *J*=8.9 Hz, 1H), 1.78 (dddd, *J*=9.7, 3.6, 2.5, 2.5 Hz, 1H), 1.31 (d, *J*=5.4 Hz, 3H), 1.07 (m, 21H) 0.9 (s, 9H), 0.09 (s, 6H). $^{13}$C NMR $\delta$ 74.4, 64.6, 61.2, 56.9, 52.6, 40.0, 25.7, 18.0, 13.5, 11.8, −4.4 and −5.1. Anal. Calcd for $C_{22}H_{48}O_4Si_2$: C, 61.05; H, 11.18. Found: C, 60.97; H, 11.37.

*4.2.9. (±)-(2S*,3R*)-2-((2R*,3R*)-3-Methyloxiran-2-yl)-3-(tert-butyldimethylsilyloxy)-4-(triisopropylsilyloxy)butan-1-ol (**11d**-anti and **11d**-syn).* $^1$H NMR $\delta$ 3.98 (dd, *J*=11.4, 3.9 Hz, 1H), 3.95 (ddd, *J*=7.7, 6.8, 5.5 Hz, 1H), 3.83 (dd, *J*=11.4, 4.0 Hz, 1H), 3.72 (dd, *J*=11.7, 3.8 Hz, 1H), 3.70 (dd, *J*=11.7, 5.5 Hz, 1H), 3.0 (dd, *J*=5.0, 1.5 Hz, 1H), 2.86 (dq, *J*=5.0, 1.5 Hz, 1H), 1.59 (dddd, *J*=7.7, 5.0, 4.0, 3.9 Hz, 1H), 1.34 (d, *J*=5.0 Hz, 3H), 1.05 (m, 21H) 0.89 (s, 9H), 0.09 (s, 6H). $^{13}$C NMR $\delta$ 72.4, 64.8, 61.0, 59.4, 54.3, 45.5, 25.7, 17.9, 17.7, 11.9, 4.4, −5.1. Anal. Calcd for $C_{22}H_{48}O_4Si_2$: C, 61.05; H, 11.18. Found: C, 60.93; H, 11.03. Spectral data for the minor isomer (±)-(2*S**,3*R**)-2-((2*S**,3*S**)-3-*methyloxiran*-2-*yl*)-3-(*tert-butyldimethylsilyloxy*)-4-(*triisopropylsilyloxy*)*butan*-1-ol (**11d**-*anti*): $^1$H NMR $\delta$ 4.12 (ddd, *J*=6.0, 5.5, 2.0 Hz, 1H), 3.97 (dd, *J*=11.5, 2.0 Hz, 1H), 3.75 (m, *J*=11.7, 6.0 Hz, 1H), 3.73 (m, *J*=11.5, 3.5 Hz, 1H), 3.72 (m, *J*=11.7, 5.5 Hz, 1H), 3.17 (d, *J*=7.9 Hz, 1H), 2.97 (m, *J*=5.8, 2.0 Hz, 1H), 2.96 (m, *J*=6.0, 2.0 Hz, 1H), 1.68 (m, *J*=6.0, 3.5, 2.0, 2.0 Hz, 1H), 1.35 (dd, *J*=5.8, 1.0 Hz, 3H), 1.05 (m, 21H) 0.89 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H). $^{13}$C NMR $\delta$ 73.9, 64.9, 60.6, 59.2, 55.0, 43.9, 25.8, 17.9, 17.8, 11.9, −4.4, −5.1. Anal. Calcd for $C_{22}H_{48}O_4Si_2$: C, 61.05; H, 11.18. Found: C, 61.01; H, 11.24.

*4.2.10. (±)-(2R*,3S*,4S*,5R*)-4,5-Epoxy-3-(tert-butyldimethylsilyloxymethyl)-1-(triisopropylsilyloxy)-2-hexanol (**12a**-anti).* $^1$H NMR $\delta$ 4.07 (ddd, *J*=8.2, 3.9, 2.2 Hz, 1H), 3.91 (dd, *J*=10.5, 8.3 Hz, 1H), 3.83 (dd, *J*=10.0, 6.2 Hz, 1H), 3.80 (dd, *J*=10.5, 3.9 Hz), 3.76 (dd, *J*=10.0, 6.2 Hz, 1H), 3.11 (dd, *J*=9.5, 4.2 Hz, 1H), 3.07 (dq, *J*=5.7, 4.3 Hz, 1H, 1H), 2.91 (s, 1H), 1.65 (dddd, *J*=9.4, 6.2, 6.1, 2.1 Hz, 1H), 1.32 (dd, *J*=5.7, 1.7 Hz, 3H), 1.08 (m, 21H) 0.92 (s, 9H), 0.09 (s, 6H). $^{13}$C NMR $\delta$ 72.4, 65.8, 62.1, 55.2, 51.6, 41.7, 25.9, 17.9, 13.9, 11.9, −5.5. Anal. Calcd for $C_{22}H_{48}O_4Si_2$: C, 61.05; H, 11.18. Found: C, 61.33; H, 11.20.

*4.2.11. (±)-(2R*,3R*,4R*,5S*)-4,5-Epoxy-3-(tert-butyldimethylsilyloxymethyl)-1-(triisopropylsilyloxy)-2-hexanol (**12c**-anti and **12c**-syn).* $^1$H NMR $\delta$ 3.94 (ddd, *J*=8.8, 6.2, 4.0 Hz, 1H), 3.93 (dd, *J*=11.2, 4.0 Hz, 1H), 3.89 (dd, *J*=10.1, 5.6 Hz, 1H), 3.84 (dd, *J*=10.1, 4.0 Hz, 1H), 3.71 (dd, *J*=11.2, 8.8 Hz, 1H), 3.09 (dq, *J*=5.3, 4.5 Hz, 1H), 2.98 (dd, *J*=8.9, 4.4 Hz, 1H), 1.55 (dddd, *J*=8.9, 6.2, 5.6, 4.0 Hz, 1H), 1.29 (d, *J*=5.5 Hz, 3H), 1.07 (m, 21H) 0.89 (s, 9H), 0.07 (s, 6H). $^{13}$C NMR $\delta$ 71.9, 66.3, 61.5, 56.8, 52.6, 41.9, 25.9, 17.9, 13.9, 11.9, −5.5. Spectral data for the minor isomer (±)-(2*R**,3*R**,4*S**,5*R**)-4,5-*Epoxy*-3-(*tert-butyldimethylsilyloxymethyl*)-1-(*triisopropylsilyloxy*)-2-*hexanol* (**12c**-*syn*): $^1$H NMR $\delta$ 3.96–3.70 (m, 5H), 3.21 (dd, *J*=9.8, 4.1 Hz, 1H), 3.17 (dq, *J*=5.3, 4.9 Hz, 1H), 1.67 (m, 1H), 1.29 (d, *J*=5.5 Hz, 3H), 1.07 (m, 21H), 0.89 (s, 9H), 0.07 (s, 6H). $^{13}$C NMR $\delta$ 72.7, 65.8, 62.2, 55.7, 53.5, 39.9, 25.9, 17.9, 13.5, 11.9, −5.5.

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## Supplementary data

Experimental details with spectroscopic data and copies of $^1$H and $^{13}$C NMR spectra for all new compounds. Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.11.079. These data include MOL files and InChIKeys of the most important compounds described in this article.

## References and notes

1. (a) Burova, S. A.; McDonald, F. E. *J. Am. Chem. Soc.* **2002**, *124*, 8188; (b) Achmatowicz, B.; Wicha, J. *Tetrahedron: Asymmetry* **1993**, 339; (c) Mohr, P. *Tetrahedron Lett.* **1992**, *33*, 2455; (d) Lipshutz, B. H.; Kozlowski, J. A. *J. Org. Chem.* **1984**, *49*, 1147.
2. (a) Waddell, T. G.; Ross, P. A. *J. Org. Chem.* **1987**, *52*, 4802; (b) Masamune, T.; Sato, S.; Abiko, A.; Ono, M.; Murai, A. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2895; (c) Murai, A.; Ono, M.; Masamune, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1226; (d) Murai, A.; Ono, M.; Masamune, T. *J.C.S. Chem. Commun.* **1976**, 864.
3. (a) Carley, S.; Brimble, M. A. *Org. Lett.* **2009**, *11*, 563; (b) Sabitha, G.; Rao, V. R. S.; Sudhakar, K.; Kumar, M. R.; Reddy, E. V.; Yadav, J. S. *J. Mol. Cat. A: Chem.* **2008**, *280*, 16; (c) Chirskaya, M. V.; Vasil'ev, A. A.; Shorshnev, S. V.; Sviridov, S. I. *Russ.*

*Chem. Bull., Int. Ed.* **2006**, *55*, 1301; (d) Blanc, A.; Toste, F. D. *Angew. Chem., Int. Ed.* **2006**, *45*, 2096; (e) Pena, P. C. A.; Roberts, S. M. *Curr. Org. Chem.* **2003**, *7*; (f) Karikomi, M.; Watanabe, S.; Kimura, Y.; Uyehara, T. *Tetrahedron Lett.* **2002**, *43*, 1495; (g) Hoppe, D.; Tarara, G.; Wilckens, M. *Synthesis* **1989**, 83; (h) Coxon, J. M.; Hartshorn, M. P.; Swallow, W. H. *Aust. J. Chem.* **1973**, *26*, 2521.

4. (a) Torres, W.; Rodriguez, R. R.; Prieto, J. A. *J. Org. Chem.* **2009**, *74*, 2447; (b) Robles, O.; McDonald, F. E. *Org. Lett.* **2008**, *10*, 1811; (c) Dávila, W.; Torres, W.; Prieto, J. A. *Tetrahedron* **2007**, *63*, 8218; (d) Kobayashi, Y.; Uchiyama, H.; Kanbara, H.; Sato, F. *J. Am. Chem. Soc.* **1985**, *107*, 5541; (e) Corey, E. J.; Hase, T. *Tetrahedron Lett.* **1979**, *20*, 335.
5. (a) Torres, G.; Torres, W.; Prieto, J. A. *Tetrahedron* **2004**, *60*, 10245; (b) Guanti, G.; Banfi, L.; Narisano, E.; Thea, S. *Tetrahedron Lett.* **1991**, *32*, 6943; (c) Hanamoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 6191; (d) Mihelich, E. D.; Daniels, K.; Eickhoff, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 7690.
6. (a) Tirado, R.; Prieto, J. A. *J. Org. Chem.* **1993**, *58*, 5666; (b) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321.
7. (a) Wang, Z.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 31; (b) Coxon, J. M.; Simpson, G. W.; Steel, P. J.; Trenerry, V. C. *Tetrahedron Lett.* **1983**, *24*, 1427; (c) Beau, J.-M.; Aburaki, S.; Pougny, J.-R.; Sinay, P. *J. Am. Chem. Soc.* **1983**, *105*, 621; (d) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1981**, *103*, 3229; (e) Johnson, M. R.; Kishi, Y. *Tetrahedron Lett.* **1979**, *20*, 4347.
8. (a) Li, Z.; Zhang, W.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7520; (b) Zhang, W.; Yamamoto, H. *J. Am. Chem. Soc.* **2007**, *129*, 286; (c) Okachi, T.; Murai, N.; Onaka, M. *Org. Lett.* **2003**, *5*, 85; (d) Makita, N.; Hoshino, Y.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2003**, *42*, 941; (e) Karjalainen, J. K.; Hormi, O. E. O.; Sherrington, D. C. *Tetrahedron: Asymmetry* **1998**, *9*, 3895; (f) Ikemagui, S.; Katsuki, T.; Yamaguchi, M. *Chem. Lett.* **1987**, 83; (g) Rossister, B. E.; Sharpless, K. B. *J. Org. Chem.* **1984**, *49*, 3707.
9. (a) Burke, C. P.; Shi, Y. *Org. Lett.* **2009**, *11*, 5150; (b) Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488; (c) Frohn, M.; Shi, Y. *Synthesis* **2000**, 1979.
10. Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.
11. (a) Krasinski, A.; Jurczak, J. *Tetrahedron: Asymmetry* **2002**, 2075; (b) Guanti, G.; Banfi, L.; Merio, V.; Narisano, E.; Thea, S. *Tetrahedron* **1993**, *49*, 9501.
12. Rodriguez, D.; Mulero, M.; Prieto, J. A. *J. Org. Chem.* **2006**, *71*, 5826.
13. Sasaki, M.; Tanino, K.; Miyashita, M. *Org. Lett.* **2001**, *3*, 1765.
14. Spartan 04 for PC, Wavefunction, Irvine, CA, 2004.
15. (a) White, P. J.; Kaus, M. J.; Edwards, J. O.; Rieger, P. H. *J. Chem. Soc., Chem. Commun.* **1976**, 429; (b) Sharpless, B. K.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.
16. Muntwyler, R.; Keller-Schierlein, W. *Helv. Chim. Acta* **1972**, *55*, 460.
17. Rinehart, K. L., Jr.; Shield, L. S. *Chem. Org. Naturst.* **1976**, *33*, 231.
18. Ishibashi, M.; Moore, R. E.; Patterson, G. M. L.; Xu, C.; Clardy, J. *J. Org. Chem.* **1986**, *51*, 5300.