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Enantioselective iminium-catalyzed epoxidation of hindered trisubstituted allylic alcohols

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Dedicated to Professor Henri Kagan on the occasion of his 80th birthday

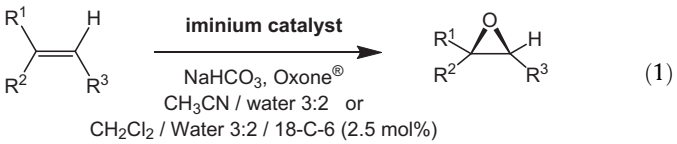
ABSTRACT

The reactivity of diastereomeric biaryl iminium cations made of a (*Ra*)-5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl core and exocyclic appendages derived from (*S*)- or (*R*)-3,3-dimethylbutyl-2-amine was investigated with hindered trisubstituted allylic alcohols—a class of alkenes which had not been previously studied in detail in epoxidation reactions with cyclic iminium catalysts (ee up to 98%). Surprisingly, generally strong matched/mismatched effects are observed not only in terms of reactivity but also on the enantioselectivity of the reaction (Δee up to 16%). Also, for the most hindered substrates, two sets of reaction conditions were tested in a preliminary study and little advantage was found in running reactions in MeCN/water instead of CH_2Cl_2/water/18-C-6. In any case, the presence of the hydroxyl group did not reveal any anchimeric effect.

1. Introduction

Non-racemic epoxides are useful precursors and building blocks in synthetic organic chemistry. Quite a few effective systems have been developed for their preparation,[1] and catalytic asymmetric epoxidation of olefins has proven to be one of the most powerful approaches. Most strategies are based on transition metal catalysis such as the Katsuki–Sharpless epoxidation of allylic alcohols with chiral titanium catalysts,[2] vanadium-catalyzed epoxidation of allylic[3] and homoallylic alcohols[4] mainly developed by Yamamoto, and the Katsuki–Jacobsen protocol with Mn(salen) catalysts for unfunctionalized olefins.[5] During the last decade, much effort has been devoted to the development of organocatalytic processes that afford metal-free procedures,[6,7] such as asymmetric epoxidation catalyzed by chiral ketones,[7,8] iminium salts,[9] peptides,[10] and phase-transfer catalysts.[11]

In this field, oxaziridinium ions are effective oxygen transfer reagents toward nucleophilic substrates[12] and electron-rich unfunctionalized olefins in particular. Moreover, the propensity of iminium ions to react with Oxone® to generate the oxaziridinium species renders the development of catalytic processes possible (Eq. 1).[13]



(1)

Recently, several successful enantioselective variants of the iminium-catalyzed epoxidation of alkenes have been reported,[14–17] and many of them are based on configurationally stable biarylazepinium skeletons.[18–20] In this family, it was recently shown that axially chiral 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl-derived iminium salts **1a** and **1b** (Fig. 1), prepared from enantiopure (*R*)-BINOL and (*R*)-/(*S*)-3,3-dimethylbutyl-2-amine, are probably the most selective catalysts of this type for enantioselective epoxidations of simple prochiral olefins.[21] These epimeric molecules provide non-racemic epoxides with the same absolute configuration and often with virtually the same enantiomeric purity (up to 98% ee) despite their diastereomeric relationship. This unusual behavior was explained by the existence of stereospecific atropisomers around the N(sp^2)–C(sp^3) bond that links the azepinium core to the chiral appendage of **1a**

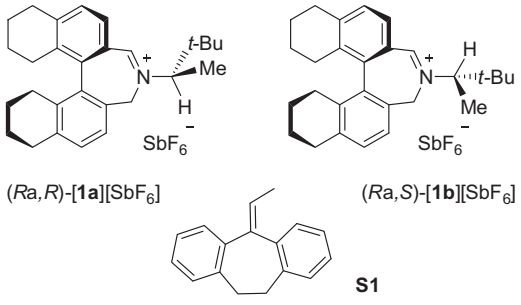


Figure 1. Diastereomeric 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl-derived iminium catalysts **1** and hindered unfunctionalized olefin **S1**. The most selective (*Ra*,*R*)-**1a** and most reactive (*Ra*,*S*)-**1b** derived from (*R*)- and (*S*)-3,3-dimethylbutyl-2-amine respectively. Compounds **1a** and **1b** have predominantly *anti*- and *syn-periplanar* conformations

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and **1b**.[22] It ensures that the same prochiral *Re* face of the iminium ions **1a** and **1b** is accessible to Oxone® and to the olefin irrelevant of the configuration of the chiral side chain.

However, if little differences were seen on the selectivity of the reaction with **1a** and **1b**, large matched/mismatched effects were observed in terms of reactivity. In fact, salts [**1a**][SbF_6] and [**1b**][SbF_6] catalyzed the reaction with rather different rates. With hindered substrates such as olefin **S1** (Fig. 1), diminished conversions and yields were obtained with the more selective salt [**1a**][SbF_6]. This forced us to use higher amounts of catalyst (up to 20 mol %) and longer reaction times (up to 4 days) to drive the reaction to completion. The only reported solution to this reactivity problem was the use of the more reactive salt [**1b**][SbF_6] that led, with **S1**, to a moderately lower enantioselectivity value (ee 93% with **1b** instead of 98% with **1a**).

We wondered about the generality of this observation and decided to study the reactivity of a similar yet different class of olefin—that of allylic alcohols which had not been previously studied in details in epoxidation reactions with cyclic iminium catalysts. Herein we report that surprisingly,[19] generally strong matched/mismatched effects are observed with the diastereomeric catalysts not only in terms of reactivity but also on the enantioselectivity of the reaction (Δee up to 16%). We wondered if the selected reaction conditions were having an influence with these polar substrates. We decided to briefly check, for the most hindered substrates, if the more traditional CH_3CN/water conditions would not be better than our strictly biphasic CH_2Cl_2/water conditions. However, preliminary data indicate that little difference can be observed for the two solvent systems.

2. Results and discussion

2.1. Enantioselective epoxidation of hindered trisubstituted allylic alcohols using [1a][SbF_6] iminium salt as catalyst

Diastereomeric iminium salts (*Ra*,*R*)-**1a** and (*Ra*,*S*)-**1b** are effective asymmetric epoxidation catalysts with lipophilic hindered alkenes that present (i) little differences in terms of the enantioselectivity but (ii) large matched/mismatched effects in terms of reactivity.[21] We wondered about the generality of this observation and decided to investigate the reactivity of these catalysts with another class of olefins.

A range of hindered trisubstituted allylic alcohols **S2**–**S11** was synthesized usually by Horner–Wadsworth–Emmons olefination of ketones and subsequent reduction with DIBAL-H, and studied in the asymmetric epoxidation reaction (Eq. 1). For all substrates, the reaction was studied under biphasic CH_2Cl_2/water. In fact, for iminium-catalyzed epoxidation reactions, we have previously introduced the use of strict biphasic CH_2Cl_2/water/18-C-6 conditions. With catalytic iminium salts associated with a lipophilic TRISPHAT counterion,[23,24] an enhancement of the selectivity was observed using these conditions in which the oxidation occurs in the organic CH_2Cl_2 phase only.[15] A similar observation was reported by Page et al. who developed strict anhydrous conditions using pure CH_2Cl_2 as a solvent and tetraphenylphosphonium monoperoxybisulfate (TPPP) as a stoichiometric oxidant.[16,20,25]

First, 3,3-diphenylprop-2-en-1-ol **S2** was successfully transformed into the corresponding epoxide in good yield and enantioselectivity using [**1a**][SbF_6] salt as the catalyst (Table 1, entry 1). However, the reaction was quite slow and required 20 mol % of iminium salt. This lack of reactivity was somewhat surprising and two possible factors were considered to explain this result: (i) an unfavorable partition of the allylic alcohol in the biphasic CH_2Cl_2/water mixture and (ii) an effect of the electron-withdrawing hydroxyl group that renders the double bound less nucleophilic. To test these hypotheses, compounds **S3** and **S4**, structurally similar to that of **S2**, were prepared. They contain an alkylated hydroxyl group in the form of a methoxy residue and two electron-donating methyl groups in *para*-position of phenyl rings, respectively. As expected, both modifications favored the reaction. The increased lipophilicity and nucleophilicity of the double bond in these two substrates accelerated the rate of the epoxidation process. A shorter reaction time was possible with **S3**. With **S4**, less catalyst [**1a**][SbF_6] (10 mol % for **S4** vs 20 mol % for **S2**, respectively) was required to get full conversion in also reduced amount of time (Table 1, entries 1 and 3). For this latter example, the reaction was clean as judged by GC–MS and ^{1}H NMR of crude reaction mixture, but unfortunately we were not able to isolate the epoxide in analytically pure form due to its very acid-sensitive nature. Despite this fact, the enantioselectivity of the 'crude' product was determined to be 88% ee. It shows, in comparison with the reaction of **S2**, that the asymmetric induction is essentially insensitive to electronic effects. A similar enantiomeric purity was obtained for the reaction with **S3** (87% ee). Then, a range of compounds containing different alkyl groups (**S5**–**S11**) was studied (see Fig. 2) to test the steric influence of the group R on both enantioselectivity and reactivity.

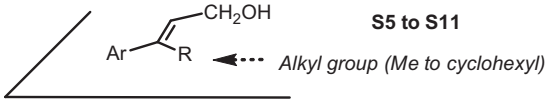


Figure 2. Hindered trisubstituted allylic alcohols.

Unexpected and disappointing results were obtained with allylic alcohol **S5** containing a methyl group as substituent R (Table 1, entry 4). In this particular case, the reaction was very capricious. If only 10 mol % of [**1a**][SbF_6] was needed to obtain full conversion of the substrate, it was not possible to isolate the desired epoxide detected in the ^{1}H NMR spectrum of the crude mixture and no measure of the enantiomeric excess of the epoxide could be made.

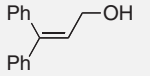
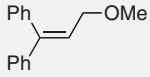
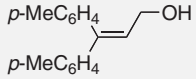
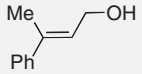
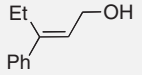
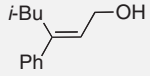
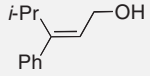
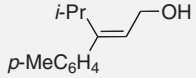
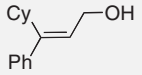
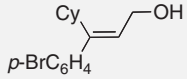
Moving to more hindered substrates **S6** (R = Et) and **S7** (R = *i*-Bu), better results were obtained. Full and clean conversions of starting materials to their corresponding epoxides were observed. The products were isolated in pure form in good yields and enantioselectivities. A higher asymmetric induction in the case of **S7** compared to **S6** (90% ee vs 87% ee) was noticed which was explained by a larger steric influence of the isobutyl group relative to the ethyl. In this spirit, moving to bulkier substrates **S8** (R = *i*-Pr) and **S10** (R = cyclohexyl), the enantioselectivity values were higher (95% and 98% ee, respectively, entries 7 and 9). Clearly the trend is conserved; the bulkier the alkyl group R, the better the enantioselectivity.

Globally, the reactions were clean. No post-decomposition or racemization of the products was observed under the reaction conditions. For example, increasing the reaction time in the epoxidation reaction of **S6** from 24 h to 48 h (full conversion is obtained in 24 h) did not yield any variation in the enantiomeric excess of the desired epoxide which was isolated in similar yield. However, whereas enantioselectivity levels increased moving from non-hindered substrates to bulky compounds, reactivity significantly dropped. Only 80% conversion of **S8** was obtained under CH_2Cl_2/water reaction conditions in 24 h. Increasing the reaction time from 24 h to 48 h or longer did not have any effect; the conversion remaining the same.

2.2. Enantioselective epoxidation of hindered trisubstituted allylic alcohols using [1b][SbF_6] iminium salt as catalyst

This lack of reactivity was disappointing. We felt that the more reactive catalyst [**1b**][SbF_6] should be tried with the more troublesome substrates—if only to tabulate the reactivity of **1b** with **1a**.

Table 1
Asymmetric epoxidation of various allylic alcohols mediated by catalyst [**1a**][SbF_6] (*most selective* catalyst) in CH_2Cl_2/H_2O conditions

Entry	Substrate		Solvent	Catalyst (mol %)	Time (h)	Yield[a] (conv.[b] %)	ee[c] (%)	Config.
1		**S2**	CH_2Cl_2[d]	20	48	80 (>97)	88	(−)-(*S*)[e]
2		**S3**	CH_2Cl_2[d]	20	24	76 (93)	87	(−)
3		**S4**	CH_2Cl_2[d]	10	24	(>99)	88	—
4		**S5**	CH_2Cl_2[d]	10	24	(>99)	n.d.	—
5		**S6**	CH_2Cl_2[d]	20	24	84 (>99)	87	(+)
6		**S7**	CH_2Cl_2[d]	20	24	69 (>99)	90	(+)
7		**S8**	CH_2Cl_2[d]	20	24	65 (80)	95	(+)
8		**S9**	CH_2Cl_2[d]	20	24	63 (85)	95	(+)
9		**S10**	CH_2Cl_2[d]	20	24	65 (75)	98 (>99[f])	(+)-(2*S*,3*S*)[e]
10		**S11**	CH_2Cl_2[d]	20	24	37 (75)	95	(+)

[a] Isolated yields of pure epoxides.
[b] Determined by GC–MS or ^1H NMR analysis of the crude reaction mixture.
[c] Determined by CSP-HPLC (see the Experimental).
[d] Conditions: substrate (0.2 mmol), catalyst (*x* mol %), 2.5 mol % of 18-C-6, 1.1 equiv Oxone®, 4.0 equiv $NaHCO_3$, CH_2Cl_2/H_2O (3:2), 0 °C.
[e] The absolute configuration of the major enantiomers was determined by comparison of the optical rotation with that reported in the literature.
[f] After single recrystallization from *n*-hexane/*i*-PrOH.

The results are presented in Table 2. They are in line with our expectations. Quite lower amounts of catalyst are necessary (5–10 with **1b** vs 20–30 mol % with **1a**) to reach full conversions.[26] However, in terms of selectivity, initial tests with challenging substrate **S10** (Table 2, entry 1 and Table 1, entry 9) indicated a very strong matched/mismatched behavior between diastereomeric catalyst [**1b**][SbF_6] and [**1a**][SbF_6]. Much lower enantiomeric excess values were obtained with the more reactive catalyst **1b** (ee 85% in CH_2Cl_2). The drop in enantiomeric excess (−13%) compared to that of **1a** is consequent. It can be perceived even more by considering enantiomeric ratios instead of enantiomeric excesses. The reaction of **S10** with [**1b**][SbF_6] in CH_2Cl_2 yields the scalemic epoxide in 13:1 ratio, whereas under the same conditions [**1a**][SbF_6] affords the product in 104:1 ratio.[27] It is the first time that such a difference of selectivity is observed with diastereomeric biaryl azepinium catalysts.

The trend was confirmed in all other experiments. Alkenes **S7**, **S8**, **S9**, and **S11** also yielded the corresponding epoxides with major losses of enantiomeric purity (−10%, −10%, −12%, and even −16% *ee*, respectively). The reason(s) for these general losses in enantiomeric purity is (are) still under evaluation.

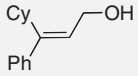
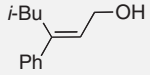
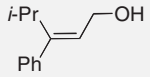
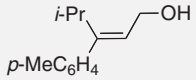
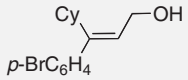
Yet, despite this major shortcoming, catalyst [**1b**][SbF_6] has the advantage of providing reproducible results that can be readily scaled-up. The selectivity issue can be offset if an effective enantioenrichment protocol can be coupled to the oxidation. For instance, the epoxidation reaction of **S10** can be readily performed with 1.0 g of substrate (4.63 mmol) and the desired epoxide was isolated with the same enantiomeric purity (86% ee) and slightly better yield (87%) than in the test reaction.[28] After a single recrystallization from *n*-hexane/*i*-PrOH (25:1), the product was obtained in enantiopure form (>99% ee) (Scheme 1).

2.3. Acetonitrile/water versus dichloromethane/water conditions. Preliminary results

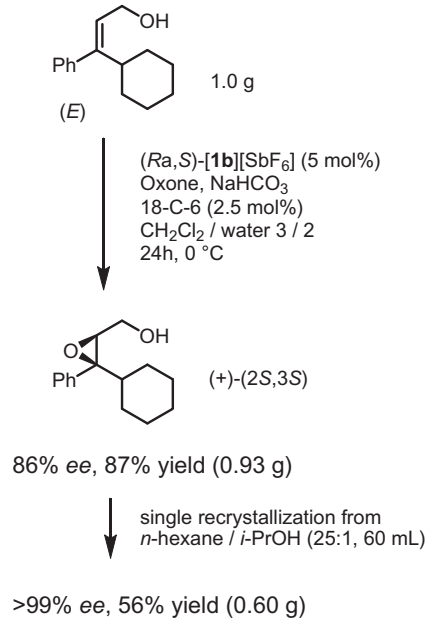
Traditionally, epoxidation reactions with iminium catalysts are not performed in CH_2Cl_2 but instead in mixtures of CH_3CN and water.[29] Both lipophilic alkenes and polar BF_4^- or PF_6^- iminium salts display usually a good solubility in CH_3CN. In some instances, the epoxidation reactions can proceed faster in the acetonitrile/water system than in the dichloromethane/water mixture.[30] We thus wondered if acetonitrile/water conditions might not be an answer to our reactivity problem with salt [**1a**][SbF_6] and hindered alcohols **S7**–**S11**. We reasoned that the higher polarity of the acetonitrile/water mixture could help the solubilization and reactivity of these polar substrates. Results are reported in Table 3 (entries 1–5) and can be compared with that in CH_2Cl_2 (Table 1).

First, the absolute configuration of the resulting epoxides remains the same under the two sets of reaction conditions. The enantioselectivity values are virtually identical (ee ±1% in CH_2Cl_2 and CH_3CN). This result is interesting as stronger differences could have been expected.[30] It should be noted that the acetonitrile/water (3:2) system is not monophasic but triphasic. Two liquid layers and one inorganic precipitate can be seen from the start to

Table 2
Asymmetric epoxidation of a selection of allylic alcohols mediated by catalyst [**1b**][SbF_6] (*most reactive* catalyst) in CH_2Cl_2/H_2O conditions[a]

Entry	Substrate		Solvent	Catalyst (mol %)	Time (h)	Yield[b] (conv.[c] %)	ee[d] (%)	ee[d] (%) with [**1a**][SbF_6]
1		**S10**	CH_2Cl_2[e]	10	24	81 (>99)	85 (96[f])	98 (>99[f])
2		**S7**	CH_2Cl_2[e]	10	24	61 (>99)	80	90
3		**S8**	CH_2Cl_2[e]	10	24	86 (>99)	85	95
4		**S9**	CH_2Cl_2[e]	5	24	86 (>99)	88	95
5		**S11**	CH_2Cl_2[e]	10	24	82 (>99)	79	95

[a] All epoxide products from the reaction of **S7**–**S11** are dextrorotatory irrespective of the use of catalyst [**1b**][SbF_6] or [**1a**][SbF_6].
[b] Isolated yields of pure epoxides.
[c] Determined by GC–MS analysis of crude reaction mixture.
[d] Determined by CSP-HPLC (see the Experimental).
[e] Conditions: substrate (0.2 mmol), catalyst (*x* mol %), 2.5 mol % of **18-C-6**, 1.1 equiv Oxone®, 4.0 equiv $NaHCO_3$, CH_2Cl_2/H_2O (3:2), 0 °C.
[f] After single recrystallization from *n*-hexane/*i*-PrOH.



Scheme 1. Enantioselective epoxidation of **S10** performed on 1.0 g of substrate.

the end of the reaction. It is then not clear in which liquid phase(s) the epoxidation reaction actually proceeds. Possibly, the epoxidation process takes place at an interface but this is short of an explanation to account for the minimal difference in selectivity between the two solvent systems. It should also be mentioned that 18-C-6, which is absolutely necessary for the phase transfer of $KHSO_5$ in the biphasic CH_2Cl_2/water conditions,[15,17] is not required anymore in the ternary MeCN/water system.

Specifically, for **S9**, the reaction proceeded faster but 20 mol % of catalyst was still needed (entry 3). For substrates **S8**, **S10**, and **S11**, full conversion to their corresponding epoxides was now achieved. Nevertheless, with these substrates, no measurable increase in reactivity was seen in the polar CH_3CN/water conditions. It was actually necessary to use a higher amount of catalyst (25–30 mol %) to reach full conversion—the CH_3CN/water combination allowing yet to increase the catalyst loading due to the better solubility of [**1a**][SbF_6] in CH_3CN.[31] Nevertheless, these MeCN/water conditions are clearly not a general answer to the reactivity problem spotted with these substrates.

Finally, in the MeCN/water medium, substrate **S10** was treated with catalyst [**1b**][SbF_6]. Again, as for reactions in CH_2Cl_2/water, a very strong matched/mismatched behavior between diastereomeric catalysts. A much lower enantiomeric excess value was obtained with the more reactive **1b** (ee 84% in CH_3CN, see the Experimental). The drop is again important in enantiomeric excess (−12%) or in enantiomeric ratios (11:1 vs 71:1) with [**1b**][SbF_6] instead of [**1a**][SbF_6].

2.4. Absolute sense of stereoinduction

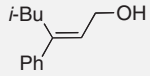
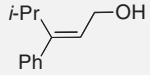
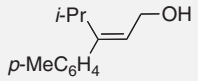
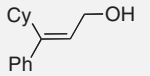
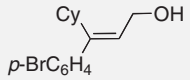
We have recently proposed that any trisubstituted alkene of type **2** with the substitution pattern displayed in Figure 3 should lead to high enantiomeric excesses in an enantioselective epoxidation reaction catalyzed by salt [**1a**][SbF_6]. Clearly, this proposition is a working model with allylic alcohols **S2**–**S11**. All epoxide products displayed rather high level of enantiomeric purity in reactions performed in CH_2Cl_2/water or in CH_3CN/water conditions.

It was also shown that the major enantiomer comes usually from the addition of the O-atom on the top face of the alkene in the geometrical disposition provided in Figure 3. With the novel alcohols, this could be verified only in the case of **S10** which is the only novel substrate for which the absolute configuration of the epoxide is known. In this case, the (+)-(2*S*,3*S*)-*trans*-3-cyclohexyl-3-phenyloxiranemethanol was obtained and this product comes indeed from a *Re* face oxidation of the alkene. Most probably, the same approach takes place for the others substrates.

3. Conclusion

The reactivity of diastereomeric biaryl iminium cations made of a (*Ra*)-5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl core and exocyclic appendages derived from (*S*)- or (*R*)-3,3-dimethylbutyl-2-amine was investigated with hindered trisubstituted allylic alcohols—a class of alkenes which had not been previously studied in detail in epoxidation reactions with such cyclic iminium catalysts. Surprisingly strong matched/mismatched effects are observed not

Table 3
Asymmetric epoxidation of various allylic alcohols mediated by catalyst [**1a**][SbF_6] (*most selective* catalyst) in MeCN/H_2O conditions

Entry	Substrate		Solvent	Catalyst (mol %)	Time (h)	Yield[a] (conv. [b] %)	ee[c] (%)	Config.[d]
1		**S7**	MeCN[e]	20	24	73 (>99)	91	(+)
2		**S8**	MeCN[e]	25	24	79 (98)	95	(+)
3		**S9**	MeCN[e]	20	24	84 (>99)	95	(+)
4		**S10**	MeCN[e]	30	24	80 (>99)	96 (>99[f])	(+)-(2*S*,3*S*)
5		**S11**	MeCN[e]	30	24	77 (98)	94	(+)

[a] Isolated yields of pure epoxides.
[b] Determined by GC–MS or ^{1}H NMR analysis of the crude reaction mixture.
[c] Determined by CSP-HPLC (see the Experimental).
[d] The absolute configuration of the major enantiomers was determined by comparison of the optical rotation with that reported in the literature.
[e] Conditions: substrate (0.2 mmol), catalyst (*x* mol %), 1.1 equiv Oxone®, 4.0 equiv $NaHCO_3$, MeCN/H_2O (3:2), 0 °C.
[f] After single recrystallization from *n*-hexane/*i*-PrOH (25:1).

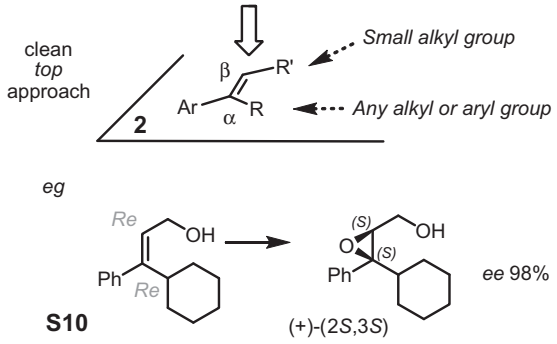


Figure 3. Proposed model type of alkenes giving epoxides with high enantiomeric excesses. Facial selectivity of the epoxide formation (*Re* face in case of allylic alcohols).

only on the reactivity but also on the enantioselectivity of the reaction (Δee up to 16%). For the most hindered substrates, two sets of conditions (CH_2Cl_2/water/18-C-6 or MeCN/water) were tested but little difference was noticed for the two systems.

Finally, if one compares the results obtained herein with hindered allylic alcohols and that previously reported with the corresponding alkenes (for instance **S2** and 1,1-diphenylpropene),[21] very similar results are obtained in term of yields and enantiomeric excesses. It seems to indicate that the hydroxyl group has no (or very little) interaction with the catalysts at play and anchimeric effects do not need to be considered.

4. Experimental

NMR spectra were recorded on 300, 400, and 500 MHz spectrometers at room temperature (25 °C) unless otherwise stated. ^{1}H NMR: chemical shifts are given in parts per million (ppm) relative to Me_4Si with the solvent resonance used as the internal standard ($CDCl_3$ δ 7.26 ppm; CD_2Cl_2 δ 5.32 ppm; DMSO-d_6 δ 2.50 ppm). ^{13}C-NMR (75, 100, 125 MHz): chemical shifts were given in ppm relative to Me_4Si, with the solvent resonance used as the internal standard ($CDCl_3$ δ 77.16 ppm; CD_2Cl_2 δ 54.0 ppm). Assignments may have been achieved using COSY, DEPT-135, HSQC, and NOESY experiments. IR spectra were recorded using a diamond ATR Golden Gate sampling. Melting points (mp) were measured in open capillary tubes and were uncorrected. MS-EI spectra were obtained with ionizing voltage 70 eV and 40 eV; *m*/z (intensity in%) by the Department of Mass Spectroscopy of the University of Geneva. Optical rotations were measured in a thermostated 10.0 cm long microcell with high pressure lamp of sodium and are reported as follows: $[\alpha]_D^t$ (*c* (g/1000 mL), solvent). HPLC analyses were performed using Chiralcel OD-H, OJ and OJ-H (0.46 × 25 cm) columns. Chiral stationary phase (CSP) chromatography was performed using a Hydrodex-β column (25 m × 0.25 mm, H_2, 40 Psi). GC–MS analysis was performed using a HP-5MS column (30 m × 0.25 mm, He 1.0 mL/min).

4.1. Typical enantioselective epoxidation procedure under CH_2Cl_2/water (3:2) conditions

All reactions were performed in a standard test tube equipped with a magnetic stirring bar. $NaHCO_3$ (67 mg, 0.80 mmol, 4.0 equiv) was dissolved in 800 μL of water. Oxone® (132 mg, 0.21 mmol, 1.1 equiv) was then added as a solid in one portion and the solution was stirred for few minutes until effervescence subsided. Five-hundred microliters of a 0.4 mol/L solution of an alkene (0.20 mmol, 1.0 equiv) in CH_2Cl_2 was added and the resulting biphasic mixture was cooled to 0 °C with a cryostat bath. A catalyst was added in CH_2Cl_2 (500 μL) in one pot followed by a solution of 18-C-6 (1.0 mg, 5.0 μmol, 2.5 mol %) in CH_2Cl_2 (200 μL) and the resulting mixture was then vigorously stirred (*very important*!) at 0 °C. After the indicated amount of time, the reaction mixture was diluted with dichloromethane (10 mL) and water (10 mL), and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, concentrated under vacuum, and purified.

4.2. Typical enantioselective epoxidation procedure under MeCN/water (3:2) conditions

The reaction procedure is similar to the CH_2Cl_2/water protocol with small modifications. All reactions were performed in a

standard test tube equipped with a magnetic stirring bar. $NaHCO_3$ (67 mg, 0.80 mmol, 4.0 equiv) was dissolved in 800 μL of water. Oxone® (132 mg, 0.21 mmol, 1.1 equiv) was then added as a solid in one portion and the solution was stirred for few minutes until effervescence subsided. Five-hundred microliters of a 0.4 mol/L solution of an alkene (0.20 mmol, 1.0 equiv) in MeCN was added (after the addition was done the mixture became triphasic: precipitation of inorganic material was observed and the liquid layer separated in two phases) with the aid of MeCN (200 μL) which was used to rinse the walls of the flask, and the resulting mixture was cooled to 0 °C with a cryostat bath. A catalyst was added as a solution in MeCN (500 μL) in one pot. After few minutes without any stirring the resulting triphasic mixture was then vigorously stirred (*very important*!) at 0 °C. After the indicated amount of time, the reaction mixture was diluted with dichloromethane (20 mL), water (10 mL), and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, concentrated under vacuum, and purified.

4.3. 3,3-Diphenylprop-2-en-1-ol S2[32]

White solid. Mp = 62.8–63.5 °C (lit. 53–56 °C[32]). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.57 (br s, 1H, OH), 4.33 (d, 2H, CH_2, J = 6.8 Hz), 6.36 (t, 1H, CH vinyl, J = 6.8 Hz), 7.24–7.53 (m, 10H, C^{ar}H) ppm.

4.4. 1,1-Diphenyl-3-methoxyprop-1-ene S3

Pale yellow oil. ^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 3.28 (s, 3H, CH_3), 3.96 (d, 2H, CH_2, J = 6.6 Hz), 6.19 (t, 1H, CH vinyl, J = 6.6 Hz), 7.14–7.19 (m, 2H, C^{ar}H), 7.22–7.42 (m, 8H, C^{ar}H) ppm. ^{13}C NMR (CD_2Cl_2, 125 MHz): δ = 58.3 (CH_3), 70.7 (CH_2), 126.5 (CH vinyl), 128.01 (CH), 128.03 (CH), 128.1 (CH), 128.7 (CH), 128.72 (CH), 130.3 (CH), 139.9 (C quat.), 142.6 (C quat.), 145.0 (C quat.) ppm. IR (neat): 3056 (w), 3027 (w), 2981 (w), 2923 (w), 2818 (w), 1599 (w), 1576 (w), 1493 (w), 1444 (w), 1378 (w), 1114 (m), 1086 (m), 757 (m), 695 (s) cm^{-1}. MS-EI *m/z* (rel intensity): 224 [M]$^+$ (42), 193 (40), 192 (100), 165 (34), 115 (61), 77 (26). HRMS-EI calcd for $C_{16}H_{16}O$ [M]$^+$ 224.1193, found 224.1201.

4.5. 3,3-Di(4-methylphenyl)prop-2-en-1-ol S4[33]

White solid. Mp = 68−69.5 °C (lit. 69–70 °C[33]). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.36 (t, 1H, OH, J = 5.5 Hz), 2.34 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 4.22 (dd, 2H, CH_2–OH, J = 6.8 Hz, 5.5 Hz), 6.18 (t, 1H, CH vinyl, J = 6.8 Hz), 7.02–7.21 (m, 8H, C^{ar}H) ppm.

4.6. (*E*)-3-Phenylpent-2-en-1-ol S6[34]

Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.93 (t, 3H, CH_3, J = 7.5 Hz), 1.27 (br s, 1H, OH), 2.48 (q, 2H, CH_2, J = 7.5 Hz), 4.29 (dd, 2H, CH_2–OH, J = 6.3 Hz, 4.3 Hz), 5.77 (t, 1H, CH vinyl, J = 6.8 Hz), 7.14–7.36 (m, 5H, C^{ar}H) ppm.

4.7. (*E*)-5-Methyl-3-phenylhex-2-en-1-ol S7

Clean colorless oil. ^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 0.84 (d, 6H, 2 × CH_3, J = 6.6 Hz), 1.43 (br s, 1H, OH), 1.49–1.59 (m, 1H, CH of *i*-Pr), 2.42 (d, 2H, CH_2, J = 7.2 Hz), 4.31 (d, 2H, CH_2–OH, J = 6.6 Hz), 5.86 (t, 1H, CH vinyl, J = 6.8 Hz), 7.22–7.39 (m, 5H, C^{ar}H) ppm. ^{13}C NMR (CD_2Cl_2, 125 MHz): δ = 22.6 (CH_3), 27.7 (CH of *i*-Pr), 39.3 (CH_2), 60.3 (CH_2–OH), 127.1 (CH), 127.6 (CH), 128.8 (CH), 129.0 (CH), 142.8 (C quat.), 143.3 (C quat.) ppm. IR (neat): 3315 (br, w), 2953 (w), 2867 (w), 1643 (w), 1599 (w), 1493 (w), 1463 (w), 1444 (w), 1366 (w), 1010 (m), 764 (m), 696 (m) cm^{-1}. MS-EI *m/z* (rel intensity): 190 [M]$^+$ (25), 133 (100), 115 (40), 91 (50), 77 (37), 55(23). HRMS-EI: calcd for $C_{13}H_{18}O$ [M]$^+$ 190.1355, found 190.1358.

4.8. (*E*)-4-Methyl-3-phenylpent-2-en-1-ol S8[35]

Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.03 (d, 6H, 2 × CH_3, J = 7.0 Hz), 1.29 (br m, 1H, OH), 3.01 (sept, 1H, CH, J = 7.0 Hz), 4.34 (dd, 2H, CH_2, J = 6.5 Hz, 5.3 Hz), 5.46 (t, 1H, CH vinyl, J = 6.8 Hz), 7.11–7.31 (m, 5H, C^{ar}H) ppm.

4.9. (*E*)-4-Methyl-3-(4-methylphenyl)pent-2-en-1-ol S9[35]

Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.05 (d, 6H, 2 × CH_3, J = 7.1 Hz), 1.30 (t, 1H, OH, J = 5.4 Hz), 2.35 (s, 3H, CH_3), 3.02 (sept., 1H, CH, J = 7.1 Hz), 4.35 (dd, 2H, CH_2, J = 6.6 Hz, 5.4 Hz), 5.47 (t, 1H, CH vinyl, J = 6.6 Hz), 7.03–7.14 (m, 4H, C^{ar}H) ppm.

4.10. (*E*)-3-Cyclohexyl-3-phenylprop-2-en-1-ol S10[32]

Colorless viscous oil.^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.19–1.39 (m, 6H), 1.56–1.80 (m, 5H), 2.55–2.68 (m, 1H), 4.36 (dd, 2H, CH_2–OH, J = 6.3 Hz, 5.3 Hz), 5.46 (t, 1H, CH vinyl, J = 6.8 Hz), 7.12–7.18 (m, 2H, C^{ar}H), 7.22–7.32 (m, 3H, C^{ar}H) ppm.

4.11. (*E*)-3-(4-Bromophehyl)-3-cyclohexylprop-2-en-1-ol S11

White solid. Mp = 69.6–70.2 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.98–1.11 (m, 1H), 1.15–1.36 (m, 4H), 1.42 (s, 1H, OH), 1.56–1.78 (m, 5H), 2.53–2.65 (m, 1H, CH of Cy), 4.34 (dd, 2H, CH_2–OH, J = 6.3 Hz, 3.3 Hz), 5.44 (t, 1H, CH vinyl, J = 6.7 Hz), 7.02 (d, 2H, CH_2, J = 8.5 Hz), 7.40 (d, 2H, CH_2, J = 8.2 Hz) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 26.0 (CH_2), 26.7 (CH_2), 32.2 (CH_2), 40.8 (CH of Cy), 59.0 (CH_2–OH), 120.8 (C quat.), 128.1 (CH vinyl), 130.2 (CH), 130.8 (CH), 141.8 (C quat.), 148.6 (C quat.) ppm. IR (neat): 3307 (br, w), 2925 (m), 2851 (m), 1646 (w), 1586 (w), 1485 (m), 1448 (w), 1009 (m), 823 (m) cm^{-1}. MS-EI *m/z* (rel intensity): 296 [M]$^+$ (11), 294 [M]$^+$ (16), 252 (19), 213 (85), 169 (40), 141 (62), 115 (96), 83 (77), 55 (100). HRMS-EI: calcd for $C_{15}H_{17}OBr$ [M−2H]$^+$ 292.0463, found 292.0463.

4.12. (−)-(*S*)-3,3-Diphenyloxiranemethanol, epoxide of S2[21]

Purification—preparative TLC on silica gel, eluent *n*-hexane/EtOAc 3:2. $[\alpha]_D^{25} = -16.6$ (*c* 0.5, $CHCl_3$) 88% ee [lit.[36] $[\alpha]_D^{25} = +33.8$ (*c* 0.42, $CHCl_3$) for 94% ee epoxide with absolute configuration (*R*)]. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 1.96 (br s, 1H, OH), 3.3–3.42 (m, 1H), 3.55–3.72 (m, 2H), 7.25–7.45 (m, 10H, C^{ar}H) ppm. ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 62.6 (CH_2), 66.2 (CH), 66.5 (C quat.), 127.4 (CH), 128.3 (CH), 128.4 (CH), 128.5 (CH), 128.8 (CH), 128.9 (CH), 137.6 (C quat.), 141.0 (C quat.) ppm. CSP-HPLC separation: Chiracel OD-H column, *n*-hexane/*i*-PrOH 95:5, 0.5 mL/min, 23 °C, λ = 210 nm); t_R (major) = 35.09 min, t_R (minor) = 40.47 min.

4.13. (−)-1,1-Diphenyl-3-methoxyprop-2-ene oxide, epoxide of S3

Purification—preparative TLC on silica gel, eluent *n*-hexane/EtOAc/Et_3N 80:20:1. R_f = 0.57. Pale yellow oil. $[\alpha]_D^{25} = -28.6$ (*c* 1.0, $CHCl_3$) 87% ee. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.16 (dd, 1H, –C*H*H–OMe, J = 11.1 Hz, 6.2 Hz), 3.33 (s, 3H, CH_3), 3.45 (dd, 1H, –CH*H*–OMe, J = 11.1 Hz, 4.2 Hz), 3.61 (dd, 1H, CH–O, J = 5.8 Hz, 4.6 Hz), 7.20–7.50 (m, 10H, C^{ar}H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 59.3 (CH_3), 64.3 (CH), 65.2 (C quat.), 71.8 (CH_2), 127.0 (CH), 128.0 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 137.0 (C quat.), 140.4 (C quat.) ppm. IR (neat): 3061 (w), 3029 (w), 2984 (w),

2928 (w), 2821 (w), 1495 (w), 1448 (m), 1122 (m), 1088 (m), 764 (m), 753 (m), 696 (s) cm^{-1}. MS-EI *m/z* (rel intensity): 240 $[M]^+$ (4), 208 (37), 195 (11), 165 (100), 105 (28), 77 (24). HRMS-EI: calcd for $C_{16}H_{16}O_2$ $[M]^+$ 240.1150, found 240.1141. CSP-HPLC separation: Chiracel OD-H column, *n*-hexane/*i*-PrOH 99:1, 0.5 mL/min, 23 °C, λ = 210 nm); t_R (minor) = 16.04 min, t_R (major) = 17.43 min.

4.14. (+)-*trans*-3-Ethyl-3-phenyloxiranemethanol, epoxide of S6

Purification—preparative TLC on silica gel, eluent *n*-hexane/EtOAc 3:2. R_f = 0.45. Pale yellow oil. $[\alpha]_D^{25} = +5.3$ (*c* 1.0, $CHCl_3$) 87% ee. ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.94 (t, 3H, CH_3, *J* = 7.4 Hz), 1.74–1.84 (m, 1H, –C*H*H–CH_3), 1.87 (dd, 1H, OH, *J* = 6.9 Hz, 5.0 Hz), 2.08–2.18 (m, 1H, –C*H*H–CH_3), 3.12 (dd, 1H, CH–O, *J* = 6.4 Hz, 4.2 Hz), 3.80–3.90 (m, 1H, –C*H*H–OH), 3.94–4.04 (m, 1H, –CH*H*–OH), 7.26–7.37 (m, 5H, $C^{ar}H$) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 9.6 (CH_3), 24.7 (–CH_2–CH_3), 61.2 (–CH_2–OH), 65.9 (C quat.), 66.0 (CH–O), 126.1 (CH), 127.6 (CH), 128.5 (CH), 140.3 (C quat.) ppm. IR (neat): 3399 (br, w), 2975 (w), 2938 (w), 2878 (w), 1496 (w), 1449 (w), 1379 (w), 1303 (w), 1030 (m), 888 (w), 761 (m), 698 (m) cm^{-1}. MS-EI *m/z* (rel intensity, 40 eV): 177 $[M-H]^+$ (9), 160 (9), 147 (14), 131 (50), 117 (100), 105 (39), 91 (83), 77 (50). HRMS-EI: calcd for $C_{11}H_{13}O_2$ $[M-H]^+$ 117.0917, found 117.0916. CSP-HPLC separation: Chiracel OJ column, *n*-hexane/*i*-PrOH 90:10, 1.0 mL/min, 23 °C, λ = 210 nm); t_R (major) = 7.51 min, t_R (minor) = 9.23 min.

4.15. (+)-*trans*-3-Isobutyl-3-phenyloxiranemethanol, epoxide of S7

Purification—preparative TLC on silica gel, eluent *n*-hexane/EtOAc/Et_3N 60:40:1. R_f = 0.65. Pale yellow oil. $[\alpha]_D^{25} = +20.4$ (*c* 1.0, $CHCl_3$) 92% ee. ^1H NMR ($CDCl_3$, 300 MHz): δ = 0.87 (d, 3H, CH_3, *J* = 6.0 Hz), 0.89 (d, 3H, CH_3, *J* = 6.0 Hz), 1.45–1.73 (m, 3H), 2.18 (dd, 1H, *i*-Pr-C*H*H–, *J* = 13.9 Hz, 5.2 Hz), 2.98 (dd, 1H, CH–O, *J* = 6.6 Hz, 4.3 Hz), 3.77–3.89 (m, 1H, –C*H*H–OH), 3.92–4.04 (m, 1H, –CH*H*–OH), 7.22–7.40 (m, 5H, $C^{ar}H$) ppm. ^{13}C NMR (CD_2Cl_2, 125 MHz): δ = 22.5 (CH_3), 23.7 (CH_3), 25.9 (CH of *i*-Pr), 40.2 (*i*-Pr-CH_2–), 61.6 (–CH_2–OH), 64.7 (C quat.), 65.1 (CH–O), 126.4 (CH), 127.8 (CH), 128.8 (CH), 141.7 (C quat.) ppm. MS-EI *m/z* (rel intensity): 205 $[M-H]^+$ (16), 176 (9), 163 (12), 147 (36), 131 (100), 105 (78), 91 (95), 77 (76). IR (neat): 3398 (w), 2955 (w), 2870 (w), 1496 (w), 1465 (w), 1450 (w), 1368 (w), 1294 (w), 1033 (m), 761 (w), 698 (m) cm^{-1}. HRMS-EI: calcd for $C_{13}H_{18}O_2$ $[M]^+$ 206.1307, found 206.1293. CSP-HPLC separation: Chiracel OJ-H column, *n*-hexane/*i*-PrOH 90:10, 1.0 mL/min, 23 °C, λ = 210 nm); t_R (major) = 8.09 -min, t_R (minor) = 9.34 min.

4.16. (+)-*trans*-3-Isopropyl-3-phenyloxiranemethanol, epoxide of S8

Purification—preparative TLC on silica gel, eluent *n*-hexane/EtOAc/Et_3N 60:40:1. R_f = 0.53 (silica gel, *n*-hexane/EtOAc 3:2). Colorless viscous oil. $[\alpha]_D^{25} = +33.0$ (*c* 1.0, $CHCl_3$) 95% ee. ^1H NMR (CD_2Cl_2, 500 MHz): δ = 0.91 (d, 3H, CH_3, *J* = 6.6 Hz), 0.99 (d, 3H, CH_3, *J* = 7.0 Hz), 1.83 (sept. 1H, CH, *J* = 7.0 Hz), 2.50 (br s, 1H, OH), 3.12 (dd, 1H, C*H*–O, *J* = 6.6 Hz, 4.4 Hz), 3.85 (dd, 1H, –C*H*H–, *J* = 12.0 Hz, 6.6 Hz), 4.02 (dd, 1H, –CH*H*–, *J* = 12.0 Hz, 4.4 Hz), 7.26–7.35 (m, 5H, $C^{ar}H$) ppm. ^{13}C NMR (CD_2Cl_2, 125 MHz): δ = 18.4 (CH_3), 19.8 (CH_3), 31.9 (CH of *i*-Pr), 61.1 (CH_2), 65.2 (CH–O), 69.9 (C quat.), 127.9 (CH), 128.0 (CH), 128.7 (CH), 138.7 (C quat.) ppm. IR (neat): 3415 (br, w), 2967 (w), 2934 (w), 2875 (w), 1497 (w), 1462 (w), 1447 (w), 1386 (w), 1365 (w), 1030 (m), 905 (w), 760 (m), 701 (m) cm^{-1}. MS-EI *m/z* (rel intensity, 40 eV): 191 $[M-H]^+$ (12), 161 (7), 149 (12), 131 (76), 117 (100), 105 (45), 91 (68), 77 (41). HRMS-EI: calcd for $C_{12}H_{16}O_2$ $[M]^+$ 192.1150, found 192.1129. CSP-HPLC separation: Chiracel OD-H column, *n*-hexane/*i*-PrOH 90:10, 0.8 mL/min, 23 °C, λ = 210 nm); t_R (major) = 9.84 min, t_R (minor) = 16.92 min.

4.17. (+)-*trans*-3-Isopropyl-3-(4-methylphenyl)oxiranemethanol epoxide of S9

Purification—preparative TLC on silica gel, eluent *n*-hexane/EtOAc/Et_3N 60:40:1. R_f = 0.53 (silica gel, *n*-hexane/EtOAc 3:2). Pale yellow viscous oil. $[\alpha]_D^{25} = +25.9$ (*c* 1.0, $CHCl_3$) 95% ee. ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.93 (d, 3H, CH_3, *J* = 6.6 Hz), 0.99 (d, 3H, CH_3, *J* = 7.3 Hz), 1.82 (sept., 1H, CH, *J* = 7.0 Hz), 1.91 (br s, 1H, OH), 2.34 (s, 3H, CH_3), 3.17 (dd, 1H, CH–O, *J* = 6.6 Hz, 4.4 Hz), 3.89 (dd, 1H, –C*H*H–, *J* = 12.1 Hz, 7.0 Hz), 4.03 (dd, 1H, –CH*H*–, *J* = 12.1 Hz, 4.6 Hz), 7.12 (d, 2H, $C^{ar}H$, *J* = 7.9 Hz), 7.20 (d, 2H, $C^{ar}H$, *J* = 7.9 Hz) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 18.2 (CH_3 of *i*-Pr), 19.7 (CH_3 of *i*-Pr), 21.3 (CH_3), 31.5 (CH of *i*-Pr), 60.8 (CH_2), 64.7 (*C*H–O), 69.8 (C quat.), 128.1 (CH), 128.4 (CH), 135.0 (C quat.), 137.3 (C quat.) ppm. IR (neat): 3416 (br, w), 2966 (w), 2874 (w), 1516 (w), 1459 (w), 1385 (w), 1365 (w), 1031 (m), 905 (w), 815 (m) cm^{-1}. MS-EI *m/z* (rel intensity, 40 eV): 205 $[M-H]^+$ (10), 191 (31), 163 (15), 145 (66), 131 (100), 105 (80), 91 (69). HRMS-EI: calcd for $C_{13}H_{18}O_2$ $[M-H]^+$ 205.1226, found 205.1229. CSP-HPLC separation: Chiracel OJ column, *n*-hexane/*i*-PrOH 90:10, 1.0 mL/min, 23 °C, λ = 210 nm); t_R (major) = 8.59 min, t_R (minor) = 13.27 min.

4.18. (+)-(2*S*,3*S*)-*trans*-3-Cyclohexyl-3-phenyloxiranemethanol, epoxide of S10[37]

Purification—preparative TLC on silica gel, eluent *n*-hexane/EtOAc/Et_3N 60:40:1. R_f = 0.53 (silica gel, *n*-hexane/EtOAc 3:2). White solid, mp = 153.8–155 °C (recrystallized from *n*-hexane/*i*-PrOH, 96% ee). $[\alpha]_D^{25} = +42.0$ (*c* 1.0, $CHCl_3$, 96% ee). [lit.[37] $[\alpha]_D^{20} = +42.0$ (*c* 1.0, $CHCl_3$) for 97% epoxide with absolute configuration (2*S*,3*S*)). ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.83–1.03 (m, 2H), 1.07–1.30 (m, 3H), 1.49 (tt, 1H, CH of Cy ring, *J* = 12.3 Hz, 3.1 Hz), 1.55–1.63 (m, 1H), 1.65–1.79 (m, 3H), 1.84–1.93 (m, 1H), 2.0 (br m, 1H, OH), 3.17 (dd, 1H, CH–O, *J* = 6.6 Hz, 4.4 Hz), 3.91 (dd, 1H, –C*H*H–OH, *J* = 12.1 Hz, 6.8 Hz), 4.03 (dd, 1H, –CH*H*–OH, *J* = 12.1 Hz, 4.4 Hz), 7.26–7.34 (m, 5H, $C^{ar}H$) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 26.0 (CH_2), 26.1 (CH_2), 26.4 (CH_2), 28.7 (CH_2), 30.1 (CH_2), 42.0 (CH of Cy), 60.8 (CH_2–OH), 64.3 (CH–O), 69.4 (C quat.), 127.6 (CH), 127.7 (CH), 128.0 (CH), 138.9 (C quat.) ppm. IR (neat): 3427 (m), 2928 (m), 2855 (w), 1495 (w), 1460 (w), 1446 (w), 1297 (w), 1279 (w), 1029 (m), 885 (w), 770 (m), 722 (w), 707 (m), 653 (w) cm^{-1}. MS-EI *m/z* (rel intensity, 40 eV): 231 [M-H]$^+$ (36), 187 (17), 131 (100), 105 (79), 91 (89), 55 (41). HRMS-EI: calcd for $C_{15}O_{20}O_2$ $[M]^+$ 232.1446, found 232.1463. CSP-HPLC separation: Chiracel OJ column, *n*-hexane/*i*-PrOH 90:10, 1.0 mL/min, 23 °C, λ = 210 nm); t_R (major) = 6.10 min, t_R (minor) = 11.14 min.

4.19. (+)-*trans*-3-(4-Bromophenyl)-3-cyclohexyloxiranemethanol epoxide of S11

Purification—preparative TLC on silica gel, eluent *n*-hexane/EtOAc/Et_3N 60:40:1. R_f = 0.4 (silica gel, *n*-hexane/EtOAc 3:2). Pale yellow tar. $[\alpha]_D^{25} = +26.1$ (*c* 1.0, $CHCl_3$) 79% *ee*. ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.75–1.38 (m, 6H), 1.47 (tt, 1H, CH of Cy, *J* = 12.3 Hz, 2.8 Hz), 1.53–1.93 (m, 7H), 3.11 (dd, 1H, CH–O, *J* = 6.6 Hz, 4.7 Hz), 3.8–4.08 (m, 2H, –CH_2–OH), 7.17 (d, 2H, $C^{ar}H$, *J* = 8.2 Hz), 7.44 (d, 2H, $C^{ar}H$, *J* = 8.5 Hz) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 26.0 (CH_2), 26.1 (CH_2), 26.4 (CH_2), 28.6 (CH_2), 30.1 (CH_2), 41.8 (CH of Cy), 60.6 (CH_2–OH), 64.2 (CH–O), 68.8 (C quat.), 121.7 (C quat.), 129.7 (CH), 130.9 (CH), 137.9 (C quat.) ppm. IR (neat): 3405 (br, w), 2927 (m), 2853 (m), 1592 (w), 1490 (w),

1451 (w), 1027 (w), 1011 (m), 884 (w), 825 (m) cm^{-1}. MS-EI *m/z* (rel intensity): 312 $[M]^+$ (13), 310 $[M]^+$ (13), 253 (28), 251 (33), 211 (76), 209 (70), 169 (97), 141 (36), 129 (72), 81 (96), 55 (100). HRMS-EI: calcd for $C_{15}H_{19}O_2Br$ $[M]^+$ 310.0568, found 310.0552. CSP-HPLC separation: Chiracel OJ-H column, *n*-hexane/*i*-PrOH 95:5, 1.0 mL/min, 23 °C, λ = 210 nm); t_R (major) = 7.76 min, t_R (minor) = 10.75 min.

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