Asymmetric Weitz−Scheffer Epoxidation of α,β-Enones by Optically Active Hydroperoxides: Control of Enantioselectivity through Metal-Coordinated or Hydrogen-Bonded Templates

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The enantioselective epoxidation of the α,β-enones **1** with the optically active hydroperoxides (–)-(*S*)-**2**, catalyzed by the bases KOH or DBU, affords the enantiomerically enriched oxo epoxides **3** in high yields and with good enantioselectivities (up to 90% *ee* for KOH and up to 72% *ee* for DBU). The preparatively useful feature of this asymmetric epoxidation is the fact that opposite senses of enantioselectivity are observed with the same optically active hydroperoxide and the same prochiral enone substrate. Thus, whereas KOH in CH_3CN affords the (α*S*,β*R*)-epoxide **3a** from chalcone **1a**, through preferential *Si*-face attack, DBU in toluene selectively provide the (α*R*,β*S*)-epoxide **3a** from this alkene, through favored *Re*-face attack. It is proposed that template structures, held together by octahedrally ligating K^+ or the hydrogen-bonding $DBUH^+$ ammonium ion, account for the observed enantioselectivities. The sense and degree of enantioselectivity are determined by steric interactions between the base-derived, templating K^+ and $DBUH^+$ agents, the chiral peroxide anion oxygen donor, and the prochiral enone substrate.

Introduction

The asymmetric Weitz−Scheffer epoxidation of electron-poor alkenes was first explored by Wynberg[1−4] and coworkers, more than two decades ago. As chiral inductors, they used quaternary ammonium salts derived from cinchona alkaloids; the chemical function of these optically active agents is to act as phase-transfer catalysts (PTCs).[5] Over recent years, this approach has enjoyed much attention. Indeed, continuous improvement of the PTCs[6−10] and extensive variation of the oxygen donor (e.g., the most commonly used H_2O_2,[6,7] *tert*-butyl hydroperoxide,[8] and cumene hydroperoxide,[9] and also hypochlorite[7,10]) have provided excellent enantioselectivities. Similarly well established and no less successful is the polyamino acid based Julia−Colonna method.[11−17] In this epoxidation, the chiral oxidant is constituted by heterogeneous poly-L-leucine in combination with $NaOH/H_2O_2$, which is employed in a triphasic system. Biphasic media with the urea/H_2O_2 adduct as oxygen source and DBU as base,[18,19] as well as with a THF-soluble poly-L-leucine copolymer,[20] have also been developed, and provide good enantioselectivities. In addition, optically active bases have been employed most recently for inducing asymmetry in the Weitz−Scheffer epoxidation.[21]

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An alternative strategy is the use of metal catalysts with optically active ligands.[5] For example, diethylzinc and molecular oxygen in the presence of (1*R*,2*R*)-*N*-methylpseudoephedrine or polybinaphthol have proven to be an effective optically active oxidant for the enantioselective epoxidation of α,β-enones.[22,23] Moreover, *tert*-butyl hydroperoxide (TBHP)[24−26] may be used as an achiral oxygen source in combination with optically active lanthanide−binols as asymmetric inductors; high enantioselectivities have been achieved with this system.

Despite the fact that optically active hydroperoxides are now conveniently available through enzymatic kinetic resolution,[27,28] such chiral inductors have so far received little if any attention for the preparation of enantiomerically enriched epoxides of α,β-enones through the Weitz−Scheffer reaction. These chiral oxygen sources have previously been utilized for the electrophilic Ti^{IV}-catalyzed asymmetric oxidation of sulfides and allylic alcohols,[29−33] which established their potential synthetic value. Recently, two reports[34,35] on the use of optically active hydroperoxides in enantioselective oxidations have appeared. In a very recent preliminary[36] report, we demonstrated the efficacy of optically active hydroperoxides for the epoxidation of α,β-enones through the asymmetric Weitz−Scheffer reaction, catalyzed by KOH (Scheme 1). For the enantiomeric enrichment, a template structure held together by K^+, in which steric interactions between the β-substituent of the enone **1** and the substituents at the chirality center of the peroxide anion $\mathbf{2}^-$ provide the necessary stereochemical differenti-

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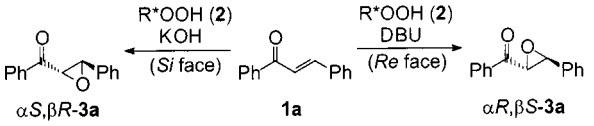
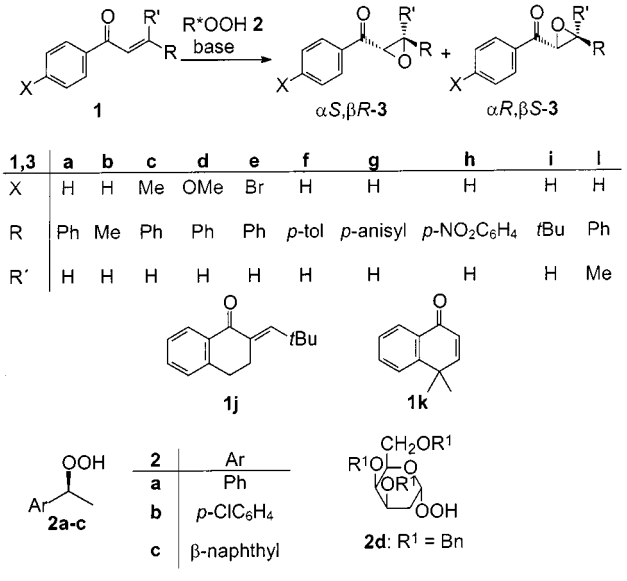
ation, was proposed to account for the observed preference for the (α*S*,β*R*)-epoxide **3**, through *Si*-face attack.



Scheme 1. Facial selectivity in the Weitz–Scheffer epoxidation with optically active hydroperoxides **2**

It was of synthetic interest and mechanistic importance to explore the performance of tertiary amines (e.g., 1,8-diazabicyclo[5.4.0]undec-7-ene, DBU) as base catalysts in combination with optically active hydroperoxides as chiral oxygen sources for the enantioselective epoxidation of α,β-enones. A preliminary experiment revealed that the epoxide was formed in a low enantiomeric excess (9% *ee*) but, more significantly, that the opposite enantiomer was expressed as the major product (Scheme 1). This unexpected dichotomous behavior in the two bases – the inorganic base KOH delivering the (α*S*,β*R*) enantiomer and the organic base the (α*R*,β*S*) congener – merited a more detailed investigation. The purpose was to explain the mechanistic circumstances that underlie the fact that, with the same prochiral α,β-enone **1** and the same optically active hydroperoxide **2**, opposite enantiomers of the epoxide **3** are favored by the mere choice of the type of base. Together with a full report on our previous preliminary results relating to the KOH-catalyzed asymmetric epoxidation of α,β-enones **1** by the optically active hydroperoxides **2**, we offer here an integrated mechanistic concept for this enantioselective oxy functionalization in terms of a common template structure for both base catalysts.



Scheme 2. Base-catalyzed enantioselective Weitz–Scheffer epoxidation of enones **1** by optically active hydroperoxides **2**

Results

For the asymmetric Weitz–Scheffer epoxidation with optically active secondary hydroperoxides, the enantiomerically pure (> 99% *ee*) (−)-(*S*)-1-phenylethyl hydroperoxide (**2a**) was selected as oxygen donor for preliminary screening (Scheme 2). In order to optimize the reaction conditions, the initial experiments were performed on chalcone **1a** as a model substrate, by varying the base, solvent and the reaction temperature. KOH as the base in CH_3CN at −40 °C proved to be the best conditions for the asymmetric epoxidation (Table 1).

Table 1. Optimization of the reaction conditions in the enantioselective Weitz–Scheffer epoxidation of the enone **1a** by (−)-(*S*)-1-phenylethyl hydroperoxide (**2a**)[a]

Entry	Base	Solvent	*T* [°C]	Conversion (%)	Yield[b] (%)	*ee*[c] [d] (%)
1	NaH	Et_2O	20	> 99	96	7
2	NaH	CH_3CN	20	> 99	95	17
3	Na_2CO_3	CH_3CN	20	95	91	18
4	Cs_2CO_3	CH_3CN	20	> 99	98	22
5	K_2CO_3	CH_3CN	20	> 95	92	25
6	K_2CO_3	DMF	20	> 95	84	20
7	K_2CO_3	neat	20	> 95	88	22
8	K_2CO_3	CH_3CN	0	94	90	33
9	K_2CO_3	CH_3CN	−10	75	72	35
10	KOH	CH_3CN	−30	> 99	96	42
11	KOH	CH_3CN	−40	> 99	99	51
12	NaOH	CH_3CN	−40	> 99	95	45
13	CsOH	CH_3CN	−40	> 99	94	48

[a] Enone **1a** (0.1–0.5 mmol), hydroperoxide **2a** (1.0 equiv.), and base (1.1–1.2 equiv.). [b] Isolated epoxide **3**. [c] HPLC analysis on a Chiracel OD column with 2-propanol/hexane (5:95) as eluent; error ≤ 3% of the stated values. [d] The configuration of the major enantiomer is (α*S*,β*R*), determined by comparison with literature data.

Initially, the reaction was carried out in Et_2O with NaH as base (Entry 1), under which conditions the reaction was complete within 2 h at ambient temperature (ca. 20 °C). Although the epoxide product **3a** was obtained in excellent yield, only poor (7% *ee*) enantioselectivity was observed. When the reaction was performed in the more polar CH_3CN as solvent, the *ee* value of the epoxide **3a** was higher, but still only 17% (Entry 2). The weaker bases Na_2CO_3, Cs_2CO_3, and K_2CO_3 in CH_3CN (Entries 3–5) gave no substantial improvement in the enantioselectivity of the epoxidation of **1a**, only up to 25% *ee* for K_2CO_3. Other polar solvents such as DMF (Entry 6), yielded the epoxide with even lower enantioselectivity (20% *ee*), as did the reaction in the absence of solvent (22% *ee*, Entry 7). An increased *ee* value of 33% and a degree of conversion of 94% was observed with the K_2CO_3/CH_3CN combination at 0 °C (Entry 8). Further lowering of the temperature to −10 °C increased the enantioselectivity only to 35% (Entry 9), with the disadvantage of a substantially reduced reactivity, that is, conversion of only 75% after 48 h. In order to shorten the reaction time and to allow even lower temper-

atures to be examined, the stronger base KOH was necessary. Thus, the KOH/CH_3CN combination afforded the (α*S*,β*R*)-epoxide **3a** in 42% *ee* at −30 °C (Entry 10) and in 51% *ee* at −40 °C (Entry 11), nearly quantitatively at both temperatures. To lower the temperature still further (CH_3CN freezes at −46 °C), toluene, CH_2Cl_2, and ethyl ether (data not shown in Table 1) were used as solvents; however, not even traces of epoxide product were detected between −40 and −78 °C under these conditions. Use of the still stronger base *n*BuLi in THF at −78 °C resulted in a complex mixture of products, presumably due to destruction of the chiral ROOH **2** (data not shown in Table 1). A change in the alkali metal ion in the hydroxide base resulted in somewhat lower *ee* values of 45% for NaOH (Entry 12) and 48% for CsOH (Entry 13). From these results, KOH/CH_3CN at −40 °C are so far the best conditions for the asymmetric Weitz−Scheffer epoxidation of enone **1a** with the optically active hydroperoxide **2a**.

Attention was next focused on the choice of the best chiral hydroperoxide (Table 2).

Table 2. Enantioselective Weitz−Scheffer epoxidation of the enones **1** with the optically active hydroperoxides **2**, base-catalyzed by KOH[a]

Entry	Enone	R*OOH	Yield (%)[b]	*ee* (%)[c] [d]
1	**1a**	**2a**	99	51
2	**1a**	**2b**	95	48
3	**1a**	**2c**	87	43
4	**1a**	**2d**	91	14
5[e]	**1a**	**2a**	94	6
6	**1b**	**2a**	99	44
7	**1b**	**2b**	96	40
8	**1b**	**2c**	86	38
9	**1b**	**2d**	92	31
10	**1c**	**2a**	98	54
11	**1d**	**2a**	97	53
12	**1e**	**2a**	95	48
13	**1f**	**2a**	97	57
14	**1g**	**2a**	96	61
15	**1h**	**2a**	98	42
16	**1i**	**2a**	95	75
17[e]	**1i**	**2a**	91	11
18	**1j**	**2a**	90	90

[a] Enone **1** (0.1−0.5 mmol), hydroperoxide **2** (1.0 equiv.), and KOH (2−3 equiv.) in CH_3CN at −40 °C; quantitative consumption of both the enone **1** and hydroperoxide **2** was observed, except for Entries 3 and 8, for which the conversions of **1a** and **1b** were 90% and 92%. [b] Isolated epoxide **3**. [c] HPLC analysis on a Chiracel OD column; except Entries 10−12 and 18 for which a Chiracel OB-H column was used; error ≤ 3% of the stated values. [d] The configuration of the major enantiomer is (α*S*,β*R*). [e] In the presence of 8-crown-6 ether.

Epoxidations of the aryl-substituted enone **1a** (Entries 1−4) and the alkyl-substituted enone **1b** (Entries 6−9) were carried out with the optically active hydroproxides **2a**−**d** under the optimized reaction conditions shown in Table 1. The *ee* values for the epoxidation of the β-methyl-substituted enone **1b** were somewhat lower (up to 44% *ee*, Entries 6−9) than for the β-phenyl-substituted substrate **1a** (up to 51% *ee*, Entries 1−4). With the standard hydroperoxide **2a**, the (α*S*,β*R*)-epoxide **3b** was obtained quantitatively in 44% *ee* (Entry 6). The 4-chloro-substituted hydroperoxide **2b** gave the epoxides **3a** and **3b** (Entries 2 and 7) with about the same *ee* values (48 and 40%) as observed with the unsubstituted hydroperoxide **2a** (Entries 1 and 6). Use of hydroperoxide **2c** (Entries 3 and 8), which bears a β-naphthyl substituent, resulted in slightly lower enantioselectivities (43 and 38% *ee*). With the sugar-derived hydroperoxide **2d** (Entries 4 and 9), the lowest *ee* values (14 and 31% *ee*) in this series were registered. The (−)-(*S*)-1-phenylethyl hydroperoxide (**2a**) was hence found to be the oxygen source of choice for this asymmetric Weitz−Scheffer epoxidation of α,β-enones.

The roles of steric and electronic factors in the enone substrate **1** were subsequently examined, in order to establish whether they influenced this asymmetric epoxidation. With the hydroperoxide **2a** under the optimized conditions, the substituents on the α,β-enone were varied in a systematic way (Table 2, Entries 1, 6, 10−16, and 18). Firstly, the aromatic ring of the enone carbonyl functionality was substituted in the *para*-position (Entries 10−12). Electron-donating 4-methyl (substrate **1c**, Entry 10) and 4-methoxy groups (substrate **1d**, Entry 11), and also the electron-withdrawing 4-bromo substituent (substrate **1e**, Entry 12) did not significantly (48−54% *ee*) influence the enantioselectivity, compared to enone **1a** (Entry 1).

Unlike the carbonyl aryl group, its counterpart in the β-position of the α,β-enone did affect the enantioselectivity. Thus, a regular trend to higher *ee* values was displayed by the electron-donating *para*-methyl group in substrate **1f** (57% *ee*, Entry 13), and even more so by the *para*-methoxy substituent in derivative **1g** (61% *ee*, Entry 14). In contrast, the electron-withdrawing 4-nitro substituent in the enone **1h** (42% *ee*, Entry 15) lowered the enantioselectivity.

In order to examine steric effects, the β-alkyl-substituted enones **1b** and **1i** were employed as substrates in this asymmetric Weitz−Scheffer epoxidation, the β-methyl-substituted enone **1b** (Table 2, Entry 6) having already been mentioned in the optimization. Its epoxidation yielded the same (α*S*,β*R*)-epoxide **3b** enantiomer as substrate **1a** (Entry 1), but with a somewhat lower *ee* value of 44%. The sterically more demanding β-*tert*-butyl-substituted enone **1i** (Entry 16) afforded the (α*S*,β*R*)-epoxide **3i** with the highest *ee* value yet observed (75%) and in 95% yield.

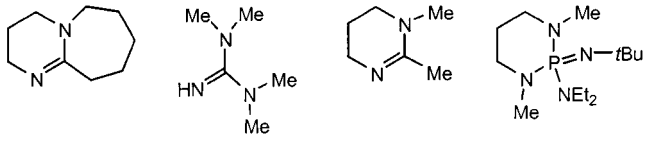
The conformation about the single bond between the carbonyl functionality and the enone double bond as a structural variable in the substrate **1** was next investigated. For this purpose, the conformationally rigid cyclic olefins **1j** and **1k** were chosen, the derivative **1j** possessing fixed *s-cis* and **1k** *s-trans* geometries. The optimized reaction conditions afforded an *ee* value of 90% in the epoxidation of *s-cis* enone **1j** (Table 2, Entry 18), the highest enantioselectivity observed so far. A contrary effect was observed with the *s-trans* enone **1k** (not shown in Table 2). At −40 °C, no trace of epoxide was detected even after 24 h; however, when the temperature was raised to −20 °C, ca. 20% of the enone

had been converted into the epoxide after 48 h, but no optical activity was observed.

The role of the potassium ion in this asymmetric Weitz−Scheffer epoxidation was tested with the aid of the potassium-chelating 18-crown-6 ether. In the case of enone **1a**, the *ee* value diminished dramatically from 51% (Table 2, Entry 1) to 6% *ee* (Entry 5) with the chelating agent present under otherwise standard conditions. The 75% *ee* found in the epoxidation of substrate **1i** (Entry 16) dropped to 11% *ee* (Entry 17) when the 18-crown-6 ether was added. Alternatively, the use of the organic base DBU (**4a**) instead of KOH in acetonitrile (Table 3, Entry 1) also gave a much decreased enantioselectivity of only 9% *ee* with the enone **1a**, with the opposite enantiomer (α*R*,β*S*)-**3a** in fact being produced.

In view of this drastic diminution in the enantioselectivity, it was important to examine the amine-mediated reaction with the enone **1a** in more detail. The epoxide **3a** was also obtained with a very small *ee* of 4% in favor of the (α*R*,β*S*) enantiomer (Entry 2) in (protic) methanol and with DBU (**4a**) as base. In the nonpolar toluene (Entry 3), the reaction proceeded with 90% conversion to yield 98% of the (α*R*,β*S*)-epoxide **3a** in 40% *ee* with DBU (**4a**).

With weaker organic bases ($pK_a \geq 11$) such as triethylamine, diisopropylamine, pyridine, DMAP, and Tröger's base, no reaction was observed even after 72 h at ca. 20 °C (data not shown in Table 3). The stronger bases **4b**−**d** yielded the desired epoxide **3a** with varying enantioselectivities (Entries 4−6).



4a **4b** **4c** **4d**

The comparatively small tetramethylguanidine (**4b**) provided a lower (9% *ee*) enantioselectivity (Entries 3 and 4) than DBU (**4a**). In the case of the base **4c**, in which the seven-membered ring of DBU is replaced by methyl groups, an enantioselectivity (38% *ee*) similar to that obtained with DBU (**4a**) was observed (Entries 3 and 5). With the noncoordinating Schwesinger base **4d**,[37,38] the reaction proceeded with a very low *ee* (4%) to afford the (α*S*,β*R*)-epoxide **3a**; that is, the opposite enantiomer to that formed with DBU (Entries 3 and 6). A similar effect was observed when LiCl was added to the DBU-mediated epoxidation, from which the (α*S*,β*R*)-epoxide **3a** was obtained with the low *ee* value of 6% (Entry 7).

Since DBU (**4a**) in toluene had proven to be the amine/solvent combination of choice in the asymmetric epoxidation with optically active hydroperoxides, the ROOH structure was varied for the enones **1a** (Entries 3 and 8−10) and **1b** (Entries 11−14) as substrates. In general, the hydroperoxide **2a** was slightly less enantioselective than **2b** and **2c**. For enone **1a**, the 4-chlorophenyl-substituted hydroperoxide **2b** afforded the (α*R*,β*S*)-epoxide with a marginally

Table 3. Enantioselective Weitz−Scheffer epoxidation of enones **1** with the optically active hydroperoxides **2**, base-catalyzed by the amines **4**[a]

Entry	Enone	R*OOH	Conversion (%)	Yield (%)[b]	*ee* (%)[c]	Configuration[d]
1[e]	**1a**	**2a**	88	95	9	(α*R*,β*S*)
2[f]	**1a**	**2a**	93	95	4	(α*R*,β*S*)
3	**1a**	**2a**	90	98	40	(α*R*,β*S*)
4[g]	**1a**	**2a**	94	96	9	(α*R*,β*S*)
5[h]	**1a**	**2a**	85	94	38	(α*R*,β*S*)
6[i]	**1a**	**2a**	> 95	93	4	(α*S*,β*R*)
7[j]	**1a**	**2a**	> 99	99	6	(α*S*,β*R*)
8	**1a**	**2b**	93	96	44	(α*R*,β*S*)
9	**1a**	**2c**	78	86	46	(α*R*,β*S*)
10	**1a**	**2d**	75	92	43	(α*R*,β*S*)
11	**1b**	**2a**	81	98	25	(α*R*,β*S*)
12	**1b**	**2b**	78	96	34	(α*R*,β*S*)
13	**1b**	**2c**	76	97	39	(α*R*,β*S*)
14	**1b**	**2d**	70	91	31	(α*R*,β*S*)
15	**1c**	**2a**	85	93	41	(α*R*,β*S*)
16	**1f**	**2a**	88	97	37	(α*R*,β*S*)
17	**1g**	**2a**	84	94	36	(α*R*,β*S*)
18	**1i**	**2a**	42	95	7	(α*S*,β*R*)
19	**1j**	**2a**	35	93	13	(α*S*,β*R*)
20	**1l**	**2a**	51	86	54	(α*R*,β*S*)
21	**1l**	**2b**	44	88	72	(α*R*,β*S*)

[a] Enone **1** (0.1−0.5 mmol), hydroperoxide **2** (1.0 equiv.), DBU (1.1−1.2 equiv.), except for Entries 4−6, in toluene, except for Entries 1 and 2, at ca. 20 °C. [b] Isolated epoxide **3** based on conversion of the enone **1**. [c] HPLC analysis on a Chiracel OD column with 2-propanol/hexane (5:95) as eluent; error ≤ 3% of the stated values. [d] Configuration of the major enantiomer is given. [e] CH_3CN was used as solvent. [f] MeOH was used as solvent. [g] Base **4b** was used. [h] Base **4c** was used. [i] Base **4d** was used. [j] LiCl was used as additive.

higher *ee* value (44%) than observed for **2a** (Entries 3 and 8). Similar enantioselectivities were obtained for the β-naphthyl-substituted hydroperoxide **2c** (46% *ee*, Entry 9) and the sugar-derived **2d** (43% *ee*, Entry 10). For the β-methyl enone **1b**, a more pronounced difference in the *ee* values was noted. Thus, while hydroperoxide **2a** displayed only 25% *ee* (Entry 11) for the (α*R*,β*S*)-epoxide, the *ee* value increased to 34% with the *para*-chloro derivative **2b** (Entry 12). The β-naphthyl-substituted hydroperoxide **2c** further improved the enantioselectivity to 39% *ee* (Entry 13), while the sugar-derived hydroperoxide **2d** afforded the epoxide **3b** in only 31% *ee* (Entry 14). Although the hydroperoxide **2c** gave the highest enantioselectivity, the degrees of conversion were higher with the simple phenyl-substituted hydroperoxide: for ROOH **2a**, they were 90% and 81% (Entries 3 and 11), while with ROOH **2c** they were only 78 and 76% (Entries 9 and 13) for the enones **1a** and **1b**, respectively. Hence, the more reactive hydroperoxide **2a** was used to assess the influence of the enone substitution pattern on the enantioselectivity.

As in the KOH-mediated epoxidation, the aryl substituents on the enone were varied first. Electron-donating substituents did not significantly change the enantioselectivity. For example, the *para*-methyl-substituted aryl group, both at the carbonyl functionality (substrate **1c**) as well as at the β-position of the enone (substrate **1f**), resulted in the corresponding epoxides with enantioselectivities close to those obtained for the phenyl derivative **1a** (Entry 3); the *ee* values thus were 41% for the substrate **1c** (Entry 15) and 37% *ee* for substrate **1f** (Entry 16), the corresponding (α*R*,β*S*)-epoxide enantiomer being observed in each case. Substrate **1g**, with a *para*-methoxy-substituted aryl group at the β-position, also afforded a similar *ee* value of 36% (Entry 17). The large *tert*-butyl substituent in the β-position of enone **1i** resulted in a very low enantioselectivity of 7% *ee* (Entry 18), with the (α*S*,β*R*) enantiomer slightly favored. Significant for this substrate is the fact that the opposite sense of enantioselectivity was obtained, since all other enones yielded the (α*R*,β*S*)-epoxide under these conditions (Entries 3, 11, 15−17). Enone **1j** also bears a β-*tert*-butyl group, but has a fixed *s-cis* conformation. Like the acyclic analog **1i**, the enone **1j** was epoxidized with a low *ee* value of only 13% *ee* (Entry 19) in favor of the (α*S*,β*R*) enantiomer. The poor enantioselectivity was matched by the sluggish reactivity of the *s-trans*-fixed enone **1k**, which was converted to an extent of only 30% after 125 h at 20 °C (in 5% *ee*; data not shown in Table 3).

The terminally disubstituted enone **1l** yielded the (α*R*,β*S*)-epoxide **3l** with an *ee* value of 54% for the hydroperoxide **2a** (Entry 20) and 72% *ee* for **2b** (Entry 21). These represent the highest enantioselectivities for this series of DBU-mediated asymmetric Weitz−Scheffer epoxidations.

Discussion

The results in Tables 1−3 show that the extent and sense of asymmetric induction in the Weitz−Scheffer epoxidation of α,β-enones **1** with the optically active hydroperoxides **2** (Scheme 2) decisively depends on the nature of the catalyzing base. Two types of base exist: On the one hand there are the alkali metal hydroxides (Tables 1 and 2), the inorganic KOH the most effective, and on the other hand the organic tertiary amine bases such as DBU (Table 3). Even though KOH and DBU induce opposite senses in the enantioselectivity with the same optically active (−)-(*S*)-hydroperoxide **2**, a common mechanistic explanation applies for the enantiofacial differentiation (Figure 1), as attested to by the similar behavior of the two types of bases (Tables 1−3).

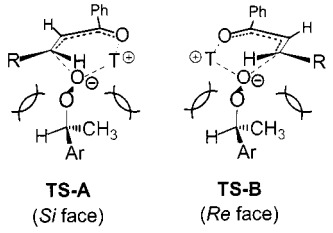


Figure 1. Template structures TS-**A** [(*Si*) face] and TS-**B** [(*Re*) face] for the base-catalyzed asymmetric oxygen transfer in the Weitz−Scheffer epoxidation of α,β-enones by optically active hydroperoxides, where T^+ (either the K^+ or R_3NH^+ ion) represents the templating agent; to facilitate the discussion, the (*Si*) face and (*Re*) face descriptors for substrate **1a** have been adopted for all others; actually the priorities differ only for substrate **1b**

The important feature pertinent for enantiocontrol in the structures TS-**A** and TS-**B** is the template-type aggregation of the enone substrate **1** and the activated peroxide ion $\mathbf{2}^-$ by the templating agent T^+, either the potassium ion (K^+) for KOH, or the ammonium ion (R_3NH^+) for the DBU. The tightness of aggregation in the template dictates the efficacy of stereodifferentiation through the steric interactions between the three components, namely the prochiral enone substrate **1**, the chiral hydroperoxide **2**, and the templating cations K^+ or $DBUH^+$. In particular, the aryl group is the largest substituent on the stereogenic center of the optically active hydroperoxide anions $\mathbf{2}^-$ and thus points away from the enone substrate **1**, exposing the smaller methyl group and the hydrogen atom for steric interaction with the enone substrate and the templating agent (T^+). Provided that the templating agent does not display any competitive steric demands (as is the case for DBU), of the two template structures TS-**A** and TS-**B**, the latter is of higher energy. TS-**B** is therefore disfavored, due to the more pronounced steric repulsion between the methyl group of the chiral hydroperoxide ion and the β-substituent of the prochiral enone substrate. To substantiate this mechanistic supposition, we shall recapitulate the salient experimental features of this asymmetric Weitz−Scheffer epoxidation implicit in Tables 1−3 (Scheme 2).

As expected from the template structures TS-**A** and TS-**B** (Figure 1), the enantioselectivity for both types of bases depends on the substitution in the enone substrate **1**. For example, the steric size of the β-substituent significantly influences the extent of asymmetric induction: a range of about 31% in the *ee* values results from the variation of the

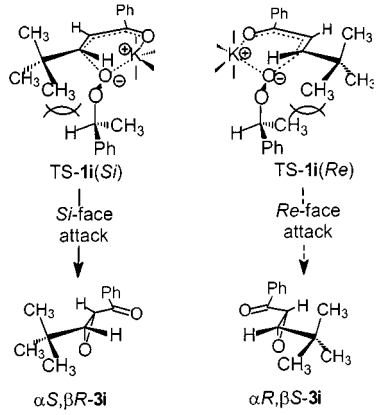
β-R substituent in the case of KOH (Table 2, Entries 1, 6 and 16), and even as much as 47% in the case of DBU (Table 3, Entries 3, 11 and 18) for the enones **1a** (R = Ph), **1b** (R = Me), and **1i** (R = *t*Bu). In contrast, electronic factors have a negligible influence on the enantioselectivity; this was tested by varying the β-aryl substituents (KOH: Table 2, Entries 13–15; DBU: Table 3, Entries 3, 16 and 17).

Furthermore, the fact that the *s-cis* conformation of the enone functionality is essential for effective enantiofacial discrimination for both the DBU- and the KOH-mediated reactions is indicative of the template structures in Figure 1. Thus, the *s-cis*-fixed enone **1j** (KOH: Table 2, Entry 18; DBU: Table 3, Entry 19) gives rise to a higher enantioselectivity than the corresponding open-chain substrate **1i** (KOH: Table 2, Entry 16; DBU: Table 3, Entry 18), whereas the *s-trans*-fixed substrate **1k** is scarcely (and, moreover, unselectively) converted (data not shown in Tables 2 and 3).

In order to achieve better enantiofacial differentiation, the catalyzing base must be available for coordination with the reactants, as depicted in structure TS-**A** and TS-**B**. If, for example, the potassium ion is sequestered by the 18-crown-6 ether (Table 2, Entry 5), or the noncoordinating Schwesinger base **4d** is used (Table 3, Entry 6), or LiCl is added to compete with DBU for coordination (Table 3, Entry 7), the enantioselectivity is significantly lower than under the normal reaction conditions (Table 2, Entry 1, Table 3, Entry 3). Thus, the nature of the base (KOH or DBU) and its coordinating ability are crucial in the control of the enantioselectivity.

All these experimental data form the basis for the proposed template structures TS-**A** and TS-**B** (Figure 1), which govern the efficacy of the asymmetric Weitz–Scheffer epoxidation with optically active hydroperoxides. In the (*Si*)-face (TS-**A**) and the (*Re*)-face (TS-**B**) attacks, the (−)-(*S*)-peroxide ion $\mathbf{2}^-$ approaches the *s-cis* conformationally aligned enone, directed by the base-derived templating agent (T^+ is either K^+ or R_3NH^+). The simultaneous coordination of the enone substrate and the peroxide anion induces the decisive steric interactions between the three aggregated species, which determines the extent and sense of the asymmetric oxygen transfer. The role of this template in the enantiofacial differentiation is now illustrated for the individual cases.

When KOH is used as base in this asymmetric Weitz–Scheffer epoxidation, the increasing size of the β-substituent [that is, the order methyl (Table 2, Entry 6), phenyl (Entry 1), and *tert*-butyl (Entry 16)] raises the enantioselectivity from 44 to 75% *ee* in favor of the (α*S*,β*R*)-epoxide enantiomer. This shows the fundamental importance of the steric interaction between the β-*R* enone substituent and the peroxide ion $\mathbf{2}^-$. In Scheme 3, this is illustrated for the *tert*-butyl-substituted enone **1i**, hitherto the most selective derivative and thus the best suited to illustrate the steric interactions that control the enantioselectivity. In the transition structures TS-**1i**(*Si*) and TS-**1i**(*Re*), the steric repulsion between the *tert*-butyl group and the hydrogen atom of the hydroperoxide in TS-**1i**(*Si*) – i.e., the (*Si*)-face attack – is clearly less serious than that with the hydroperoxide methyl group in TS-**1i**(*Re*) of the (*Re*)-face attack. Thus, in the KOH-catalyzed reaction, the sterically less hindered (*Si*)-face attack is favored and provides the (α*S*,β*R*)-epoxides **3**, as confirmed experimentally (Table 2, Entry 16).



Scheme 3. Potassium-coordinated template for the enantioselective epoxidation of the *tert*-butyl-substituted enone **1i** with the optically active hydroperoxide **2a**, catalyzed by KOH

To relieve the entropic constraint of the required *s-cis* conformation in the template (Scheme 3), the enone **1j**, the rigid geometry of which obligates this conformation, was chosen as substrate. This indeed resulted in the highest enantioselectivity yet observed with this oxidation system, 90% *ee* in favor of the (α*S*,β*R*)-epoxide **3j**. This fact nicely corroborates the validity of the proposed template effect in Figure 1. In contrast, for the conformationally fixed *s-trans* enone **1k**, the enantiodifferentiating coordination of the enone substrate and the optically active hydroperoxide anion by the templating K^+ ion in the proposed way (Scheme 3) is difficult, since the carbonyl oxygen atom and the β-carbon atom of the enone substrate are too far apart for effective coordination with the K^+ ion and the peroxide anion. Consequently, the substrate **1k** is epoxidized unselectively (ca. 0% *ee*). Moreover, the *s-trans*-fixed substrate is comparatively unreactive, which indicates that the *s-cis* conformation of the enone in the template is not only a prerequisite for effective enantiofacial discrimination, but also beneficial for the reactivity.

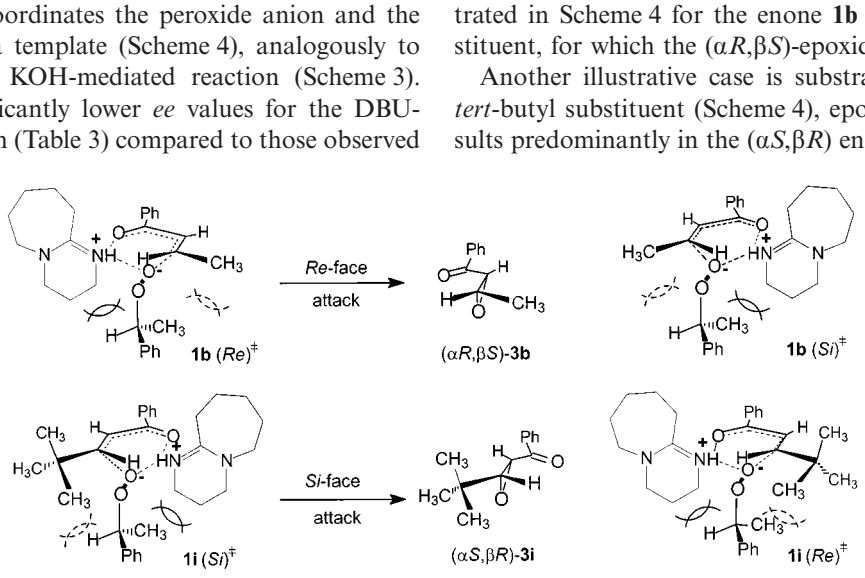
The vital importance of the templating potassium ion for enantiofacial differentiation, as presumed in Scheme 3, is unequivocally demonstrated when 18-crown-6 is employed as a sequestering agent. The drop in enantioselectivity, both for enone **1a** (Table 2, Entries 1 and 5) and for enone **1i** (Table 2, Entries 16 and 17), observed on addition of the potassium-complexing crown ether, substantiates the proposed mechanism in Scheme 3. Thus, the potassium ion coordinates the prochiral enone **1i** and the chiral peroxide anion $\mathbf{2a}^-$ to afford the two diastereomorphic transition structures TS-**1i**(*Si*) and TS-**1i**(*Re*), of which the former is preferred and the epoxide (α*S*,β*R*)-**3i** prevails (Scheme 3; Table 2, Entry 16).

The use of the amine base DBU (**4a**) in CH_3CN at 20 °C (Table 3, Entry 1) in place of KOH (Table 2, Entry 1), shows two additional revealing aspects of the asymmetric Weitz−Scheffer reaction with optically active hydroperoxides **2**: On one hand, the extent of the enantioselectivity is much lower; on the other hand, while KOH selects the (α*S*,β*R*)-configured epoxide **3a**, DBU selects the opposite (α*R*,β*S*) enantiomer. Clearly, this indicates a change in the oxygen-transfer process, since none of the factors that have been addressed so far would explain the preference for the (*Re*)-face attack observed with DBU. Thus, DBU and KOH differ significantly in their enantiofacial control; that is, DBU facilitates the (*Re*)-face attack [(α*R*,β*S*)-epoxide] and KOH the (*Si*)-face attack [(α*S*,β*R*)-epoxide]. This dichotomy demands a more detailed scrutiny of the interactions between the substrate, the ammonium ion, and the peroxide anion in the template structures.

The DBU results in Table 3 suggest that a nonpolar, aprotic solvent such as toluene (44% *ee*, Entry 3) promotes (α*R*,β*S*) selectivity, compared to that seen with the polar acetonitrile (9% *ee*, Entry 1), while the protic methanol (4% *ee*, Entry 2) reduces it even further. The addition of LiCl to the DBU-mediated reaction in toluene counteracts the effect of the amine base on the enantioselectivity (Table 3, Entry 3), and provides the opposite (α*S*,β*R*)-epoxide enantiomer in only 6% *ee* (Table 3, Entry 7). A similar low enantioselectivity (4% *ee*) of opposite configuration (α*S*,β*R*) is observed for the noncoordinating (no hydrogen bonding) Schwesinger base **4d** (Table 3, Entry 6). These experiments implicate hydrogen bonding as the mode of the aggregation, and we therefore propose the protonated amine ($DBUH^+$) as the hydrogen bond donor. Hydrogen bonding is known to be obstructed by polar (CH_3CN) or protic solvents (MeOH),[39] and the Schwesinger base **4d** is incapable of hydrogen bonding, facts that explain the poor enantioselectivity. Consequently, in the template structures of Figure 1, the protonated amine $DBUH^+$ acts as the templating agent and coordinates the peroxide anion and the enone substrate in a template (Scheme 4), analogously to the K^+ ion in the KOH-mediated reaction (Scheme 3). Evidently, the significantly lower *ee* values for the DBU-catalyzed epoxidation (Table 3) compared to those observed in the KOH-mediated case (Table 2) imply that the hydrogen-bonded template (Scheme 4) for the $DBUH^+$ ion is a looser aggregate than that produced by the oxygen atom ligating K^+ ion (Scheme 3), and the steric interactions for the enone/R*OOH/DBU system are thus weaker.

Be that as it may, the opposite senses of enantioselectivity found for the DBU- and the KOH-mediated asymmetric Weitz−Scheffer epoxidations still need to be accounted for. In this context, the size of the organic base (Table 3, Entries 3−5) appears to be important. The substantially lower (9% *ee*) enantioselectivity observed with the smaller tetramethylguanidine (**4b**) in Table 3 (Entry 4) and the similar *ee* values (ca. 40%) for the larger bases **4c** (Entry 5) and DBU (Entry 3) indicate that the large ammonium ions derived from the amine bases **4a** and **4c** favor the (*Re*)-face attack of the peroxide anion on the enone substrate in the hydrogen-bonded template **1b**$(Si)^{\neq}$ (Scheme 4). Indeed, the template structures reveal that the protonated amine interacts sterically with the substituents at the chirality center of the peroxide anion in competition with the steric repulsions of the β-substituent of the enone. Hence, the steric effects of the $DBUH^+$ ion counteract those of the β-enone substituent, the net stereochemical outcome being a balance between these two opposing trends. In particular, dominance of the steric interaction by the large DBU favors (*Re*)-face attack and affords an excess of the (α*R*,β*S*)-epoxide, while dominance by the β-substituent on the enone double bond, as in the case of the β-*tert*-butyl-substituted enone **1i**, favors the (*Si*)-face attack and the (α*S*,β*R*) enantiomer prevails. Thus, the observed (α*R*,β*S*) selectivity for the majority of the substrates in Table 3 indicates that the steric interactions between the $DBUH^+$ ion and the small hydrogen atom at the stereogenic center of the peroxide anion are minimized in the template structure **1**$(Re)^{\neq}$. In comparison, for the higher energy **1**$(Si)^{\neq}$ alternative, the more obstructive methyl substituent at the chirality center of the peroxide anion interacts with the $DBUH^+$ ion. This case is illustrated in Scheme 4 for the enone **1b** with a β-methyl substituent, for which the (α*R*,β*S*)-epoxide **3b** is favored.

Another illustrative case is substrate **1i**, with the large *tert*-butyl substituent (Scheme 4), epoxidation of which results predominantly in the (α*S*,β*R*) enantiomer of the epox-

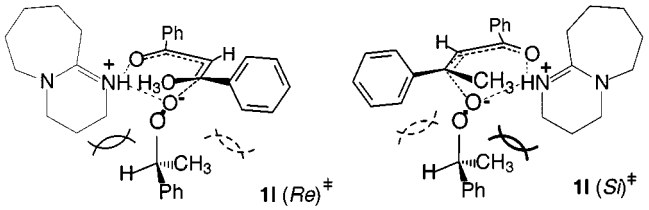


Scheme 4. Hydrogen-bonded template for the enantioselective epoxidation of the enones **1b** and **1i** with the optically active hydroperoxide **2a**, base-catalyzed by DBU

ide **3i**. Thus, the large *tert*-butyl substituent in this case overcompensates for the effect of the DBU base. The larger steric repulsion occurs between the β-*tert*-butyl group and the methyl substituent of the stereogenic center in the peroxide anion during (*Re*)-face attack, represented by the template structure **1i**(*Re*)$^{\neq}$. Thus, the (*Si*)-face approach is favored, since the smaller hydrogen atom is encountered by the enone *tert*-butyl group in the alternative template structure **1i**(*Si*)$^{\neq}$. The competing steric effects between DBU and the enone β-substituent not only explain the opposite senses of the enantioselectivities for the various substrates in Table 3, but also justify the lower *ee* values of the DBU-mediated asymmetric Weitz−Scheffer epoxidation.

As in the KOH-mediated epoxidations, the validity of the *s-cis* conformation depicted in the template structures is corroborated by the conformationally fixed substrates **1j** and **1k**. The *s-cis*-configured enone **1j** facilitates the formation of the enantiodifferentiating template and thus results in a higher enantioselectivity (Table 3, Entry 19) than seen with the corresponding conformationally flexible enone **1i** (Entry 18). In contrast, the *s-trans*-fixed enone **1k** is again less reactive and unselective (5% *ee*) in its epoxidation under the DBU-mediated reaction conditions (data not listed in Table 3).

In the epoxidation of the terminally disubstituted enone **1l**, the steric effect of the β-*cis* substituent in the enone and the steric demand of the DBU combine to yield the highest (up to 72% *ee*) enantioselectivities so far achieved with the DBU base (Table 3, Entries 20 and 21). Analysis of the steric congestion in the template structures **1l**(*Re*) and **1l**(*Si*) clarifies this significant improvement in the extent of asymmetric induction.



The (*Si*)-face attack brings the hydrogen atom at the stereogenic center of the hydroperoxide ion into close proximity to the phenyl group on the enone double bond, while the methyl group of the peroxide anion is positioned proximate to the $DBUH^+$ ion and also to the methyl group of the enone double bond in the $DBUH^+$-coordinated template **1l**(*Si*)$^{\neq}$. In contrast, for the (*Re*)-face attack, the methyl group of the peroxide anion is positioned proximate to the phenyl group on the enone double bond and the hydrogen atom toward the $DBUH^+$ ion and also toward the methyl group of the enone double bond. The latter steric repulsion of the hydrogen atom of the peroxide anion with $DBUH^+$ and the enone methyl group is evidently less serious and the (α*R*,β*S*) enantiomer of the epoxide **3l** is thus preferentially generated by a substantial margin (up to 72% *ee*).

Conclusion

In summary, a template effect has been proposed in order to interpret the extent and sense of the enantioselectivity in the base-catalyzed, asymmetric Weitz−Scheffer epoxidation of α,β-enone substrates with optically active hydroperoxides. In the template structure, made up of the enone substrate, hydroperoxide, and base catalyst, the enantiofacial differentiation is governed by the steric interactions between the aggregated species. When KOH is used as base, the (α*S*,β*R*) enantiomer of the epoxide **3** enantiomer is formed in up to 90% *ee*, due to the less severe steric repulsions between the β-substituent of the enone and the substituent at the chirality center of the peroxide anion during the (*Si*)-face attack. In the DBU-mediated epoxidation, competition between the steric interactions of the optically active peroxide anion with the enone β-substituent and the $DBUH^+$ (usually dominant) favor the (*Re*)-face attack, which results in the (α*R*,β*S*) enantiomer of the epoxide **3** in up to 72% *ee*. The asymmetric Weitz−Scheffer epoxidation of the α,β-enones **1** with the optically active hydroperoxides **2**, catalyzed by KOH or DBU, affords both enantiomers of the epoxides **3** with *ee* values that range up to good, which should be valuable for asymmetric organic synthesis.

Experimental Section

General Remarks: ^1H and ^{13}C NMR spectra were recorded with Bruker AC 200 (^1H: 200 MHz, ^{13}C: 50 MHz) or Bruker AC 250 (^1H: 250 MHz, ^{13}C: 63 MHz) spectrometers, IR spectra were measured with a Perkin−Elmer 1600 FT-IR spectrophotometer. The HPLC analyses were carried out on chiral columns (Daicel CHIRALCEL OD and OB-H) with a Kontron instrument, furnished with a UVIKON 720 spectrophotometer and an IBZ Messtechnik (Hannover, Germany) CHIRALYSER 1.6. The optical rotations were determined with a Perkin−Elmer 241 MC polarimeter. Solvents and commercially available chemicals were purified by standard procedures. Enone **1a** is commercially available (Riedel-de Haën). Enones **1b**−**l** were prepared according to literature procedures (**1b**,[8] **1c**,[40] **1d**,[41] **1e**,[42] **1f**,[43] **1g**,[44] **1h**,[45] **1i**,[46] **1k**,[47] **1l**[48]).

(*E*)-2-(2′,2′-Dimethylpropylidene)-1,2,3,4-tetrahydronaphthalene-1-one (1j): NaOH solution (10%, 1.20 mL) was added to a mixture of tetralone (1.46 g, 10.0 mmol) and pivalaldehyde (1.20 g, 11.0 mmol) in 6.5 mL of ethanol (77% in water) and the mixture was stirred for 48 h at 25 °C. The ethanol was removed in a rotary evaporator (25 °C, 20 Torr) and the residue was diluted with 10 mL of water and extracted with ether (3 × 15 mL). The combined organic phases were washed with water (5 mL) and brine (5 mL) and dried with $MgSO_4$, and subsequent silica gel chromatography (Et_2O/petroleum ether, 1:9) yielded 1.21 g (56%) of a colorless oil. ^1H NMR (200 MHz. $CDCl_3$): δ = 1.25 (s, 9 H, CH_3), 2.95 (s, 4 H, CH_2), 6.97 (s, 1 H, CH), 7.21−7.36 (m, 2 H, aromatic), 7.42−7.50 (m, 1 H, aromatic), 8.06−8.11 (m, 1 H, aromatic). ^{13}C NMR (50 MHz. $CDCl_3$): δ = 26.3, 27.8, 30.2, 32.6, 127.1, 128.4, 128.6, 133.3, 133.8, 134.9, 144.1, 149.8, 189.3. $C_{15}H_{18}O$ (214.14): calcd. C 84.07, H 8.47; found C 83.68, H 8.56.

Enzymatic Kinetic Resolution of 1-(2-Naphthyl)ethyl Hydroperoxide (2c):[49] Horseradish peroxidase (1.00 mg) was added to a stirred

mixture of the racemic hydroperoxide **2c** (47.0 mg, 0.250 mmol) and guaiacol (12.0 mg, 0.100 mmol) in a 0.1 M phosphate buffer (pH = 6, 2.5 mL). The reaction was monitored by HPLC, which showed 99% *ee* of the hydroperoxide after 1 h. The reaction mixture was filtered through Celite and extracted with ether (3 × 15 mL), and the combined organic layers were dried ($MgSO_4$), concentrated (20 °C, 30 Torr), and purified by silica gel chromatography (petroleum ether/Et_2O, 8:1) to yield 17.9 mg (76%) of the (−)-(*S*)-hydroperoxide **2c** (> 99% *ee*) and 17.8 mg (82%) of the corresponding alcohol (96% *ee*). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.56 (d, *J* = 6.6 Hz, 3 H, CH_3), 5.26 (q, *J* = 6.6 Hz, 1 H, CH), 7.48−7.54 (m, 3 H, aromatic), 7.83−7.91 (m, 4 H, aromatic). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.9, 78.8, 118.8, 120.7, 121.0, 121.1, 122.6, 122.8, 123.5, 128.1, 128.1, 133.6. $[\alpha]_D^{20}$ = −91.5 (*c* = 1.0, $CHCl_3$, > 99% *ee*). HPLC: (−) 16.64, (+) 22.28 min (OD column; *i*PrOH/hexane, 9:1; flow 0.9 mL/min).

Epoxides 3

Representative Procedure A for the Epoxidation of Enone 1a by the Optically Active Hydroperoxides 2a with KOH as a Base: A precooled (−40 °C) solution of enone **1a** (104 mg, 0.500 mmol) and the optically active hydroperoxide (−)-(*S*)-**2a** (69.0 mg, 0.500 mmol) in dry CH_3CN (3 mL) was added slowly to a suspension of powdered KOH (56.0 mg, 1.00 mmol) in dry CH_3CN (2 mL) at −40 °C under nitrogen. The reaction mixture was stirred for 20−30 min at −40 °C, decanted into ice/water (10 mL), and extracted with ether (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent was evaporated (20 °C, 30 Torr). Purification by silica gel flash chromatography, with a petroleum ether/ethyl ether (15:1) mixture as eluent, afforded 110 mg (99%) of epoxy ketone (α*S*,β*R*)-**3a** (51% *ee*) as colorless needles (m.p. 62−63°C). The spectroscopic data were in accordance with those reported.[50] The optically active epoxides **3b**−**j** were prepared from the corresponding enones **1b**−**j** according to the above procedure, and the results are given in Table 2.

Representative Procedure B for the Epoxidation of the Enone 1a by the Optically Active Hydroperoxide 2a with DBU as a Base: DBU (91.0 mg, 0.600 mmol) was added under nitrogen to a solution of enone **1a** (104 mg, 0.500 mmol) and the optically active hydroperoxide (−)-(*S*)-**2a** (69.0 mg, 0.500 mmol) in dry toluene (4 mL). The reaction mixture was stirred magnetically for 24 h at ca. 20°C, poured into water (8 mL), and extracted with ether (3 × 8 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated (20 °C, 30 Torr). Purification by silica gel flash chromatography, with a petroleum ether/ethyl ether (15:1) mixture as eluent, afforded 98.0 mg (88%) of the known epoxy ketone (α*S*,β*R*)-**3a** (40% *ee*). The spectroscopic data were in accordance with those reported.[50] The enones **1b**, **1c**, **1f**, **1g**, **1i**, **1j**, and **1l** were also epoxidized according to this procedure and the results are given in Table 3. The epoxides **3a**−**i** and **3l** are known; their spectroscopic data were identical to those described in the literature. The configuration of the major enantiomer was in each case determined by comparison with the literature data (**3a**,[50] **3b**,[51] **3c**,[6] **3d**,[14] **3e**,[8] **3f**,[52] **3g**,[8] **3h**,[12] **3i**,[6] **3j**,[36] **3k**,[9] **3l**[53]). The configuration of **3j** was tentatively assigned by comparison of the HPLC retention times and the optical rotation of the reported isopropyl derivative.[22] Because of the very low enantiomeric excess (5% *ee*) observed for **3k**, the absolute configuration was not determined.

(2*S*,3′*R*)-3′-*tert*-Butyl-1,2,3,4-tetrahydrospiro[naphthalene-2,2′-oxirane]-1-one (3j): Epoxide **3j** was prepared according to the above general epoxidation Procedure A in 90% yield as a white powder; m.p. 62−63 °C. ^{1}H NMR (200 MHz. $CDCl_3$): δ = 1.10 (s, 9 H, CH_3), 2.38−2.62 (m, 2 H, CH_2), 2.97 (s, 1 H, CH), 3.12−3.19 (m, 2 H, CH_2), 7.26−7.38 (m, 2 H, aromatic), 7.48−7.56 (m, 1 H, aromatic), 8.03−8.08 (m, 1 H, aromatic). ^{13}C NMR (50 MHz. $CDCl_3$): δ = 26.2, 27.9, 28.4, 32.3, 63.8, 72.4, 126.7, 127.7, 128.6, 132.6, 133.9, 143.5, 194.7. $[\alpha]_D^{20}$ = + 68.4 (*c* = 1.0, $CHCl_3$, for 100% *ee*). $C_{15}H_{18}O_2$ (230.13): calcd.: C 78.23, H 7.88; found C 78.04, H 7.93.

7,7a-Dihydro-7,7-dimethylnaphth[2,3-*b*]oxiren-2(1a*H*)-one (3k): The epoxidation of the enone **1k** according to the general Procedures A and B resulted in only 30% conversion and very low (5%) *ee* values. For this reason, the racemic epoxide was prepared as described below.[54] A solution of DMD in acetone (0.89 M, 4.90 mL, 440 mmol) at 0 °C was added to a magnetically stirred solution of 4,4-dimethyl-4*H*-naphthalene-1-one (44.0 mg, 440 mmol) in dichloromethane (3 mL). After this had stirred for 12 h at ca. 20 °C, another batch of the DMD solution (440 mmol) was added and stirred until complete conversion of the enone, as determined by TLC. The reaction mixture was dried ($MgSO_4$), and the solvent was evaporated (20 °C, 20 mbar). Silica gel chromatography (petroleum ether/ether, 95:5) afforded 44.4 mg (87%) of the racemic epoxide **3k** as white needles, m.p. 68−69 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, CH_3), 1.69 (s, 3 H, CH_3), 3.56 (d, *J* = 4.3 Hz, 1 H, CH), 3.72 (d, *J* = 4.3 Hz, 1 H, CH), 7.32−7.40 (m, 2 H, aromatic), 7.55−7.62 (m, 1 H, aromatic), 7.88−7.92 (m, 1 H, aromatic). ^{13}C NMR (63 MHz, $CDCl_3$): δ = 25.2, 30.1, 36.0, 55.4, 62.5, 126.0, 127.0 127.5, 128.8, 134.2, 147.1, 194.7. $C_{12}H_{12}O_2$ (188.08): calcd.: C 76.57, H 6.43; found C 76.11, H 6.85.

Acknowledgments

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