Diastereoselective and Regioselective Singlet Oxygen Ene Oxyfunctionalization (Schenck Reaction): Photooxygenation of Allylic Amines and Their Acyl Derivatives

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Abstract: The photooxygenations of the chiral allylic amine **1a**, its ammonium chloride **1b**, and the acylated derivatives **1c−f** and **1h** gave the corresponding regio- and diastereomeric allylic α-amino hydroperoxides **2** and **2′** through the ene reaction with singlet oxygen. For comparison purposes, also the unfunctionalized chiral alkene 2,4,5,5-tetramethyl-2-hexene (**1g**) was photooxygenated. While the reactions of the free amine **1a** and its ammonium chloride **1b** proceeded *threo*-diastereoselectively, for the acylated allylic amines **1c−f** and (*Z*)-**1h**, as well as for the chiral alkene **1g**, *erythro* selectivity was observed. The larger the nitrogen-containing moiety, the higher the *erythro* selectivity; however, for all acylated allylic amines, the stereocontrol was higher than for the alkene **1g**. These findings are explained in terms of the formation of diastereomeric perepoxide-like structured exciplexes **Ex** or *bona fide* perepoxide **D** intermediates during the oxyfunctionalization step. With the help of 1,3-allylic strain, the diastereotopic sides of the olefinic plane are differentiated by hindered rotation at the allylic chirality center. The high *threo* selectivities for the functionalized substrates **1a,b** are then dictated by attractive interactions between the incipient, negatively charged oxygen atom in the *threo*-**Ex** and *threo*-**D** structures with the amino and ammonium substituents by hydrogen bonding. This makes the relative energy content of the *threo* structures lower than for the *erythro* diastereomers. In contrast, the observed *erythro* selectivities for the acylated allylic amines **1c,f** and (*Z*)-**1h** and the alkene **1g** are best reconciled in terms of the steric repulsion between the terminal oxygen atoms of the *threo*-**Ex** and *threo*-**D** structures and the bulky substituents at the allylic positions. Consequently, the *erythro*-**Ex** and *erythro*-**D** structures are now energetically favored. In addition, the *threo*-**Ex** and *threo*-**D** structures of the acylated allylic amines are destabilized by the repulsive, electrostatic interactions between the incipient, negatively charged oxygen atoms and the polarized carbonyl functionalities. This manifests itself in the higher *erythro* selectivity of the acylated allylic amines compared to the alkene **1g**, despite the very large *tert*-butyl group of the latter. Therefore, by the proper choice of the allylic nitrogen functionality, i.e. the free amine *versus* its acylated derivative, either the *threo* or *erythro* diastereomer of allylic α-amino alcohols can be prepared selectively.

Introduction

The ene reaction of singlet oxygen ($^1O_2$) with alkenes, the so-called Schenck reaction,[1] constitutes a convenient route to allylic hydroperoxides.[2] Much work has been carried out in recent years on such photooxygenations, particularly on their diastereo- and regioselectivity.[3−11] The prominent controlling factor for the regioselectivity in the Schenck reaction[1] is the by now classical *cis* effect,[3] but more recently, *gem*-directing[4] and "nonbonding large group" interactions have been recognized.[5] Furthermore, very high regioselectivity is exercised by silyl[6] and stannyl substituents[7] on the olefin.

In regard to the diastereoselectivity for the $^1O_2$ ene reaction, π-facial differentiation has been abundantly documented[8] for cyclic and bicyclic substrates, whereas for acyclic olefins, such diastereomeric control has been described only recently.[9−11] Among the earliest examples count the acyclic olefins with silyloxy[9] and phenyl substituents[10] at an allylic chirality center, for which again the *cis* effect in conjunction with 1,3-allylic strain is held responsible as the steering factor. Most recently, for chiral allylic alcohols,[11] the *threo*-directing effect of the hydroxy group was documented, which promises valuable preparative applications in the stereoselective synthesis of oxyfunctionalized target molecules.

Although it has been well established[12] that amines quench efficiently $^1O_2$, we demonstrated[13] that chiral allylic primary

† Dedicated to Prof. Dr. H.-D. Scharf on the occasion of his 65th birthday.

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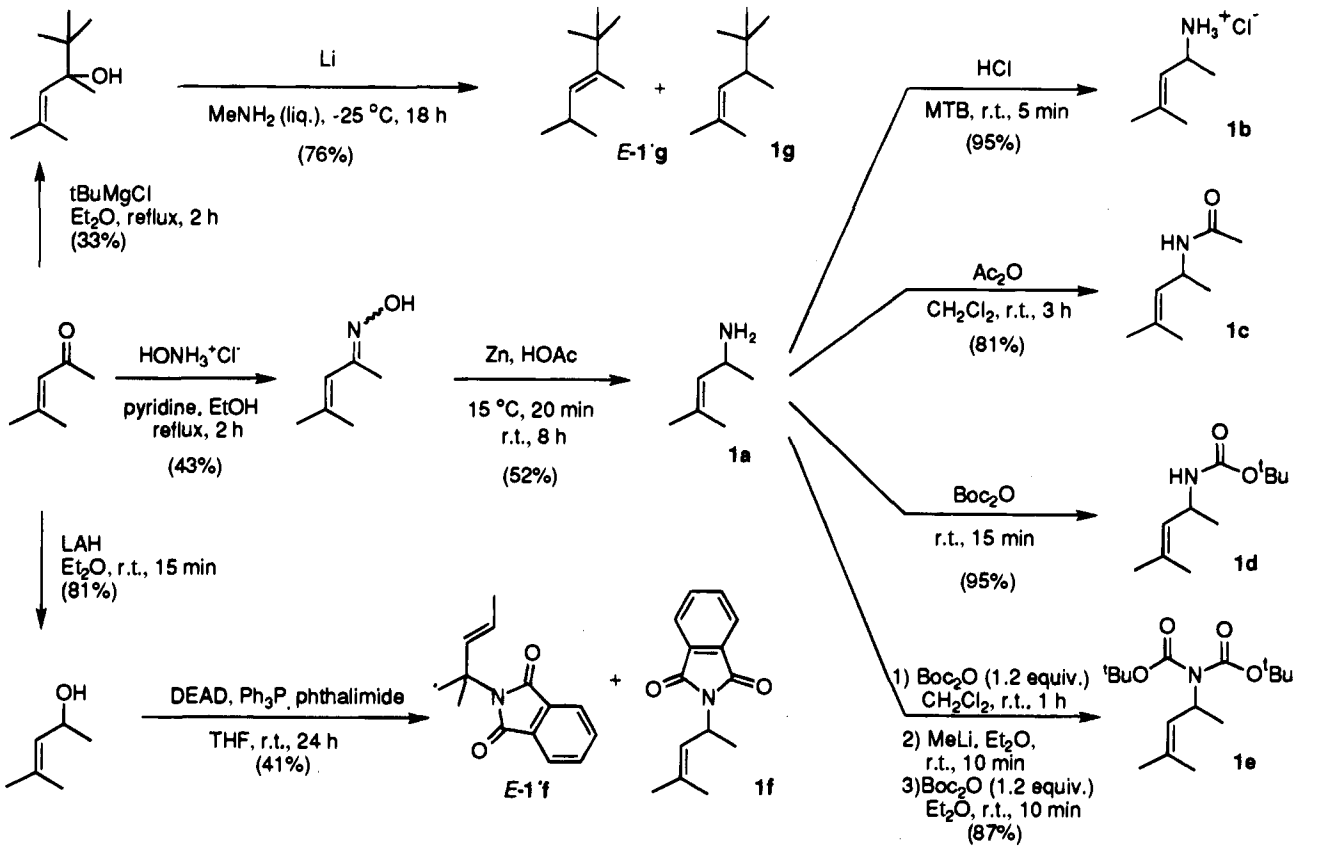
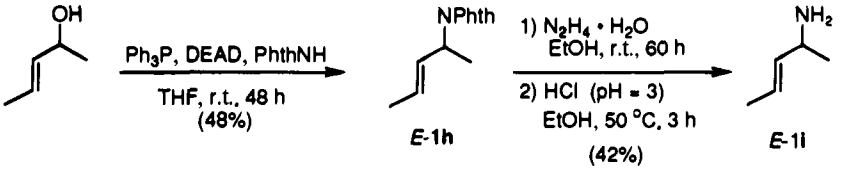
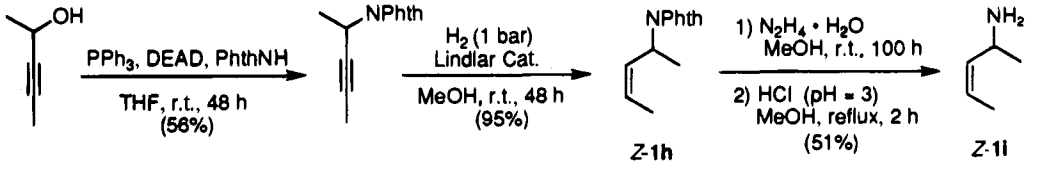
Scheme 1



Scheme 2



Scheme 3



amines and their acylated derivatives undergo efficient diastereo- and regioselective ene reactions with singlet oxygen. The high *threo* selectivity for the free amine has been rationalized in terms of a directing effect of the amino functionality similar to that proposed for the hydroxy group[11] in chiral allylic alcohols. In contrast to the free amine, the acetyl and phthalimide derivatives display predominantly *erythro* selectivity, which has been rationalized on the basis of the more usual steric effects.

Herein we report the full experimental details on the regio- and diastereoselective photooxygenations of chiral allylic amines and their acylated derivatives. The mechanistic features of the stereocontrolled ene reactions of singlet oxygen will be discussed.

Results

Scheme 1 outlines the synthesis of starting materials **1a–g** from mesityl oxide. The allylic amine **1a** was obtained in 52% yield from the 4-methyl-3-penten-2-one oxime[14] by reduction with zinc in acetic acid. From amine **1a**, the hydrochloride **1b**, the acetamide **1c**, the carbonate **1d**, and the imidodicarbonate **1e** were synthesized. A Mitsunobu reaction[15] was used to prepare the phthalimide **1f** from 4-methyl-3-penten-2-ol,[16] which was obtained with its regioisomer (*E*)-**1'f** and constitutes a difficult to separate mixture. The alkene **1g** was prepared from 2,2,3,5-tetramethyl-4-hexen-3-ol[17] by reduction with lithium in liquid methylamine as an inseparable mixture with its isomer (*E*)-**1'g**. The phthalimide (*E*)-**1h** was made from (*E*)-3-penten-2-ol[18] (Scheme 2) and (*Z*)-**1h** from 3-pentyn-2-ol[19] by reduction of the alkyne, which again was made available through the Mitsunobu reaction (Scheme 3). Deprotection of the phthal-

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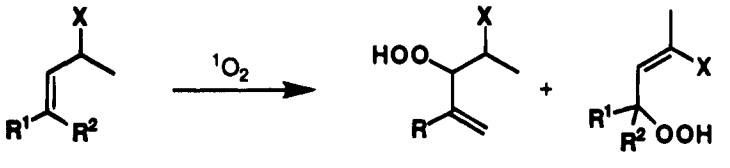
Table 1. Regio- and Diastereoselectivity in the Photooxygenation of Chiral Allylic Amines, Alcohols, and Derivatives



2 2'

								regioselectivity[c]	diastereoselectivity[c]	
entry	substrate	X	R^1	R^2	solvent[a]	time[b] (h)	yield[c] (%)	2:2'	*threo*:*erythro*	*Z*:*E*
1[d]	**1a**	NH_2	Me	Me	CCl_4	2	87	*e*	>95:5	*e*
2[d]	**1a**	NH_2	Me	Me	$CDCl_3$	3	90	*e*	92:8	*e*
3[d]	**1a**	NH_2	Me	Me	D_3COD	4	87	*e*	85:15	*e*
4	**1b**	$NH_3^+Cl^-$	Me	Me	CCl_4	30	93	*e*	64:36	*e*
5	**1b**	$NH_3^+Cl^-$	Me	Me	$CDCl_3$	48	90	*e*	94:6	*e*
6	**1b**	$NH_3^+Cl^-$	Me	Me	D_3COD	48	90	*e*	87:13	*e*
7	**1c**	NHAc	Me	Me	CCl_4	4	93	*e*	28:72	*e*
8	**1c**	NHAc	Me	Me	$CDCl_3$	8	90	*e*	36:64	*e*
9	**1c**	NHAc	Me	Me	D_3COD	8	90	*e*	29:71	*e*
10	**1d**	NHBoc	Me	Me	CCl_4	14	80	*e*	24:76	*e*
11	**1d**	NHBoc	Me	Me	$CDCl_3$	20	84	*e*	35:65	*e*
12	**1d**	NHBoc	Me	Me	D_3COD	20	84	*e*	29:71	*e*
13	**1e**	$NBoc_2$	Me	Me	CCl_4	3[f]	91[g]	86:14	5:95	>90:10
14	**1f**	NPhth	Me	Me	CCl_4	4	87[g]	90:10	11:89	>95:5
15	**1f**	NPhth	Me	Me	$CDCl_3$	8	>95	92:8	22:78	>95:5
16	**1f**	NPhth	Me	Me	D_3COD	8	>95	89:11	15:85	>95:5
17	**1g**	^{t}Bu	Me	Me	CCl_4	5	>95	>95:5	29:71	*e*
18	(*Z*)-**1h**	NPhth	H	Me	CCl_4	50[f]	91[g]	88:12	13:87	87:13
19	(*E*)-**1h**	NPhth	Me	H	CCl_4	120[h]	87[g]	81:19	50:50	60:40
20	(*Z*)-**1i**	NH_2	H	Me	CCl_4	3	0[i]			
21	(*E*)-**1i**	NH_2	Me	H	CCl_4	3	0[i]			
22[k]	**1k**	OH	Me	Me	CCl_4	4	89[g]	96:4	93:7	*l*
23[k]	**1k**	OH	Me	Me	D_3COD	6	89[g]	96:4	73:27	*l*
24[k]	(*Z*)-**1l**	OH	H	Me	CCl_4	6	73[g]	*e*	93:7	*e*
25[k]	(*E*)-**1l**	OH	Me	H	CCl_4	20	75[g]	96:4	54:46	*l*
26[k]	**1m**	OMe	Me	Me	CCl_4	8	57[g]	80:20	72:28	*m*
27[k]	**1n**	$OSiMe_3$	Me	Me	CCl_4	8	63[g]	74:26	80:20	*m*

[a] Tetraphenylporphine as the sensitizer in CCl_4 and $CDCl_3$, Rose Bengal in methanol-d_4. [b] Reaction time necessary for full conversion. [c] Yields, diastereomeric ratios, and regioselectivities were determined directly on the crude reaction mixture by ^1H NMR spectroscopy against naphthalene as the internal standard (error ±5% of the stated value). [d] After reduction, isolated as the corresponding amino alcohols. [e] No regioisomeric products were detected. [f] Irradiation by two external 250 W sodium lamps. [g] Yield of isolated material. [h] Conversion 79%. [i] No ene reaction. [k] Reference 11. [l] The regioisomer was observed in the form of its ring tautomer. [m] The resulting enol ether products were unstable under the reaction conditions.

imides (*Z*,*E*)-**1h** according to the usual procedures gave the allylic amines (*E*,*Z*)-**1i** (Schemes 2 and 3).[20]

Photooxygenations of the allylic amine **1a**, its derivatives **1b**–**f**,**h**, and the olefin **1g** afforded the corresponding allylic hydroperoxides **2** by means of the singlet oxygen ene reaction. The observed product ratios in Table 1 were determined by ^1H NMR spectroscopy directly on the crude reaction mixtures. Control experiments such as irradiation of **1a**–**h** in the absence of sensitizer and prolonged photooxygenations of the corresponding hydroperoxides established that all starting materials and products, except for (*E*)-**2'h**, were stable under the reaction conditions. In the case of hydroperoxide (*E*)-**2'h** (entry 19), a second $^1O_2$ ene reaction occurred during the prolonged irradiation times and, thus, the ratio of (*Z*,*E*)-**2'h** was determined at low conversion.

The photooxygenation of the allylic amine **1a** afforded in high regio- and diastereoselectivity predominantly the *threo*-configurated hydroperoxide (*S**,*S**)-**2a** (d.r. > 95:5, in CCl_4, entry 1). Due to the thermal lability of the free amino hydroperoxide (*S**,*S**)-**2a**, the latter was reduced with triphenylphosphine to its amino alcohol (*S**,*S**)-**3a**, which was fully characterized. Regioisomeric products were not detected.

The degree of the *threo* selectivity depended on the solvent in which the photooxygenation was performed. For example, in the polar, protic solvent methanol, the selectivity was significantly lower than in the nonpolar, aprotic CCl_4 (entries 1–3).

The photooxygenation of the hydrochloride **1b** afforded also predominantly the *threo*-configurated product (*S**,*S**)-**2b**. In deuterochloroform and in methanol the diastereoselectivity was as high as for the free amine **1a** (94:6 in $CDCl_3$ and 87:13 in methanol, entries 5 and 6). Only in CCl_4 was the selectivity significantly lower (64:36, entry 4). Again no regioisomeric products were observed.

The acylated derivatives **1c**–**f** (entries 7–16) and (*Z*)-**1h** (entry 18) gave in moderate to good *erythro* selectivities the corresponding hydroperoxides **2**. The lowest *erythro* selectivity was found for the acetamide **1c** (72:28 in CCl_4, entry 7), but the larger the nitrogen-containing moiety, the higher the *erythro* selectivity. Accordingly, for the carbamate **1d**, the selectivity in CCl_4 was 76:24 (entry 10); for the phthalimide (*Z*)-**1h** 87:13 (entry 18), for the phthalimide **1f** 89:11 (entry 14), and for the sterically very crowded imidodicarbonate **1e**, it was 95:5 (entry 13). For the substrates **1c**,**d**,**f**, the diastereoselectivities were higher in CCl_4 (entries 7, 10, and 14) than in deuterochloroform (entries 8, 11, and 15) and methanol (entries 9, 12, and 16).

The formation of the regioisomeric products **2'** also occurred

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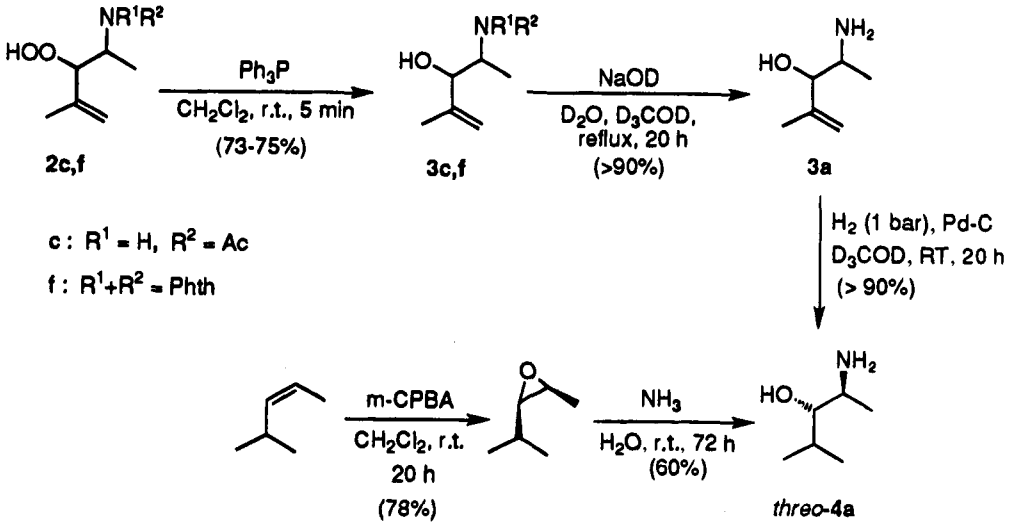
Scheme 4



in a highly diastereoselective manner. For substrates **1e,f** only the (*Z*)-**2′e,f** isomers were observed (entries 13 and 14). The photooxygenation of (*Z*)-**1h** (entry 18) produced both regioisomers (*Z,E*)-**2′h** in appreciable amounts, but with a high *Z* selectivity (*Z*:*E* = 87:13). For the acylated substrates **1c,d** (entries 7−12) no regioisomeric products were observed. Moreover, the regioselectivities of all reactions in which regioisomeric products **2** and **2′** were obtained were also high, i.e. the **2**:**2′** ratio ranged from 86:14 for **1e** (entry 13) to 92:8 for **1f** (entry 15).

The photooxygenation of the phthalimide (*E*)-**1h**, which unlike all the other substrates possesses no 1,3-allylic strain, exhibited a significantly lower selectivity than all other substrates (entry 19). The main product **2h** was not formed stereoselectively (*threo*-**2h**:*erythro*-**2h** = 50:50). The *Z*:*E* ratio of the regioisomeric product (*Z,E*)-**2′h** was only 60:40, but the **2**:**2′** regioselectivity was still quite high, i.e. 81:19.

The $^1O_2$ ene reaction of the chiral alkene **1g** occurred, like the photooxygenation of the corresponding acylated allylic amines, in an *erythro*-selective manner. Astonishingly, the diastereoselectivity was in spite of the high steric demand of the *tert*-butyl group not very high (71:29, entry 17). Regioisomeric products were not observed.

Unfortunately, the allylic amines (*Z,E*)-**1i** (entries 20 and 21) did not undergo ene reaction with $^1O_2$. Instead, a complex mixture of products was obtained.

Stereochemical Assignments

The relative configuration of the diastereomeric alcohol **3a** was determined by chemical correlation (Scheme 4). The allylic amino alcohol **3a** was catalytically reduced to the saturated derivative (*S**,*S**)-**4a**, whose *threo* stereochemistry was assigned by independent synthesis from *cis*-4-methyl-3-pentene by epoxidation[21] and subsequent ammonolysis.

To assess the stereochemistry of hydroperoxides **2c,f**, these were reduced by triphenylphosphine to the corresponding alcohols **3c,f** and the latter hydrolyzed to the amino alcohol **3a**. Comparison of the NMR spectra with those of *threo*-**3a**, obtained directly from the allylic amine **1a**, revealed that the photooxygenation of the acylated derivatives **1c,f** had afforded the *erythro*-configurated product as the main isomer.

The configuration of the hydroperoxide **2d** was determined by comparing the coupling constants of the α protons at the nitrogen- and oxygen-bearing carbon atoms in the hydroperoxide **2c**. The configuration of the hydroperoxide **2g** was similarly assessed by the coupling constants of the protons α to the *tert*-butyl and α to the hydroperoxy groups. The configuration of the di-Boc hydroperoxide **2e** could then be obtained by correlating it with the mono-Boc derivative **2d** through selective hydrolysis of one of the Boc-protecting groups[22] with trifluoroacetic acid.

The configurations of all regioisomeric products **2′** were determined by NOE experiments. For the *Z* isomers, significant enhancements (10−12%) of the olefinic proton signals were found on irradiation of the methyl group attached to the double bond. In contrast, for the *E* isomers, such enhancements were not observed.

Discussion

The present and earlier[11,13] results of the singlet ene reaction for the allylic amines, allylic alcohols, and their acylated derivatives will now be analyzed critically in terms of the established[9−11,13] mechanism. As will become evident, earlier suggested mechanisms[9−11,13] will have to be revised and a more complete picture will be offered.

Any rational mechanism for these regio- and diastereoselective ene reactions must take into account the following observations:

(1) Only acyclic chiral olefins which possess 1,3-allylic strain[23] are photooxygenated diastereoselectively (entries 19 and 25).

(2) The singlet oxygen ene reactions of allylic amines, ammonium chlorides, and alcohols which possess 1,3-allylic strain proceed in a highly *threo*-selective manner, i.e. predominantly the (*S**,*S**)-configurated products are formed (entries 1−6 and 22−24).

(3) For the *threo*-selective photooxygenations of allylic amines and alcohols, the diastereoselectivity is significantly lower in the polar, protic methanol than in the unpolar, nonprotic CCl_4 as solvents (entries 1, 3, and 22−23). No significant solvent effects are observed in the case of the *erythro*-selective ene reactions of the acylated allylic amines.

(4) The photooxygenations of all substrates are highly regioselective.

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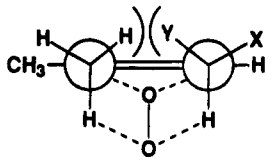
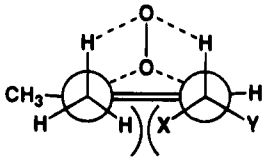
(23) Hofmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.

(5) The regioisomer **2′** is also formed in high diastereoselectivity, in favor of the *Z* isomer for those cases in which 1,3-allylic strain applies (entries 13 and 14).

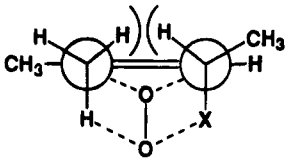
Several mechanisms have been suggested to rationalize the diastereoselectivity in the singlet oxygen ene reaction of acyclic, chiral olefins.[9-11,13] One of the earliest versions[9] explained the high diastereoselectivity in the photooxygenation of silyl cyanohydrins of α,β-unsaturated aldehydes in terms of perepoxide-like transition states. In these transition states the favorable conformation is determined by the interaction of the allylic hydrogen atoms with the perepoxide oxygen atom analogous to that proposed in the classical *cis* effect.[3] The high diastereoselectivity is then controlled by the 1,3-allylic strain in the two diastereomeric transition state structures *threo*-**A**$^{\neq}$ and *erythro*-**A**$^{\neq}$. However, this classical *cis* effect cannot



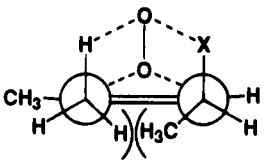
threo-**A**$^{\neq}$



erythro-**A**$^{\neq}$



threo-**B**$^{\neq}$



erythro-**B**$^{\neq}$

X = OH, NH_2

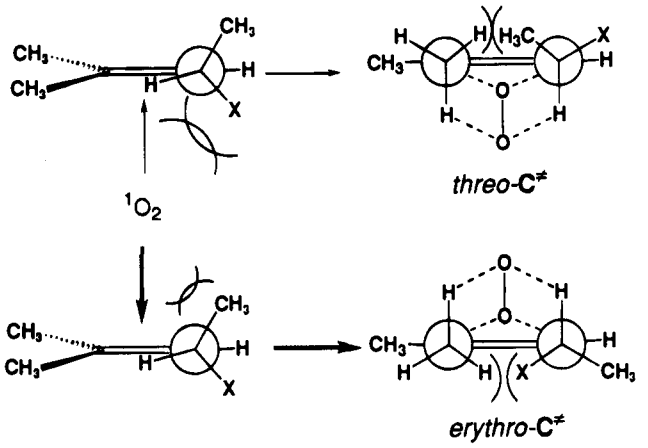
operate in the diastereoselective ene reactions of the allylic amine **1a** (entries 1−3) and the alcohols **1k** and (*Z*)-**1l** (entries 22−24) because singlet oxygen reacts with these chiral substrates in a highly *threo*-selective manner.[11,13] Besides the fact that a low *erythro* selectivity would have been expected because of the small difference in the steric demand of the methyl *versus* the hydroxy or amino group, more significant, the opposite sense, i.e. *threo* rather then *erythro* diastereoselectivity, has been observed (compare the *threo*- and *erythro*-**A**$^{\neq}$ structures).

The pronounced *threo* selectivity was rationalized[11,13] in terms of an electrophile−nucleophile attraction between the incoming electrophilic singlet oxygen[24] and the nucleophilic hydroxy or amino functionality. The difference in the 1,3-allylic strain between the two diastereomeric structures *threo*- and *erythro*-**B**$^{\neq}$ was then held responsible for the preferred formation of the *threo*-configurated products.

A further argument against the classical *cis* effect is that the *erythro* selectivity in the photooxygenation of the allylic acetamide **1c** (entries 7−9) and phthalimide **1f** (entries 14−17) increases with the steric demand of the nitrogen functionality.[13] Were the *cis* effect to operate, one would expect for X = Me and X = NHAc and NPhth in structure **A**$^{\neq}$ a higher *threo* selectivity for the larger X group. Thus, the observed *erythro* selectivity was rationalized in terms of simple steric effects[10b,13] (Scheme 5) in which the singlet oxygen attack from the side opposite of the bulky nitrogen functionality is decisive rather than 1,3-allylic strain in the *cis*-coordinated *erythro*-**C**$^{\neq}$ transition state.

(24) Thomas, M. J.; Foote, C. S. *Photochem. Photobiol.* **1978**, *27*, 683.

Scheme 5



X = HNAc, NPhth

Our originally proposed mechanisms[11,13] for the *threo*-selective photooxygenations (chiral alcohols and amines) and the *erythro*-selective ones (chiral amides and imides) must be extended to accommodate satisfactorily all facts. For example, the previous hypothesis of the steering effect by the nucleophilic hydroxy or amino groups does not explain why the photooxygenations of the allylic methyl and trimethylsilyl ethers **1m,n** (entries 26 and 27) occurred with a significantly lower *threo* selectivity than the free alcohols (entries 22−24).[11b]

Still more puzzling are our present results that the ammonium chloride **1b** (entries 5 and 6) in deuterochloroform and methanol undergoes photooxygenation with the same *threo* selectivity as the free amine **1a** (entries 2−3). This highly *threo*-selective reaction (especially in $CDCl_3$; entry 5) of the non-nucleophilic ammonium chloride clearly implies that the originally proposed electrophile−nucleophile electrostatic attraction cannot alone be responsible for the high *threo* diastereoselectivity in the photooxygenations of allylic amines and alcohols.

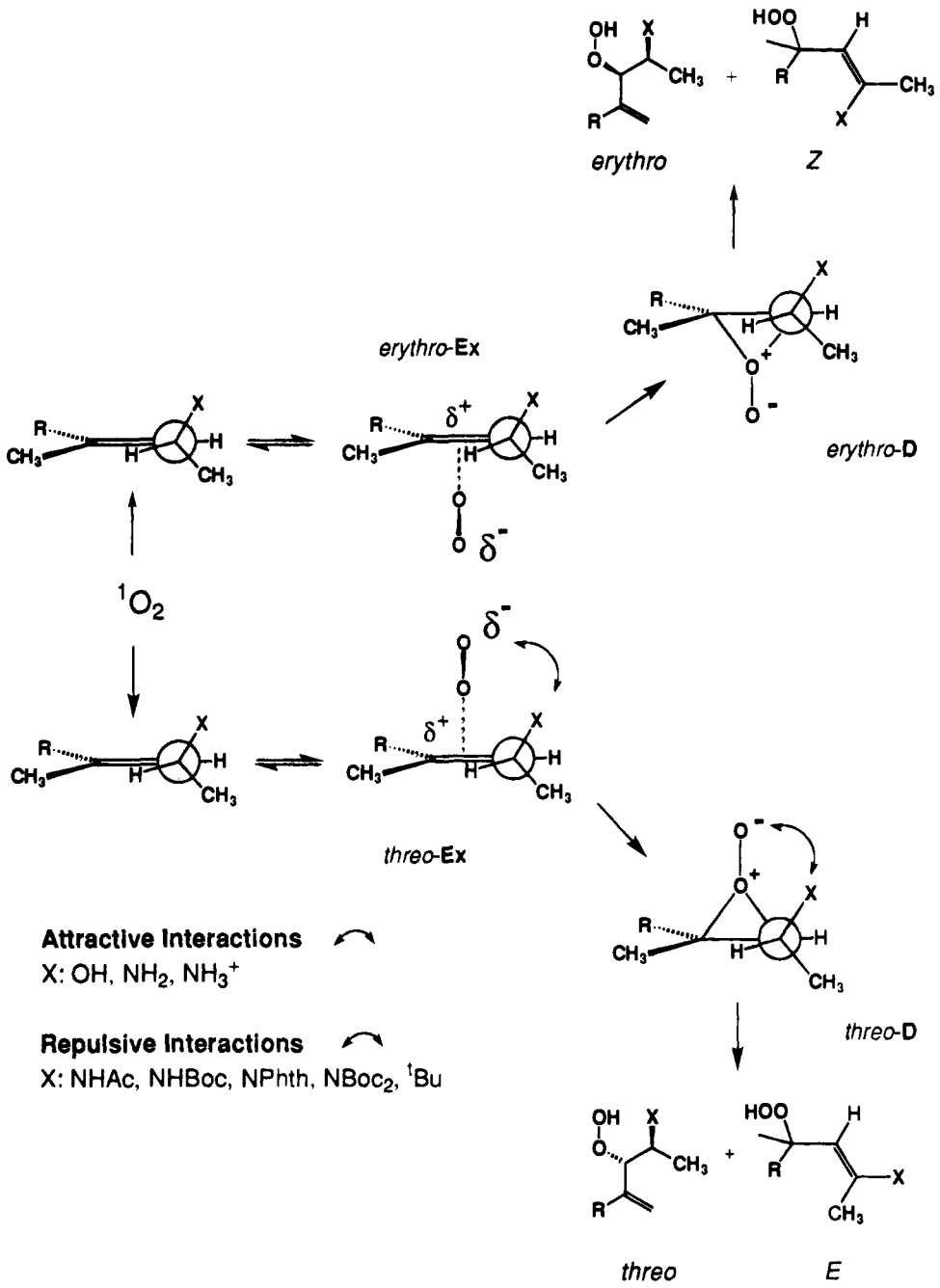
Moreover, the observed *erythro* selectivity in the singlet oxygen ene reactions of amides and imides (entries 7−16) cannot only depend on steric factors, as was demonstrated by the photooxygenation of the alkene **1g** (entry 17). In fact, the *erythro* selectivity of the alkene **1g** is even lower than for all acylated allylic amines **1c−f** and (*Z*)-**1h** (entries 7, 10, 13, 14, and 18), which suggests that besides steric also electronic factors play a role.

The extended mechanism in Scheme 6 is proposed to account for all the present experimental facts. The exciplexes **Ex**, the precursors to the perepoxides **D**, comprise the new and stereocontrolling feature. Although the geminal methyl groups in the allylic substrates **1** have not been differentiated through deuteration to establish their regioselectivities, in view of the fact that the isotopically labeled (*E*)-4-methyl-2-(trideuteromethyl)-2-pentene[3a] undergoes predominant hydrogen atom abstraction at the geminal CH_3 rather than CD_3 group, the same regioselectivity is assumed to apply for our chiral olefins.

The reversible formation of exciplexes in photooxygenations is abundantly documented.[25] Although the geometry of these complexes is not known,[25d] kinetic data suggest that the exciplex

(25) (a) Frimer, A. A.; Bartlett, P. D.; Boschung, A. F.; Jewett, J. G. *J. Am. Chem. Soc.* **1977**, *99*, 7977. (b) Gorman, A. A.; Gould, I. R.; Hamblett, I.; Standen, M. C. *J. Am. Chem. Soc.* **1984**, *106*, 6956. (c) Gorman, A. A.; Gould, I. R.; Hamblett, I. *J. Am. Chem. Soc.* **1982**, *104*, 7098. (d) Hurst, J. R.; Wilson, S. L.; Schuster, G. B. *Tetrahedron* **1985**, *41*, 2191. (e) Gorman, A. A.; Hamblett, I.; Lambert, C.; Spencer, B.; Standen, M. C. *J. Am. Chem. Soc.* **1988**, *110*, 8053. (f) Orfanopoulos, M.; Smonou, I.; Foote, C. S. *J. Am. Chem. Soc.* **1990**, *112*, 3607.

Scheme 6



is a highly ordered species[25c,e] and it is assumed that the geometry is perepoxide-like.[25f] In view of the established *cis* effect,[3] the terminal oxygen atom in the perepoxide-like structured exciplex points toward the higher substituted side of the double bond.

The attractive force between the oxygen and the π system of the olefin in these exciplexes derives from charge transfer, which results in a partially negatively charged dioxygen molecule and a partially positively charged olefinic π system.[25a-c] In the case of chiral olefins, the two diastereomeric exciplexes *threo*- and *erythro*-**Ex** are possible (Scheme 6). These exciplexes transform to the corresponding *threo*- and *erythro*-**D** perepoxides, which finally produce the *threo*- and *erythro*-hydroperoxides as major and the *Z*- and *E*-hydroperoxides as minor regioisomers.

The favored π-facial approach of singlet oxygen in the formation of these diastereomeric exciplexes **Ex** and perepoxides **D** is energetically controlled by the interaction of the incipient negatively charged dioxygen molecule with the substituents at the chirality center, while conformational preference is fixed by 1,3-allylic strain. The importance of the latter discriminating steric features is exemplified in the *E*-configurated substrates (*E*)-**1h** and (*E*)-**1l**, for which no diastereoselectivity is observed in the photooxygenation (entries 19 and 25).

The postulated electronic interaction between the incipient negatively charged dioxygen and the functionality X at the chirality center can be of repulsive or attractive nature. An attractive interaction results in a stabilization of the exciplex *threo*-**Ex** with the consequence that the *threo*- or *E*-configurated hydroperoxides are formed preferentially, while a repulsive interaction promotes formation of the *erythro*- and *Z*-configurated hydroperoxides. For all substrates, irrespective of whether the formation of the exciplex **Ex** or the perepoxide **D** is the product-determining step, all substituents X which stabilize the exciplex *threo*-**Ex** influence also the stability of the perepoxide *threo*-**D** in the same manner.

Let us now examine how this extended mechanism (Scheme

6) accounts for the observed diastereoselectivities of the various X functionalities at the stereogenic site. When X is OH, NH_2, or NH_3^+, we propose that the *threo*-**Ex** exciplex and correspondingly the *threo*-**D** perepoxide are stabilized by hydrogen bonding. The degree of this stabilization can be influenced by the solvent used, as manifested by the polar, protic methanol (entries 3, 6, and 23) for which the diastereoselectivity is significantly lower than in deuterochloroform (entries 2 and 5) or CCl_4 (entries 1 and 22). The low *threo* selectivity observed in the photooxygenation of the ammonium chloride **1b** in CCl_4 (entry 4) may be due to the formation of ion pairs in this unpolar solvent. The repulsive interaction of the chloride ion and the incipient negatively charged oxygen atom would be expected to compensate to some extent the stabilizing effect due to hydrogen bonding.

The X substituents like NHAc, NHBoc, NPhth, $NBoc_2$, and *tert*-butyl destabilize the *threo*-**Ex** exciplex and *threo*-**D** perepoxide and, therefore, lead to the *erythro*- and *Z*-configurated hydroperoxides. Two factors seem to be responsible for the repulsive interaction of the X substituent and the incipient negatively charged oxygen. On one hand, it is the steric demand of the X substituent and the bigger the X the higher the *erythro* selectivity. This was shown for the acylated allylic amines, for which the *erythro* selectivity increases in the order NHAc < NHBoc < NPhth < $NBoc_2$ (entries 7−16). On the other hand, the repulsive, electrostatic interaction of the polarized carbonyl moiety and the incipient negatively charged oxygen additionally destabilizes the *threo*-**Ex** exciplex. This is manifested by the fact that the singlet oxygen ene reactions of all here investigated acylated allylic amines exhibit a higher *erythro* selectivity than the alkene **1g** (entry 17), for which the large but unpolar *tert*-butyl substituent can only operate by steric repulsions.

The high regioselectivities of the *threo*-selective photooxygenations derive from the fact that the conformation of the allylic chirality centers in the *threo*-**Ex** exciplex and the *threo*-**D** perepoxide are fixed by hydrogen bonding. Therefore, the allylic hydrogen atom at the chirality center is encumbered to acquire the essential perpendicular conformation to the olefinic plane and hydrogen atom abstraction is suppressed.

Last, but not least, the high regioselectivities of the *erythro*-selective singlet oxygen ene reactions can be explained in terms of the hindered rotation about the allylic chirality center. Because of 1,3-allylic strain, the allylic hydrogen at the tertiary carbon atom can hardly achieve a conformation perpendicular to the olefinic plane and is, thus, not abstracted. Moreover, it is well established that hydrogen abstraction by singlet oxygen at allylic methinyl sites, e.g. isopropyl groups, is notoriously poor and this alone would account for a low regioselectivity at the stereogenic site in our substrates **1**.

Conclusions

The regio- and diastereoselective singlet oxygen ene reactions of chiral allylic amines and their acylated and protonated derivatives make readily and conveniently available the corresponding β-amino allylic hydroperoxides. Both the (S^*,S^*)- and (S^*,R^*)-configurated hydroperoxides can be obtained highly selectively by the proper choice of the substituents at the nitrogen. Thus, the free amine and its ammonium salt afford preferentially the *threo* products, while the acylated derivatives lead predominantly to the *erythro* products. The offered mechanism explains the observed diastereo- and regioselectivity for the ene reaction of singlet oxygen with acyclic chiral olefins in that for polar, protic groups (−OH, $-NH_2$, and $-NH_3^+$) hydrogen bonding provides the attractive interaction for the *threo* π-facial control, while for electron-withdrawing substituents (NHAc, NHBoc, $NBoc_2$, and NPhth) electrostatic repulsions are responsible for *erythro* π-facial control. However, the chiral allylic substrate must possess 1,3-allylic strain for conformational discrimination in the exciplex and perepoxide. In this manner, oxyfunctionalized molecules of defined stereochemistry can be designed for organic synthesis.

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Supplementary Material Available: Text giving experimental details for the preparation, purification, and characterization of all mentioned compounds (18 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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