Diastereoselective Reactions of the Tiglic Acid Functionality Mediated by Oxazolidine Chiral Auxiliaries: A Mechanistic Comparison of DMD and *m*-CPBA Epoxidations versus Singlet Oxygen and PTAD Ene Reactions

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2,2-Dimethyloxazolidines have been utilized as chiral auxiliaries for the diastereoselective functionalization of the optically active tiglic acid derivatives (*S*)-**1** by means of epoxidation with DMD or *m*-CPBA and ene reactions with $^1O_2$ or PTAD. In the DMD and *m*-CPBA epoxidations, high diastereoselectivities but opposite senses of diastereomer selection were observed. In contrast, the stereochemistry of the $^1O_2$ and PTAD ene reactions depended on the size of the attacking enophile: whereas essentially perfect diastereoselectivity was obtained with PTAD, much lower stereoselection was observed with $^1O_2$. The stereochemical results for the DMD and *m*-CPBA epoxidations and the PTAD ene reaction are explained in terms of the energy differences for the corresponding diastereomeric transition states, dictated by steric and electronic effects. The PTAD ene reaction for these tiglic acids (*S*)-**1** provides, after removal of the chiral auxiliaries, an attractive synthetic route for optically active β-amino acid derivatives.

Introduction

Evans' chiral 2-oxazolidinones are well known as efficient chiral auxiliaries in enolate chemistry.[1] Unfortunately, the presence of a Lewis acid, required for metal chelation, is not compatible with a large number of common oxidants. In the 1990s, Porter and Kanemasa reported the induction of effective diastereochemical control by chiral 2,2-dimethyloxazolidines, in radical additions,[2] nitrile oxide cycloadditions,[3] and conjugate additions of organocuprates[4] to α,β-unsaturated amides. The efficacy of these auxiliaries originates from the conformational alignment of the amide linkage and the shielding of one of the faces of the CC double bond by the proximate substituent at the C-4 position of the oxazolidine ring,[3b] with the steric hindrance imposed by the two methyl groups at the C-2 position of the oxazolidine ring, which forces the amide fragment predominantly to occupy the *syn*/*s*-*cis* conformation **A** (Figure 1).[3b] The highest efficiencies were observed with 2,2,5,5-tetramethyloxazolidines **C**, in which the two methyl groups at the 5-position enhance the shielding of the *N*-acryloyl reaction site by the benzylic phenyl group (Figure 1).[3c]

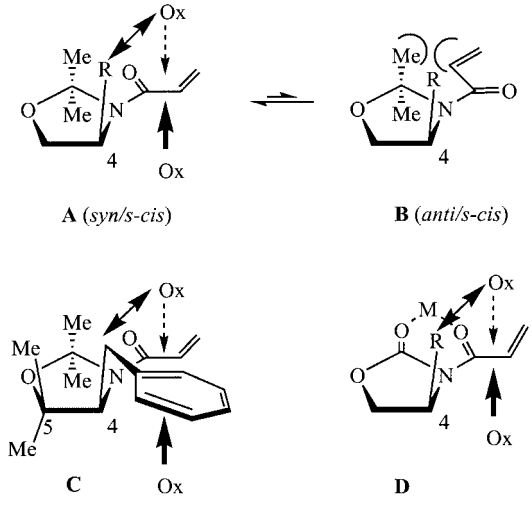

Figure 1. The preferred conformation **A** (*syn*/*s*-*cis*) vs. **B** (*anti*/*s*-*cis*) for the favored oxidative attack in *N*-acryloyl-2,2-dimethyloxazolidines; structure **C** displays the increased shielding by the two methyl groups at the C-5 position of the oxazolidine ring and structure **D** shows the metal chelation in *N*-acryloyloxazolidinones.

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Enantiomerically enriched α-epoxy amides are useful building blocks for stereoselective chemical transformations.[5] In particular, the epoxides derived from tiglic acid and alkyl tiglates are parts of some natural products[6] or are used as precursors in the synthesis of biologically and pharmaceutically important compounds, such as the phytotoxin phomozin.[7] Its preparative relevance notwithstanding, diastereoselective epoxidation of tiglic acid derivatives has so far furnished discouraging results,[8] probably because direct epoxidation by alkaline hydrogen peroxide[9] (the Weitz–Scheffer conditions commonly used for the epoxidation of electron-poor olefins) usually proceeds nonstereoselectively. Furthermore, electrophilic oxidants such as peracids[10] either react very slowly with alkenes that bear electron-withdrawing groups[11] or, alternatively, are ring-opened to the corresponding diol ester by the liberated *m*-CBA.[11] In contrast, it is well established that dioxiranes[12] efficiently epoxidize α,β-unsaturated carbonyl compounds under mild conditions, an oxidation method that should be advantageous for this purpose.[13]

It should be evident in this context that the convenient and efficient preparation of optically active heteroatom-functionalized acid derivatives constitutes an attractive goal in view of their versatile synthetic utility.[14] Indeed, the as yet still relatively little explored β-amino acids and the peptides derived from them are of special pharmaceutical significance in modern drug design.[15] Such heteroatom-containing functionalities may be readily prepared through regioselective ene reactions between tiglic acid substrates and either singlet oxygen ($^1O_2$), to afford oxygen-functionalized products, or the 1,2,4-triazoline-3,5-dione (TAD) enophile for nitrogen-functionalized ones. In the latter case, the use of the TAD enophile is preparatively quite valuable, since it offers a useful method for the synthesis of β-amino acids through the carbanion-assisted cleavage of the urazole NN bond.[16] Despite its potential, this promising concept has yet to be exploited. Only the highly diastereoselective $^1O_2$ ene reactions of the tiglic acid functionality, with the employment of chiral auxiliaries to achieve high diastereoselectivity, have been reported to date.[17] Similarly, excellent results have also been obtained with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) for the diastereoselective preparation of nitrogen-functionalized products.[17b]

Here we present an efficient method for the diastereoselective oxidation of the tiglic acid functionality through the use of 2,2-dimethyloxazolidines as chiral auxiliaries. In particular, the diastereoselective reactions investigated involve the epoxidation of chiral tiglic acid derivatives by common epoxidants such as DMD and *m*-CPBA, to afford optically active α-epoxy amides. Alternatively, the $^1O_2$ and PTAD enophiles have been employed to obtain enantioenriched β-hydroperoxy and β-amino acid derivatives, all useful chiral building blocks in synthetic organic chemistry. Furthermore, a comparative mechanistic explanation of the stereochemical control in the heteroatom-transferring process is offered, providing a comprehensive interpretation of the diastereoselectivity in terms of the interplay between the chiral auxiliary structure and the reaction type.

Results

The enantiomerically pure tiglic amides (*S*)-**1** with substituents of different size at the C-4 position of the oxazolidine ring were obtained in good yields by acylation of the appropriate oxazolidine with tiglic acid chloride (cf. Experimental Section). Subsequent functionalization of the tiglic amide fragment was achieved by epoxidation with DMD and *m*-CPBA or through ene reactions between singlet oxygen and PTAD (Scheme 1).

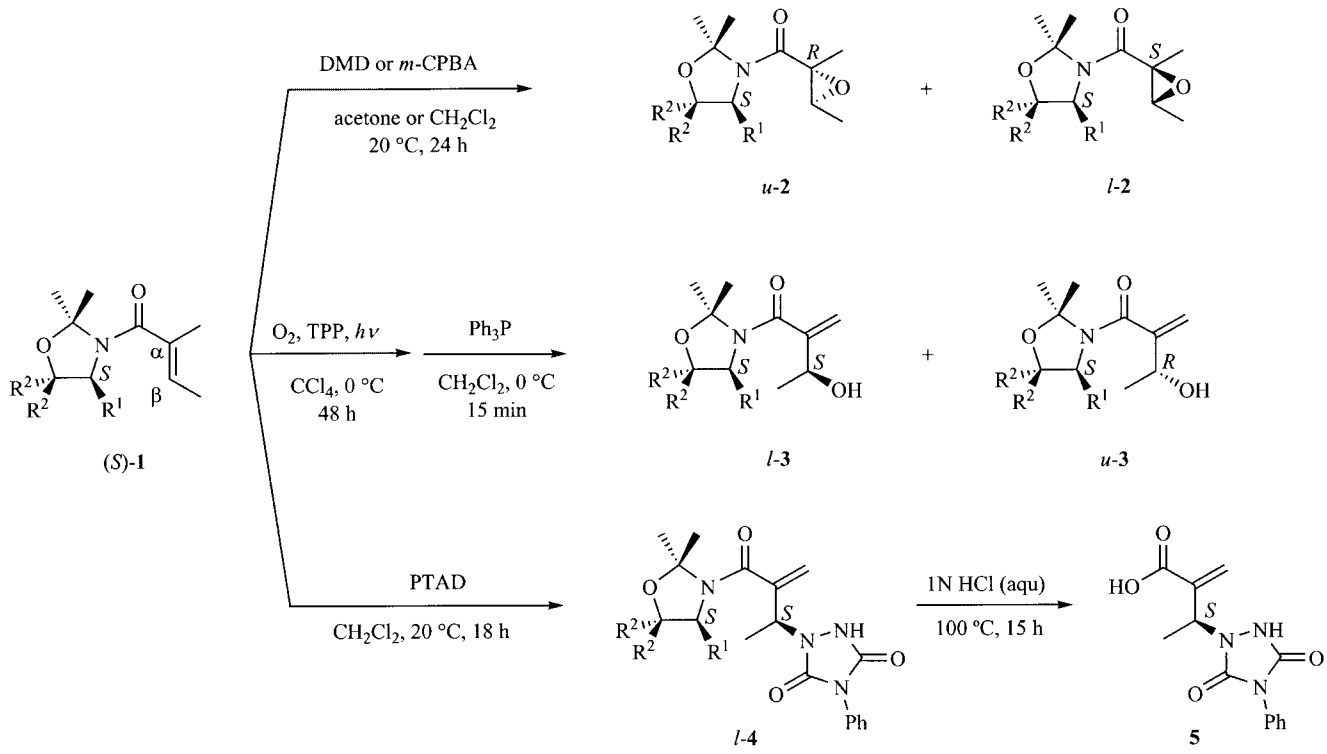
Treatment of the tiglic amides (*S*)-**1c**, (*S*)-**1e**, and (*S*)-**1f** with DMD (three equiv.) in acetone or *m*-CPBA (two equiv.) in CH_2Cl_2 at 20 °C for 24 h provided the corresponding diastereomeric epoxides *u*-**2** and *l*-**2** (Table 1; Entries 3 and 5–6) in good to excellent yields (72–95%).[18] Evidently, despite the electron-poor character of the tiglic acid fragment, these oxidations proceeded with high levels of conversion (above 88%) with both electrophilic reagents.

Both oxidants, DMD and *m*-CPBA, gave high diastereoselectivities (up to 86% de; see Table 1). Surprisingly, these epoxidations take place with opposite stereochemical senses: with DMD the major diastereomer is *u*-**2** while with *m*-CPBA it is *l*-**2**. Also mechanistically significant is the fact that, contrary to expectation, the C-4 (R^1) and C-5 (R^2) substituents at the oxazolidine ring have only a minor influence on the diastereoselectivity of the epoxidation process.

The *m*-CPBA epoxidation of (*S*)-**1e** was conducted in several solvents, to assess the influence of solvent polarity and hydrogen bonding on the diastereoselectivity and on the degree of conversion. Although only a small effect on the diastereoselectivity was found [24:76 (MeCN), 22:78 (*t*BuOH), and 34:66 (MeOH)], a dramatic drop was observed for the conversion in MeOH: >95% in CH_2Cl_2, MeCN, or *t*BuOH and only 7% in MeOH.[18]

The photooxygenation of the amides (*S*)-**1** was performed at 0 °C in CCl_4 with tetraphenylporphine (TPP) as sensitizer, to give the corresponding hydroperoxides as single regioisomers. Because of their labile natures, the hydroperoxides were reduced in situ with Ph_3P to the allylic alcohols **3**, which were isolated in good yields (57–79%) as diastereomeric mixtures (Table 1; Entries 2–6). These ene reactions of $^1O_2$ took place nondiastereoselectively, except in the case of (*S*)-**1e**, in which the *de* value was only 20%. As in the epoxidations of (*S*)-**1** with DMD and *m*-CPBA, the influence of the substituents at the C-4 and C-5 positions of the oxazolidine on the diastereomeric ratio is negligible. For this reason, the singlet-oxygen ene reaction of (*S*)-**1a**, with the small methyl group attached to the C-4 position of the oxazolidine ring, was not investigated (Table 1; Entry 1).

The ene reactions between the amides (*S*)-**1** and PTAD at 20 °C in CH_2Cl_2 gave the corresponding ene adducts *l*-**4** with complete regioselectivity in up to 81% yield. Essentially perfect diastereoselection was observed irrespective of the substituents at the C-4 position of the oxazolidine ring, even for the derivative (*S*)-**1a** with the small methyl group (Table 1; Entries 1–5). For this reason, the *gem*-dimethyl



Scheme 1.

Table 1. Diastereoselectivities for the DMD and *m*-CPBA epoxidations and $^1O_2$ and PTAD ene reactions of amides (*S*)-**1**.

Entry	Amide	R^1	R^2	Epoxidation DMD[a] *u*-**2**:*l*-**2**[d]	*m*-CPBA[b] *u*-**2**:*l*-**2**[d]	Ene reaction $^1O_2$[c] *l*-**3**:*u*-**3**[d] [e]	PTAD[b] *l*-**4**: *u*-**4**[f]
1	(*S*)–**1a**	Me	H	–[g]	–[g]	–[g]	>98:02
2	(*S*)–**1b**	CH_2tBu	H	–[g]	–[g]	50:50	>98:02
3	(*S*)–**1c**	CH_2Ph	H	91:09[h]	15:85[h]	50:50[i]	>98:02[i]
4	(*S*)–**1d**	*i*Pr	H	–[g]	–[g]	50:50[i]	>98:02[i]
5	(*S*)–**1e**	Ph	H	83:17[h]	15:85[h]	60:40[j]	>98:02
6	(*S*)–**1f**	CH_2Ph	Me	90:10[h]	07:93[h]	50:50	–[g]

[a] Conducted in acetone. [b] Conducted in CH_2Cl_2. [c] Conducted in CCl_4. [d] Determined by ^1H NMR (200 or 600 MHz) analysis of characteristic signals directly on the crude reaction mixture (error ± 5% of the stated values). [e] Determined from the diastereomeric mixture of allylic hydroperoxides before treatment with Ph_3P. [f] Determined by ^{13}C NMR (50 MHz) analysis of characteristic signals directly on the crude reaction mixture (error ± 2% of the stated values). [g] Not examined. [h] cf. ref. [18]. [i] cf. Ref. [20]. [j] Configuration tentatively assigned.

substrate (*S*)-**1f** was not investigated for the PTAD reaction (Table 1; Entry 6).

The assignment of the relative configurations of the epoxides **2** is based on the X-ray structure of *l*-**2e**.[19] By analogy, the configurations of the major diastereomers obtained in the *m*-CPBA epoxidations of amides (*S*)-**1c** and (*S*)-**1f** were assigned as *l*-**2c** and *l*-**2f**; consequently, the minor diastereomers are *u*-**2c** and *u*-**2e/f**. The (*S*) configurations of the newly formed stereogenic centers in the urazoles *l*-**4d**[20] and *l*-**4e**[21] was determined by X-ray structural analysis. The configurations of the other urazoles *l*-**4a**–**c** were assessed by chemical correlation. For this purpose, the oxazolidine chiral auxiliaries in *l*-**4a**–**e** were removed by acid-catalyzed hydrolysis (cf. Supporting Information; for Supporting Information see also the footnote on the first page of this article), to form the same (*S*)-configured carboxylic acid **5** in each case (Scheme 1).

Discussion

The observed diastereoselectivities for the epoxidations of the substrates (*S*)-**1** with DMD and *m*-CPBA and their ene reactions with $^1O_2$ and PTAD convey a number of unexpected results that need to be interpreted mechanistically. In particular, detailed comparison of our results obtained for the four reactants obliged us to revise the previously suggested transition structures and we now offer a more consistent mechanistic view.[18,20] The diastereomeric control of the vast majority of the reported epoxidations and

ene reactions with these oxidants is based on directing effects that favor the approach of the reagent onto the face possessing a polar functional group for attractive interactions.[22] In the absence of such a steering phenomenon, the oxidation normally takes place on the sterically less hindered side. In the case of flexible substrates, in particular acyclic ones such as examined here, detailed conformational analysis is essential in order to explain the π-facial selectivity of the oxygen transfer; consequently, the preferred conformations of the tiglic amides (*S*)-**1** had to be scrutinized.

In this context, analogously to the *N*-acryloyloxazolidines described by Kanemasa and Porter (Figure 1),[3b] our conformational analysis reveals, on the basis of molecular models, that the *N*-tigloyl fragment in (*S*)-**1** should be located *syn* with respect to the oxazolidine ring, to avoid steric interactions with the two methyl groups at the C-2 position in the auxiliary. Unlike in the case of the Kanemasa and Porter auxiliaries, the CC double bond cannot be coplanar (*s-trans* or *s-cis*) with respect to the carbonyl group, due to steric interactions with the substituent at the C-4 position of the oxazolidine ring (Figure 2). The nonplanar conformational preference of the double bond relative to the carbonyl group is general for methacrylate and tiglate derivatives of imides and amides.[23]

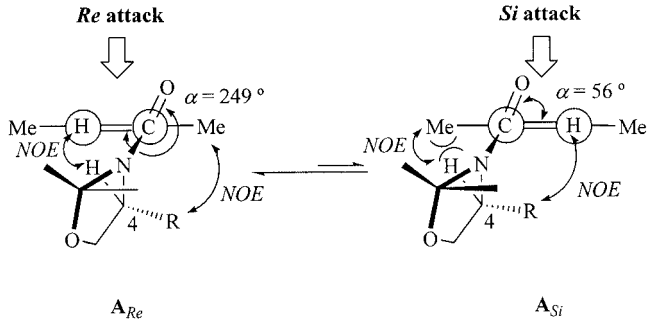


Figure 2. The two lowest-energy conformers, $\mathbf{A}_{Re}$ and $\mathbf{A}_{Si}$, of the tiglic amide (*S*)-**1a** (R = Me), determined from AM1 semiempirical calculations (α is the dihedral angle between the double bond and the carbonyl group). Also shown are the NOE contacts within the (*S*)-**1c** (R = CH_2Ph) substrate, which support the coexistence of both conformers ($\mathbf{A}_{Re}$ and $\mathbf{A}_{Si}$) in solution.

Semiempirical calculations[18] confirmed our intuitive conformational analysis for the tiglic amides (*S*)-**1**: the values for the dihedral angles between the double bond and the carbonyl group of the lowest-energy conformations were computed to be 249° (conformer $\mathbf{A}_{Re}$ in Figure 2) and 56° (conformer $\mathbf{A}_{Si}$). In these two conformers, one of the π faces of the double bound is well shielded from attack by the oxidant by the chiral auxiliary; specifically, the *Si* face is shielded in conformer $\mathbf{A}_{Re}$ and the *Re* face in conformer $\mathbf{A}_{Si}$. The energy difference, however, amounts to only ca. 1.4 kcal·mol^{-1} in favor of the conformer $\mathbf{A}_{Re}$. We presume that this is due to the destabilization of the $\mathbf{A}_{Si}$ conformation on account of the steric interaction between the H-4 atom in the oxazolidine ring and the α-methyl group of the tigloyl functionality.

As would be expected from the above computational results, the ^{1}H NMR spectra of the tiglic amides (*S*)-**1** each show one set of signals at 293 K, a spectral feature that is interpreted in terms of the two coexisting, rapidly interconverting conformers $\mathbf{A}_{Re}$ and $\mathbf{A}_{Si}$. Additionally, a ^{1}H/^{1}H-NOESY spectrum of (*S*)-**1c** (see Supporting Information) reveals prominent NOE contacts between the tiglic acid functionality and the oxazolidine chiral auxiliary, which substantiate the simultaneous presence of conformers $\mathbf{A}_{Re}$ and $\mathbf{A}_{Si}$, rapidly interchanging in solution (Figure 2).

On the basis of the Curtin–Hammett principle,[24] no significant diastereoselective control should be expected from the relatively low energy difference in the ground-state conformations of (*S*)-**1**. Since the values of the free energy of activation for the DMD and *m*-CPBA epoxidations, as well as for the $^1O_2$ and PTAD ene reactions, are notably higher than the computed rotational barriers,[25] the Curtin–Hammett principle requires that the product ratio should depend solely on the free energy differences between the transition states.

The established preferred mode for dioxirane attack is a concerted, oxenoid-type *spiro* transition state, with the plane of the peroxide ring oriented perpendicularly to and bisecting the π system of the double bond.[12,26] This mechanism has been corroborated by theoretical work,[27] which identified additional structural and electronic features in the transition state for the two forming CO bonds. Therefore, in addition to the available experimental evidence, the calculations indicate that dioxiranes are polar species, for which electronic effects such as dipole–dipole interactions become important factors in the transition state for the oxygen transfer, besides steric and conformational effects.[22a–c,28] Accordingly, we propose that the *spiro* transition states $\mathbf{B}_{Re}^{\neq}$ and $\mathbf{B}_{Si}^{\neq}$ (Figure 3) best account for the observed diastereoselectivity of the DMD epoxidations of (*S*)-**1**, in which the oxidant attacks the unshielded faces of the CC double bond in the two ground-state conformers $\mathbf{A}_{Re}$ and $\mathbf{A}_{Si}$ (Figure 3).

Closer inspection of the early transition states **B** suggests that in the $\mathbf{B}_{Si}^{\neq}$ structure the DMD attack is disfavored by the steric interactions between the amide carbonyl pointing towards the center of the double bond and the DMD methyl groups, directed away from the allylic hydrogen atoms of the tiglic substrate. In contrast, these steric interactions are negligible in the $\mathbf{B}_{Re}^{\neq}$ transition structure. In addition, electronic effects also disfavor the $\mathbf{B}_{Si}$ transition state, due to the higher electrostatic repulsion between the more proximate polarized DMD and the polar carbonyl group of the tiglic amide, oriented towards the center of the double bond. On the basis of this mechanistic scrutiny, it is to be expected that the transition state $\mathbf{B}_{Re}^{\neq}$ should be preferred over $\mathbf{B}_{Si}^{\neq}$, which implicates *unlike* diastereoselectivity, as observed (Table 1; Entries 3, 5 and 6).

In the accepted "butterfly" mechanism for the peracid epoxidation,[25b–c,27b] theoretical work suggests a preference for *spiro* attack. As in the DMD case, the olefinic carbons have undergone only a small degree of rehybridization with little change in the bonding of the peroxy acid oxidant, as

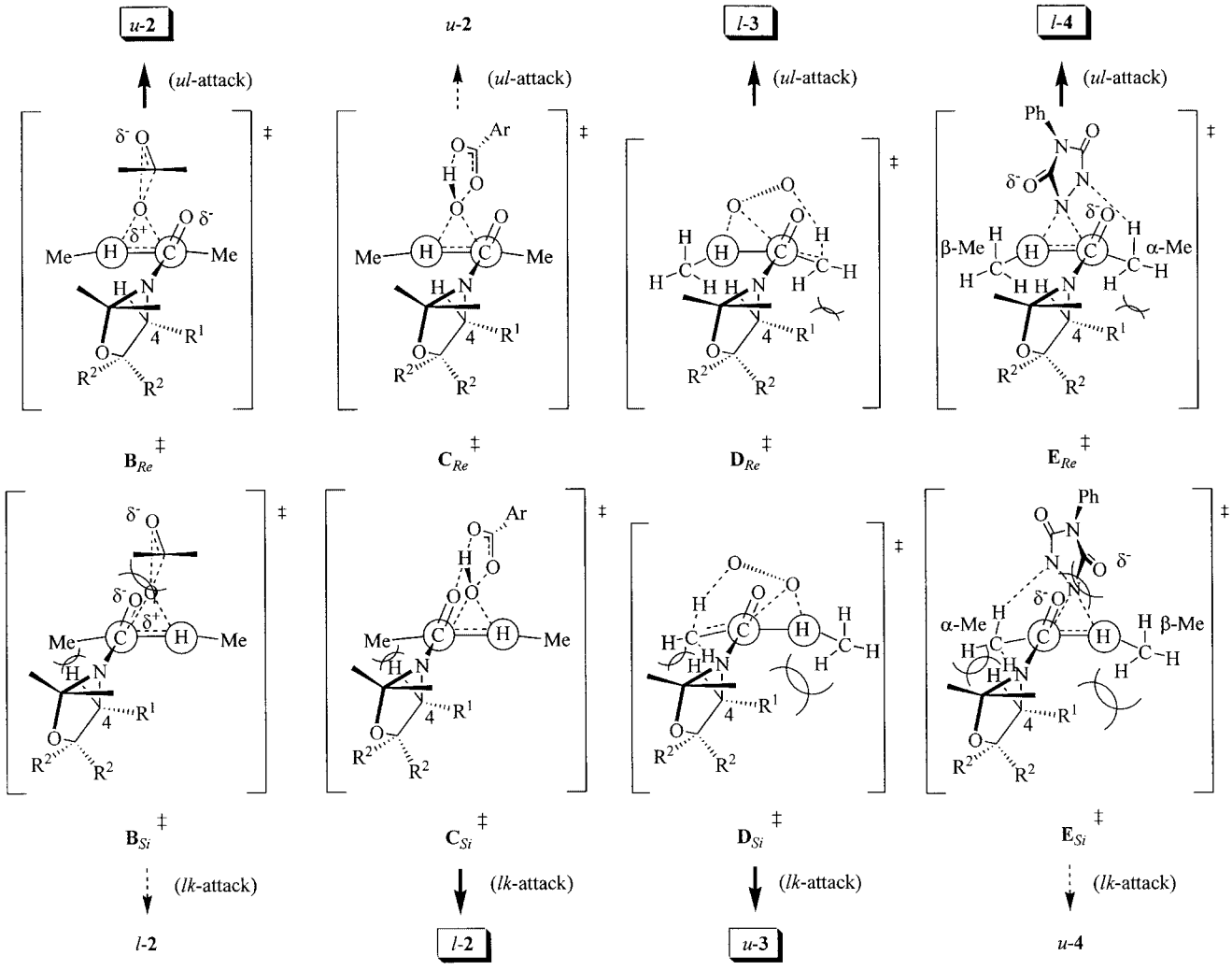


Figure 3. Proposed transition structures $\mathbf{B}_{Re}$ through $\mathbf{E}_{Si}$ for the attack on the tiglic amides (*S*)-**1** by the epoxidants DMD and *m*-CPBA and the enophiles $^1O_2$ and PTAD.

displayed in the $\mathbf{C}_{Re}^{\neq}$ and $\mathbf{C}_{Si}^{\neq}$ transitions structures.[29] The opposite sense in the observed stereoselectivity for *m*-CPBA vs. DMD implies that the transition structure $\mathbf{C}_{Si}^{\neq}$ is favored over the $\mathbf{C}_{Re}^{\neq}$ (Figure 3); consequently, factors other than those for DMD must be operative in this case. Indeed, it has previously been established that in peracid epoxidations of substrates containing carbonyl groups (carbamates,[30a–30d] amides,[30c,30e] esters,[30d–30e] ketones[30f]), the effective hydrogen bonding between the peracid proton and the carbonyl group specifies *syn* stereoselectivity. We propose that similar three-center hydrogen bonding[31] lowers the energy of the transition structure $\mathbf{C}_{Si}^{\neq}$ relative to $\mathbf{C}_{Re}^{\neq}$ and thus accounts for the experimentally observed *like* diastereoselectivity (Table 1; Entries 3, 5 and 6). This propitious interaction is less pronounced in the transition structure $\mathbf{C}_{Re}^{\neq}$ because the carbonyl group and the peracid hydrogen atom are too far apart. Such hydrogen bonding in the $\mathbf{C}_{Si}^{\neq}$ structure also substantially increases the reactivity of the tiglic amide towards *m*-CPBA epoxidation, as evidenced by the fact that the level of conversion dramatically dropped from >95% to 7% when the solvent was changed from the nonpolar CH_2Cl_2 to the hydrogen-bonding MeOH. Evidently, the "external" hydrogen bonding between the substrate and MeOH solvent disrupts the favorable "internal" hydrogen bonding between the substrate and the peracid in the transition structure $\mathbf{C}_{Si}^{\neq}$.

The mechanism for the $^1O_2$ ene reaction has been intensively debated, but the current consensus favors the stepwise mechanism, with a perepoxide-like oxygen transfer.[32] Indeed, such an epoxide-type trajectory resembles the peracid epoxidation reaction and justifies a mechanistic comparison of the singlet-oxygen ene reaction with the peracid epoxidation. For the particular case of the electron-deficient alkenes investigated here, a fast reversible step operates to give the perepoxide intermediate first and, subsequently, in the second, rate-determining step, the allylic hydrogen abstraction takes place, as established by isotope effect studies.[33] High levels of geminal regioselectivity have been observed in such substrates (similar to tiglic amides (*S*)-**1**),[34] again interpreted in terms of perepoxide intermediates.[35]

Isotope effect studies[36] and other experimental[37] and theoretical work[25e] have also established that PTAD reacts

through a three-membered ring intermediate, namely an aziridinium imide (AI). Stereochemical characteristics analogous to the perepoxide structures in the $^1O_2$ ene reactions apply in this mechanism. In the case of electron-deficient alkenes as the ene substrate, however, contrary to the $^1O_2$ ene reaction, the formation of the intermediate takes place during the rate-determining step with a large change in the hybridization (from sp^2 to sp^3).[33,38]

The puzzling stereochemical fact demanding mechanistic scrutiny of the $^1O_2$ and PTAD ene reactions in relation to the DMD and *m*-CPBA epoxidations is the essentially complete lack of diastereoselectivity for $^1O_2$, in conjunction with the essentially perfect stereocontrol for PTAD (Table 1). There is little purpose in analyzing the two possible transitions structures $\mathbf{D}_{Re}^{\neq}$ and $\mathbf{D}_{Si}^{\neq}$ in detail, except to state that – irrespective of steric, electronic, and conformational features – the attack by the small $^1O_2$ enophile is not discriminated by the oxazolidine chiral auxiliary; this also includes the carbonyl group of the tiglic amide. For the PTAD ene reaction, the observed diastereomeric ratio depends on the energy differences of the transition states $\mathbf{E}_{Re}^{\neq}$ and $\mathbf{E}_{Si}^{\neq}$ (Figure 3) giving rise to the corresponding AI intermediates. As in the case of the DMD epoxidations, the higher energy of $\mathbf{E}_{Si}^{\neq}$ may be interpreted in terms of steric and electrostatic effects. Thus, the steric and electrostatic repulsions between the carbonyl groups of the enophile (directed towards the other side of the double bond system, away from the tiglic allylic hydrogen atoms) and the amide would be expected to be stronger in the transition structure $\mathbf{E}_{Si}^{\neq}$ than in $\mathbf{E}_{Re}^{\neq}$, resulting in the major diastereomer *l*-**4** (Table 1; Entries 1–5). Additionally, closer inspection of the transition state $\mathbf{E}_{Si}^{\neq}$, which would produce *u*-**4** but is not detected, suggests that the PTAD attack is highly disfavored by steric interactions between the H-4 atom and the R^1 substituent in the oxazolidine ring and the α- and β-methyl groups of the tiglate functionality. Unlike in the transition structure $\mathbf{B}_{Si}^{\neq}$ for DMD, these steric repulsions now become important, due to the high degree of rehybridization of the carbon atoms in the late transition states **E**. Thus, electrostatic and steric factors work together in this process to provide the observed high levels of diastereoselection.

Conclusions

We have shown that 2,2-dimethyloxazolidines are efficient chiral auxiliaries for diastereoselective functionalization of tiglic acid derivatives by epoxidation with *m*-CPBA or DMD and through ene reactions with PTAD. Notably, the diastereoselectivity in the epoxide formation may be tuned through judicious choice of the oxidant: DMD, for example, gives an epoxide ratio of up to 91:09 in favor of the epoxide *u*-**2**, while with *m*-CPBA the ratio inverts to 93:07 in favor of the *l*-**2** diastereomer. The sense and the extent of the diastereoselectivity in these oxidations are controlled by a combination of conformational, electrostatic, hydrogen-bonding, and steric interactions in the corresponding diastereomeric transition states. The essentially perfect diastereoselectivity obtained in the PTAD ene reaction provides an attractive synthetic route for the optically active β-amino acid derivative **5**, after removal of the chiral auxiliary. The highlight of this study is the stereochemical efficacy displayed by the 2,2-dimethyloxazolidine chiral auxiliary in the oxidation of the α-substituted α,β-unsaturated carbonyl substrates.

Experimental Section

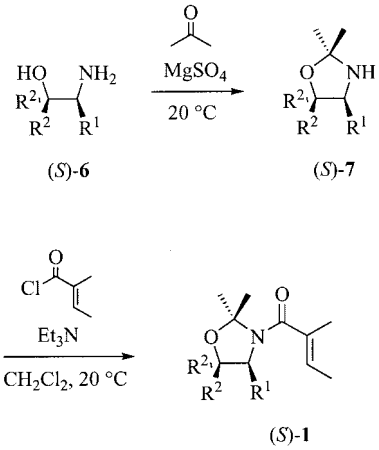
Here we report the synthetic details and characteristic spectroscopic data of the tiglic amides (*S*)-**1a,** (*S*)-**1b**, and (*S*)-**1d** [(*S*)-**1c,** (*S*)-**1e,** and (*S*)-**1f** have already been reported[18]], the allylic alcohols *l*-**3b**, *l*-**3e**, and *l*-**3f** and *u*-**3b**, *u*-**3e**, and *u*-**3f** as diastereomeric mixtures (*l*-**3c**, *l*-**3d**, *u*-**3c**, and *u*-**3d** have already been reported[20]), and the allylic urazoles ***l*-4a**, ***l*-4b**, and ***l*-4e** (*l*-**4c**, *l*-**4d** have already been reported[20]), as well as the hydrolysis of the allylic urazoles ***l*-4a**–**e** to the carboxylic acid **5**.

General Aspects: ^1H and ^{13}C NMR spectra were measured on Bruker AC 200 (^1H: 200 MHz, ^{13}C: 50 MHz) or Bruker AC 250 (^1H: 250 MHz, ^{13}C: 63 MHz) instruments with $CHCl_3$ as internal standard. IR spectra were recorded on a Perkin–Elmer 1600 FT-IR Infrared Ratio-Recording spectrophotometer. The TLC analysis was conducted on precoated silica gel foils (Polygram SIL G/UV254, 40 × 80 mm) from Machery and Nagel. The spots were viewed by irradiation under an UV lamp or with the phosphomolybdic acid test spray. Silica gel (20–63 mm, Woelm) was used for flash chromatography. The optical rotations were measured on a Perkin–Elmer 241 MC polarimeter.

Materials: Solvents and commercially available chemicals were purified by standard procedures. Carbon tetrachloride, the solvent for the photooxygenations, was stirred over basic Al_2O_3 and filtered immediately before use. All the optically active amino alcohols were supplied as gift samples by Degussa AG, Hanau, for which we are very grateful. The tigloyl chloride, prepared from tiglic acid by literature procedures,[39] was freshly distilled before use. The 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) was freshly sublimed before use.[40]

Synthesis of 2,2-Dimethyl-3-tigloyloxazolidines (*S*)-1a, (*S*)-1b, and (*S*)-1d: The optically active 2,2-dimethyl-3-tigloyloxazolidines (*S*)-**1** were synthesized in two steps. The appropriate amino alcohol (*S*)-**6** was first acetalated with acetone in the presence of $MgSO_4$ to give the unstable oxazolidines (*S*)-**7**, which were subsequently used without further purification, being acylated with tigloyl chloride and triethylamine as base (Scheme 2).

General Procedure for the Preparation of the Oxazolidines (*S*)-7a and (*S*)-7b: Anhydrous $MgSO_4$ (2.0 g) was added to a solution of the amino alcohol (*S*)-**6** (10.0 mmol) in acetone (20 mL). The suspension was stirred at 20 °C for 3 h and, after filtration, the solvent was removed under reduced pressure (20 °C/7.5 Torr) to give the oxazolidines (*S*)-**7** (in the case of 2,2,4-trimethyloxazolidine (*S*)-**7a**, the solvent was removed by distillation at normal pressure). Only the ^1H NMR and ^{13}C NMR spectroscopic data for (*S*)-2,2,4-trimethyloxazolidine ((*S*)-**7a**) and (*S*)-4-(2,2-dimethylpropyl)-2,2-dimethyloxazolidine ((*S*)-**7b**) are listed below since they are too labile for rigorous purification and characterization on account of facile hydrolysis. Their purity was satisfactory, however, to be used without further purification in the next step. The fully characterized derivatives (*S*)-**7c**–**f** have already been reported.[3b]



Scheme 2.

(*S*)-2,2,4-Trimethyloxazolidine ((*S*)-7a): 75% yield (0.89 g). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17 (d, J = 6.1 Hz, 3 H), 1.25 (s, 3 H), 1.39 (s, 3 H), 1.97 (br. s, 1 H), 3.11 (dd, J = 7.6, J = 6.7 Hz, 1 H), 3.48–3.38 (m, 1 H), 3.91 (dd, J = 8.2, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 17.7 (q), 26.7 (q), 27.8 (q), 53.5 (d), 72.3 (t), 95.3 (s) ppm.

(*S*)-4-(2,2-Dimethylpropyl)-2,2-dimethyloxazolidine ((*S*)-7b): 85% yield (1.46 g). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.90 (s, 9 H), 1.26 (s, 3 H), 1.32 (dd, J = 13.7, J = 7.3 Hz, 1 H), 1.39 (s, 3 H), 1.55 (dd, J = 13.7, J = 4.6 Hz, 1 H), 1.56–1.70 (br. s, 1 H), 3.13 (t, J = 7.9 Hz, 1 H), 3.33–3.44 (m, 1 H), 3.95 (t, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 26.6 (q), 27.8 (q), 30.0 (3×q), 30.2 (s), 47.8 (t), 55.6 (d), 72.3 (t), 94.3 (s) ppm.

General Procedure for the Preparation of the 2,2-Dimethyl-3-tigloyloxazolidines (*S*)-1a, (*S*)-1b, and (*S*)-1d: The appropriate oxazolidine (*S*)-**7** (25.0 mmol) was dissolved under argon in CH_2Cl_2 (50 mL), together with Et_3N (25.0 mmol). *N*-Tigloyl chloride (25.0 mmol) was slowly added at 0 °C, and the mixture was stirred at this temperature for 0.5 h and then warmed to 20 °C and stirred for 16 h more. The reaction mixture was treated with saturated, aqueous $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (4×20 mL). The combined extracts were dried ($MgSO_4$), the solvent was evaporated (20 °C/7.5 Torr), and the residue was purified by column chromatography or kugelrohr distillation.

[(*S*)-(*E*)]-2,2,4-Trimethyl-3-(2-methyl-1-oxo-2-butenyl)oxazolidine ((*S*)-1a): Colorless oil (kugelrohr distillation at 70 °C/0.075 Torr), 63% yield (3.11 g). $[a]_D^{25}$ = +4.81 (c = 1.31, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.18 (d, J = 6.1 Hz, 3 H), 1.51 (s, 3 H), 1.63 (s, 3 H), 1.65 (dq, J = 7.0, J = 1.3 Hz, 3 H), 1.81 (q, J = 1.3 Hz, 3 H), 3.59–3.63 (m, 1 H), 3.98–4.08 (m, 2 H), 5.55–5.67 (m, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 13.1 (q), 13.9 (q), 20.5 (q), 24.1 (q), 26.6 (q), 54.1 (d), 69.4 (t), 94.9 (s), 124.9 (d), 133.8 (s), 170.6 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1625 ($\nu_{C=O}$) cm^{-1}. $C_{11}H_{19}NO_2$ (197.3): calcd. C 66.97, H 9.71, N 7.10; found C 66.81, H 9.47, N 7.54.

[(*S*)-(*E*)]-4-(2,2-Dimethylpropyl)-2,2-dimethyl-3-(2-methyl-1-oxo-2-butenyl)oxazolidine ((*S*)-1b): Colorless oil (by silica gel chromatography, eluted with petroleum ether/Et_2O 2:1), 81% yield (5.13 g). An analytical sample was obtained by kugelrohr distillation (130 °C/0.015 Torr). $[a]_D^{25}$ = +15.7 (c = 1.00, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.82 (s, 9 H), 1.31 (d, J = 13.4 Hz, 1 H), 1.50 (s, 3 H), 1.57 (s, 3 H), 1.55–1.65 (m, 1 H), 1.61 (dq, J = 6.7, J = 1.1 Hz, 3 H), 1.78 (q, J = 1.2 Hz, 3 H), 3.71–3.75 (m, 1 H), 3.95–4.01 (m, 2 H), 5.59 (q, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 13.0 (q), 14.0 (q), 23.8 (q), 26.5 (q), 29.6 (3×q), 30.2 (s), 48.8 (t), 56.1 (d), 69.1 (t), 94.0 (s), 125.4 (d), 133.9 (s), 170.4 (s) ppm. IR (Nujol): $\tilde{\nu}$ = 1625 ($\nu_{C=O}$) cm^{-1}. $C_{15}H_{27}NO_2$ (253.4): calcd. C 71.10, H 10.74, N 5.53; found C 70.67, H 10.86, N 5.63.

[(*S*)-(*E*)]-2,2-Dimethyl-4-(1-methylethyl)-3-(2-methyl-1-oxo-2-butenyl)oxazolidine ((*S*)-1d): Colorless needles (silica gel chromatography, eluted with petroleum ether/Et_2O, 4:1), 70% yield (3.94 g). An analytical sample was obtained by recrystallization from petroleum ether, m.p. 45–46 °C. $[a]_D^{25}$ = –11.5 (c = 1.00, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.83 (d, J = 7.0 Hz, 3 H), 0.87 (d, J = 7.0 Hz, 3 H), 1.51 (s, 3 H), 1.63 (s, 3 H), 1.68 (dq, J = 6.8, J = 1.1 Hz, 3 H), 1.78–1.84 (m, 3 H), 1.85–2.08 (m, 1 H), 3.79–4.00 (m, 3 H), 5.67 (qq, J = 6.8, J = 1.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 13.0 (q), 13.8 (q), 17.0 (q), 19.4 (q), 24.0 (q), 26.1 (q), 29.9 (d), 63.0 (d), 64.1 (t), 94.8 (s), 125.5 (d), 133.8 (s), 171.2 (s) ppm. IR (KBr): $\tilde{\nu}$ = 1607 ($\nu_{C=O}$) cm^{-1}. $C_{13}H_{23}NO_2$ (225.3): calcd. C 69.29, H 10.29, N 6.22; found C 69.04, H 9.92, N 6.35.

CAUTION! Hydroperoxides are potentially explosive and should be handled with care!

General Procedure for the Preparation of the Allylic Alcohols *l*-3b, *l*-3e, *l*-3f and *u*-3b, *u*-3e, *u*-3f: A solution of the appropriate tiglic amide (*S*)-**1** (1.10 mmol) and TPP (20.0 mg) in CCl_4 (10 mL) was placed in a test tube and cooled to 0 °C. The photooxygenation was conducted by continually passing a slow stream of dried ($CaCl_2$, silica gel, P_4O_{10}) oxygen gas through the solution by means of a disposable pipette and external irradiation with two 400 W sodium lamps until complete consumption (ca. 48 h) of the starting material (TLC monitoring, silica gel, Et_2O/petroleum ether 1:1). The solvent was removed (20 °C/7.5 Torr) and the residue was dissolved in CH_2Cl_2 (5 mL) at 0 °C. After addition of Ph_3P (0.320 g, 1.20 mmol), the solution was stirred for 15 min. Removal of the solvent (20 °C/7.5 Torr) gave the crude alcohols *l*-**3b**, *l*-**3e**, *l*-**3f** and *u*-**3b**, *u*-**3e**, *u*-**3f**, which were isolated as diastereomeric mixtures; their diastereomeric ratios (^{1}H NMR analysis) are listed in Table 1.

[(*S*)-(*R,*R**)]-4-(2,2-Dimethylpropyl)-3-(3-hydroxy-2-methylidene-1-oxobutyl)-2,2-dimethyloxazolidine (*l*-3b) and [(*S*)-(*R**,*S**)]-4-(2,2-Dimethylpropyl)-3-(3-hydroxy-2-methylidene-1-oxobutyl)-2,2-dimethyloxazolidine (*u*-3b):** These isomers were isolated by silica gel chromatography, eluted with petroleum ether/Et_2O 1:1, 57% yield (0.17 g). An analytical sample was obtained by recrystallization from petroleum ether/Et_2O 3:1 at –20 °C, colorless needles, m.p. 70–71 °C. $[a]_D^{25}$ = +50.1 (c = 1.00, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (s, 18 H), 1.35 (d, J = 6.7 Hz, 3 H), 1.36 (d, J = 6.4 Hz, 3 H), 1.44–1.50 (m, 2 H), 1.54 (s, 6 H), 1.67 (s, 6 H), 1.62–1.73 (m, 2 H), 3.48 (d, J = 6.4 Hz, 1 H), 3.61 (d, J = 4.6 Hz, 1 H), 3.80 (d, J = 8.8 Hz, 2 H), 3.94–4.05 (m, 2 H), 4.05–4.21 (m, 2 H), 4.42–4.54 (m, 2 H), 5.22 (s, 1 H), 5.24 (s, 1 H), 5.38 (d, J = 1.2 Hz, 1 H), 5.44 (d, J = 1.5 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.6 (q), 22.1 (q), 25.5 (2×q), 26.6 (2×q), 29.88 (3×q), 29.91 (3×q), 30.3 (2×s), 47.8 (t), 48.1 (t), 56.4 (d), 56.6 (d), 67.8 (d), 68.9 (2×t), 69.1 (d), 94.5 (2×s), 114.2 (t), 115.1 (t), 148.2 (s), 148.5 (s), 167.9 (s), 168.4 (s) ppm. IR (KBr): $\tilde{\nu}$ = 3352 (ν_{OH}), 1644 ($\nu_{C=O}$) cm^{-1}. Calcd for $C_{15}H_{27}NO_3$ (269.4): C 66.88, H 10.10, N 5.20; found C 66.45, H 9.94, N 5.59.

[(*S*)-(*R,*R**)]-3-(3-Hydroxy-2-methylidene-1-oxobutyl)-2,2-dimethyl-4-phenyloxazolidine (*l*-3e) and [(*S*)-(*R**,*S**)]-3-(3-Hydroxy-2-methylidene-1-oxobutyl)-2,2-dimethyl-4-phenyloxazolidine (*u*-3e):** These isomers were isolated by silica gel chromatography, eluted with Et_2O, colorless oil, 71% yield (0.22 g). An analytical sample

was obtained by kugelrohr distillation (135 °C/0.015 Torr). $[\alpha]_D^{25}$ = +97.7 (c = 1.60, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.93 (d, J = 6.4 Hz, 3 H), 1.04 (d, J = 6.4 Hz, 3 H), 1.68 (s, 3 H), 1.69 (s, 3 H), 1.88 (s, 6 H), 2.38–2.61 (br. s, 1 H), 3.38–3.52 (br. s, 1 H), 3.85 (dd, J = 9.2, J = 4.0 Hz, 1 H), 3.86 (dd, J = 9.2, J = 4.0 Hz, 1 H), 3.95–4.10 (m, 2 H), 4.32 (dd, J = 9.2, J = 6.4 Hz, 2 H), 4.92 (s, 2 H), 4.96–5.03 (m, 2 H), 5.18 (s, 1 H), 5.21 (s, 1 H), 7.18–7.35 (m, 10 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 22.2 (q), 22.3 (q), 23.7 (2×q), 25.2 (2×q), 62.8 (d), 63.0 (d), 67.5 (d), 68.9 (d), 71.3 (2×t), 96.3 (2×s), 114.4 (2×t), 126.9 (2×d), 127.0 (2×d), 127.8 (d), 127.9 (d), 128.7 (2×d), 128.8 (2×d), 141.4 (s), 141.7 (s), 147.8 (s), 149.0 (s), 168.9 (s), 169.7 (s) ppm. IR (film): $\tilde{\nu}$ = 3413 (ν_{OH}), 1643 ($\nu_{C=O}$) cm^{-1}. Calcd for $C_{16}H_{21}NO_3$ (275.4): C 69.79, H 7.69, N 5.09; found C 69.48, H 7.62, N 5.28.

[(*S*)-(*R,*R**)]-3-(3-Hydroxy-2-methylidene-1-oxobutyl)-2,2,5,5-tetramethyl-4-phenylmethyloxazolidine (*l*-3f) and [(*S*)-(*R**,*S**)]-3-(3-Hydroxy-2-methylidene-1-oxobutyl)-2,2,5,5-tetramethyl-4-phenylmethyloxazolidine (*u*-3f):** These isomers were isolated by silica gel chromatography, eluted with petroleum ether/Et_2O 1:1, colorless oil, 79% yield (0.28 g). An analytical sample was obtained by kugelrohr distillation (195 °C/0.015Torr). $[\alpha]_D^{25}$ = –75.6 (c = 1.01, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.15 (s, 3 H), 1.20 (d, J = 6.4 Hz, 3 H), 1.21 (s, 3 H), 1.36 (s, 3 H), 1.38 (d, J = 6.4 Hz, 3 H), 1.39 (s, 3 H), 1.72 (s, 3 H), 1.74 (s, 6 H), 1.77 (s, 3 H), 2.66–2.75 (br. s, 1 H), 2.83–3.05 (m, 4 H), 3.71–3.84 (m, 2 H), 4.21–4.28 (m, 1 H), 4.30–4.45 (m, 2 H), 5.28 (s, 2 H), 5.52 (s, 1 H), 5.54 (d, J = 0.9 Hz, 1 H), 7.32–7.12 (m, 10 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.9 (q), 22.9 (q), 24.2 (q), 24.4 (q), 27.8 (2×q), 29.1 (q), 29.2 (3×q), 39.0 (t), 39.1 (t), 66.9 (d), 67.4 (2×d), 68.6 (d), 80.5 (s), 80.8 (s), 94.3 (s), 94.4 (s), 114.9 (t), 115.4 (t), 126.5 (d), 126.6 (d), 128.6 (2×d), 128.8 (2×d), 129.1 (2×d), 129.3 (2×d), 137.7 (s), 138.3 (s), 148.2 (s), 149.7 (s), 168.5 (s), 169.6 (s) ppm. IR (film): $\tilde{\nu}$ = 3419 (ν_{OH}), 1612 ($\nu_{C=O}$) cm^{-1}. Calcd for $C_{19}H_{27}NO_3$ (317.4): C 71.89, H 8.57, N 4.41; found C 71.80, H 8.68, N 4.74.

General Procedure for the PTAD Adducts *l*-4a, *l*-4b, and *l*-4e: A solution of the corresponding tiglic amide (*S*)-**1** (0.4 mmol) and PTAD (0.4 mmol) in CH_2Cl_2 (5 mL) was stirred at 20 °C for 18 h. The solvent was removed (20 °C/7.5 Torr) and the crude product was purified by recrystallization to give the diastereomerically pure allylurazoles ***l*-4a**, ***l*-4b**, and ***l*-4e**.

[(*S*)-(*R,*R**)]-2-[1-Methyl-2-methylidene-3-oxo-3-(2,2,4-trimethyloxazolidin-3-yl)propyl]-4-phenyl-1,2,4-triazolidine-3,5-dione (*l*-4a):** Colorless prisms from CH_2Cl_2/Et_2O 1:4 at –20 °C, m.p. 107–108 °C, 63% yield (0.09 g). $[\alpha]_D^{25}$ = +41.3 (c = 1.02, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.28 (d, J = 6.7 Hz, 3 H), 1.46 (d, J = 7.0 Hz, 3 H), 1.54 (s, 3 H), 1.71 (s, 3 H), 3.72 (d, J = 7.0 Hz, 1 H), 4.04–4.13 (m, 2 H), 5.15 (q, J = 6.7 Hz, 1 H), 5.51 (d, J = 1.1 Hz, 1 H), 5.65 (d, J = 1.1 Hz, 1 H), 7.31–7.52 (m, 5 H), 9.26 (br. s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.1 (q), 21.0 (q), 23.2 (q), 26.6 (q), 53.3 (d), 54.3 (d), 69.6 (t), 96.0 (s), 120.1 (t), 125.6 (2×d), 128.1 (d), 129.1 (2×d), 131.5 (s), 143.8 (s), 151.6 (s), 152.8 (s), 166.7 (s) ppm. IR (KBr): $\tilde{\nu}$ = 3084 (ν_{NH}), 1767 ($\nu_{C=O}$), 1689 ($\nu_{C=O}$), 1630 ($\nu_{C=O}$) cm^{-1}. $C_{19}H_{24}N_4O_4$ (372.4): calcd. C 61.28, H 6.50, N 15.04; found C 60.96, H 6.58, N 14.79.

[(*S*)-(*R,*R**)]-2-{3-[4-(2,2-Dimethylpropyl)-2,2-dimethyloxazolidin-3-yl]-1-methyl-2-methylidene-3-oxopropyl}-4-phenyl-1,2,4-triazolidine-3,5-dione (*l*-4b):** Colorless needles from CH_2Cl_2/Et_2O 1:4 at –20 °C, m.p. 201–202 °C, 58% yield (0.10 g). $[\alpha]_D^{25}$ = +42.9 (c = 1.02, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.89 (s, 9 H), 1.36 (d, J = 13.7 Hz, 1 H), 1.46 (d, J = 6.8 Hz, 3 H), 1.53 (s, 3 H), 1.67 (s, 3 H), 1.81 (dd, J = 13.7, J = 11.3 Hz, 1 H), 3.87 (d, J = 8.0 Hz, 1 H), 3.98–4.03 (m, 2 H), 5.14 (q, J = 6.8 Hz, 1 H), 5.53 (d, J = 0.9 Hz, 1 H), 5.65 (d, J = 0.9 Hz, 1 H), 7.52–7.31 (m, 5 H), 9.23 (br. s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.0 (q), 22.9 (q), 26.5 (q), 29.8 (3×q), 30.3 (s), 48.4 (t), 53.2 (d), 56.3 (d), 68.9 (t), 95.1 (s), 120.8 (t), 125.5 (2×d), 128.0 (d), 129.1 (2×d), 131.5 (s), 143.7 (s), 151.7 (s), 152.8 (s), 166.6 (s) ppm. IR (KBr): $\tilde{\nu}$ = 3088 (ν_{NH}), 1769 ($\nu_{C=O}$), 1694 ($\nu_{C=O}$), 1633 ($\nu_{C=O}$) cm^{-1}. Calcd for $C_{23}H_{32}N_4O_4$ (428.5): C 64.47, H 7.53, N 13.07; found C 64.26, H 7.64, N 13.26.

[(*S*)-(*R,*R**)]-2-[3-(2,2-Dimethyl-4-phenyloxazolidin-3-yl)-1-methyl-2-methylidene-3-oxopropyl]-4-phenyl-1,2,4-triazolidine-3,5-dione (*l*-4e):** Colorless prisms from CH_2Cl_2/Et_2O 1:4 at –20 °C, m.p. 182–183 °C, 81% yield (0.14 g). $[\alpha]_D^{25}$ = +146.6 (c = 1.00, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.77 (d, J = 7.0 Hz, 3 H), 1.69 (s, 3 H), 1.93 (s, 3 H), 3.97 (dd, J = 9.3, J = 4.0 Hz, 1 H), 4.40 (dd, J = 9.3, J = 6.7 Hz, 1 H), 4.87 (q, J = 6.8 Hz, 1 H), 5.02 (dd, J = 6.7, J = 4.0 Hz, 1 H), 5.39 (s, 1 H), 5.55 (d, J = 0.9 Hz, 1 H), 7.24–7.51 (m, 10 H), 8.96 (br. s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.6 (q), 23.7 (q), 25.2 (q), 53.1 (d), 62.6 (d), 71.4 (t), 96.9 (s), 121.2 (t), 125.5 (2×d), 127.5 (2×d), 127.9 (d), 128.3 (d), 128.9 (2×d), 129.0 (2×d), 131.5 (s), 140.4 (s), 143.3 (s), 151.1 (s), 152.5 (s), 167.5 (s) ppm. IR (KBr): $\tilde{\nu}$ = 3096 (ν_{NH}), 1766 ($\nu_{C=O}$), 1690 ($\nu_{C=O}$), 1637 ($\nu_{C=O}$) cm^{-1}. Calcd for $C_{24}H_{26}N_4O_4$ (434.5): C 66.34, H 6.03, N 12.89; found C 66.27, H 6.05, N 12.77.

General Procedure for the Hydrolysis of the Urazoles *l*-4a–e. Preparation of (*S*)-3-(3,5-Dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methylidenebutanoic Acid (5): A suspension of the urazole ***l*-4** (0.50 mmol) in aqueous HCl (1 N, 25 mL) was heated at 100 °C for 15 h. After the mixture had cooled to 20 °C, the aqueous phase was extracted with Et_2O (4×10 mL) and dried over $MgSO_4$. The solvent was removed (20 °C/8 Torr), to give the urazole **5** as single product; the yields and optical rotations are listed in Table S1 in the Supporting Information. An analytical sample of **5** was obtained by recrystallization from Et_2O/*n*-pentane/MeOH 2:4:1, colorless prisms, m.p. 197–209 °C. $[\alpha]_D^{25}$ = +64.2 (c = 1.00, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.67 (d, J = 7.4 Hz, 3 H), 5.21 (q, J = 7.4 Hz, 1 H), 6.06 (s, 1 H), 6.39 (s, 1 H), 7.38–7.52 (m, 5 H), 10.68 (s, 1 H), 12.62 (br. s, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 17.7 (q), 54.9 (d), 125.7 (2×d), 128.5 (d), 129.2 (2×d), 130.6 (s), 130.9 (s), 138.6 (t), 150.7 (s), 154.1 (s), 170.0 (s) ppm. IR (KBr): $\tilde{\nu}$ = 3413–2508 (ν_{OH}), 1772 ($\nu_{C=O}$), 1713 ($\nu_{C=O}$), 1674 ($\nu_{C=O}$) cm^{-1}. Calcd for $C_{13}H_{13}N_3O_4$ (275.3): C 56.73, H 4.76, N 15.27; found C 56.82, H 4.51, N 15.18.

Supporting Information: Supporting Information for this article (optical rotations and yields of **5**, obtained from the corresponding urazoles ***l*-4a–e**, and the $^1H/^1H$-NOESY spectrum of a $CDCl_3$ solution of the tiglic amide (*S*)-**1c**) is available (see also the footnote on the first page of this article).

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