Photooxygenation of Olefins in the Presence of Titanium(IV) Catalyst: A Convenient "One-Pot" Synthesis of Epoxy Alcohols

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Abstract: The photooxygenation of olefins in the presence of transition-metal complexes derived from Ti, V, and Mo constitutes a convenient and efficient "one-pot" synthesis of epoxy alcohols. First, singlet oxygen transforms the olefin via an ene reaction into its allylic hydroperoxide, and subsequently, the allylic hydroperoxide is converted via transition-metal-catalyzed oxygen transfer into its epoxy alcohol. From the point of view of the olefinic substrate, the oxygen transfer is intermolecular, one allylic hydroperoxide molecule serving as oxygen donor and the other as oxygen acceptor in the form of its allylic alcohol, the transition metal playing the role of a template for both as in the Sharpless epoxidation. Unlike the latter process, the hydroperoxide donor and the allylic alcohol acceptor are generated in situ and continually consumed via a novel oxygen-transfer chain sequence. The chain reaction is initiated by transition-metal-catalyzed reduction of the allylic hydroperoxide into its allylic alcohol, presumably involving a complex redox process. Consequently, the advantages of the present synthetic method over classical epoxidation procedures (including the Sharpless reaction) is that the peroxidic oxygen donor is generated in situ, does not accumulate, and serves as source for the allylic alcohol. Like the Sharpless epoxidation, the epoxy alcohols are obtained in good chemical yields and in high diastereomeric ratios (dr). The prerequisite is that the olefin must exhibit ene reactivity with singlet oxygen. By use of this "one-pot" oxygen functionalization method, a number of acyclic alkenes could be converted into their epoxy alcohols, including *trans*-2-butene (**1**), *trans*-2,5-dimethyl-3-hexene (**2**), 2,3,3-trimethyl-1-butene (**3**), 2-methyl-2-butene (**7**), α,α-dimethylstilbene (**8**), and ethyl tiglate (**9**), as cyclic and bicyclic olefins served as cyclohexene (**11**), α-pinene (**12**), β-pinene (**13**), and $\Delta^{9,10}$-octalin (**14**). With diethyl tartrate as chiral auxiliary, the 2,3,3-trimethyl-1-butene (**3**) was transformed into its optical active epoxy alcohol in respectable enantiomeric excess (ee 72%). Side reactions figured reduction of the allylic hydroperoxides to their allylic alcohols or oxidation to their enones. Characterization of the epoxy alcohols rests on chemical correlations and spectral assignments.

One of the most valuable recent organic reactions for preparative purposes is the Sharpless epoxidation[2] of allylic alcohols, in which epoxy alcohols are produced diastereoselectively and in the presence of chiral auxiliaries in high enantioselectivity (eq 1).

(1)

Few transformations can rival this synthetic conquest, as witnessed by the abundant use of the now conveniently accessible epoxy alcohols of defined configuration as synthetic building blocks especially in the synthesis of highly functionalized natural products.[3] Of the numerous methods available for the preparation of allylic alcohols, the ene reaction of olefins with singlet oxygen ($^1O_2$) figures as one of the attractive routes, since reduction of the resulting allylic hydroperoxides is usually unproblematic (eq 2).[4] As it is evident in eq 2, in the conversion of the olefin into

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the epoxy alcohol, an oxygen atom is removed from the allylic hydroperoxide by reduction, to be reintroduced in the resulting allylic alcohol by epoxidation with an external oxygen donor. A more efficient synthetic pathway would be short cutting that sequence by directly converting the allylic hydroperoxide into the epoxy alcohol; better yet would be the direct oxygen functionalization of the olefin. The feasibility of transforming allylic hydroperoxides into epoxy alcohols was demonstrated by using $VO(acac)_2$ as catalyst,[5] while the direct oxygen functionalization of olefins $CpV(CO)_4$[6a] (where Cp stands for cyclopentadienyl) or $VO(acac)_2$/AIBN[6b] [where AIBN stands for α,α-azobis(isobutyronitrile)] gave a modest yield of the desired epoxy alcohol. While our work[7] was in progress, we became aware of a patent[8]

Table I. Photooxygenation of Acyclic Olefins in the Presence of Titanium Tetraisopropoxide[a]

	substrate				epoxy alcohols		
	R^1	R^2	R^3	R^4		$R^*,S^*:R^*,R^{*\,b}$	yield, %[c]
1	H	Me	H	H	**1a**	47:53	68
2	H	*i*-Pr	H	Me	**2a**	90:10	75
3	H	H	*t*-Bu	H	**3a**		87
4	Me	H	Me	H	**4a**	83:17	32[d]
5	Et	H	Me	H	**5a**	79:21	28[d]
6	*t*-Bu	H	Me	H	**6a**	95:5	84
7	Me	Me	Me	H	**7a**		84
8	Ph	Me	Ph	H	**8a**	55:45	84
9	Me	H	CO_2Et	H	**9a**	90:10	57

[a] All reactions were run in CH_2Cl_2 at −20 °C to 0 °C; tetraphenylporphine (TPP, ca. 5×10^{-4} M) as sensitizer; complete conversion of olefin. [b] Diastereomeric ratios (dr) determined by ^1H NMR (200/400 MHz); error ca. 5%; structures are given in eq 3. [c] Yields are reported for isolated, purified products. [d] The regioisomeric epoxy alcohols were formed in 39% and 32% yields starting from olefins **4** and **5**, respectively (cf. Experimental Section).

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(1) Undergraduate Research Participant, University of Würzburg, Spring 1986.
(2) Finn, G. M.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, FL, 1985; Vol. V, 247.
(3) (a) Pfenninger, A. *Synthesis* **1986**, 89. (b) Rossiter, B. E. in ref 2, p 193.
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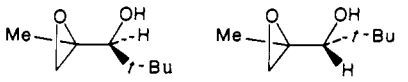
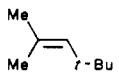
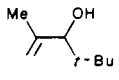
Table II. Yields[a] and Diastereomeric Ratios (dr)[b] in the Preparation of Epoxy Alcohol **6a** Using Various Oxidants



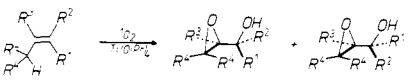
substrate	oxidant	yield, %[c]	(*R**,*S**)-**6a**:(*R**,*R**)-**6a** (erythro) (threo)
 **6**	$^1O_2$/Ti(O-*i*-Pr)$_4$	84	95:5
	$^1O_2$/VO(acac)$_2$	91	99:1
	$^1O_2$/MoO$_2$(acac)$_2$	53	88:12
 **6c**	*m*-CPBA	48	56:44

[a] Isolated yields after distillation except entry 3: relative yields (normalized to 100%) determined by ^{13}C NMR (100 MHz). [b] Determined by ^1H NMR (400 MHz); error ca. 5%. [c] All reactions were run in CH_2Cl_2 at 0 °C; complete conversion of starting material, mass balance >90%.

which illustrates that photooxygenation of olefins in the presence of titanium or vanadium catalysts provides an effective one-pot preparation of the synthetically precious epoxy alcohols. In this full report we demonstrate that this synthetic methodology is general, covering di-, tri-, and tetrasubstituted acyclic olefins, as well as monocyclic and bicyclic ones. With appropriate substrates, this functionalization proceeds diastereo- and enantioselectively.

Results

Product Studies. The results for the acyclic substrates (eq 3) are given in Table I. For all cases, except **8** and **9**, the epoxy



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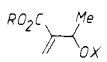
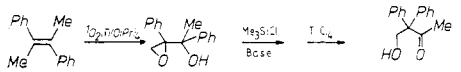
alcohols were the only oxygenated products, as confirmed by 400-MHz ^1H NMR directly on the crude reaction mixture. In the reaction of dimethylstilbene (**8**) and ethyl tiglate (**9**), the allylic alcohols **8c** and **9c** were obtained in 5% and 25% yields, respec-

8c



9b: R = Me, Et; X = OH
c: R = Me, Et; X = H

tively, as confirmed by spectral comparison with the authentic materials.[9,10] Another side product of the photooxygenation of **8** in the presence of Ti(O-*i*-Pr)$_4$ was the hydroxy ketone **8e**, formed in low yield (ca. 5%) by Ti(O-*i*-Pr)$_4$-catalyzed ring opening of the epoxy alcohol **8a** (eq 4). Indeed, the epoxy alcohol **8a**[11] could



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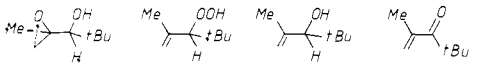
8 **8a** **8e**

be quantitatively converted into **8e** by silylation with subsequent rearrangement with $TiCl_4$.[12]

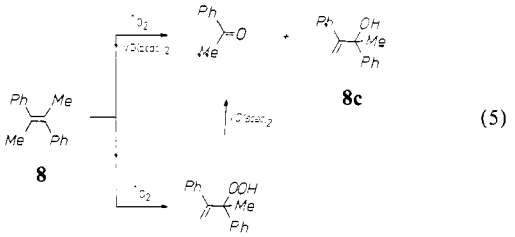
Olefin **6** was chosen as a model substrate to examine the influence of the catalyst on the product composition, especially the diastereoselectivity. The results are given in Table II. Clearly, titanium and vanadium are superior to molybdenum. The latter gave rise to a complex product mixture, containing only 53% of the desired epoxy alcohol **6a** in lower stereoselectivity (88:12),



6a **6b** **6c** **6d**

21% of the allylic hydroperoxide **6b**,[13a] 15% allylic alcohol **6c**,[13b] and 11% enone **6d**.[13c] The structures were assigned by spectral matching with authentic samples. For comparison, the *m*-CPBA epoxidation of the allylic alcohols **6c** was conducted, which led to the two diastereomeric epoxy alcohols **6a** in a 56:44 ratio (Table II).

In view of the excellent results with VO(acac)$_2$ on the olefin **6** (Table II), we also submitted the stilbene **8** to photooxygenation in the presence of this catalyst. However, the ^1H NMR of the crude product mixture showed that instead of the desired epoxy alcohol **8a**, acetophenone and allylic alcohol **8c** had been formed in a 67:33 ratio (eq 5). A control experiment confirmed that the



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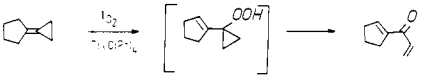
8 **8c** **8b**

allylic hydroperoxide **8b** decomposed into acetophenone (Hock cleavage) in the presence of the vanadium catalyst. This Hock cleavage could be completely suppressed by using Ti(O-*i*-Pr)$_4$ as catalyst (Table I). However, even with the weaker Lewis acid, the cyclopropylidene substrate **10**[14a] gave the dienone **10d**[14b] as rearrangement product of the intermediary allylic hydroperoxide **10b**[14b] in 6% yield (eq 6). Difficulties in using VO(acac)$_2$ were



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10 **10b** **10d**

also encountered with methyl tiglate **9** (R = Me) as substrate, for which the intermediary allylic hydroperoxide **9b**[15] was exclusively reduced to the allylic alcohol **9c** (R = Me). These problems could be largely circumvented by employing Ti(O-*i*-Pr)$_4$ as catalyst with these labile substrates (Table I).

An additional complication was observed in using VO(acac)$_2$ as well as MoO$_2$(acac)$_2$. These catalysts absorb in the visible region in which the photosensitized formation of $^1O_2$ is conducted. Thus, the concentration of the catalyst is crucial, a suitable concentration range being between 10^{-3} and 10^{-2} M for VO(acac)$_2$. Lower concentrations result in incomplete conversion, while at higher concentrations no reaction occurred, despite the fact that sufficient sensitizer was employed. Consequently, Ti(O-*i*-Pr)$_4$ catalyst is the choice for these one-pot oxygen functionalization of acyclic olefins into their corresponding epoxy alcohols (Table I).

The results for the cyclic substrates cyclohexene (**11**), α-pinene (**12**), β-pinene (**13**), and $\Delta^{9,10}$-octalin (**14**) are summarized in Table III. Although not as clean as most of the acyclic systems (Table I), this direct oxygen functionalization is also of preparative value

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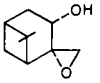
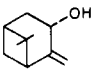
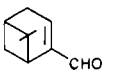
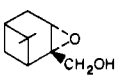
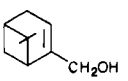
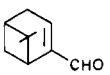
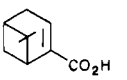
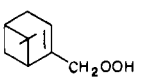
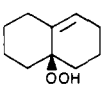
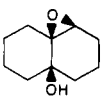
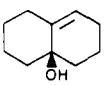
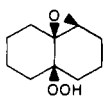
Table III. Photooxygenation[a] of Cyclic and Bicyclic Olefins in the Presence of Titanium and Vanadium Catalysts

substrate	catalyst (mol %)	relative yields, %[b] epoxy alcohol	allylic alcohol	enone	other	
						
11		**11a**[c]	**11c**	**11d**	**11e**	
	$Ti(O\text{-}i\text{-}Pr)_4$ (100)	60	7	4	29	
	$Ti(O\text{-}i\text{-}Pr)_4$ (16)	91	7	3		
	$VO(acac)_2$ (5)	51	29	18		
						
12		**12a**	**12c**	**12d**	**12e**	**13d**
	$Ti(O\text{-}i\text{-}Pr)_4$ (100)	0	37	23	37	3
	$Ti(O\text{-}i\text{-}Pr)_4$ (16)	81	9	5		2
	$VO(acac)_2$ (2)	46	28	8	10	8
						
13		**13a**	**13c**	**13d**	**13e**	**13b**
	$Ti(O\text{-}i\text{-}Pr)_4$ (100)			72	28	
	$Ti(O\text{-}t\text{-}Bu)_4$ (10)	23	16	18		43
	$VO(acac)_2$ (1)	67	10	18		5
						
14b		*cis*-**14a**	**14c**	*cis*-**14e**		
	$Ti(O\text{-}i\text{-}Pr)_4$ (100)	87	7	6		

[a] Run in CH_2Cl_2; TPP (ca. 5×10^{-4} M) as sensitizer; conversion 100%, mass balance 85–95%. [b] Determined by ^1H NMR (400 MHz), error ±2%; all products are known compounds and authentic samples were available for spectral identification. [c] Cis/trans ratio determined by capillary GC; 98:2 for Ti and >98:2 for V.

for such olefins. The choice of the transition-metal catalyst and its concentration, as Table III reveals, was most critical in optimizing the desired epoxy alcohol product. Thus, catalytic amounts (10–15 mol %) of $Ti(O\text{-}i\text{-}Pr)_4$ proved advantageous for cyclohexene (**11**) and α-pinene (**12**), but surprisingly, $VO(acac)_2$ gave the best results for β-pinene (**13**). For the octalin **14**, only $Ti(O\text{-}i\text{-}Pr)_4$ was tried, which gave good results.

The use of catalytic quantities of $Ti(O\text{-}i\text{-}Pr)_4$ completely eliminated direct epoxidation of cyclohexene (**11**) and α-pinene (**12**) to their respective oxides **11e** and **12e** (Table III); but it also substantially suppressed the formation of the allylic alcohols **11c** and **12c**, respectively, as well as the enones **11d** and **12d**. These allylic alcohols are derived from the intermediate allylic hydroperoxides **11b** and **12b** via reduction, while the enones result from rearrangement of the respective epoxy alcohols, as confirmed by control experiments. Thus, shortcomings are but minor, considering that in such a one-pot process cheap starting materials such as cyclohexene (**11**) and α-pinene (**12**) are converted in high yields to the valuable epoxy alcohols **11a**[16a] and **12a**[16b] diastereoselectively (Table III).

The functionalization of β-pinene (**13**) was not quite as satisfactory. Even catalytic amounts of $Ti(O\text{-}t\text{-}Bu)_4$ hardly presented the desired improvement (Table III). With this reagent, large quantities of the allylic hydroperoxide **13b**[17] accumulated. However, the use of $VO(acac)_2$ led in good yield (67%) to the diastereomerically pure epoxy alcohol **13a**.[16c]

In the case of $\Delta^{9,10}$-octalin **14**, instead of the one-pot procedure, it proved advantageous to run the photooxygenation and the oxygen transfer separately. Thus, treatment of the allylic hydroperoxide **14b**[18b] (derived from the ene reaction of **14** with $^1O_2$) with $Ti(O\text{-}i\text{-}Pr)_4$ gave a high yield (82%) of the diastereomerically pure epoxy alcohol *cis*-**14a**, together with ca. 6% each of the allylic alcohol **14c**[18] (reduction of the allylic hydroperoxide **14b**) and the epoxy hydroperoxide *cis*-**14e** (oxygen transfer to the hydroperoxide **14b**). That no epoxy alcohol *trans*-**14a** and epoxy hydroperoxide *trans*-**14e** were formed in the $Ti(O\text{-}i\text{-}Pr)_4$-catalyzed functionalization was certified by authentic samples, prepared via epoxidation of the allylic alcohol **14c** and the allylic hydroperoxide **14b** with *m*-CPBA, respectively. The allylic alcohol **14c** gave in 83% yield a 86:14 mixture of *cis*- and *trans*-**14a**, while the allylic hydroperoxide **14b** led in 81% yield to a 90:10 mixture of *cis*- and *trans*-**14e**. The fact that the epoxy hydroperoxide *cis*-**14e** accumulated in the $Ti(O\text{-}i\text{-}Pr)_4$ functionalization has important mechanistic implications, as shall become apparent in the Discussion.

Diastereomeric Assignments. Except for the stereochemistry of the diastereomers, the characterization of the epoxy alcohols was straightforward, resting mainly on spectral data (IR, ^1H and ^{13}C NMR, MS) and comparison with authentic materials, when readily available. For all new compounds, satisfactory elemental analyses were provided (cf. Experimental Section).

More cumbersome was the configurational assignment of the diastereomers. Besides spectral data (^1H and ^{13}C NMR), extensive chemical correlations were necessary. The diastereomeric ratios (dr) were determined by quantitative NMR, utilizing appropriate characteristic ^1H and ^{13}C chemical shifts. The more important features of the structural assignments for the individual cases follow below.

Fortunately, the epoxy alcohols (*R**,*R**)- and (*R**,*S**)-**1a** derived from *trans*-2-butene (**1**) are reported,[19] which simplified

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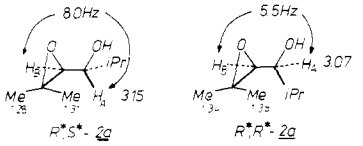
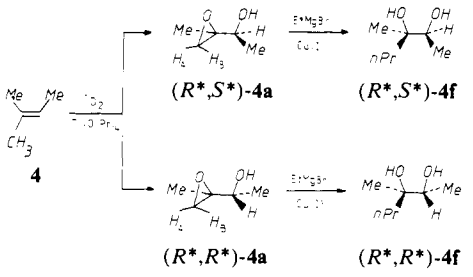
the determination of their configurations. An authentic R^*,-$R^*/R^*,S^*$ mixture was prepared by *m*-CPBA epoxidation of the allylic alcohol **1c**, and the spectral data coincided well with those obtained in the $^1O_2$ functionalization of *trans*-2-butene (**1**).

For the $R^*,S^*/R^*,R^*$ epoxy alcohols **2a** derived from *trans*-2,5-dimethyl-3-hexene (**2**), the stereochemistry was assessed by means of ^{1}H NMR. Use was made of the observation[20] that for



such diastereomeric epoxy alcohols the H_A proton of the R^*,S^* isomer absorbs at lower field than the corresponding proton of the R^*,R^* isomer; furthermore, the J_{AB} coupling is larger for the R^*,S^* isomer. The same ^{1}H NMR spectral characteristics also obtained in the diastereomeric epoxy alcohols (R^*,S^*)- and (R^*,R^*)-**4a**.

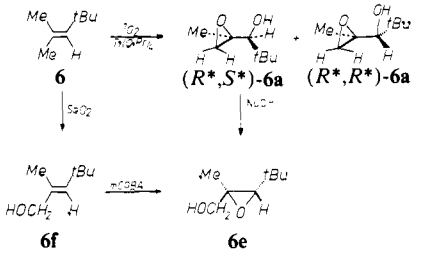
In addition to these spectral data, a chemical correlation with the diastereomeric *vic*-diols **4f** was described by Sharpless et al.,[19] as illustrated in eq 7. The spectral data of the latter matched



(7)

perfectly those reported for these diols. Furthermore the A branch of the AB pattern for the R^*,S^* isomer is displaced to higher field than that of the R^*,R^* isomer and the B branch to lower field. This ^{1}H NMR criterion was utilized to define the stereochemistry of the diastereomeric epoxy alcohols **5a**, derived from 2-methyl-2-pentene (**5**) in its $^1O_2/Ti(O\text{-}i\text{-}Pr)_4$ functionalization.

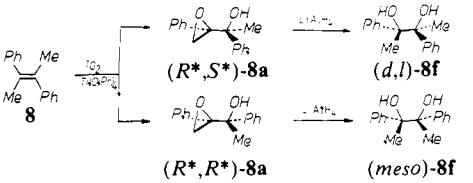
Besides such spectral criteria, for the epoxy alcohols (R^*,S^*)- and (R^*,R^*)-**6a**, resulting from 2,4,4-trimethyl-2-pentene (**6**), the chemical correlation shown in eq 8 was performed. With the help



(8)

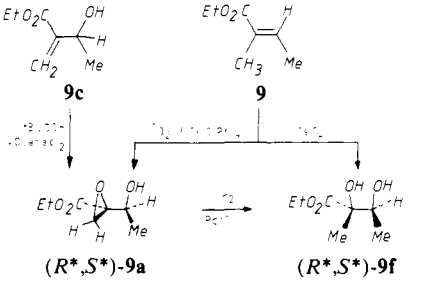
of the Payne rearrangement,[21] the major isomer (R^*,S^*)-**6a** was converted to the isomeric epoxy alcohol **6e**. The latter was prepared via the authentic sequence **6** → **6f** → **6e** by oxidation with SeO_2[22] and subsequent epoxidation with *m*-CPBA. To be certain of the reported[23] *E* configuration for the allylic alcohol **6f**, a differential ^{1}H NMR nuclear Overhauser enhancement (NOE) experiment was conducted. Saturation of the hydroxymethyl protons at 3.92 ppm resulted in a strong (8.3%) enhancement of the olefinic proton at 5.42 ppm and an appreciable (1.7%) enhancement of the geminal hydroxy protons, and vice versa. However, saturation of the methyl protons at 1.77 ppm did not affect the olefinic proton. This unequivocally fixes the *E* configuration in the allylic alcohol **6f** and in the epoxy alcohol **6e**. The latter was identical in its physical and spectral properties with those of the Payne rearrangement product of the R^*,S^* isomer **6a**.

The chemical correlations for the configurational assignment of the R^*,S^* and R^*,R^* epoxy alcohols **8a**, obtained from the stilbene **8**, are displayed in eq 9. Thus, $LiAlH_4$ reduction of the



(9)

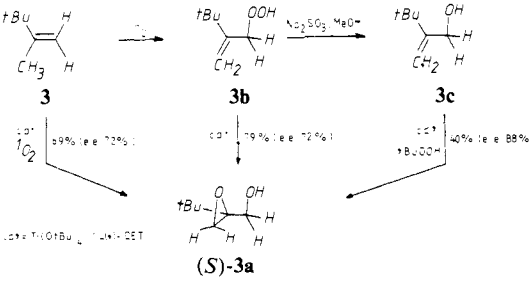
55:45 diastereomeric mixture of epoxy alcohols **8a** gave the known[24] *vic*-diols and *d,l*- and *meso*-**8f**. The spectral data matched those reported.[24] Finally, the stereochemistry of the epoxy alcohols (R^*,S^*)- and (R^*,R^*)-**9a** obtained from ethyl tiglate (**9**; R = Et), was elucidated according to the correlation shown in eq 10. The



(10)

major diastereomer (R^*,S^*)-**9a**, isolated in pure form from the $^1O_2/Ti(O\text{-}i\text{-}Pr)_4$ functionalization of ethyl tiglate (**9**) by chromatography, was converted to the *vic*-diol (R^*,S^*)-**9f** by catalytic hydrogenation.[25] It was identical in its physical and spectral properties with that obtained directly by OsO_4 *vic* dihydroxylation of ethyl tiglate (**9**). Furthermore, the allylic alcohol **9c**[10] led to the same major diastereomer (R^*,S^*)-**9a** on Sharples epoxidation with $VO(acac)_2$ and *t*-BuOOH.

Enantioselectivity Studies. Analogous to the Sharpless epoxidation,[2] diethyl tartrate (L-(+)-DET) was used as chiral auxiliary. For this purpose we chose the olefins **3** and **7**. With $Ti(O\text{-}i\text{-}Pr)_4$ as catalyst, the former gave in low (ca. 10%) chemical yield the epoxy alcohol **3a**, which possessed an enantiomeric excess (ee) of only 26%. The complex reaction mixture was evidently the result of $Ti(O\text{-}i\text{-}Pr)_4$-catalyzed ring opening of the epoxide product.[26] This problem could be in part avoided by employing $Ti(O\text{-}t\text{-}Bu)_4$ as catalyst instead of $Ti(O\text{-}i\text{-}Pr)_4$. The epoxy alcohol (*S*)-**3a** was obtained in good yield (69%) with ee of 72% (eq 11).



(11)

An authentic sample of (*S*)-**3a** was prepared by Sharpless epoxidation[27] of the allylic alcohol **3c**, which in turn was made by reduction of the allylic hydroperoxide **3b** formed in the photooxygenation of **3**. The same enantiomeric excess (ee 72%) but higher chemical yield was obtained in the treatment of the allylic hydroperoxide **3b** with $Ti(O\text{-}t\text{-}Bu)_4$/L-(+)-DET. In all of these

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runs the enantiomeric excess was determined by quantitative 400-MHz ^{1}H NMR studies on the corresponding methyl (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetate (MTPA ester)[28] and the Eu(tfc)$_3$-shifted epoxy acetate.

The asymmetric epoxidation of 2,3-dimethyl-2-butene (**7**) with $^1O_2$/Ti(O-*i*-Pr)$_4$/L-(+)-DET gave poor results. After 6 days a 60:30:10 mixture of the epoxy alcohol **7a** (ee <5%), allylic alcohol **7c**, and allylic hydroperoxide **7b** was observed. The poor results, especially the low enantioselectivity, is not surprising for this substrate, because attempted Sharpless epoxidation of the corresponding allylic alcohol **7c** stopped at ca. 20% conversion.

Mechanistic Studies. A number of control experiments were performed to understand the mechanistic course of this novel hydroxy epoxidation reaction. The main interest, unquestionably, was to elucidate whether the oxygen atom was transferred intramolecularly (within the same allylic hydroperoxide molecule) or intermolecularly (between two different allylic hydroperoxide molecules). With more complex metal catalysts, Lyons[6a] also demonstrated intermolecularity.

First of all, which is particularly important for the one-pot procedure, it was established that singlet oxygen is not being quenched by the Ti(IV) catalyst. Thus, the β-values[29] ranged between 0.0058 and 0.0066 and the rate constants k_r[29] between 1.7×10^6 and 1.4×10^6 M^{-1} s^{-1} when [Ti(O-*i*-Pr)$_4$] was varied from 0 to 100 mol%, with 2-methyl-2-butene (**4**) as olefinic substrate; the first values refer to no Ti(IV) catalyst, the second to stoichiometric amounts, respectively. This fact enables use of Ti(O-*i*-Pr)$_4$ directly in the photooxygenation of the alkene and constitutes the success of the one-pot process.

Furthermore, it was shown in this experiment that the regioisomeric epoxy alcohols **4a** and **4a′** were formed in 54:46 ratio over the entire [Ti(O-*i*-Pr)$_4$] range. This result also reveals that the regioselectivity in the formation of the allylic hydroperoxides **4b** and **4b′** is not affected by the Ti(IV) catalyst during the photooxygenation of olefin **4**. Thus, the Ti(O-*i*-Pr)$_4$ catalyst appears not to complex in an appreciable extent to the olefinic substrate.

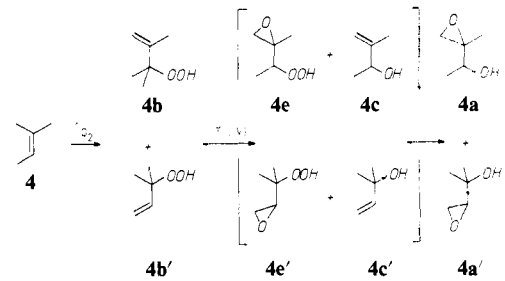
A pronounced induction period was observed when the oxygen transfer of allylic hydroperoxide **7b** with Ti(O-*i*-Pr)$_4$ was monitored by 400-MHz ^{1}H NMR at ambient temperatures directly in the spectrometer. This latent period was variable in time (10–30 min), depending on the reaction conditions. For example, larger amounts of catalyst and higher temperature diminished the induction period; but once the oxygen transfer was initiated, it preceeded vigorously until complete consumption of the allylic hydroperoxide. Most significant, by addition of a few mole percent of allylic alcohol **7c**, the induction period could be completely eliminated and oxygen atom transfer took place essentially on mixing.

In this context it is important to recall (cf. Tables I and III) that allylic alcohols accumulate as final products. For example, a most pronounced case constitutes the tiglic ester **9** (R = Et), which afforded as much as 25% allylic alcohol **9c**. Thus, for less reactive substrates, as is the case with tiglic ester, Ti(O-*i*-Pr)$_4$ causes reduction of the allylic hydroperoxide **9b** to the allylic alcohol **9c** in competition with oxygen transfer, affording the desired epoxy alcohol **9a**. In fact, for such cases as much as 100 mol % Ti(IV) catalyst had to be used to drive the oxygen transfer to completion. Presumably the catalyst was being consumed in these more sluggish epoxidations. Indeed, significant amounts of acetone could be observed when the oxygen-transfer progress of the hydroperoxides **4b** and **4b′** was monitored by ^{1}H NMR directly in the 400-MHz spectrometer. Thus, the induction period derives from the necessity of generating in situ some allylic alcohol from the allylic hydroperoxide by a complex redox process involving the Ti(O-*i*-Pr)$_4$ catalyst, the former being reduced and the latter suffering oxidation of the isopropoxy ligand to acetone.

Furthermore, of relevance for the induction period is the isolation of the epoxy hydroperoxide *cis*-**14e** in the Ti(IV)-catalyzed oxygen transfer of the allylic hydroperoxide **14b** (Table III). Control experiments revealed that *cis*-**14e** also served as oxygen atom donor, converting the allylic alcohol **14c** to the epoxy alcohol *cis*-**14a** under the action of Ti(O-*i*-Pr)$_4$ as catalyst. However, in the absence of a suitable oxygen atom acceptor such as allylic alcohol **14c**, Ti(O-*i*-Pr)$_4$ leads to reduction of *cis*-**14e** to the epoxy alcohol *cis*-**14a**, presumably under degradation of the isopropoxy ligand to acetone. That more complex redox processes are also involved is indicated by the fact that epoxy hydroperoxide **7e** afforded epoxy alcohol **7a** when treated with Ti(O-*t*-Bu)$_4$ as shown in eq 12. In this case, more complex redox chemistry, presumably of the free-radical type,[30] appears to play a role.

7e **7a** (12)

A most informative experiment, which convincingly uncovers the complexity of the present oxygen-transfer process, concerns direct ^{1}H NMR monitoring of the Ti(O-*i*-Pr)$_4$ reaction with the allylic hydroperoxides **4b** and **4b′** derived from 2-methyl-2-butene (eq 13). Authentic samples of the final products, i.e., the epoxy



4b **4e** **4c** **4a**

4 (13)

4b′ **4e′** **4c′** **4a′**

alcohols **4a** and **4a′**, the allylic alcohols **4c** and **4c′**, and the epoxy hydroperoxides **4e** and **4e′**, were on hand to allow observation of each component of this complex reaction mixture as a function of amount of the Ti(O-*i*-Pr)$_4$ during the transcourse of the oxygen transfer. The substrate–Ti(O-*i*-Pr)$_4$ profiles are displayed in Figure 1. The final product compositions at a particular concentration of Ti(O-*i*-Pr)$_4$ are shown after completion of the oxygen transfer. For these particular allylic alcohols **4c** and **4c′**, the oxygen transfer is sufficiently slow so that the Ti(O-*i*-Pr)$_4$ is destroyed via complex redox processes as already pointed out above for the tiglate case.

It is clearly evident that the allylic hydroperoxide **4b** disappears faster than its regioisomer **4b′**, showing the former to be a more efficient oxygen atom donor. Furthermore, the intermediary allylic alcohol **4c** accumulates to a smaller extent than its regioisomer **4c′**, implying that the latter is a less reactive oxygen atom acceptor. It is, therefore, of no surprise that the epoxy alcohol **4a** appears faster than its regioisomer **4a′** or that the intermediate epoxy hydroperoxide **4e** accumulates to a lesser degree than **4e′**.

The intermolecularity of the oxygen-transfer process, while implied by the above results, could be substantiated by adding the more reactive allylic alcohol 3-methyl-2-buten-1-ol to a mixture of allylic hydroperoxide **7b** and Ti(O-*i*-Pr)$_4$. As shown in eq 14,

7b **7c** (14)

the 2,3-epoxy-3-methyl-1-butanol is formed practically exclusively as oxygen-transfer product. Unquestionably, the allylic hydroperoxide **7b** served as oxygen atom donor and the allylic alcohol as acceptor in this intermolecular oxygen transfer. Quite analogously, addition of the external allylic alcohol **4c** to a mixture of hydroperoxide **7b** and Ti(O-*i*-Pr)$_4$ led to the epoxy alcohols **7a** and **4a′** in 70:30 ratio. In the latter case, the less reactive monosubstituted allylic alcohol **4c′** competed only partially with the

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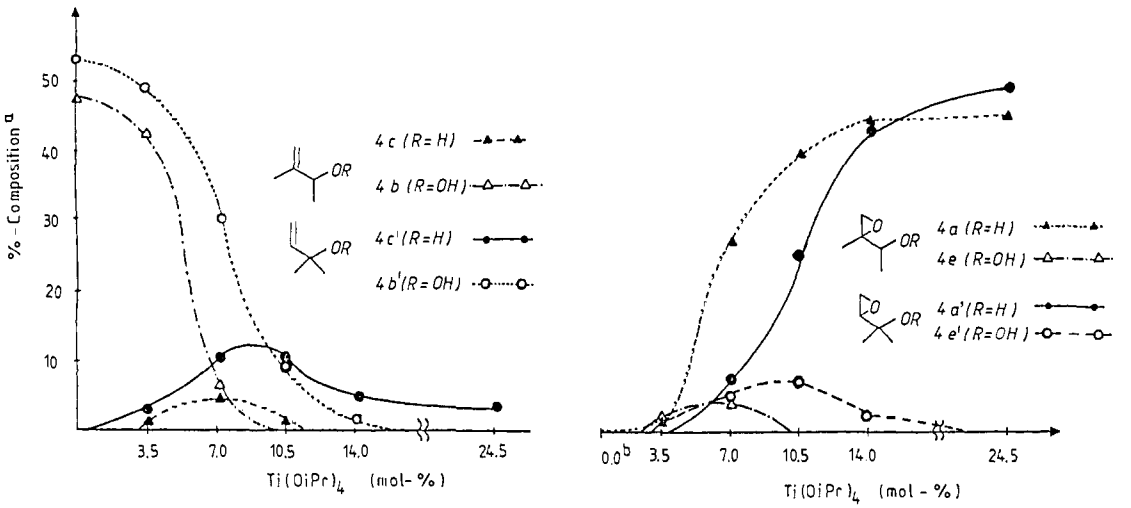


Figure 1. Substrate–Ti(O-*i*-Pr)$_4$ profiles for the oxygen transfer of a 47:53 mixture of allylic hydroperoxides **4b** and **4b'**, catalyzed by Ti(O-*i*-Pr)$_4$ in $CDCl_3$ at 30 °C (monitored by 400-MHz ^1H NMR). (a) The sum of all eight components **4b**, **4b'**, **4c**, **4c'**, **4e**, and **4e'** corresponds to 100% at any particular mole percent Ti(O-*i*-Pr)$_4$; (b) For convenience these sets of products are presented separately, i.e., the two origin points (0.0) should be superimposed.

more reactive allylic alcohol **7c** that is being released in situ from the allylic hydroperoxide **7b** during oxygen atom transfer.

Discussion

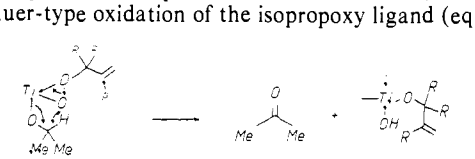
The above results unmistakingly uncover the novel transformation of allylic hydroperoxides into epoxy alcohols under the action of titanium tetraisopropoxide (eq 2) as a masked Sharpless epoxidation of allylic alcohols (eq 1). In other words, during a pronounced induction period a small amount of the allylic hydroperoxide is reduced to the allylic alcohol. The Ti(IV) catalyst serves as template, binding simultaneously the released allylic alcohol (oxygen atom acceptor) and allylic hydroperoxide (oxygen atom donor), the latter being activated by coordination to titanium for oxygen transfer. Thus, the actual oxygen transfer is intramolecular (similar conclusions were reached by Lyons[6a] for more complex metal catalysts) from the point of view of the titanium catalyst but intermolecular from the point of view of the allylic hydroperoxide substrate in that the oxygen atom is being transferred between two distinct molecules. In Scheme I the complex sequence of events are summarized for the generalized case. In contrast to the normal Sharpless epoxidation (eq 1), the allylic hydroperoxide serves on one hand as oxygen atom donor (analogous to *tert*-butyl hydroperoxide) and on the other hand as oxygen atom acceptor (after being reduced to its allylic alcohol, the actual substrate in the Sharpless process).

The reduction of the allylic hydroperoxide to its allylic alcohol is the critical step in the mechanism of Scheme I responsible for the induction period. In principle, at least three pathways are feasible, which are characterized by steps k_1 and k_2 (Scheme I). Step k_1 is analogous to the Sharpless epoxidation of homoallylic alcohols by *tert*-butyl hydroperoxide and Ti(O-*i*-Pr)$_4$, except that one of the allylic hydroperoxide molecules plays the role of the homoallylic alcohol (as oxa-substituted heteroanalogue) and the other the *tert*-butyl hydroperoxide (eq 15). It is a notorious fact

(15)

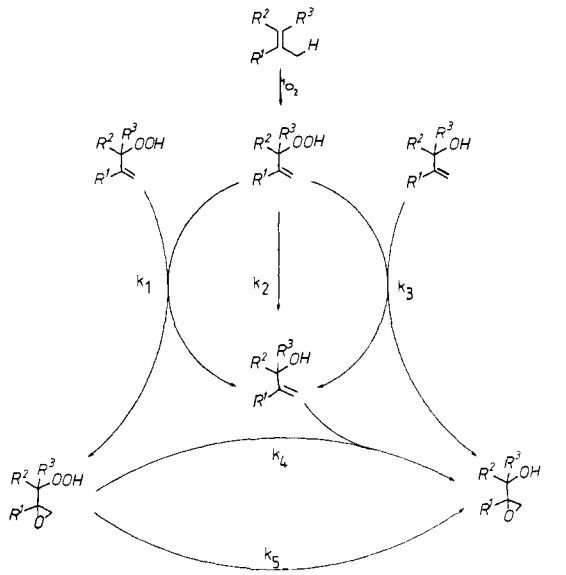
that homoallylic alcohols are poor substrates in the Sharpless reaction, so that the release of the required allylic alcohol should be a slow process and thus an induction period would be expected.

The step k_2 encompasses two alternatives, namely the Oppenauer-type oxidation of the isopropoxy ligand (eq 16) and



(16)

Scheme I



a complex free-radical-type redox process catalyzed by the transition metal (eq 17).[30] As initiation steps, those in eq 18 and,

$$2RO_2H \rightarrow 2ROH + O_2 \quad (17)$$

$$M^{n+} + RO_2H \rightarrow M^{(n-1)+} + RO_2^{\bullet} + H^+$$

$$M^{(n-1)+} + RO_2H \rightarrow M^{n+} + RO^{\bullet} + OH^- \quad (18)$$

$$2RO^{\bullet} + 2RO_2H \rightarrow 2ROH + 2RO_2^{\bullet}$$

$$2RO_2^{\bullet} \rightarrow 2RO^{\bullet} + O_2 \quad (19)$$

as propagation steps, those in eq 19 may serve. For Ti(O-*i*-Pr)$_4$, this sequence of events should be of minor importance in view of its low oxidizing power, i.e., $E° = 0.06$ eV[30] for the half-reaction Ti(IV) + e^- → Ti(III); but for VO(acac)$_2$ ($E° = 1.0$ eV), this is a very likely source of allylic alcohol.

Be this as it may, once the allylic alcohol is released from the allylic hydroperoxide via the reduction steps k_1 and k_2, the major product-forming route is the propagation step k_3. Thereafter the oxygen transfer is analogous to the Sharples epoxidation, so that all conditions that dictate the latter also apply here. By adding the allylic alcohol from the start, the induction period can be bypassed. When the allylic alcohol that is being released in situ is a relatively unreactive substrate, e.g., electronically deactivated as in the case of **9c**, then large quantities (ca. 25%) of it accu-

mulate and up to stoichiometric amounts of $Ti(O\text{-}i\text{-}Pr)_4$ must be utilized to promote oxygen transfer. In special cases, such as the allylic hydroperoxide **14b**, appreciable amounts of epoxy hydroperoxide *cis*-**14e** accumulate via step k_1, presumably due to steric encumbrance.

A revealing experiment, providing convincing evidence for the complex mechanism in Scheme I, is the conversion of the allylic hydroperoxides **4b** and **4b′** to the epoxy alcohols **4a** and **4a′** (eq 13). The substrate–catalyst profiles (Figure 1) show that the possible allylic alcohols **4c** and **4c′** and epoxy hydroperoxides **4e** and **4e′** intervene as intermediate products. Thus, the minor product-forming step k_4 in Scheme I becomes plausible. This step has been independently established by employing epoxy hydroperoxide *cis*-**14e** and showing that it serves as oxygen atom donor for allylic alcohol **14c**, affording the epoxy alcohol *cis*-**14a** under $Ti(O\text{-}i\text{-}Pr)_4$ action. The reduction of epoxy hydroperoxide to epoxy alcohol (step k_5 in Scheme I) is analogous to step k_2 and was illustrated for the epoxy hydroperoxides **7e** and *cis*-**14e**, using $Ti(O\text{-}t\text{-}Bu)_4$ and $Ti(O\text{-}i\text{-}Pr)_4$, respectively.

Now that it is established that mechanistically the transformation of allylic hydroperoxides to epoxy alcohols under the action of $Ti(O\text{-}i\text{-}Pr)_4$ is a "disguised" Sharpless epoxidation (Scheme I), it should not be surprising that the pronounced diastereoselectivity and impressive enantioselectivity of the latter also applies in our case. The results in Table I amply document the diastereoselectivity for acyclic substrates, while allylic hydroperoxide **3b** (eq 11) verifies the high degree of asymmetric induction when diethyl tartrate is employed as chiral auxiliary.

In summary, the salient features of the present oxygen functionalization of olefins via the ene reaction of singlet oxygen, coupled with the $Ti(O\text{-}i\text{-}Pr)_4$-catalyzed epoxidation, seem worthwhile reiterating:

(1) The one-pot hydroxy epoxidation of olefins consists of two steps, namely, photooxygenation with formation of an allylic hydroperoxide and subsequent oxygen transfer to give the epoxy alcohol.

(2) In contrast to autoxidation procedures, the use of singlet oxygen allows fast and complete conversion of the olefins under mild conditions.

(3) Titanium tetraisopropoxylate is the catalyst of choice, since side reactions are minimized and the diastereoselectivity is high.

(4) No external hydroperoxide has to be used in the epoxidation step, and thus in most cases, the epoxy alcohol is the sole product in the reaction mixture and can easily be separated from the Ti(IV) catalyst.

(5) The oxygen transfer is *intermolecular*, i.e., oxygen donor and oxygen acceptor are located in different molecules.

(6) The high diastereoselectivity, however, derives from an *intermolecular* reaction, i.e., oxygen donor and acceptor are coordinated at the *same* metal center.

(7) The allylic alcohol serves as chain carrier, being formed by redox pathways from the allylic hydroperoxide intermediate, by Oppenauer-like oxidation of the isopropoxide ligand, or by transition-metal-catalyzed oxygen transfer between two allylic hydroperoxide molecules.

(8) Epoxy hydroperoxides are formed which serve as oxygen atom donors.

(9) The reaction is applicable to all olefins that undergo ene reaction with singlet oxygen, although olefins with electron-deficient double bonds are poor substrates, cyclic olefins yield appreciable amounts of side products, and tetrasubstituted acyclic olefins show poor diastereoselectivity.

(10) The asymmetric version of the one-pot oxygen functionalization allows the formation of epoxy alcohols in high enantioselectivity.

The advantages outweigh by far the disadvantages, thereby making this oxygen functionalization of olefins a valuable synthetic route for the preparation of epoxy alcohols.

Experimental Section

General Aspects. Melting points are uncorrected and were taken on a Reichert Thermovar Kofler apparatus. Instrumentation was as follows: infrared (IR) spectra, Perkin-Elmer 1420; ^1H NMR spectra, Bruker WM 400 (400 MHz), TMS (δ 0.00) as internal standard; ^{13}C NMR spectra, Bruker AC 200 (50 MHz), $CDCl_3$ (δ 77.0) as internal standard; ^{13}C NMR spectra, Bruker WM 400 (100 MHz), $CDCl_3$ (δ 77.0) as internal standard; mass spectra (MS), Varian MAT CH 7; thin-layer chromatography (TLC), Polygram SIL/G/UV (40 × 80 mm), Machery & Nagel. Combustion analysis were obtained in-house. For the photooxygenation, a 150-W sodium street lamp with tetraphenylporphine (TPP) as sensitizer was used. Stirring was performed magnetically, room temperature was ca. 20 °C, and rotoevaporation was performed at water aspirator pressure (ca. 20 °C at 20 Torr). Reagents and solvents were purchased from standard chemical suppliers and purified to match the reported physical and spectral data.

General Procedure for the Photooxygenation of Olefins in the Presence of Transition-Metal Catalysts [Ti(IV), V(V), Mo(VI)]. Unless otherwise noted, ca. 20 mmol of olefin in CH_2Cl_2 (100 mL) was photooxygenated by passing a slow stream of dry oxygen gas while externally irradiating with a 150-W sodium street lamp (Philips G/28/2 SON) at the appropriate temperature in the presence of catalytic or stoichiometric amounts of $Ti(O\text{-}i\text{-}Pr)_4$, $VO(acac)_2$, or $MoO_2(acac)_2$ and TPP (ca. 5×10^{-4} M) as sensitizer until complete consumption of the olefin and the intermediary hydroperoxide (TLC, KI test). For exact amounts of catalyst, specific temperatures, and photooxygenation times, consult the individual experiment. For titanium-catalyzed reactions, the reaction mixture was diluted with ether (200 mL), and water (1 mL/mmol of Ti used) was added under vigorous stirring. After 20–30 min, the solid matter was removed by filtration over Celite (ca. 10 g), and the filtrate was dried over $MgSO_4$ and rotoevaporated at ca. 20 °C (20 Torr). Final purification was achieved by distillation, chromatography, or recrystallization. The product distribution was determined by 200/400-MHz ^1H NMR spectroscopy immediately after the removal of the catalyst. For vanadium- and molybdenum-catalyzed reactions, the solvent was rotoevaporated [ca. 20 °C (20 Torr)] and the product was directly distilled from the catalyst, or the residue was filtered over silica gel (ca. 10 g) with ether as eluent.

Epoxy alcohols (*R*,R)- and (*R*,S**)-1a**: from 2.24 g (40.0 mmol) of **1** and 2.28 g (8.00 mmol) of $Ti(O\text{-}i\text{-}Pr)_4$, which afforded after photooxygenation at −20 °C for 48 h on distillation 2.39 g (68%) of **1a** as 53:47 *R*,R*/R*,S** mixture: bp 80 °C (20 Torr) [lit.[21] bp 52–55 °C (10 Torr)]. An authentic sample was obtained by *m*-CPBA epoxidation of **1c**.[19]

(*R*,R)-α-Methyloxiranemethanol (1a)**: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.28 (d, J = 6.5 Hz, 3 H, Me), 2.20 (br s, 1 H, OH), 2.71, 2.80, and 2.99 (m, 3 H, oxirane H), 3.59 (dq, J = 6.5, 6.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.3 (q), 45.0 (t), 55.4 (d), 68.3 (d).

(*R*,S)-α-Methyloxiranemethanol (1a)**: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.24 (d, J = 6.5 Hz, 3 H, Me), 2.20 (br s, 1 H, OH), 2.67, 2.77, and 2.95 (m, 3 H, oxirane H), 3.97 (dq, J = 6.5, 3.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.4 (q), 43.5 (t), 56.5 (d), 64.3 (d).

(*R*,S)-3,3-Dimethyl-α-(1-methylethyl)oxiranemethanol (2a).** From 2.30 g (20.5 mmol) of **2** and 5.85 g (20.5 mmol) of $Ti(O\text{-}i\text{-}Pr)_4$ after photooxygenation at 0 °C for 60 h was obtained on distillation 2.21 g (75%) of **2a** as a 90:10 *R*,S*/R*,R** mixture, bp 70 °C (oven) (0.1 Torr). Isomerically pure (*R*,S**)-**2a** was obtained by fractional distillation: IR (CCl_4) 3540, 3060, 2990, 2915, 2870, 1480, 1385, 1360, 1085 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.90 and 1.00 (d, J = 7.0 Hz, 6 H), 1.28 and 1.31 (s, 6 H, oxirane Me), 1.76 (dqq, J = 8.0, 7.0, 7.0 Hz, 1 H), 2.40 (br s, 1 H, OH), 2.71 (d, J = 8.0 Hz, 1 H), 3.15 (dd, J = 8.0, 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.0 (q), 18.1 (q), 19.6 (q), 24.7 (q), 32.1 (d), 60.2 (s), 66.8 (d), 74.6 (d); MS (70 eV) m/z (rel abund) 143 (0.04, $M^+ - 1$), 142 (0.07, $M^+ - 2$), 129 (1, $M^+ - Me$), 99 (11), 87 (22), 70 (56), 58 (35), 57 (100), 43 (60), 41 (79), 31 (13). Anal. Calcd for $C_8H_{14}O_2$ (144.2): C, 66.63; H, 11.18. Found: C, 66.39; H, 11.30.

2-(1,1-Dimethylethyl)oxiranemethanol (3a).[27] From 1.47 g (15.0 mmol) of **3** and 4.26 g (15.0 mmol) of $Ti(O\text{-}i\text{-}Pr)_4$ after photooxygenation at 0 °C for 70 h was obtained on distillation 1.70 g (87%) of **3a**: bp 80 °C (oven) (0.1 Torr); IR (film) 3430, 3035, 2980, 2890, 1480, 1395, 1365, 1210, 1060, 1045, 1020, 915, 825 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 9 H, *t*-Bu), 1.80 (br s, 1 H, OH), AB system (δ_A 2.76, δ_B 2.82, $J_{A,B}$ = 4.4 Hz, oxirane H), AB system (δ_A 3.96, δ_B 4.34, $J_{A,B}$ = 12.5 Hz, CH_2OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.9 (q), 29.7 (s), 47.9 (t), 62.7 (s), 77.2 (t).

Epoxy Alcohols (*R*,R)- and (*R*,S**)-4a[19] and 4a′.**[21] From 7.00 g (0.100 mol) of **4** and 7.10 g (25.0 mmol) of $Ti(O\text{-}i\text{-}Pr)_4$ after photooxygenation at −10 °C for 19 h was obtained on distillation 8.10 g of a mixture of **4a** (32%, 83:17 *R*,S*/R*,R** ratio) and **4a′** (39%), bp 42–44 °C (0.08 Torr), which was characterized without further purification: IR (CCl_4) 3415, 2990, 2939, 2879, 1450, 1370, 1266, 1234, 1060, 916, 868 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) for (*R*,S**)-2-methyl-α-methyloxiranemethanol (**4a**) δ 1.22 (d, J = 6.2 Hz, 3 H), 1.30 (s, 3 H), 2.58

(d, J = 4.9 Hz, 1 H), 2.86 (d, J = 4.9 Hz, 1 H), 2.85 (s, OH), 3.74 (q, J = 6.2 Hz, 1 H); ^{1}H NMR for (R^*,R^*)-2-methyl-α-methyloxiranemethanol (**4a**) δ 1.21 (d, J = 6.2 Hz, 3 H) 1.31 (s, 3 H), 2.62 (d, J = 4.8 Hz, 1 H), 2.76 (d, J = 4.8 Hz, 1 H), 2.85 (br s, OH); ^{1}H NMR for α,α-dimethyloxiranemethanol (**4a′**) δ 1.20 (s, 3 H), 1.32 (s, 3 H), 2.70 (dd, J = 5.0, 4.1 Hz, 1 H), 2.77 (dd, J = 3.0, 5.0 Hz, 1 H), 2.94 (dd, J = 4.1, 3.0 Hz, 1 H), 3.12 (br s, OH).

Epoxy Alcohols (R^*,R^*)- and (R^*,S^*)-5a and 5a′. From 420 mg (5.00 mmol) of **5** and 284 mg (1.00 mmol) of Ti(O-i-Pr)$_4$ after photooxygenation at −5 °C for 24 h was obtained on distillation a mixture of 441 mg of **5a** (28%, 79:21 R^*,S^*/R^*,R^* ratio) and **5a′** (32%): bp 46–51 °C (0.1 Torr); IR (film) 3400, 2980, 2918, 2932, 1450, 1370, 1265, 1235, 1060, 915, 868 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) for (R^*,S^*)-α-ethyl-2-methyloxiranemethanol (**5a**) δ 0.91 (q, J = 7 Hz, 2 H), 1.02 (t, J = 7 Hz, 3 H), 1.30 (s, 3 H), 2.61 (d, J = 4.8 Hz, 1 H), 2.92 (d, J = 4.8 Hz, 1 H), 3.60 dd, J = 3.2, 8.4 Hz, 1 H); ^{1}H NMR for (R^*,R^*)-α-ethyl-2-methyloxiranemethanol (**5a**) δ 0.86 (q, J = 6.8 Hz, 2 H), 0.99 (t, J = 6.8 Hz, 3 H), 1.31 (s, 3 H), 2.69 (d, J = 4.4 Hz, 1 H), 2.78 (d, J = 4.4 Hz, 1 H), 3.24 (dd, J = 5.6, 7.6 Hz, 1 H); ^{1}H NMR for α,-α,3-trimethyloxiranemethanol (**5a′**) δ 1.33 (s, 3 H), 1.34 (d, J = 5.6 Hz, 3 H), 1.35 (s, 3 H), 2.68 (d, J = 2.4 Hz, 1 H), 3.09 (dq, J = 2.4, 5.6 Hz, 1 H).

(R^*,S^*)-α-(1,1-Dimethylethyl)-2-methyloxiranemethanol (6a). From 2.00 g (17.8 mmol) of **6** and 5.07 g (17.8 mmol) of Ti(O-i-Pr)$_4$ after photooxygenation at 0 °C for 19 h was obtained after distillation 2.15 g (84%) of **6a** in 95:5 R^*,S^*/R^*,R^* ratio, bp 80 °C (oven) (0.08 Torr). Further distillation gave (R^*,S^*)-**6a** in isomeric purity of ≥98%. With VO(acac)$_2$ as catalyst (23.6 mg, 0.16 mmol) and starting with 1.00 g (8.91 mmol) of **6**, 1.17 g (91%) of **6a** was obtained at 0 °C after 24 h as a 99:1 R^*,S^*/R^*,R^* mixture. With MoO_2(acac)$_2$ as catalyst (174 mg, 0.535 mmol), from 1.00 g (8.91 mmol) of **6** was obtained at 0 °C after 15 h a mixture consisting of 53% **6a** (88:12 R^*,S^*/R^*,R^* ratio), 21% **6b**, 15% **6c**, and 11% **6d**: IR (CCl_4) 3540, 3040, 2980, 2910, 2870, 1480, 1385, 1360, 1080, 1010, 940 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.97 (s, 9 H, t-Bu), 1.40 (d, J = 0.8 Hz, 3 H, Me), 2.60 (br s, 1 H, OH), 2.65 (d, J = 8.0 Hz, 1 H), 2.98 (ddq, J = 8.0, 0.8, 0.8 Hz, 1 H), 3.33 (br s, 1 H, 3-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6 (q), 26.7 (q), 34.6 (s), 50.9 (t), 57.7 (s), 78.9 (d); MS (70 eV) m/z (rel abund) 142 (0.1, M$^+$ − 2), 129 (1), 99 (11), 87 (22), 70 (60), 58 (38), 57 (100), 43 (32), 41 (73), 28 (44). Anal. Calcd for $C_8H_{16}O_2$ (144.2): C, 66.63; H, 11.18. Found: C, 66.60; H, 11.34.

α,α,2-Trimethyloxiranemethanol (7a).[31] From 1.00 g (11.9 mmol) of **7** and 3.38 g (11.9 mmol) of Ti(O-i-Pr)$_4$ after photooxygenation at 0 °C for 4 h was obtained on distillation 1.16 g (84%) of **7a**: bp 100 °C (oven) (20 Torr); IR (CCl_4) 3570, 3070, 2980, 2940, 1380, 1365, 1340, 1190, 1160, 960, 845 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21 and 1.28 (s, 6 H, Me), 1.31 (d, J = 0.8 Hz, 3 H), 2.05 (br s, 1 H, OH), 2.46 (d, J = 4.8 Hz, 1 H), 2.94 (dq, J = 0.8, 4.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 17.7 (q), 25.1 (q), 25.9 (q), 51.4 (t), 62.0 (s), 69.6 (s).

Epoxy Alcohols (R^*,R^*)- and (R^*,S^*)-8a.[11] From 510 mg (2.45 mmol) of **8**[32] and 696 mg (2.45 mmol) of Ti(O-i-Pr)$_4$ after photooxygenation at 0 °C for 5.5 h was obtained a mixture consisting of **8a** (90%, 55:45 R^*,S^*/R^*,R^* ratio), **8c** (5%), and **8e** (5%). Radial chromatography using a Chromatotron (silica gel, 10:1 CH_2Cl_2/EtOAc) afforded 494 mg (84%) of **8a**, which solidified on cooling. Recrystallization (petroleum ether/CH_2Cl_2) gave colorless prisms, mp 102–103 °C. As a second fraction 20.0 mg (4%) of pure **8c**[9] was isolated, mp 31–33 °C (lit.[9b] mp 33–34 °C). A third fraction consisted of a mixture of **8c** and **8e**. With VO(acac)$_2$ as catalyst (63.6 mg, 0.240 mmol), 1.00 g (4.80 mmol) of **8** led at 0 °C after 15 h to a mixture of acetophenone and **8c** in a 67% yield.

(R^*,S^*)-α,2-Diphenyl-α-methyloxiranemethanol (**8a**): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.78 (s, 3 H, Me), 2.84 (br s, OH, 1 H), 2.90 and 3.40 (d, J = 5.3 Hz, 2 H, oxirane H), 7.00–7.40 (m, arom H, 10 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9 (q), 51.0 (t), 67.1 (s), 74.2 (s), the aromatic carbon resonances could not be assigned.

(R^*,R^*)-α,2-Diphenyl-α-methyloxiranemethanol (**8a**): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.71 (s, Me, 3 H), 2.81 and 3.73 (d, J = 5.4 Hz, 2 H, oxirane H), 3.02 (br s, 1 H, OH), 7.00–7.40 (m, 10 H, arom H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.7 (q), 51.5 (t), 66.5 (s), 73.4 (s), the aromatic carbon resonances could not be assigned.

(R^*,S^*/R^*,R^*)-**8a**: ^{13}C NMR ($CDCl_3$, 100 MHz) δ 125.9, 126.7, 127.1, 127.2, 127.3, 127.7, 128.4, 128.7, 142.8, 143.8; IR (CCl_4) 3620, 3585, 3065, 3035, 2990, 2930, 1490, 1445, 915, 700 cm^{-1}; MS (70 eV) m/z (rel abund) 240 (0.04, M$^+$), 222 (1, M$^+$ − H_2O), 210 (1, M$^+$ − CH_2O), 178 (2), 167 (10), 152 (4), 120 (66), 105 (41), 91 (23), 77 (26), 43 (100). Anal. Calcd for $C_{16}H_{16}O_2$ (240.3): C, 79.97; H, 6.71. Found: C, 80.17; H, 6.93.

(R^*,S^*)-2-(1-Hydroxyethyl)oxiranecarboxylate (9a). From 2.50 g (19.5 mmol) of ethyl tiglate (**9**) and 4.44 g (15.6 mmol) of Ti(O-i-Pr)$_4$ after photooxygenation at 0 °C for 68 h was obtained a mixture of 2.45 g of **9a** (68%, 90:10 R^*,S^*/R^*,R^* ratio) and **9c** (25%). Radial chromatography using a Chromatotron (silica gel, eluting first with CH_2Cl_2 and subsequently with 5:1 CH_2Cl_2/EtOAc) yielded 1.78 g (57%) of isomerically pure (R^*,S^*)-**9a**: IR (CCl_4) 3585, 2985, 2940, 2905, 1735, 1720, 1375, 1300, 1270, 1090, 1030, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.25 (t, J = 7.0 Hz, 3 H, OCH_2Me), 1.27 (d, J = 6.5 Hz, 3 H, OCHMe), 2.74 (br s, 1 H, OH), AB system (δ_A 2.92, δ_B 3.05, $J_{A,B}$ = 5.9 Hz, oxirane H), 4.13 (q, J = 6.5 Hz, 1 H, OCHMe), 4.17 and 4.22 (dq, J = 11.0 and 7.0 Hz, 2 H, OCH_2Me); ^{13}C NMR ($CDCl_3$, 100 MHz), δ 13.9 (q), 18.4 (q), 49.3 (t), 58.8 (s), 61.7 (t), 65.4 (d), 169.4 (s); MS (70 eV) m/z (rel abund) 161 (0.2, M$^+$ + 1), 145 (6), 117 (12), 88 (24), 60 (22), 56 (20), 45 (89), 43 (84), 42 (100), 29 (53). Anal. Calcd for $C_7H_{14}O_4$ (160.2): C, 52.49; H, 7.55. Found: C, 52.64; H, 7.79.

Photooxygenation of Cyclopropylidene Cyclopentane 10 in the Presence of Ti(O-i-Pr)$_4$. The photooxygenation of 1.00 g (9.24 mmol) of **10**[14a] in the presence of 2.63 g (9.24 mmol) of Ti(O-i-Pr)$_4$ at −40 °C for 3 h gave a complex mixture by ^{1}H NMR. On chromatography (silica gel, CH_2Cl_2) only 66.0 mg (6%) of dienone **10d**[14a] could be isolated.

7-Oxabicyclo[4.1.0]heptan-2-ol (11a).[16a] Photooxygenation at 0 °C for 49 h of 2.00 g (24.3 mmol) of cyclohexene (**11**) in the presence of 6.42 g (24.3 mmol) of Ti(O-i-Pr)$_4$ gave 2.05 g of a mixture of **11a** (60%, 98:2 cis/trans ratio), **11c** (7%), **11d** (4%), and **11e** (29%). With catalytic amounts of Ti(O-i-Pr)$_4$ (1.42 g, 5.00 mmol), 2.46 g (30.0 mmol) of **11** led at 0 °C after 47 h to 3.12 g of a mixture of **11a** (91%, 98:2 cis/trans ratio), **11c** (7%), and **11d** (3%). With VO(acac)$_2$ as catalyst (322 mg, 1.22 mmol), starting with 2.00 g (24.3 mmol) of **11** gave at 0 °C after 45 h 2.52 g of a mixture of **11a** (51%, >98:2 cis/trans ratio), **11c** (29%), and **11d** (20%).

6,6-Dimethylspirobicyclo[3.1.1]heptan-3-ol-2,2′-oxirane (12a).[16b] Photooxygenation at 0 °C for 64 h of 2.50 g (18.4 mmol) of α-pinene (**12**) in the presence of 5.22 g (18.4 mmol) of Ti(O-i-Pr)$_4$ gave 2.76 g of a mixture of **12c** (37%), **12d** (23%), **12e** (37%), and **13d** (3%). With catalytic amounts of Ti(O-i-Pr)$_4$ (522 mg, 1.84 mmol) at 0 °C after 20 h there was obtained 2.91 g of a mixture of **12a** (81%), **12c** (9%), **12d** (5%), and **13d** (3%). With VO(acac)$_2$ as catalyst (243 mg, 0.920 mmol), starting with 2.50 g (18.4 mmol) of **12** gave 2.60 g of a mixture of **12a** (46%), **12c** (28%), **12d** (8%), **12e** (10%), and **13d** (8%).

7,7-Dimethyl-3-oxatricyclo[4.1.1.0^{2,4}]octane-2-methanol (13a). Photooxygenation at 0 °C for 72 h of 2.50 g (18.4 mmol) of β-pinene (**13**) in the presence of 5.22 g (18.4 mmol) of Ti(O-i-Pr)$_4$ gave 2.16 g of a mixture of **13d** (72%) and **13e** (28%). With catalytic amounts of Ti(O-t-Bu)$_4$ (12.9 mg, 0.038 mmol) and starting from 51.5 mg (0.378 mmol) of **13** in $CDCl_3$ at 0 °C after 28 h there was obtained 48.0 mg of a mixture of **13a** (23%), **13b**[17] (43%), **13c** (16%), and **13d** (18%). Use of VO(acac)$_2$ as catalyst (133 mg, 0.500 mmol) and 6.81 g (50 mmol) of β-pinene in 50 mL of benzene at 8 °C after 15 h gave at 60% conversion (photooxygenation was discontinued because of precipitation) 5.70 g of a mixture of **13a**, **13b**, **13c**, and **13d** in 67:5:10:18 relative proportions (normalized to 100%), respectively.

Transformation of Allylic Hydroperoxides into Epoxy Alcohols by Means of Transition-Metal Catalysts [Ti(IV), V(V)]. Epoxy Alcohol 8a.[11] A solution of 30.0 mg (0.144 mmol) of **8** in 5 mL of $CDCl_3$ was photooxygenated at 0 °C to complete consumption (ca. 2 h) by using TPP (ca. 5 × 10^{-4} M) as sensitizer. To this mixture was added 1.0 mL of a 1.0 M $CDCl_3$ solution of VO(acac)$_2$ (0.0010 mmol), and the reaction progress was monitored by ^{1}H NMR. After 10 min the **8b** was completely consumed, resulting in a 67:33 mixture of acetophenone and **8c**. No **8a** could be detected by 400-MHz ^{1}H NMR.

Attempted Preparation of Epoxy Alcohol 9a. To a solution of 400 mg (3.06 mmol) of **9b** (methyl ester) in CH_2Cl_2 (50 mL) was added at 0 °C 40.5 mg (0.153 mmol) of VO(acac)$_2$ in CH_2Cl_2 (5 mL). After 2 h, the solvent was rotoevaporated [ca. 20 °C (20 Torr)] and the residue distilled to give 283 mg (73%) of **9c** (methyl ester). No other products could be detected by ^{1}H NMR (400 MHz).

(1α,3α,7α)-2-Oxatricyclo[5.4.0.0^{1,3}]undecan-7-ol (14a). A solution of 680 mg of **14b**[18] and 1.14 g (4.05 mmol) of Ti(O-i-Pr)$_4$ in 50 mL of CH_2Cl_2 was stirred for 24 h at 0 °C. After this time all starting material was consumed. The usual workup (cf. the general procedure) gave 660 mg of a mixture of *cis*-**14a** (82%), **14c** (6%), *cis*-**14e** (6%), and an unidentified product. Radial chromatography using a chromatotron (silica gel, CH_2Cl_2) yielded 530 mg (78%) of *cis*-**14a** as colorless oil, which solidified upon standing as a wax: mp 33–35 °C; IR ($CDCl_3$) 3590, 2950, 2880, 1460, 1305, 1185, 1095, 1000, 835 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.0–2.2 (m, 15 H), 3.08 (d, J = 4.7 Hz, 1 H, oxirane H), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.3, 20.7, 23.6, 25.2, 30.6, 35.3 and

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35.6 (all t), 63.9 (d), 64.0 (s), 71.2 (s); MS (70 eV) *m/z* (rel abund) 168 (0.3, M^+), 150 (6, $M^+ - H_2O$), 124 (30), 111 (100), 98 (26), 83 (29), 67 (27), 55 (68), 43 (31), 41 (37). Anal. Calcd for $C_{10}H_{16}O_2$ (168.2): C, 71.39; H, 9.74. Found: C, 71.72; H, 9.83.

General Procedure of *m*-Chloroperbenzoic Acid (*m*-CPBA) Epoxidations. To a solution of 1.0 equiv of olefin in CH_2Cl_2 (100 mL) was added at 0 °C portionwise 1.5 equiv of *m*-CPBA (80% purity). After the mixture was stirred overnight, the solid matter was removed by filtration, and the filtrate was washed with aqueous Na_2SO_3 (2 × 50 mL), saturated Na_2CO_3 (2 × 50 mL), and water (50 mL) and dried ($MgSO_4$). Rotoevaporation of the solvent at 20 °C (20 Torr) gave the crude epoxy alcohol, which was purified by distillation or chromatography.

Epoxy Alcohols (*R*,R)- and (*R*,S**)-6a.** A mixture of 1.01 g (7.87 mmol) of **6c** and 2.02 g (11.7 mmol) of *m*-CPBA gave 540 mg (48%) of **6a** as *R*,S*/R*,R** diastereomers in 60:40 ratio, bp 80 °C (oven) (0.1 Torr). The NMR data of the (*R*,R**)-**6a** diastereomer were extracted from the *R*,S*/R*,R** mixture by comparison with the pure (*R*,S**)-**6a** diastereomer.

(*R*,R**)-**6a**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.96 (s, 9 H, *t*-Bu), 1.35 (s, 3 H, Me), 2.40 (br s, 1 H, OH), AB system (δ_A 2.73, δ_B 2.75, $J_{A,B}$ = 3.5 Hz), 2.81 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.3 (q), 27.1 (q), 34.5 (s), 54.0 (t), 58.8 (s), 84.4 (d).

Epoxy Alcohol (*R*,R)-6e.** A 76:24 mixture of 1.00 g of **6f** and (*E*)-2,4,4-trimethyl-2-pentenal (obtained in the SeO_2 oxidation of olefin **6**, see below) and 2.05 g (11.7 mmol) of *m*-CPBA gave 870 mg of a 80:20 mixture of (*R*,R**)-**6e** and (*E*)-2,4,4-trimethyl-2-pentenal, bp 70 °C (oven) (0.08 Torr).

Epoxy Alcohols *cis*- and *trans*-14a. A mixture of 120 mg (0.788 mmol) of **14c** and 204 mg (1.18 mmol) of *m*-CPBA led to 132 mg (83%) of **14a** in 86:14 ratio. The NMR data of the *trans*-**14a** diastereomer were extracted from the cis/trans mixture by comparison with the pure *cis*-**14a** diastereomer: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.0–2.2 (m, 15 H), 2.97 (d, *J* = 4.6 Hz, 1 H, oxirane H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.5, 21.0, 22.7, 23.2, 29.5, 33.3, 37.6 (all t), 60.4 (d), 62.2 (s); carbinol carbons were not observed as a result either of overlapping or too low intensity.

(1α,3α,7α)-7-Hydroperoxy-2-oxatricyclo[5.4.0.0^{1,3}]undecane (14e). Starting with 168 mg (1.00 mmol) of **14b** and 259 mg (1.50 mmol) of *m*-CPBA there was obtained 149 mg (81%) of crude **14e** as a 90:10 cis/trans mixture. Radial chromatography using a Chromatotron (silica gel, eluting first with CH_2Cl_2 and subsequently with ether) gave 121 mg (66%) of *cis*-**14e** as a colorless oil, which solidified upon cooling to −30 °C. Recrystallization from petroleum ether/CCl_4 gave colorless prisms, mp 55–57 °C.

***cis*-14e**: IR (KBr) 3340, 2980, 2940, 2860, 1440, 1400, 990, 930, 890, 860 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.0–2.3 (m, 14 H), 2.93 (d, *J* = 4.4 Hz, 1 H, oxirane H), 8.20 (br s, 1 H, OOH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.6, 20.5, 23.0, 25.3, 28.5, 30.8, 32.8 (all t), 60.4 (d), 62.3 (s), 83.0 (s); MS (70 eV) *m/z* (rel abund) 151 (58, $M^+ - H_2O_2$), 135 (45), 111 (20), 107 (16), 91 (56), 81 (56), 67 (82), 55 (100), 41 (58), 27 (34). Anal. Calcd for $C_{10}H_{16}O_3$ (184.2): C, 65.19; H, 8.75. Found: C, 65.32; H, 8.48.

***trans*-14e**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.0–2.3 (m, 14 H), 3.10 (d, *J* = 4.9 Hz, 1 H, oxirane H), 8.20 (br s, 1 H, OOH).

Chemical Correlations. Payne Rearrangement[21] of Epoxy Alcohol (*R*,S)-6a into Epoxy Alcohol (*R*,R**)-6e.** A solution of 4.20 g (29.1 mmol) of (*R*,S**)-**6a** in 50 mL of 2 N NaOH was stirred for 1 h at room temperature. After saturation with ammonium sulfate (ca. 12 g), the solution was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with 20% aqueous ammonium sulfate (2 × 50 mL), dried ($MgSO_4$), and rotoevaporated [ca. 20 °C (20 Torr)]. Distillation of the residue gave 2.70 g (64%) of (*R*,R**)-**6e**, bp 70 °C (0.08 mm) in 94% purity, besides 6% of the starting material **6a**: IR ($CDCl_3$) 3650, 3000, 2900, 1505, 1450, 1400, 1380, 1220, 1065, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 9 H, *t*-Bu), 1.36 (s, 3 H, Me), 2.55 (br s, 1 H, OH), 2.73 (s, 1 H, oxirane H), AB system (δ_A 3.45, δ_B 3.51, $J_{A,B}$ = 12.0 Hz, CH_2O); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.7 (q), 27.6 (q), 31.1 (s), 61.5 (s), 66.8 (t), 67.7 (d); MS (70 eV) *m/z* (rel abund) 143 (0.1, $M^+ - 1$), 142 (0.2 $M^+ - 2$), 127 (1), 111 (3), 87 (35), 70 (43), 58 (47), 55 (100), 43 (87), 41 (65). anal. Calcd for $C_8H_{16}O_2$ (144.2): C, 66.66; H, 11.18. Found: C, 66.83; H, 11.10.

$LiAlH_4$ Reduction of Epoxy Alcohols (*R*,R*/R*,S)-8a to the (*R*,R*/R*,S**)-2,3-Diphenyl-2,3-butanediol (8f).** A solution of 600 mg (2.50 mmol) of a 55:45 *R*,S*/R*,R** mixture of **8a** in ether (5 mL) was added to 285 mg (7.50 mmol) of $LiAlH_4$ in ether (50 mL) and refluxed for 30 min. Addition of water (0.3 mL), 2 N NaOH (0.3 mL), and again water (1.2 mL) resulted in a precipitate, which was removed by filtration. The solution was dried ($MgSO_4$) and rotoevaporated [ca. 20 °C (20 Torr)] to give 580 mg of a 55:45 *R*,R*/R*,S** mixture of **8f**. The spectral data of this crude product was in accordance with that published.[33]

Catalytic Hydrogenolysis of Epoxy Alcohol (*R*,S)-9a (R = Et) to the (*R*,S**)-Ethyl 2,3-Dihydroxy-2-methylbutanoate (9f).** A solution of 250 mg (1.56 mmol) of (*R*,S**)-**9a** in EtOH (50 mL) was hydrogenated[34] at room temperature and normal pressure with 20 mg of Pd/C (10%). The catalyst was removed by filtration and the solvent rotoevaporated at 40 °C (20 Torr). The viscous residue (230 mg) crystallized at −20 °C to give (*R*,S**)-**9f**, mp 41–43 °C. This material was identical with that obtained below.

Osmium Tetroxide Cis Dihydroxylation of Ethyl Tiglate to 1,2-Diol (*R*,S)-9f.** Following the procedure of Sharpless et al.,[35] 3.70 mL of 70% aqueous *t*-BuOOH (16.2 mmol) and 1.70 mL of 40% aqueous tetraethylammonium hydroxide (4.00 mmol) were added to 2.00 g (15.6 mmol) of **9** (R = Et) in acetone (100 mL). The mixture was cooled to 0 °C, and 100 mg (0.393 mmol) of OsO_4 was added. After being stirred for 1 h, the reaction was diluted with ether (200 mL), saturated aqueous Na_2SO_3 (50 mL) was added, and the resultant mixture was stirred for 1 h. The layers were separated, the aqueous layer was extracted with ether (2 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and rotoevaporated [ca. 20 °C (20 Torr)]. The residue was distilled to give 600 mg (24%) of (*R*,S**)-**9b** (R = Et), bp 60 °C (0.1 mm). The material crystallized upon standing, mp 42–43 °C. It was identical with that obtained above.

Epoxy Alcohol (*R*,S)-9a by Sharpless[36] Epoxidation of Allylic Alcohol 9c (R = Et) with *t*-BuOOH/VO(acac)$_2$.** A mixture of 0.95 mL of 3.8 M *t*-BuOOH (3.60 mmol) in CH_2Cl_2, 400 mg (2.77 mmol) of **9c**, and 10.0 mg (0.388 mmol) of $VO(acac)_2$ in benzene (30 mL) was refluxed for 5 h. The solvent was rotoevaporated [ca. 20 °C (20 Torr)] and the residue distilled to give 310 mg (69%) of (*R*,S**)-**9a** (isomeric purity ≥ 98%), bp 70 °C (oven) (0.1 Torr).

3,3-Diphenyl-4-hydroxy-2-butanone (8e). Following the procedure of Yamamoto et al.,[12] 1.20 g of the mixture obtained in the photooxygenation of **8** in the presence of Ti(O-*i*-Pr)$_4$, containing ca. 1.08 g (4.50 mmol) of epoxy alcohol **8a**, was added at room temperature with stirring to 710 mg (6.02 mmol) of Me_3SiCl and 480 mg (7.04 mmol) imidazole in DMF (50 mL). After 12 h, the mixture was poured into ether (50 mL) and washed with 2 N aqueous HCl (20 mL) and saturated aqueous $NaHCO_3$ (20 mL). The organic layer was dried ($MgSO_4$) and rotoevaporated [ca. 20 °C (20 Torr)] to give 475 mg of the crude silyl ether of the epoxy alcohol **8a**, which was used without further purification. To a solution of this silyl ether in CH_2Cl_2 (30 mL) was added at −78 °C 345 mg (1.82 mmol) of $TiCl_4$. The mixture was stirred for 15 min, poured into 2 N aqueous HCl (20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The organic layer was washed with saturated brine (20 mL), dried ($MgSO_4$), and rotoevaporated [ca. 20 °C (20 Torr)]. The residual oil was chromatographed (silica gel, CH_2Cl_2) to give 295 mg (25% starting from **8**) of **8e** as pale yellow needles: mp 75–76 °C (MeOH, petroleum ether); IR ($CDCl_3$) 3590, 3070, 3040, 2940, 1695, 1600, 1495, 1445, 1360, 1065 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.13 (s, 3 H, Me), 2.40 (br s, 1 H, OH), 4.32 (s, 2 H, CH_2O), 7.22–7.42 (m, 10 H, arom H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 28.6 (q), 67.5 (s), 68.3 (t), 127.4 (d), 128.5 (d), 140.0 (s), 210.4 (s); MS (70 eV) *m/z* (rel abund) 222 (0.2, $M^+ - H_2O$), 210 (3), 167 (100), 152 (17), 139 (3), 128 (2), 115 (5), 89 (2), 77 (2), 43 (10). Anal. Calcd for $C_{16}H_{16}O_2$ (240.3): C, 79.97; H, 6.71. Found: C, 80.05; H, 6.80.

(*E*)-2,4,4-Trimethyl-2-penten-1-ol (6f) via SeO_2 Oxidation of Olefin 6. Following the reported[22] procedure, 50 mL of 2.9 M *t*-BuOOH in CH_2Cl_2 was poured at 0 °C into a stirred suspension of 550 mg (4.95 mmol) of SeO_2 and 700 mg (5.07 mmol) of salicylic acid in CH_2Cl_2 (40 mL). While this mixture was being stirred there was added portionwise 5.50 g (50.0 mmol) of **6** in CH_2Cl_2 (10 mL), and the resulting solution was allowed to stir for 3 days at room temperature. Benzene (50 mL) was added, and the CH_2Cl_2 was removed by distillation. Ether (100 mL) and saturated aqueous Na_2SO_4 (25 mL) were added and the resultant mixture was stirred for 1 h. The organic layer was washed with 2 N aqueous NaOH (4 × 30 mL) and saturated brine (30 mL), dried ($MgSO_4$), and rotoevaporated [ca. 20 °C (20 Torr)]. The ^{1}H NMR showed **6f** (57%) as major product, besides (*E*)-2,4,4-trimethyl-2-pentenal (18%) and 4,4-dimethyl-2-hydroxymethyl-2-penten-1-ol (23%). Distillation at 75 °C (20 mm) gave 1.90 g of a 76:24 mixture consisting of **6f** and the (*E*)-2,4,4-trimethyl-2-pentenal. Recrystallization of the distillation res-

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idue from petroleum ether (30–50 °C) gave 250 mg of the unsaturated diol.

2,4,4-Trimethyl-1-penten-3-one (6d).[13c] Following the reported procedure,[37] 2.24 g (20.0 mmol) of olefin **6** in CH_2Cl_2 (50 mL) was photooxygenated in the presence of 2.25 g (22.0 mmol) of acetic anhydride, 1.03 g (13.0 mmol) of pyridine, and 4-(dimethylamino)pyridine (ca. 5 mg), using TPP (ca. 20 mg) as sensitizer. After complete conversion of **6** (ca. 6 h), the reaction mixture was kept for 3 days at room temperature. At this the time, ^1H NMR showed 80% conversion of **6b** into enone **6d**. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with saturated aqueous $NaHCO_3$ (2 × 20 mL), 1 N aqueous HCl (2 × 10 mL), saturated copper sulfate (10 mL), and saturated brine (30 mL), dried ($MgSO_4$), and rotoevaporated [ca. 20 °C (20 Torr)]. Radical chromatography on a Chromatotron (silica gel, CH_2Cl_2) gave 1.76 g (64%) of enone **6d** as a colorless liquid: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.20 (s, 9 H, *t*-Bu) 1.86 (dd, J = 1.0, 1.0 Hz, 3 H, Me), 5.34 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.1 (q), 27.5 (q), 43.9 (s), 118.0 (t), 144.3 (s), 211.3 (s).

Mechanistic Studies. The β-values were determined as described in the literature.[29,38] Product ratios of **4a**/**4a**′ were determined by quantitative ^1H NMR analysis of the crude reaction mixtures.

^1H NMR monitoring of the reaction progress was performed by first preparing the stock solutions: (a) 10^{-2} M **7b**, (b) 10^{-2} M Ti(O-*i*-Pr)$_4$, and (c) 10^{-2} M **7c**, all in $CDCl_3$. These stock solutions were mixed as described below and placed into an NMR tube and the ^1H NMR spectra continuously recorded.

Run A. Injection of 0.1 mL of solution b into 1 mL of solution a at room temperature led to an immediate exothermic reaction with complete formation of the epoxy alcohol **7a**.

Run B. Following injection of 0.1 mL of solution b into 1 mL of solution a, which was precooled to −30 °C, and allowing the mixture to warm up to 0 °C, **7a** began to form after 10–20 min (several measurements), and conversion was complete after ca. 80–90 min.

Run C. Following injection of 0.1 mL of solution b into a mixture of 1 mL of solution a and 0.1 mL of solution c, which was precooled to −30 °C, the mixture was allowed to warm up to 0 °C. After 10 min the products **7b**/**7c**/**7a** were formed in the ratio 34:11:55, respectively, after 15 min in a ratio of 10:10:80, and after 20 min the reaction was complete, affording a ratio of 0:9:91.

Run D. The same procedure as described in run C was followed but using 0.3 mL of solution c: after 2 min the reaction was complete, affording the products **7b**/**7c**/**7a** in a ratio of 0:23:76, respectively.

Substrate–Catalyst Profile for the Reaction of 4b and 4b′ with Ti(O-*i*-Pr)$_4$. To 2.0 mL of a 10^{-3} M solution of **4b** and **4b**′ in $CDCl_3$ was added 0.25 mL of a 10^{-4} M solution of Ti(O-*i*-Pr)$_4$ in $CDCl_3$ at −50 °C. The solution was warmed up to 20 °C (ca. 10 min), and the ^1H NMR (400 MHz) was taken. The same procedure was performed several times, injecting different amounts of Ti(O-*i*-Pr)$_4$ stock solution. All signals in the ^1H NMR spectra of the reaction mixtures could be assigned with certainty by comparison with authentic samples. The product ratios were determined by integration of the respective signals and normalizing to 100%. The results are displayed in Figure 1, the individual ^1H NMR spectra are given below.

Allylic Hydroperoxides. 4b: ($CDCl_3$, 400 MHz) δ 1.21 (d, J = 6.9 Hz, 3 H), 1.73 (s, 3 H), 4.39 (q, J = 6.9 Hz, 1 H), 4.88 (m, 2 H), 7.22 (s, 1 H, OOH).

4b′: ($CDCl_3$, 400 MHz) δ 1.29 (s, 6 H), 5.07 (dd, J = 1.8, 10.8, 1 H), 5.14 (dd, J = 1.8, 17.5, 1 H), 5.92 (dd, J = 10.8, 17.5, 1 H).

Allylic Alcohols. 4c: ($CDCl_3$, 400 MHz) δ 1.18 (d, J = 7.2 Hz, 3 H), 1.77 (s, 3 H), 4.25 (q, J = 7.2 Hz, 1 H), 4.81 (m, 2 H), 8.01 (s, 1 H, OOH).

4c′ ($CDCl_3$, 400 MHz) δ 1.20 (s, 6 H), 4.96 (dd, J = 1.6, 10.4 Hz, 1 H), 5.19 (dd, J = 1.6, 17.2 Hz, 1 H), 5.98 (dd, J = 10.4, 17.2 Hz, 1 H).

Epoxy Hydroperoxides. 4e: ($CDCl_3$, 400 MHz) δ 1.24 (d, J = 6.3 Hz, 3 H), 1.33 (s, 3 H), 2.72 (d, J = 4.8 Hz, 1 H), 3.03 (d, J = 4.8 Hz, 1 H), 3.83 (q, J = 6.3 Hz, 1 H).

4e′ ($CDCl_3$, 400 MHz) δ 1.22 (s, 1 H), 1.31 (s, 1 H), 2.67 (dd, J = 4.0, 9.6 Hz, 1 H), 2.79 (dd, J = 4.0, 9.6 Hz, 1 H), 3.17 (dd, J = 4.0, 4.0 Hz).

Asymmetric Hydroxy Epoxidation. Photooxygenation of 3 in the Presence of Ti(O-*t*-Bu)$_4$/Diethyl Tartrate. At 0 °C, 3.50 g (10.3 mmol) of Ti(O-*t*-Bu)$_4$ and 2.55 g (12.4 mmol) of L-(+)-diethyl tartrate in CH_2Cl_2 (100 mL) were stirred for 30 min. After addition of ca. 20 mg of TPP and 982 mg (10.0 mmol) of **3**, the mixture was cooled to −20 °C and photooxygenated until complete consumption of **3** (ca. 24 h). Under vigorous stirring, the reaction mixture was poured into 10% aqueous tartaric acid (30 mL) and stirred for 1 h. The layers were separated, the organic layer was dried ($MgSO_4$), and the solvents were rotoevaporated at 20 °C (20 Torr). The residue was diluted with ether (100 mL) and, after being cooled to 0 °C, stirred with 1 N NaOH (30 mL) for 20 min. The layers were separated, the organic layer was dried ($MgSO_4$), and the solvent was evaporated. Radial chromatography on the Chromatotron (silica gel, CH_2Cl_2) gave 897 mg (69%) of (*S*)-**3a** (ee = 72%) as a colorless liquid.

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Registry No. 1, 624-64-6; (*R**,*S**)-**1a**, 53837-91-5; (*R**,*R**)-**1a**, 53837-90-4; **2**, 692-70-6; (*R**,*S**)-**2a**, 107784-04-3; (*R**,*R**)-**2a**, 107784-03-2; **3**, 594-56-9; **3a**, 100841-12-1; (*S*)-**3a**, 100038-14-0; **4**, 513-35-9; (*R**,*S**)-**4a**, 22520-26-9; (*R**,*R**)-**4a**, 22520-27-0; **4a**′, 19482-44-1; **4b**, 13249-73-5; **4b**′, 15315-30-7; **4c**′, 115-18-4; **4e**, 117202-98-9; **4e**′, 117202-99-0; **5**, 625-27-4; (*R**,*S**)-**5a**, 84599-41-7; (*R**,*R**)-**5a**, 81280-10-6; **5a**′, 1193-04-0; **6**, 107-40-4; (*R**,*S**)-**6a**, 100841-14-3; (*R**,*R**)-**6a**, 100841-13-2; **6c**, 7432-48-6; **6d**, 7432-56-6; **6e**, 117202-95-6; **7**, 563-79-1; **7a**, 22515-23-7; **7b**, 13249-73-5; **7c**, 10473-13-9; **8**, 782-06-9; (*R**,*S**)-**8a**, 117202-90-1; (*R**,*R**)-**8a**, 117202-91-2; **8e**, 89867-88-9; (*R**,*S**)-**8f**, 4217-65-6; (*R**,*R**)-**8f**, 22985-90-6; **9**, 5837-78-5; (*R**,*S**)-**9a**, 100841-15-4; (*R**,*R**)-**9a**, 100858-09-1; **9c**, 14362-99-3; **9f**, 117202-96-7; **10**, 14949-48-5; **10d**, 62672-81-5; **11**, 110-83-8; *cis*-**11a**, 26828-73-9; *trans*-**11a**, 26828-72-8; **11c**, 822-67-3; **11d**, 930-68-7; **11e**, 286-20-4; **12**, 80-56-8; **12a**, 33081-46-8; **12c**, 1674-08-4; **12d**, 16812-40-1; **12e**, 32162-27-9; **13**, 127-91-3; **13a**, 105815-51-8; **13b**, 58434-29-0; **13c**, 515-00-4; **14d**, 564-94-3; **13e**, 19250-17-0; *cis*-**14a**, 117202-92-3; *trans*-**14a**, 117305-64-3; **14b**, 117202-89-8; **14c**, 34130-86-4; *cis*-**14e**, 117202-93-4; *trans*-**14e**, 117305-65-4; Ti(O-*i*-Pr)$_4$, 546-68-9; VO(acac)$_2$, 3153-26-2; MoO_2(acac)$_2$, 17524-05-9; Ti(O-*t*-Bu)$_4$, 7425-80-1; (*E*)-2,4,4-trimethyl-2-pentenal, 117202-94-5; 4,4-dimethyl-2-(hydroxymethyl)-2-penten-1-ol, 117202-97-8.

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