Communications

Geminal Selectivity in Singlet Oxygen Reactions

Summary: Replacement of a hydrogen on tetramethylethylene with a variety of functional groups produces a family of substrates which react preferentially with singlet oxygen by abstraction of a geminal hydrogen to form allylic hydroperoxides.

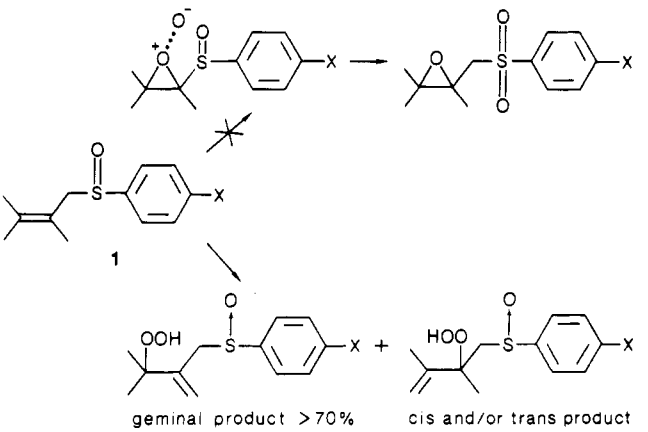
Sir: In the late 1970's the remarkable cis regioselectivity of singlet oxygen ene reactions[1] was first recognized.[2] In 1985[3] Schuster discovered that cis olefins and trans olefins have distinctly different normalized entropies of activation, suggesting that an interaction between singlet oxygen and the allylic hydrogens is developing in the rate-determining step. These important contributions have led to the suggestion that a species with perepoxide symmetry is on the singlet oxygen ene reaction surface. We report here a new regioselective singlet oxygen ene reaction and provide speculation on the origin of the regioselectivity.

Additions of singlet oxygen to allylic sulfoxides 1 did not result in trapping of a perepoxide (Scheme I) as anticipated[4] but ene reactions with greater than 70% geminal selectivity were observed.[5] In addition no abstraction of hydrogen α to the sulfoxide group occurred.

Geminal regioselectivity has previously been reported in the singlet oxidations of α,β-unsaturated ketones,[6] aldehydes,[7] acids,[8] and esters.[9] In these cases 4 + 2 cycloaddition to form a trioxene intermediate which subsequently cleaved and abstracted hydrogen (Scheme II) was utilized to rationalize the high degree of geminal regioselectivity.[10] Clearly such a mechanism is not adequate to explain the geminal selectivity in sulfoxides 1.

The ability of an allylic substituent to direct hydrogen abstraction to the geminal position is a general phenomenon. A wide variety of substituents including halides, ethers, sulfones, and sulfides enhances the geminal selectivity of singlet oxygen (Table I). In each of the cases examined, except for the allylic cyano compound, geminal hydrogen abstraction in excess of the statistically anticipated 33% was observed. Abstraction of hydrogen adjacent to the substituent occurred only in the reactions of the methoxy and ethoxy substituted tetramethylethylenes (eq 1; 9% in each case).[11]

Scheme I



Scheme II

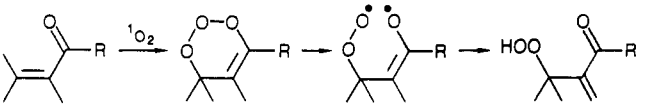
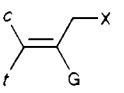
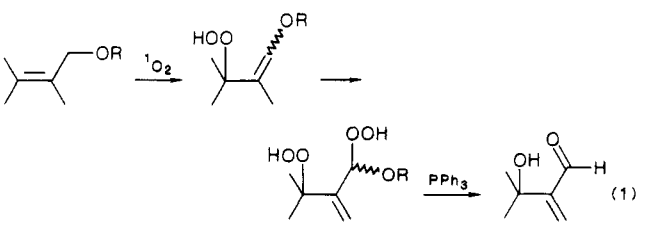


Table I. Product Distributions in the Ene Reactions of Allylically Substituted Tetramethylethylenes[a]



X	G[b]	%(c + t)[c]
SO_2(*p*-MePh)	81	19
SO(*p*-NO_2Ph)	75	25
SOPh	74	26
SO(*p*-MePh)	73	27
SO(*p*-MeOPh)	72	28
Br	54	46
S(*p*-MePh)[e]	52	48
S(*p*-NO_2Ph)	52	48
OMe	39	52[d]
OEt	39	52[d]
CN	32	68

[a] Reactions conducted in acetone-d_6 at −78 °C using Rose Bengal as a sensitizer. [b] Percent geminal hydrogen abstraction. [c] Percent cis and trans hydrogen abstraction. [d] 9% methylene hydrogen abstraction was observed. [e] At 16 °C.



(1) Frimer, A. A.; Stephenson, L. M. in *Singlet O_2. Reaction Modes and Products*; Frimer, A. A., Ed.; CRC: Boca Raton, FL, 1985; Vol II, Part 1, Chapter 3, p 67.

(2) (a) Stephenson, L. M.; Grdina, M. J.; Orfanopoulos, M. *Acc. Chem. Res.* **1980**, *13*, 419. (b) Rousseau, G.; LePerchec, P.; Conia, J. M. *Tetrahedron Lett.* **1977**, 2517. (c) Lerdal, D.; Foote, C. S. *Ibid.* **1978**, 3227. (d) Schulte-Elte, K. H.; Multer, B. L.; Rautenstrauch, V. *Helv. Chim. Acta* **1978**, *61*, 2777. (e) Orfanopoulos, M.; Bellarmine, G. M.; Stephenson, L. M. *J. Am. Chem. Soc.* **1979**, *101*, 275.

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(10) An exciplex intermediate resembling the 4 + 2 intermediate has been suggested in order to rationalize geminal selectivity in α,β-unsaturated aldimines. Akasaka, T.; Takeuchi, K.; Ando, W. *Tetrahedron Lett.* **1987**, 6633.

(11) After reduction with triphenylphosphine the same aldehyde was formed in the reactions of both ethers. 2-(1-Hydroxy-1-methylethyl)-acrolein: ^{1}H NMR (acetone-d_6) δ 1.39 (s, 6 H), 6.11 (br s, 1 H), 6.68 (br s, 1 H), 9.12 (s, 1 H).

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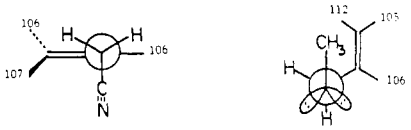
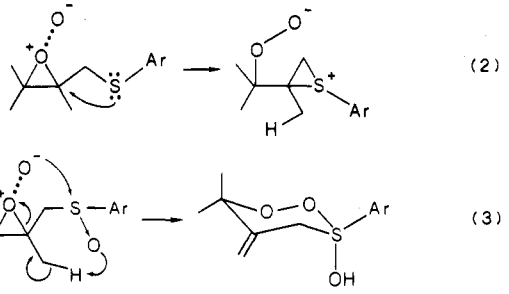


Figure 1. MM2[14] minimized structures for the cyano- and methoxy-substituted tetramethylethylenes. The dihedral angle relative to the olefinic plane for the most favorably aligned hydrogen on each methyl are given.

Anchimeric assistance from the allylic substituent resulting in regiochemically preferred opening of the perepoxide (eq 2 or 3) and subsequent, geminal hydrogen abstraction is an unlikely explanation for this phenomenon.



(2)

(3)

A change in the geminal selectivity, as the para substituent on the allylic phenyl sulfide or sulfoxide is varied, is not observed as anticipated for neighboring group assistance.

Two possible contributing factors to the geminal selectivity observed in these reactions are as follows.

(1) Electronic repulsion between lone pairs on the substituent and the pendant oxygen of the nascent perepoxide favors formation of the perepoxide on the distal side of the olefin. Eliel[12] and others have previously invoked a repulsive interaction between sulfur and oxygen in order to explain the greater equatorial preference in 5-(methylthio)-1,3-dioxane in comparison to (methylthio)cyclohexane. However, if the cis methyls on the distal side of the olefin are equally reactive exclusive formation of the distal perepoxide would result in 50% geminal hydrogen abstraction. The observation of 81% geminal selectivity (Table 1), although not excluding a role for electron repulsion, requires operation of an additional mechanism(s) enhancing the reactivity of the geminal methyls.

(2) The substituted tetramethylethylenes exist in conformations in which the geminal hydrogens are closer to and/or can reach the perpendicular geometry necessary for abstraction easier than the hydrogens on the cis and/or trans methyl groups. Houk[13] has previously utilized a very similar argument to explain the cis effect observed in the singlet oxygen ene reaction. Minor differences in conformational energetics are important because they contribute significantly to the near zero activation barriers for singlet oxygen reactions. Consistent with this explanation are MM2 calculations performed on the methoxy and cyano compounds. In the lowest energy conformation of the cyano compound (Figure 1) which exhibits no geminal selectivity the conformational dispositions of all three methyl groups are identical. In the lowest energy conformation of the methoxy compound, which does exhibit a moderate selectivity, the cis methyl is less favorably disposed for hydrogen abstraction.

Further work to delineate the factors which contribute to geminal selectivity, and additional attempts to trap a perepoxide are currently in progress and will be communicated in the near future.

Acknowledgment. We thank the National Science Foundation and the donors of the Petroleum Research Foundation, administered by the American Chemical Society, for their generous support of this research.

Registry No. O_2, 7782-44-7; $Me_2C{=}C(Me)CH_2SO_2(p\text{-}MePh)$, 86925-63-5; $Me_2C(OOH)C(=CH_2)CH_2SO_2(p\text{-}MePh)$, 114597-44-3; $CH_2{=}C(Me)CMe(OOH)CH_2SO_2(p\text{-}MePh)$, 114597-45-4; $Me_2C{=}C(Me)CH_2SO(p\text{-}NO_2Ph)$, 114597-46-5; $Me_2C(OOH)C(=CH_2)CH_2SO(p\text{-}NO_2Ph)$, 114614-33-4; $CH_2{=}C(Me)CMe(OOH)CH_2SO\ (p\text{-}NO_2Ph)$, 114597-47-6; $Me_2C{=}C(Me)CH_2SOPh$, 101384-22-9; $Me_2C(OOH)C(=CH_2)CH_2SOPh$, 114597-48-7; $CH_2{=}C(Me)CMe(OOH)CH_2SOPh$, 114597-49-8; $Me_2C{=}C(Me)CH_2SO(p\text{-}MePh)$, 51954-48-4; $Me_2C(OOH)C(=CH_2)CH_2SO(o\text{-}MePh)$, 114597-50-1; $CH_2{=}C(Me)CMe(OOH)CH_2SO(p\text{-}MePh)$, 114597-51-2; $Me_2C{=}C(Me)CH_2SO(p\text{-}MeOPh)$, 114597-52-3; $Me_2C(OOH)C(=CH_2)CH_2SO(p\text{-}MeOPh)$, 114597-53-4; $CH_2{=}C(Me)CMe(OOH)CH_2SO(p\text{-}MeOPh)$, 114597-54-5; $Me_2C{=}C(Me)CH_2Br$, 5072-70-8; $Me_2C(OOH)C(=CH_2)CH_2Br$, 67228-75-5; $CH_2{=}C(Me)CMe(OOH)CH_2Br$, 114597-55-6; $Me_2C{=}C(Me)CH_2SPh$, 79597-54-9; $Me_2C(OOH)C(=CH_2)CH_2SPh$, 114597-56-7; $CH_2{=}C(Me)CMe(OOH)CH_2SPh$, 114597-57-8; $Me_2C{=}C(Me)CH_2S(p\text{-}NO_2Ph)$, 114597-58-9; $Me_2C(OOH)C(=CH_2)CH_2S(p\text{-}NO_2Ph)$, 114597-59-0; $CH_2{=}C(Me)CMe(OOH)CH_2S(p\text{-}NO_2Ph)$, 114597-60-3; $Me_2C{=}C(Me)CH_2OMe$, 20518-48-3; $Me_2C(OOH)C(=CH_2)CH_2OMe$, 114597-61-4; $CH_2{=}C(Me)CMe(OOH)CH_2OMe$, 114597-62-5; $Me_2C(OH)C(=CH_2)CHO$, 114597-67-0; $Me_2C{=}C(Me)CH_2OEt$, 20174-79-2; $Me_2C(OOH)C(=CH_2)CH_2OEt$, 114597-63-6; $CH_2{=}C(Me)CMe(OOH)CH_2OEt$, 114597-64-7; $Me_2C{=}C(Me)CH_2CN$, 4786-36-1; $Me_2C(OOH)C(=CH_2)CH_2CN$, 114597-65-8; $CH_2{=}C(Me)CMe(OOH)CH_2CN$, 114597-66-9.

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Nucleophilic and Electrophilic Mercaptanylations via 2-(Trimethylsilyl)ethanethiol-Derived Reagents[1]

Summary: 2-(Trimethylsilyl)ethanethiol reacts with carboxylic acids, alkyl halides, epoxides, and enones to provide acyl- and alkyl-substituted 2-(trimethylsilyl)ethyl sulfides. Electrophilic mercaptanylation is effected by a thiol-sulfonate reagent derived from 2-(trimethylsilyl)ethanethiol.

Sir: In conjunction with a pair of projects in our laboratory, we needed methods for nucleophilic and electrophilic introduction of the sulfhydryl moiety into highly functionalized substrates. The desired nucleophilic application required an efficient transformation of a carboxylic acid into a thiol acid. We anticipated that acylation of an alkyl mercaptan[2,3] followed by dealkylation of the resulting thiol

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