Dramatic Diastereoselectivity Differences in the Asymmetric Ene Reactions of Triazolinediones and Singlet Oxygen with Chiral 2,2-Dimethyloxazolidine Derivatives of Tiglic Acid

Waldemar Adam[a], Thomas Wirth*[a], Aurelia Pastor[a], and Karl Peters[b]

Institut für Organische Chemie, Universtät Würzburg[a],
Am Hubland, D-97074 Würzburg, Germany
Fax: (internat.) +49(0)931/888−4756
E-mail: adam@chemie.uni-wuerzburg.de

Max-Planck-Institut für Festkörperforschung[b]
Heisenbergstraße 1, D-70506 Stuttgart, Germany
Fax: (internat.) +49(0)711/689−1503

Received October 24, 1997

Keywords: Ene reactions / Chiral tiglic acid 2,2-dimethyloxazolidines / Triazolinedione / Singlet oxygen / Evans' oxazolidinones

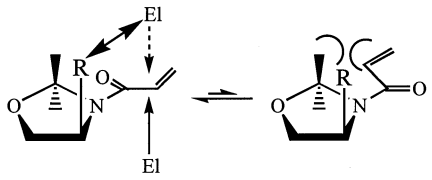
The diastereoselectivity in the ene reactions of triazolinedinone and singlet oxygen with chiral oxazolidine or oxazolidinone derivatives of tiglic acid depends both on the chiral auxiliary used and the size of the attacking enophile. While chiral 2,2-dimethyloxazolidine amides of tiglic acid give with triazolinediones TAD only one single ene adduct, the corresponding chiral oxazolidinone derivatives (Evans' auxiliaries) display a very low diastereoselectivity. No selectivity is observed in the singlet-oxygen ene reaction with dimethyloxazolidine amides of tiglic acid. These stereochemical results are rationalized in terms of the differences in the steric demand of the singlet oxygen and TAD enophiles rather than electronic factors.

The ene[1] reaction of triazolinediones (TAD)[2] and singlet oxygen ($^1O_2$)[3] of alkenes with allylic hydrogens has attracted much attention in the last years from both the synthetic[4] and mechanistic[5] points of view. A problem that remains, however, is the stereochemical control of the new stereogenic center that is formed in this process.[6] In the present communication we report an unprecedented asymmetric ene reaction[7] of chiral amides of tiglic acid with 2,2-dimethyloxazolidines as chiral auxiliaries.[8] These auxiliaries are readily prepared in two steps from commercially available amino alcohols and are easily removed from the resulting product by acid hydrolysis. The stereoselectivity with these auxiliaries is based on the conformational control of the amide linkage (Scheme 1).[8c]

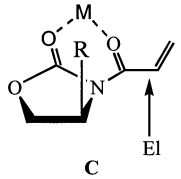
In α,β-unsaturated acryloyl amide derivatives, the amide functionality predominantly occupies the *syn*/*s-cis* conformation **A** to minimize steric hinderance such that one of the diastereotopic faces of the reacting π system may be effectively shielded by the proximate substituent at the 4 position (Scheme 1). The related 2-oxazolidinones **C** are well-known as Evans' chirality-controlling auxiliaries,[9] with which highly efficient chiral induction has been achieved in asymmetric reactions when a Lewis acid or a metal ion is utilized for fixing the amide conformation.

The preparation of α,β-unsaturated tiglic acid amides (*S*)-**1** derived from oxazolidines is straightforward and followed analogous literature procedures.[8d] *N*-Tigloyl amides (*S*)-**1** were allowed to react with the triazolinediones PTAD

Scheme 1. Preferred conformation **A** (*syn*/*s-cis*) *versus* **B** (*anti*/*s-cis*) and favored electrophilic attack for *N*-acryloyl-2,2-dimethyloxazolidines; metal-locked conformation **C** of *N*-acryloyloxazolidinones



A (*syn*/*s-cis*) **B** (*anti*/*s-cis*)



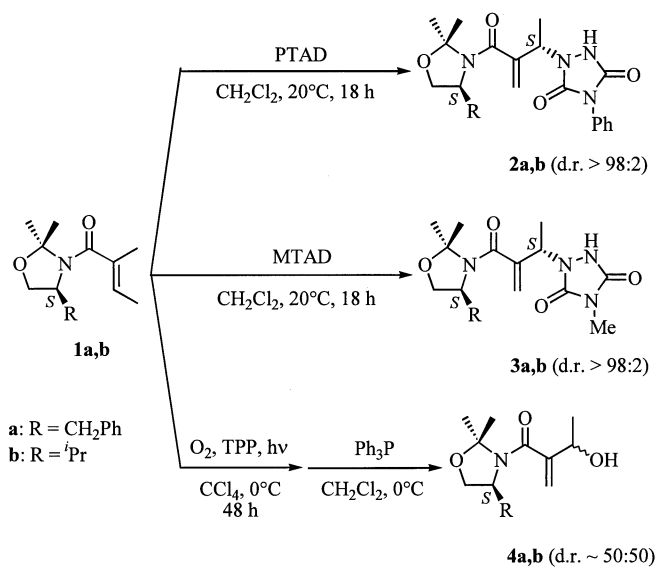
C

(phenyl) or MTAD (methyl) to give the corresponding ene products **2** or **3** in 65−81% yield. ^{13}C-NMR (63 MHz) spectroscopy unequivocally showed that only one diastereomeric ene adduct (d.r. > 98:2) was formed (Scheme 2).

In contrast, the photooxygenation of substrates (*S*)-**1** at 0°C in CCl_4 for 48 h with tetraphenylporphine (TPP) as sensitizer afforded a 50:50 mixture of the diastereomeric allylic hydroperoxides. These labile hydroperoxides were reduced with triphenylphosphine at 0°C in dichloromethane

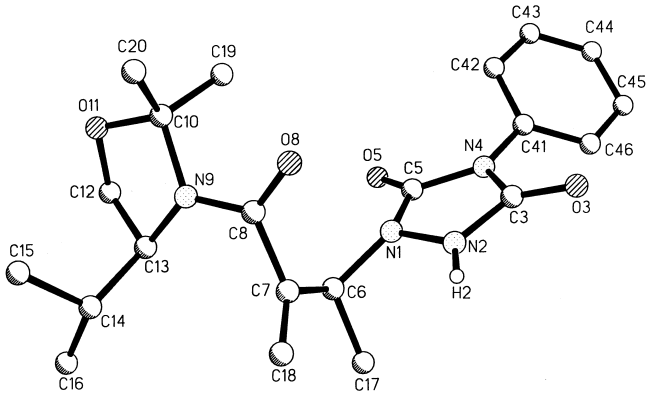
  1434−193X/98/0303−0501 $ 17.50+.50/0

Scheme 2. Diastereoselectivities in the ene reactions of oxazolidines (*S*)-**1a,b** with TAD and $^1O_2$



to the allylic alcohols **4**, isolated in 61−65% overall yields. From the X-ray structures of the ene products **2b** and **3a** (Figures 1 and 2), the configurations of the newly formed chirality centers are assigned to be *S* in the adducts **2** and **3**. Thus, while TAD reacts perfectly (d.r. > 98:2) diastereoselectively with oxazolidines **1**, $^1O_2$ is completely (d.r. ≈ 50:50) unselective.

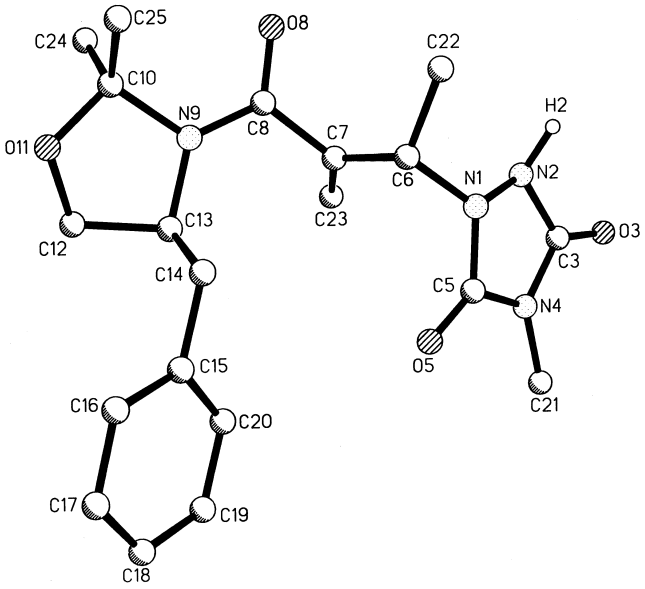
Figure 1. Crystal structure of **2b**



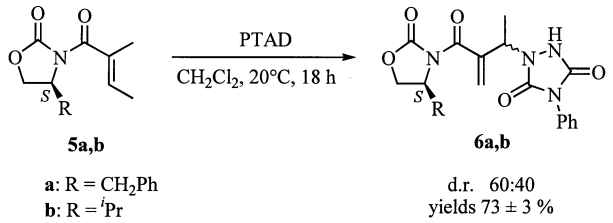
For comparison, the diastereoselectivities in the PTAD ene reaction of the optically pure *N*-tigloyl amides (*S*)-**5** with Evans′ oxazolidinones as chiral auxiliaries, prepared by standard methods,[10] are given in Scheme 3. The ene reactions were carried out at 20°C in dichloromethane to give the corresponding ene adducts **6**, but in very low diastereoselectivities (d.r. = 60:40) compared to the oxazolidines **1** (d.r. > 98:2).

To rationalize the dramatic differences in the stereoselectivities between the electrophilic TAD (d.r. > 98:2) and $^1O_2$ (d.r. = 50:50) in their ene reactions with 2,2-dimethyloxazolidines (*S*)-**1** and the much lower (d.r. = 60:40) stereocontrol for TAD with the corresponding oxazolidinones (*S*)-**5**, electronic factors can hardly apply. Both enophiles follow

Figure 2. Crystal structure of **3a**



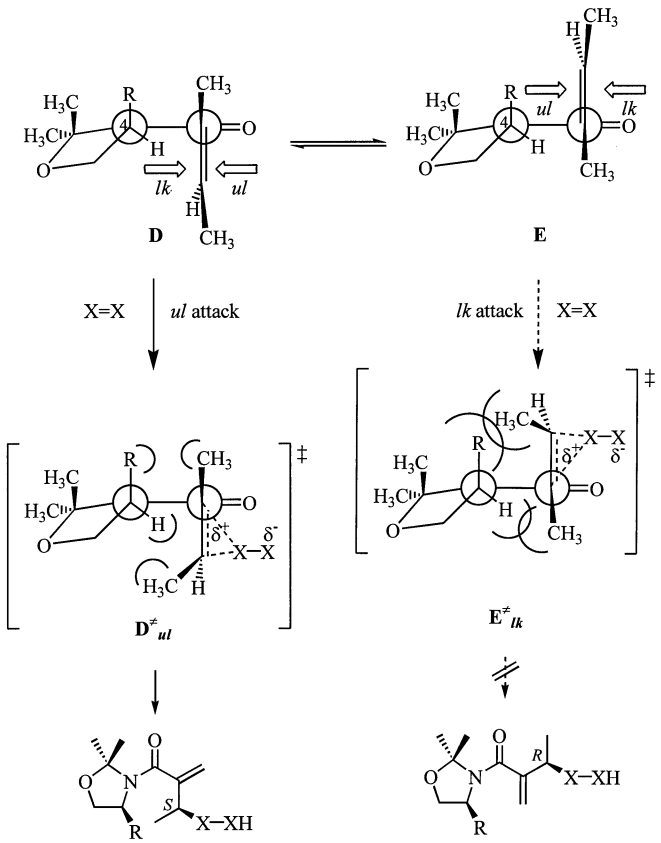
Scheme 3. Diastereoselectivities in the ene reactions of oxazolidinones (*S*)-**5a,b** with PTAD



the same reaction mechanism, i. e. TAD proceeds through the aziridinium imide as intermediate and $^1O_2$ an the analogous perepoxide-like exciplex.[11] Instead of electronic factors, the dramatic difference in the steric demand of these two reagents is likely to be responsible. We propose that the stereochemical control in the reaction of the 2,2-dimethyloxazolidines (*S*)-**1** with TAD derives from the attack of this bulky enophile on the π system from the side opposite to the substituent at the 4 position in the conformers **D** and **E** fixed by the restricted rotation around the amide linkage (Scheme 4).

In contrast to the *N*-acryloyl oxazolidines with the preferred conformation **A** (Scheme 1), the situation for the *N*-tigloyl oxazolidines (*S*)-**1** is different: while the favored conformation of the *N*-tigloyl fragment is also *syn* with respect to the oxazolidine ring (**D** and **E**, Scheme 4), the double bond is twisted with respect to the carbonyl group to avoid steric interactions. This perpendicular conformational arrangement with respect to the carbonyl group is general for methacrylate and tiglate derivatives of imides and amides since the planar rotamers (*s-trans* and *s-cis*) cannot be accommodated for steric reasons.[12] The approach of the large TAD enophile is then controlled by steric shielding of either the oxazolidine ring for the conformer **D** (*lk* attack unfavorable) or of the substituent at the 4 position for the conformer **E** (*ul* attack unfavorable) such that the *unlike*

Scheme 4. Possible *like* (*lk*) and *unlike* (*ul*) attacks in the ene reactions of oxazolidines (*S*)-**1** with TAD and $^1O_2$



trajectory applies for $\mathbf{D}^{\neq}{}_{ul}$ and the *like* one for $\mathbf{E}^{\neq}{}_{lk}$. The pronounced *ul* diastereoselectivity (Scheme 2) is then rationalized in terms of the lower energy of the transition state $\mathbf{D}^{\neq}{}_{ul}$ due to the smaller interactions between the methyl groups of the incipient aziridinium imide functionality and the R substituents at the 4 position of the oxazolidine ring as observed (Scheme 4). Also, the low diastereoselectivities (d.r. = 60:40) in the reaction of the oxazolidinones (*S*)-**5** with TAD are expected because in the absence of chelating Lewis acids the conformational control around the amide linkage is not guaranteed.

Like in the case of TAD, also for the smaller $^1O_2$ enophile the transition state $\mathbf{E}^{\neq}{}_{lk}$ (Scheme 4) is unfavorable due to steric interactions. The decrease in the diastereoselectivity may be explained by the fact that the π-facial differentiation of the obstructing oxazolidine ring in the conformer **D** is not effective. Consequently, both sides of the π system are attacked with equal facility to afford two diastereomorphic transition states $\mathbf{D}^{\neq}{}_{ul}$ and $\mathbf{D}^{\neq}{}_{lk}$ (not shown) of equal energy. Thus, little if any diastereoselectivity is expected, as is observed.

We gratefully thank the *Deutsche Forschungsgemeinschaft* (Schwerpunktprogramm: Sauerstofftransfer/Peroxidchemie), the *Fonds der Chemischen Industrie* (doctoral fellowship for T. W. during 1996−1998) and the *Spanish Ministerio de Educación y Cultura* (postdoctoral fellowship for A. P.) for financial support and Dr. *M. Schwarm* and Prof. *K.-H. Drauz* (Degussa AG, Hanau) for generous gifts of optically active amino alcohols and oxazolidinones.

Experimental Section

General: IR: Perkin-Elmer 1420 Ratio Recording Infrared Spectrophotometer. − ^{1}H NMR: Bruker AC 250 MHz (250 MHz) ($CHCl_3$, at δ = 7.26 ppm as internal standard). − ^{13}C NMR: Bruker AC 250 MHz (63 MHz) ($CHCl_3$, at δ = 77.0 ppm as internal standard). − Melting points: Büchi B-545 (uncorrected values). − Column chromatography was performed on silica gel (60−230 mesh, Merck).

General Procedure for the Ene Adducts from (S)-2,2-Dimethyl-3-tigloyloxazolidines **1** *and TAD:* A solution of the *N*-tigloylamide (0.4 mmol) and TAD (0.4 mmol) in CH_2Cl_2 (5 ml) was stirred at room temp. for 18 h. The solvent was removed (20°C/7.5 Torr) and the residue was purified by recrystallization.

Ene Adduct **2a** *from (S)-4-Benzyl-2,2-dimethyl-3-tigloyloxazolidine and PTAD:* Recrystallized from CH_2Cl_2/Et_2O (1:4) at −20°C (65%), colorless prisms, m.p. 131.9−132.0°C. − IR (KBr): $\tilde{\nu}$ = 3434 (NH) cm^{-1}, 1766 (C=O), 1690 (C=O), 1631 (C=O). − ^{1}H NMR ($CDCl_3$): δ = 9.24 (br s, 1 H, NH), 7.52−7.10 (m, 10 H, Ar-H), 5.75 (s, 1 H, C=CH_2), 5.60 (s, 1 H, C=CH_2), 5.23 (q, ^3J = 6.7 Hz, 1 H, 3′-H), 4.14−4.10 (m, 1 H, 4-H), 3.85 (s, 1 H, 5 H), 3.84 (s, 1 H, 5-H), 2.97 (m, 1 H, CH_2Ph), 2.83 (dd, ^2J = 13.1 Hz, ^3J = 11.0 Hz, 1 H, CH_2Ph), 1.79 (s, 3 H, CH_3-C-2), 1.56 (s, 3 H, CH_3-C-2), 1.54 (d, ^3J = 7.0 Hz, 3 H, 4′-H). − ^{13}C NMR ($CDCl_3$): δ = 166.7 (s, C-1′), 152.9 (s, C=O), 151.8 (s, C=O), 144. 2 (s, C-2′), 136.9 (s), 131.4 (s), 129.1 (d), 129.0 (d), 128.9 (d), 128.0 (d), 127.1 (d), 125.5 (d), 119.7 (t, C=CH_2), 96.1 (s, C-2), 66.1 (t, C-5), 60.2 (d, C-4), 53.3 (d, C-3′), 40.5 (t, CH_2Ph), 26.8 (q, CH_3-C-2), 22.8 (q, CH_3-C-2), 15.2 (q, C-4′). − $[\alpha]^{25}_D$ = +22.4 (*c* = 1.01, $CHCl_3$). − $C_{25}H_{28}N_4O_4$ (448.5): calcd. C 66.95, H 6.29, N 12.49; found C 66.71, H 6.59, N 12.56.

Ene Adduct **2b** *from (S)-4-Isopropyl-2,2-dimethyl-3-tigloyloxazolidine and PTAD:* Recrystallized from CH_2Cl_2/Et_2O (1:4) at −20°C (71%), colorless needles, m.p. 171.9−174.4°C. − IR (KBr): $\tilde{\nu}$ = 3448 (NH) cm^{-1}, 1767 (C=O), 1693 (C=O), 1633 (C=O). − ^{1}H NMR ($CDCl_3$): δ = 9.36 (br s, 1 H, NH), 7.51−7.29 (m, 5 H, Ar-H), 5.65 (d, ^2J = 1.2 Hz, 1 H, C=CH_2), 5.52 (d, ^2J = 0.6 Hz, 1 H, C=CH_2), 5.16 (q, ^3J = 6.8 Hz, 1 H, 3′-H), 4.00−3.90 (m, 3 H, 4-H, 5-H), 2.05−1.95 (m, 1 H, $CH(CH_3)_2$), 1.71 (s, 3 H, CH_3-C-2), 1.51 (s, 3 H, CH_3-C-2), 1.43 (d, ^3J = 6.7 Hz, 3 H, 4′-H), 0.90 (d, ^3J = 6.7 Hz, 3 H, $CH(CH_3)_2$), 0.86 (d, ^3J = 6.7 Hz, 3 H, $CH(CH_3)_2$). − ^{13}C NMR ($CDCl_3$): δ = 167.1 (s, C-1′), 152.5 (s, C=O), 151.3 (s, C=O), 144.0 (s, C-2′), 131.5 (s), 129.0 (d), 127.9 (d), 125.5 (d), 120.2 (t, C=CH_2), 96.2 (s, C-2), 63.5 (t, C-5), 62.7 (d, C-4), 53.1 (d, C-3′), 30.4 (d, $CH(CH_3)_2$), 25.4 (q, CH_3-C-2), 22.8 (q, CH_3-C-2), 19.7 (q, $CH(CH_3)_2$), 16.0 (q, $CH(CH_3)_2$), 15.0 (q, C-4′). − $[\alpha]^{25}_D$ = +42.9 (*c* = 1.00, $CHCl_3$). − $C_{21}H_{28}N_4O_4$ (400.5): calcd. C 62.98, H 7.05, N 13.99; found C 62.97, H 6.97, N 13.53.

Ene Adduct **3a** *from (S)-4-Benzyl-2,2-dimethyl-3-tigloyloxazolidine and MTAD:* Recrystallized from CH_2Cl_2/Et_2O (1:4) at −20°C (81%), colorless prisms, m.p. 159.1−160.2°C. − IR (KBr): $\tilde{\nu}$ = 3436 (NH) cm^{-1}, 1766 (C=O), 1684 (C=O), 1643 (C=O). − ^{1}H NMR ($CDCl_3$): δ = 8.86 (br s, 1 H, NH), 7.33−7.22 (m, 3 H, Ar-H), 7.07 (d, ^3J = 6.7 Hz, 2 H, Ar-H), 5.64 (s, 1 H, C=CH_2), 5.53 (s, 1 H, C=CH_2), 5.09 (q, ^3J = 6.7 Hz, 1 H, 3′-H), 4.05−4.01 (m, 1 H, 4-H), 3.82 (s, 1 H, 5-H), 3.81 (s, 1 H, 5-H), 3.01 (s, 3 H, N-CH_3), 2.93 (dd, ^2J = 13.4 Hz, ^3J = 3.1 Hz, 1 H, CH_2Ph), 2.79 (dd, ^2J = 13.1 Hz, ^3J = 11.0 Hz, 1 H, CH_2Ph), 1.73 (s, 3 H, CH_3-C-2),

1.49 (s, 3 H, CH_3-C-2), 1.44 (d, ^3J = 6.7 Hz, 3 H, 4′-H). − ^{13}C NMR ($CDCl_3$): δ = 166.8 (s, C-1′), 154.5 (s, C=O), 153.6 (s, C=O), 144.5 (s, C-2′), 137.0 (s), 129.0 (d), 128.9 (d), 127.0 (d), 119.0 (t, C=CH_2), 96.0 (s, C-2), 66.1 (t, C-5), 60.1 (d, C-4), 53.3 (d, C-3′), 40.5 (t, CH_2Ph), 26.8 (q, CH_3-C-2), 25.1 (q, N-CH_3), 22.6 (q, CH_3-C-2), 15.0 (q, C-4′). − $[\alpha]^{25}_D$ = -14.4 (*c* = 1.00, $CHCl_3$). − $C_{20}H_{26}N_4O_4$ (386.5): calcd. C 62.16, H 6.78, N 14.50; found C 61.80, H 6.71, N 14.09.

Ene Adduct **3b** *from (S)-4-Isopropyl-2,2-dimethyl-3-tigloyloxazolidine and MTAD:* Recrystallized from 1:3:1 CH_2Cl_2/Et_2O/PE at −20°C (73%), colorless prisms, m.p. 96.1−96.2°C. − IR (KBr): $\tilde{\nu}$ = 3436 (NH) cm^{-1}, 1766 (C=O), 1696 (C=O), 1631 (C=O). − ^{1}H NMR ($CDCl_3$): δ = 8.93 (br s, 1 H, NH), 5.54 (d, ^2J = 1.2 Hz, 1 H, C=CH_2), 5.45 (d, ^2J = 0.9 Hz, 1 H, C=CH_2), 5.01 (q, ^3J = 6.7 Hz, 1 H, 3′-H), 3.96−3.80 (m, 3 H, 4-H, 5-H), 3.01 (s, 3 H, N-CH_3), 2.09−1.89 (m, 1 H, $CH(CH_3)_2$), 1.64 (s, 3 H, CH_3-C-2), 1.44 (s, 3 H, CH_3-C-2), 1.32 (d, ^3J = 6.7 Hz, 3 H, 4′-H), 0.86 (d, ^3J = 7.0 Hz, 3 H, $CH(CH_3)_2$), 0.83 (d, ^3J = 7.0 Hz, 3 H, $CH(CH_3)_2$). − ^{13}C NMR ($CDCl_3$): δ = 167.3 (s, C-1′), 154.3 (s, C=O), 153.1 (s, C=O), 144.3 (s, C-2′), 119.8 (t, C=CH_2), 96.2 (s, C-2), 63.6 (t, C-5), 62.6 (d, C-4), 53.2 (d, C-3′), 30.5 (d, $CH(CH_3)_2$), 25.5 (q, CH_3-C-2), 25.1 (q, N-CH_3), 22.7 (q, CH_3-C-2), 19.8 (q, $CH(CH_3)_2$), 16.0 (q, $CH(CH_3)_2$), 14.8 (q, C-4′). − $[\alpha]^{25}_D$ = +22.0 (*c* = 1.01, $CHCl_3$). − $C_{16}H_{26}N_4O_4$ (338.4): calcd. C 56.79, H 7.74, N 16.56; found C 57.06, H 8.00, N 16.20.

General Procedure for the Allylic Alcohols **4a** *and* **4b**: A solution of the *N*-tigloylamide (1.1 mmol) and TPP (20 mg) in 10 ml of CCl_4 (freshly dried over basic alumina) was placed in a test tube and cooled to 0°C. The photooxygenation was conducted by continuously 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, 1:2 Et_2O/PE). The solvent was removed (0°C/7.5 Torr), the residue was dissolved in CH_2Cl_2 (5 ml) at 0°C, and Ph_3P (0.320 g., 1.2 mmol) was added. The solution was stirred at this temp. for 15 min, the solvent was removed (20°C/7.5 Torr) and the residue was purified by silica-gel chromatography with 1:1 Et_2O/PE as eluent to give the corresponding alcohol.

(S)-4-Benzyl-3-(3-hydroxy-2-methylenebutanoyl)-2,2-dimethyloxazolidine (**4a**): Yield 65%. − IR (neat): $\tilde{\nu}$ = 3417 (OH) cm^{-1}, 1614 (C=O). − ^{1}H NMR ($CDCl_3$) for both diastereomers: δ = 7.30−7.10 (m, 10 H, Ar-H), 5.56 (s, 1 H, C=CH_2), 5.51 (s, 1 H, C=CH_2), 5.33 (s, 1 H, C=CH_2), 5.31 (s, 1 H, C=CH_2), 4.62−4.52 (m, 2 H, 3′-H), 4.23 (br d, ^3J = 8.9 Hz, 2 H, 4-H), 3.77 (s, 6 H, 5-H, OH), 3.10 (dd, ^2J = 13.4 Hz, ^3J = 2.5 Hz, 1 H, CH_2Ph), 3.01 (dd, ^2J = 13.4 Hz, ^3J = 2.4 Hz, 1 H, CH_2Ph), 2.76 (t, ^2J = 12.2 Hz, ^3J = 12.2 Hz, 2 H, CH_2Ph), 1.73 (s, 6 H, CH_3-C-2), 1.57 (s, 6 H, CH_3-C-2), 1.42 (d, ^3J = 6.1 Hz, 3 H, 4′-H), 1.40 (d, ^3J = 6.4 Hz, 3 H, 4′-H). − ^{13}C NMR ($CDCl_3$) for both diastereomers: δ = 168.3 (s, C-1′), 168.0 (s, C-1′), 149.7 (s, C-2′), 149.5 (s, C-2′), 137.6 (s), 137.4 (s), 129.0 (2×d), 128.7 (d), 128.6 (d), 126.74 (d), 126.68 (d), 113.5 (t, C=CH_2), 113.3 (t, C=CH_2), 95.5 (2×s, C-2), 68.5 (d, C-3′), 67.8 (d, C-3′), 65.9 (2×t, C-5), 60.3 (2×d, C-4), 40.2 (2×t, CH_2Ph), 26.9 (2×q, CH_3-C-2), 23.1 (2×q, CH_3-C-2), 22.2 (q, C-4′), 22.0 (q, C-4′). − $[\alpha]^{25}_D$ = -46.8 (*c* = 1.00, $CHCl_3$). − An analytical sample was obtained by bulb-to-bulb destillation (185°C/0.004 Torr). − $C_{17}H_{23}NO_3$ (289.4): calcd. C 70.56, H 8.01, N 4.84; found C 70.71, H 8.18, N 4.88.

(S)-3-(3-Hydroxy-2-methylenebutanoyl)-4-isopropyl-2,2-dimethyloxazolidine (**4b**): Yield 61%. IR (nujol): $\tilde{\nu}$ = 3358 (OH) cm^{-1}, 1643 (C=O). − ^{1}H NMR ($CDCl_3$): δ = 5.41 (s, 1 H, C=CH_2), 5.33 (s, 1 H, C=CH_2), 5.19 (s, 1 H, C=CH_2), 5.16 (s, 1 H, C=CH_2), 4.47−4.36 (m, 2 H, 3′-H), 3.88−3.78 (m, 8 H, 4-H, 5-H, OH), 2.08−1.94 (m, 2 H, $CH(CH_3)_2$), 1.59 (s, 6 H, CH_3-C-2), 1.46 (s, 6 H, CH_3-C-2), 1.30 (d, ^3J = 6.4 Hz, 3 H, 4′-H), 1.26 (d, ^3J = 6.4 Hz, 3 H, 4′-H), 0.80 (d, ^3J = 7.0 Hz, 6 H, $CH(CH_3)_2$), 0.75 (d, ^3J = 7.0 Hz, 6 H, $CH(CH_3)_2$). − ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 168.9 (2×s, C-1′), 149.3 (s, C-2′), 148.9 (s, C-2′), 113.9 (t, C=CH_2), 113.1 (t, C=CH_2), 95.3 (2×s, C-2), 68.6 (d, C-3′), 67.2 (d, C-3′), 63.5 (t, C-5), 63.3 (t, C-5), 62.7 (d, C-4), 62.5 (d, C-4), 30.0 (d, $CH(CH_3)_2$), 29.9 (d, $CH(CH_3)_2$), 25.5 (2×q, CH_3-C-2), 23.0 (2×q, CH_3-C-2), 22.2 (q, C-4′), 21.3 (q, C-4′), 19.44 (q, $CH(CH_3)_2$), 19.41 (q, C-$CH(CH_3)_2$), 16.2 (q, $CH(CH_3)_2$), 15.9 (q, $CH(CH_3)_2$). − $[\alpha]^{25}_D$ = +29.7 (*c* = 1.01, $CHCl_3$). An analytical sample was obtained by bulb-to-bulb destillation (125°C/0.004 Torr). − $C_{13}H_{23}NO_3$ (241.3): calcd. C 64.70, H 9.61, N 5.80; found C 64.70, H 9.90, N 5.53.

General Procedure for the Ene Adducts from (S)-3-Tigloyl-2-oxazolidinones and PTAD: A solution of the *N*-tigloylamide (1.0 mmol) and PTAD (1.0 mmol) in CH_2Cl_2 (15 ml) was stirred at room temp. for 18 h. The solvent was removed at reduced pressure (20°C/7.5 Torr) and analytical samples were prepared by recrystallization.

Ene Adduct **6a** *from (S)-4-Benzyl-3-tigloyl-2-oxazolidinone and PTAD:* Yield 94%. − IR (KBr): $\tilde{\nu}$ = 3448 (NH) cm^{-1}, 1778 (C=O), 1719 (C=O), 1690 (C=O). − ^{1}H NMR ($CDCl_3$) for the major diastereomer: δ = 7.99 (br s, 1 H, NH), 7.56−7.16 (m, 10 H, Ar-H), 5.80 (s, 1 H, C=CH_2), 5.68 (s, 1 H, C=CH_2), 5.42 (q, ^3J = 6.7 Hz, 1 H, 3′-H), 4.88−4.77 (m, 1 H, 4-H), 4.36−4.17 (m, 2 H, 5-H), 3.32 (dd, ^2J = 13.4 Hz, ^3J = 3.4 Hz, 1 H, CH_2Ph), 2.89 (dd, ^2J = 13.4 Hz, ^3J = 8.9 Hz, 1 H, CH_2Ph), 1.49 (d, ^3J = 6.7 Hz, 3 H, 4′-H). − ^{1}H NMR ($CDCl_3$) for the minor diastereomer: δ = 7.99 (br s, 1 H, NH), 7.56−7.16 (m, 10 H, Ar-H), 5.72 (s, 1 H, C=CH_2), 5.61 (s, 1 H, C=CH_2), 5.37 (q, ^3J = 6.6 Hz, 1 H, 3′-H), 4.69−4.62 (m, 1 H, 4-H), 4.36−4.17 (m, 2 H, 5-H), 3.26 (dd, ^2J = 13.1 Hz, ^3J = 3.1 Hz, 1 H, CH_2Ph), 3.08 (dd, ^2J = 13.7 Hz, ^3J = 8.2 Hz, 1 H, CH_2Ph), 1.49 (d, ^3J = 6.7 Hz, 3 H, 4′-H). − ^{13}C NMR ($CDCl_3$) for the major diastereomer: δ = 169.4 (s, C-1′), 154.0 (s, C=O), 153.7 (s, C=O), 153.6 (s, C=O), 141.0 (s, C-2′), 134.4 (s), 131.3 (s), 129.4 (d), 129.2 (d), 129.1 (d), 128.2 (d), 127.6 (d), 125.5 (d), 123.1 (t, C=CH_2), 67.0 (t, C-5), 54.9 (d, C-4), 53.0 (d, C-3′), 37.1 (t, CH_2Ph), 13.1 (q, C-4′). − ^{13}C NMR ($CDCl_3$) for the minor diastereomer: δ = 169.1 (s, C-1′), 154.5 (s, C=O), 153.8 (s, C=O), 153.7 (s, C=O), 141.1 (s, C-2′), 134.4 (s), 131.2 (s), 129.4 (d), 129.1 (d), 128.9 (d), 128.1 (d), 127.7 (d), 125.4 (d), 121.3 (t, C=CH_2), 67.2 (t, C-5), 54.9 (d, C-4), 53.5 (d, C-3′), 37.3 (t, CH_2Ph), 13.1 (q, C-4′). − $[\alpha]^{25}_D$ = +48.7 (*c* = 1.02, $CHCl_3$). − An analytical sample was obtained by recrystallization from CH_2Cl_2/Et_2O (1:4), colorless prisms, m.p. 138.6−142.1°C. − $C_{23}H_{22}N_4O_5$ (434.5): calcd. C 63.59, H 5.10, N 12.90; found C 63.33, H 5.09, N 12.83.

Ene Adduct **6b** *from (S)-4-Isopropyl-3-tigloyl-2-oxazolidinone and PTAD:* 91%. − IR (KBr): $\tilde{\nu}$ = 3460 (NH) cm^{-1}, 1778 (C=O), 1760 (C=O), 1719 (C=O), 1690 (C=O). − ^{1}H NMR ($CDCl_3$) for the major diastereomer: δ = 8.01 (br s, 1 H, NH), 7.50−7.31 (m, 5 H, Ar-H), 5.79 (m, 1 H, C=CH_2), 5.73 (m, 1 H, C=CH_2), 5.36 (br q, ^3J = 6.6 Hz, 1 H, 3′-H), 4.60−4.52 (m, 1 H, 4-H), 4.39−4.17 (m, 2 H, 5-H), 2.39−2.31 (m, 1 H, $CH(CH_3)_2$), 1.46 (d, ^3J = 6.7 Hz, 3 H, 4′-H), 0.90 (d, ^3J = 6.7 Hz, 6 H, $CH(CH_3)_2$). -^{1}H NMR ($CDCl_3$) for the minor diastereomer: δ = 8.01 (br s, 1 H, NH), 7.50−7.31 (m, 5 H, Ar-H), 5.64 (m, 1 H, C=CH_2), 5.53 (m, 1 H, C=CH_2), 5.24 (br q, ^3J = 6.6 Hz, 1 H, 3′-H), 4.39−4.17 (m, 3 H, 4-H, 5-H), 2.55−2.48 (m, 1 H, $CH(CH_3)_2$), 1.46 (d, ^3J = 6.7 Hz,

Table 1. Crystal data and parameters of data collection, structural analysis and refinement for **2b** and **3a**

	2b	**3a**
Crystallographic Section		
Formula	$C_{21}H_{28}N_4O_4$	$C_{20}H_{26}N_4O_4$
Mol.weight	400.48	386.45
Crystal system	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a [pm]	981.2(3)	1101.9(1)
b [pm]	1438.1(4)	1220.1(1)
c [pm]	1573.3(3)	1496.7(1)
V [pm^3]	2220(1) $\times 10^6$	2012.2(3) $\times 10^6$
Z	4	4
Calcd. density [g cm^{-3}]	1.198	1.276
Data Collection		
Crystal size [mm]	0.2 × 0.15 × 0.7	0.25 × 0.25 × 1.15
Diffractometer	Siemens P4	Siemens P4
Radiation	Mo-K_α	Mo-K_α
Monochromator	graphite	graphite
Data collection mode	ω-scan	ω-scan
Recip. latt. segment	$h = -1 \rightarrow 12$ $k = -1 \rightarrow 18$ $l = -20 \rightarrow 20$	$h = -14 \rightarrow 1$ $k = -15 \rightarrow 1$ $l = -19 \rightarrow 19$
Θ_{max} [°]	1.75−27.5	1.75−27.5
No. refl. measd.	6704	6091
No. unique refl.	5107	4624
No. refl. $F>3\sigma(F)$	2998	3185
Lin. abs. coeff. [mm^{-1}]	0.08	0.09
Abs. correction	Ψ-scan	Ψ-scan
Structural Analysis and Refinement		
Solution by	direct phase determination	direct phase determination
Method of refinement	Full-Matrix LSQ. Hydrogen positions of riding model with fixed isotropic U	Full-Matrix LSQ. Hydrogen positions of riding model with fixed isotropic U
Data-to-parameter ratio	11.44	12.59
R, R_w	0.069, 0.056	0.068, 0.059
Weighting scheme	$w = 1/\sigma^2(F)$	$w = 1/\sigma^2(F)$
Largest difference peak	0.40 eÅ^{-3}	0.36 eÅ^{-3}
Larges difference hole	0.35 eÅ^{-3}	0.40 eÅ^{-3}
Program used	Siemens SHELXTL PLUS	Siemens SHELXTL PLUS

3 H, 4′-H), 0.84 (d, ^3J = 7.0 Hz, 6 H, CH(CH_3)$_2$). − ^{13}C NMR ($CDCl_3$) for the major diastereomer: δ = 169.3 (s, C-1′), 154.8 (s, C=O), 153.64 (s, C=O), 153.61 (s, C=O), 141.2 (s, C-2′), 131.2 (s), 129.0 (d), 128.1 (d), 125.4 (d), 122.9 (t, C=CH_2), 63.9 (t, C-5), 58.0 (d, C-4), 52.9 (d, C-3′), 27.8 (d, CH(CH$_3$)$_2$), 17.7 (q, CH(CH_3)$_2$), 14.8 (q, CH(CH_3)$_2$), 13.0 (q, C-4′). − ^{13}C NMR ($CDCl_3$) for the minor diastereomer: δ = 168.9 (s, C-1′), 154.4 (s, C=O), 153.6 (s, C=O), 153.5 (s, C=O), 140.8 (s, C-2′), 131.2 (s), 129.0 (d), 128.1 (d), 125.5 (d), 120.4 (t, C=CH_2), 64.1 (t, C-5), 59.5 (d, C-4), 53.5 (d, C-3′), 28.3 (d, CH(CH$_3$)$_2$), 17.8 (q, CH(CH_3)$_2$), 14.6 (q, CH(CH_3)$_2$), 13.5 (q, C-4′). − $[\alpha]^{25}_D$ = +72.2 (c = 1.00, $CHCl_3$). An analytical sample was obtained by recrystallization from CH_2Cl_2/Et_2O (1:4), colorless prisms, m.p. 136.3−141.9°C. − $C_{19}H_{22}N_4O_5$ (386.4): calcd. C 59.06, H 5.74, N 14.50; found C 58.62, H 5.79, N 14.19.

X-ray Structural Analysis of **2b**: Data were obtained from a crystal with approximate dimensions 0.2 × 0.15 × 0.7 mm by using a Siemens P4 diffractometer (Mo-K_α radiation, graphite monochromator). Cell dimensions were refined from 2l reflections; a = 981.2(3), b = 1438.1(4), c = 1573.3(3) pm, V = 2220(l) × 10^6 pm^3, orthorhombic, space group $P2_12_12_1$, Z = 4, $\rho_{calcd.}$ = 1.198 g/cm^3, 5107 unique intensities of which 2998 [$F_o \geq 3\sigma(F_o)$] were observed in the θ range 1.75−27.5°, measured with ω scan technique. The structure was solved by using direct phase determination and refined on F by using SHELXTL PLUS. Atomic coordinates and anisotropic displacement parameters of the non-hydrogen atoms were refined by the full-matrix least-squares method. The positions of the hydrogen atoms were calculated according to the ideal geometry (C−H 95 pm) and were refined by the riding method with fixed isotropic U values.

X-ray Structural Analysis of **3a**: Data were obtained from a crystal with approximate dimensions 0.25 × 0.25 × 1.15 mm by using a Siemens P4 diffractometer (Mo-K_α radiation, graphite monochromator). Cell dimensions were refined from 59 reflections; a = 1101.9(1), b = 1220.1(1), c = 1496.7(1) pm, V = 2012.2(3) ×10^6 pm^3, orthorhombic, space group $P2_12_12_1$, Z = 4, $\rho_{calcd.}$ = 1.276 g/cm^3, 4624 unique intensities of which 3185 [$F_o \geq 3\sigma(F_o)$] were observed in the θ range 1.75−27.5°, measured with ω scan technique. For further information see text above.[13]

[1] H. M. R. Hoffmann, *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556−557.
[2] [2a] W. H. Pirkle, J. C. Stickler, *J. Chem. Soc., Chem. Commun.* **1967**, 760−761. − [2b] S. Ohashi, K. W. Leong, K. Matyjaszewski, G. B. Butler, *J. Org. Chem.* **1980**, *45*, 3467−3471. − [2c] S. Ohashi, G. B. Butler, *J. Org. Chem.* **1980**, *45*, 3472−3476.
[3] [3a] K. Gollnick, H. J. Kuhn in *Singlet O_2* (Eds.: H. H. Wasserman, R. W. Murray), Academic Press: New York, **1979**, 287−429. − [3b] A. A. Frimer, I. M. Stephenson in *Singlet O_2* (Ed.: A. A. Frimer), CRC Press, Boca Raton, FL, **1985**, 68−87. − [3c] M. Matsumoto in *Singlet O_2* (Ed.: A. A. Frimer), CRC Press, Boca Raton, FL, **1985**, 205−272.
[4] [4a] E. J. Corey, B. B. Snider, *Tetrahedron Lett.* **1973**, 3091−3094. − [4b] W. Adam, A. Griesbeck, *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1070−1071. − [4c] W. Adam, B. Nestler, *Liebigs Ann. Chem.*, **1990**, 1051−1053.

[5] [5a] M. Orfanopoulos, M. Stratakis, Y. Elemes, *Tetrahedron Lett.* **1989**, *30*, 4875−4879. − [5b] Y. Elemes, M. Stratakis, M. Orfanopoulos, *Tetrahedron Lett.* **1989**, *30*, 6903−6906. − [5c] E. L. Clennan, X. Chen, J. J. Koola, *J. Am. Chem. Soc.* **1990**, *112*, 5193−5199. − [5d] S. Yamada, K. Hamano, M. Shimizu, *Tetrahedron Lett.* **1991**, *32*, 2379−2382.

[6] W. Adam, M. Prein, *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 477−494.

[7] Chiral auxiliaries in $^1O_2$ ene reactions: [7a] W. Adam, H.-G. Brünker, B. Nestler, *Tetrahedron Lett.* **1991**, *32*, 1957−1960. − [7b] P. H. Dussault, K. R. Woller, M. C. Hillier, *Tetrahedron* **1994**, *50*, 8929−8940.

[8] [8a] S. Kanemasa, K. Onimura, E. Wada, J. Tanaka, *Tetrahedron Asymmetry* **1991**, *2*, 1185−1188. − [8b] N. A. Porter, J. D. Bruhnke, W.-X. Wu, I. J. Rosenstein, R. A. Breyer, *J. Am. Chem. Soc.* **1991**, *113*, 7788−7790. − [8c] S. Kanemasa, K. Onimura, *Tetrahedron* **1992**, *48*, 8631−8644. − [8d] S. Kanemasa, K. Onimura, *Tetrahedron* **1992**, *48*, 8645−8658. − [8e] N. A. Porter, I. J. Rosenstein, R. A. Breyer, J. D. Bruhnke, W. X. Wu, A. T. McPhail, *J. Am. Chem. Soc.* **1992**, *114*, 7664−7676. − [8f] D. M. Scott, A. T. McPhail, N. A. Porter, *J. Org. Chem.* **1993**, *58*, 1178−1186. − [8g] S. Kanemasa, H. Suenaga, K. Onimura, *J. Org. Chem.* **1994**, *59*, 6949−6954. − [8h] S. Kanemasa, K. Ueno, K. Onimura, T. Kikukawa, H. Yamamoto, *Tetrahedron* **1995**, *51*, 10453−10462.

[9] [9a] D. A. Evans, J. Bartroli, T. L. Shih, *J. Am. Chem. Soc.* **1981**, *103*, 2127−2129. − [9b] D. J. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.* **1996**, *96*, 835−875.

[10] D. A. Evans, K. T. Chapman, J. Bisaha, *J. Am. Chem. Soc.* **1988**, *110*, 1238−1256.

[11] Y. Elemes, C. S. Foote, *J. Am. Chem. Soc.* **1992**, *114*, 6044−6050.

[12] [12a] W. Oppolzer, R. J. Mills, M. Réglier, *Tetrahedron Lett.* **1986**, *27*, 183−186. − [12b] W. Oppolzer, J.-P. Barras, *Helv. Chim. Acta* **1987**, *70*, 1666−1675. − [12c] D. P. Curran, T. A. Heffner, *J. Org. Chem.* **1990**, *55*, 4585−4595. − [12d] H. Kim, D. P. Curran, *Tetrahedron* **1993**, *49*, 293−318.

[13] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-100773. Copies of the data can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK.

[97322]