higher order interaction constants are the predominant factor contributing to the disparity in the empirical and semiempirical **F** matrices. Presuming that the higher order interactions are as important as suggested by the QCFF/PI calculation, force constants reflecting such interactions should also be included in empirical calculations. In this regard, Li and Zgierski found that the inclusion of certain 1,4 interaction constants was important in obtaining an accurate force field for porphines.[65] In our calculations on CuOEC, the effects of 1,4 interactions were explored only in a limited fashion. A detailed assessment of the effects of these (and higher order) interactions is not possible because there are a large number of these types of interactions and the experimental information is too limited to allow an evaluation of their importance.

Summary and Conclusions

The empirical force-field calculations reported herein indicate that various force fields satisfactorily reproduce the general features of the vibrational spectra of CuOEC. However, none of these force fields reproduces the frequencies and *meso*-deuteriation shift patterns of all of the modes. All of the empirical force fields predict that the eigenvectors of certain skeletal modes are localized onto sectors of the macrocycle. This result is in general agreement with the prediction of the QCFF/PI calculations and with the data available for CuOEC, ZnOEC, and their selectively *meso*-deuteriated isotopomers presented here and in our previous work.[37,42] Quantitative comparison of the empirical and semiempirical force fields indicates that 1,4 and higher interaction constants make substantial contributions to the latter force fields. These interactions are not included in the empirical force field calculations. Accordingly, the values of the force constants used in the empirical calculations are not necessarily representative of the actual force field effective in the macrocycle. The fact that a large number of important interaction force constants are probably excluded from the empirical calculations indicates that the constraint requiring the force constants to faithfully reflect the bond lengths is necessarily artificial. Accordingly, the most important criterion for evaluating the merit of a force field should be its ability to predict accurately specific isotope shift patterns, regardless of the values of the force constants.

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Communications to the Editor

Photooxygenation of Chiral Allylic Alcohols: Hydroxy-Directed Regio- and Diastereoselective Ene Reaction of Singlet Oxygen

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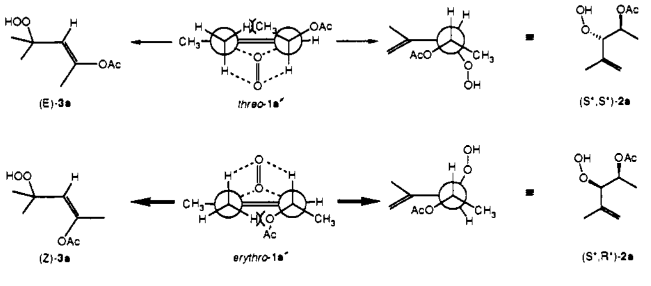
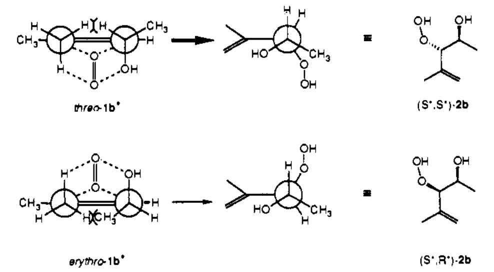
A recent communication,[1] in which it was quite generally stated that singlet oxygen ($^1O_2$) exhibits poor regio- and diastereoselectivity in its ene reaction with olefins, obliges us to report our preliminary results on the photooxygenation of chiral allylic alcohols **1**. In an appropriate environment, in this particular case the coordinating effect of the hydroxy group, regio- and diastereocontrol can be very high even for acyclic substrates (Table I). The directing effect of the hydroxy functionality, which is well-recognized in epoxidations by peracids[2] and transition metals[2c,d,3] and in nitrile oxide cycloadditions,[4] is novel for $^1O_2$. It permits, through its ene reaction, the introduction of a new stereogenic center with an oxygen functionality adjacent to the hydroxy group of the chiral allylic alcohol.

The by now classical cis effect[5] constitutes one of the prominent factors in controlling the regio- and stereochemistry of the protropic ene reaction with $^1O_2$. Diastereofacial control was recently reported[5c,d,6] for a few acyclic olefins, which was attributed to the cis effect.[5]

Scheme I



Scheme II



The photooxygenation of the allylic acetate **1a** (Table I, entry 1) illustrates the point under discussion (Scheme I). The pronounced regioselectivity (82:18) for **2** and **3** and moderate diastereoselectivity (d.r. = 32:68) for both (*S**,*S**)-/(*S**,*R**)-**2a** and (*E*)-/(*Z*)-**3a** can be rationalized in terms of the cis effect.[5] In fact, the same d.r. values for both sets of diastereomers demand a common transition state, namely, the perepoxide-like geometry shown in *erythro*-**1a**‡ for the major diastereomers (*S**,*R**)-**2a** and (*Z*)-**3a** and in *threo*-**1a**‡ for the minor diastereomers (*S**,*S**)-**2a**

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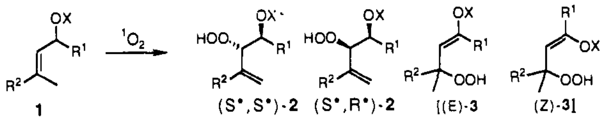
Table I. Regio- and Diastereoselectivity[a] in the Photooxygenation[b] of Chiral Allylic Acetate **1a** and Alcohols **1b–f**



entry		X	R^1	R^2	solvent	diastereoselectivity (*S**,*S**)-**2** [(*E*)-**3**]	 (*S**,*R**)-**2** [(*Z*)-**3**]	regio-selectivity **2**	 **3**
1	**1a**	Ac	Me	Me	CCl_4	39 [38]	61 [62]	82	18
2	**1b**	H	Me	Me	CCl_4	93	7	96	4[c]
3	**1b**	H	Me	Me	MeOH[d]	73	27	96	4[c]
4	**1c**	H	Me	H	CCl_4	93	7	>97	<3[e]
5	**1d**	H	tBu	H	CCl_4[f]	95	5	>97	<3[e]

[a] Product ratios were determined by ^1H NMR spectroscopy directly in the crude reaction mixture after evaporation of the solvent. [b] Unless otherwise stated, solutions containing 4 mmol of **1** and tetraphenylporphine (TPP) as sensitizer were irradiated with two 150-W sodium lamps at 0 °C while a gentle stream of dry oxygen gas was passed through the solution; full conversion was achieved for **1b** after 4 h, for **1c,d** after 6–8 h, and for **1a** after 9 h. Isolated yields were **2a** 62%, **2b–d** 73–89%. [c] The regioisomer **3b** was observed in the form of its ring tautomer 3-hydroxy-3,5,5-trimethyl-1,2-dioxolane, produced by ketonization of the initial enol and cyclization. [d] Rose bengal was used as sensitizer; 80% conversion after 24 h. [e] No products from **3c,d** could be detected. [f] The photooxygenation was conducted in the presence of 10 mol % 2,6-di-*tert*-butyl-4-methylphenol as radical scavenger.

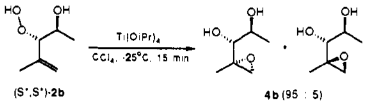
and (*E*)-**3a**. Despite the fact that the chirality center is an inherent part of the reaction coordinate,[5c,d] diastereofacial discrimination is only moderate because the allylic strain[7] of the acetoxy group (*erythro* approach) is only slightly smaller than that of the methyl group (*threo* approach).

On the grounds of the cis effect,[5] all of the above was as expected; however, in the photooxygenation of the allylic alcohol **1b** (Table I, entry 2) in CCl_4, not only was a much higher regioselectivity (96:4) and excellent diastereoselectivity (d.r. = 93:7) observed but in the latter case the sence of the stereocontrol was opposite, i.e., *threo* instead of *erythro* attack (Scheme II). The normal cis effect[5] *cannot* account for the observed selectivities! Instead, we propose coordination of the hydroxy functionality at the chiral allylic site with the incoming $^1O_2$ to generate the two diastereomeric perepoxide-like transition states *threo*-**1b**‡ (precursor to the major diastereomer (*S**,*S**)-**2b**) and *erythro*-**1b**‡ (precursor to the minor diastereomer (*S**,*R**)-**2b**). In other words, we are dealing with a novel "cis effect" in which the hydroxy group dictates regio- and diastereocontrol (Scheme II). The *threo* diastereoselectivity dominates because allylic strain[7] is minimal, i.e., H/H versus H/Me interactions.

Several additional experimental observations support the postulated hydroxy-directing effect. For example, when the photooxygenation of the allylic alcohol **1b** was conducted in methanol (Table I, entry 3), the diastereoselectivity dropped significantly (d.r. = 73:27). Expectedly, hydrogen bonding with methanol provides for less effective stereocontrol by the hydroxy group, and hence the normal cis effect[5] assumes proportionate importance. A similar high degree of diastereoselectivity with predominant formation of the (*S**,*S**)-configurated hydroperoxides is also observed in the photooxygenations of alcohols **1c,d**, in which R^1 groups of different sizes are located at the allylic stereogenic center.

The regio- and diastereoselective oxyfunctionalization of allylic alcohols through the ene reaction with $^1O_2$, in which a hydroperoxy functionality is introduced *vicinally* to the existing allylic hydroxy group with both attached to chirality centers, is undoubtly of synthetic utility. Indeed, when the β-hydroperoxy homoallylic alcohol (*S**,*S**)-**2b** was submitted to the $Ti(OiPr)_4$-catalyzed hydroxy epoxidation,[8] the epoxy diols **4b** (Scheme III) were obtained in high diastereoselectivity (d.r. = 95:5).

Scheme III



In this simple way, two additional chirality centers can be introduced regio- and diastereoselectively in successive adjacent positions to the already existing chiral allylic alcohol moiety. Thus, the present ene reaction of $^1O_2$ with chiral allylic alcohols, coupled with the $Ti(OiPr)_4$-catalyzed hydroxy epoxidation,[8] constitutes a convenient methodology for multiple oxygenation, in which the novel feature is the directing effect of the chiral allylic hydroxy functionality.

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Supplementary Material Available: Details on the stereochemical assignments (2 pages). Ordering information is given on any current masthead page.

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The First topa-Containing Copper(II) Complex, [Cu(DL-topa)(bpy)(H_2O)]BF_4·$3H_2O$, as a Model for the Active Site in Copper-Containing Amine Oxidase

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Copper-containing amine oxidases are distributed widely in plants, mammals, and microorganisms. They contain "nonblue" copper and an organic cofactor which is covalently bound to the proteins.[1] In 1984 Duine's[2] and Ameyama's[3] groups independently reported that the covalently bound organic cofactor was pyrroloquinoline quinone (PQQ). However, the evidence for PQQ in copper-containing amine oxidases has not been universally accepted. Recently, topa quinone (6-hydroxydopa quinone) residue has been identified as the cofactor in bovine serum amine oxidase.[4] The cupric site indicated a square pyramidal geometry with three imidazoles and two water molecules.[5] Dooley and co-workers presented the evidence for the generation of a Cu(I) semiquinone state by room-temperature electron paramagnetic resonance (EPR) measurements and suggested that the Cu(I) semiquinone may be the catalytic intermediate which reacts directly with dioxygen.[6]

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