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Effect of Allylic Oxygen on the Reaction Pathways of Singlet Oxygenation: Selective Formation of 1,2-Dioxetanes from 1-Alkoxymethyl-2-aryl-1-*tert*-butyl-2-methoxyethylenes

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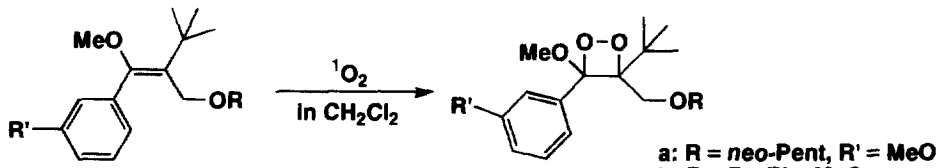
Abstract: Olefins bearing an allylic oxygen **1** undergo 1,2-addition of singlet oxygen to afford exclusively the corresponding 1,2-dioxetanes **2**, whereas their methylene analogues **3** suffer competitively 1,2-addition and ene reaction. The reactivity of **1** preferring 1,2-addition is likely attributed to the steering effect by an allylic oxygen.

It has very recently been reported that the ene reaction of singlet oxygen with olefins bearing an allylic oxygen, especially allylic alcohols, exhibits high regio- and diastereoselectivity, which are attributed to coordination of the allylic oxygen with the incoming singlet oxygen (steering effect or directing effect).[1-3] The steering effect has been further confirmed by the singlet oxygenation of chiral naphthyl alcohols to yield 1,4-endoperoxides with high diastereoselectivity.[4] The steering effect controls π-facial selectivity of the singlet oxygen attacking the olefinic plane as well as the side selectivity. The latter is recognized by the now classical cis effect for non-functionalized olefins and enol ethers,[5-9] and has been reported to influence significantly also on the reaction pathways of singlet oxygen with β-methoxystyrenes.[8,9] The π-facial selectivity should reflect as well on the reaction pathways of singlet oxygen. In the course of our investigation on the synthesis of highly efficient chemiluminescent substrates, we found a singlet oxygenation of allylic ethers suggesting that π-facial selectivity due to the steering effect by an allylic oxygen influences significantly the pathways of singlet oxygenation ; the 1,2-addition of singlet oxygen takes place exclusively for 1-alkoxymethyl-2-aryl-1-*tert*-butyl-2-methoxyethylenes **1**, whereas the ene reaction and the 1,2-addition of singlet oxygen occur concurrently for the methylene analogues **3**.

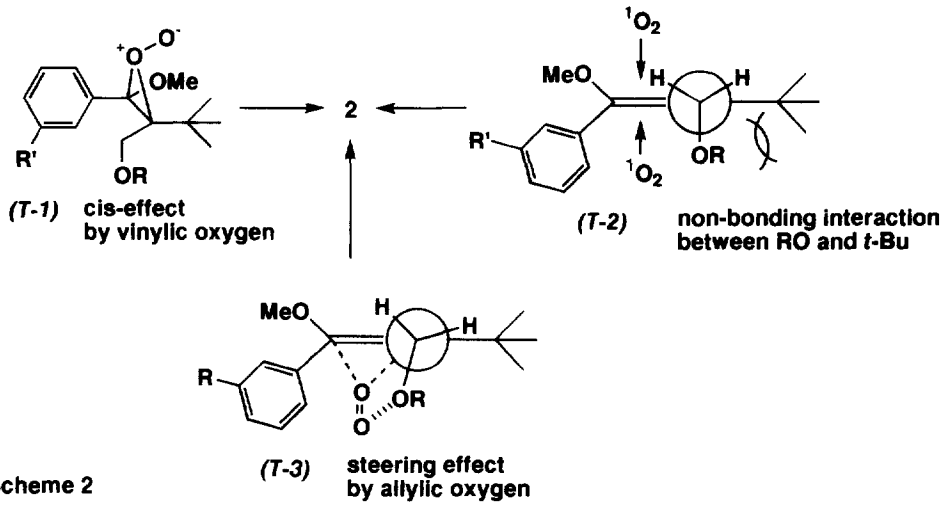


1 **2**

a: R = *neo*-Pent, R' = MeO
b: R = Pr, R' = MeO
c: R = Et, R' = MeO
d: R = Me, R' = MeO
e: R = Me, R' = H
f : R = H, R' = H

Scheme 1

An ethylene **1a** (100 mg) and tetraphenylporphin (5 mg) in dichloromethane (10 ml) was externally irradiated with a 940W sodium vapor lamp under an oxygen atmosphere at 0 °C for 2 h. After the irradiation, the photolysate was concentrated and the residue was chromatographed on silica gel. Elution with hexane-ethyl acetate (10 : 1) gave a dioxetane **2a** as a pale yellow viscous oil in 89% isolated yield.[10,11] The dioxetane **2a** was quantitatively decomposed into the corresponding carbonyl fragments in hot benzene-d_6 and was estimated to have a half life $t_{1/2}$ = 1.40 year at 25 °C after variable temperature thermolysis study. Neither the reaction temperature (room temp. to -78 °C) nor the solvent such as $CHCl_3$ (Rose Bengal supported on silica gel was used as a sensitizer), acetone, and methanol (Rose Bengal was used as a sensitizer) had marked effect on the reaction pathway and **2a** was obtained exclusively. Allylic ethers **1b-d** similarly underwent the 1,2-addition of singlet oxygen to afford the corresponding dioxetanes **2b-d** without detectable amounts of ene reaction products; half lives of **2** $t_{1/2}$ at 25 °C were **2b**: 2.46 year, **2c**: 2.75 year, **2d**: 2.31 year. Phenyl analogue **1e** gave also a dioxetane **2e** ($t_{1/2}$ = 2.80 year at 25°C) as the sole product. Photooxygenation of the parent alcohol **1f** was also found to form a dioxetane **2f** exclusively ($t_{1/2}$ = 0.74 year at 25 °C), although **1f** has a substituent (CH_2OH) smaller than the case of **1a-e**. These results showed that the 1,2-addition of singlet oxygen occurs exclusively for the present olefins **1** irrespective of bulkiness of the allylic functionality, although they possess allylic hydrogens not fixed sterically to prevent the prototropic ene reaction.

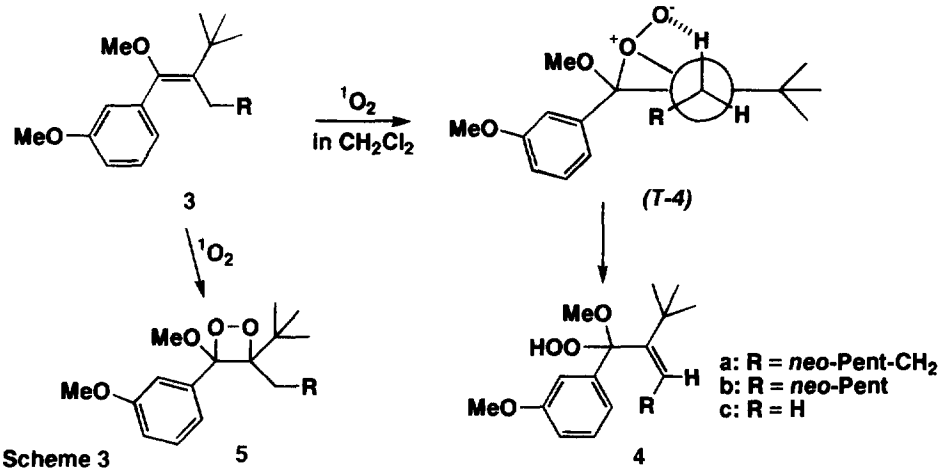


Scheme 2

There are several plausible mechanisms to interpret the high preference for the 1,2-addition mode in the present system:[12,13] a) cis effect by the vinylic oxygen in the enol ether skeleton of **1** causes orientation of the incoming singlet oxygen to the *tert*-butyl group side, shown as *(T-1)* in **Scheme 2**, where no allylic hydrogen exists to be abstracted, b) non-bonding interaction of the alkoxymethyl group with the *tert*-butyl at the *geminal* position prevents an allylic hydrogen of the alkoxymethyl group to lie at ca. 90° dihedral angle with respect to the plane of the double bond *(T-2)*, and c) the allylic oxygen steers the incoming singlet oxygen to a face where no allylic hydrogen exists *(T-3)*.

The singlet oxygenation of methylene analogues **3** gave results significantly different from the case of allylic ethers (alcohol) **1**. When the olefin **3a** was photooxygenated in dichloromethane at 0 °C similarly to the case of

1, an allylic hydroperoxide **4a** was produced together with a dioxetane **5a** (**4a** : **5a** = 46 : 54). It is noteworthy that the ene reaction of **3a** gave solely a stereoisomer whose *tert*-butyl and a hydrogen attached to the C-C double bond lie in *cis*-relation to each other according to a NOE experiment. Competition between the 1,2-addition and the ene reaction was also observed for an olefin **3b** (hydroperoxide **4b** : dioxetane **5b** = 34 : 66). The ene selectivity was more marked for a methyl analogue **3c** (hydroperoxide **4c** : dioxetane **5c** = 76 : 24). The ratio of hydroperoxide **4** to dioxetane **5** changed little even if the oxygenation was carried out at -78 °C.



Scheme 3

These results revealed that, for the singlet oxygenation of **3**, a) cis effect by the vinylic oxygen is minimal or competes with anti cis effect by the bulky *tert*-butyl group,[14] b) the non-bonding interaction of the alkyl group with adjacent *tert*-butyl scarcely prevents an allylic hydrogen suffering prototropic ene reaction to lie in a conformation shown as *(T-4)* at a transition state for the ene reaction (**Scheme 3**). Furthermore, the conformation as in (*T-4*) was suggested to be easily accessible by the fact that the reaction temperature has little effect on the reaction pathways.

There is probably little critical difference in stereochemistry[15] between olefins **3** and their oxygen analogues **1**, though the bond length of C-O and the bond angle of C-O-C (C-O-H) in **1** are, of course, different from those of the carbon chain in **3**. Thus, the oxygen analogues **3** should have a similar chance to exist in a conformation such as *(T-4)*, which is capable of undergoing the ene reaction. Accordingly, the exclusive formation of the dioxetanes **2** from **1** is hardly accounted for by the cis effect by the vinylic oxygen or the nonbonding interaction of the allylic oxygen functionality with the *tert*-butyl group. The significant difference in the reactivity between **1** and **3** is likely attributed to existence of an allylic oxygen which steers the incoming singlet oxygen opposite the face where an allylic hydrogen is oriented. The repulsive interaction of an unshared electron pair of singlet oxygen with a neighboring π-electron system has been very recently suggested to lead the π-facial selectivity for singlet oxygenation of 6,6-dialkoxyfulvenes.[16] Such an interaction may, however, cause little difference in the reaction pathways for the present systems **1** and **3**, because both olefins **1** and **3** possess a (aromatic) π-system in similar circumstances. It should be noted that the steering effect by allylic oxygen seems not to accelerate necessarily the oxygenation with singlet oxygen;[17-19] a control experiment using **1a** and an equimolar amount of **3a** showed that **3a** reacts ca four times faster than **1a** at 0 °C.

References and Notes

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10. The ^{1}HNMR (400 MHz in $CDCl_3$) analysis showed that the crude photolysate of **1a** included no detectable amount of an ene reaction product.
11. **2a**: 1HNMR (400 MHz in $CDCl_3$) δ 0.66 (s, 9H), 1.30 (s, 9H), 2.14 (d, J = 8.1 Hz, 1H), 2.59 (d, J = 8.1 Hz, 1H), 3.06 (s, 3H), 3.45 (d, J = 10.1 Hz, 1H), 3.79 (d, J = 10.1 Hz, 1H), 3.82 (s, 3H), 6.88 - 7.31 (m, 4H) ppm; IR (liquid film) 2956, 1603, 1481, 1268, and 1102 cm^{-1}.
12. A peroxirane type transition state as shown in **Schemes 2** and **3** is likely the most plausible among several transition states or intermediates proposed for ene reaction and 1,2-addition of singlet oxygen with olefins,[13] though it is still debatable whether both reaction modes proceed through a common transition state.
13. Reviews: a) *Singlet Oxygen;* Wasserman, H. H.; Murray, R. W. Eds.; Academic, New York, 1979; b) *Singlet O_2;* Frimer, A. A. Ed.; CRC, Florida, 1985, Vol I- IV; c) *Organic Peroxide;* Ando, W.; Wiley, New York, 1992.
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15. A MM2 calculation suggested that both olefins **1a** and **3a** exist in a conformation like *(T-3)* at the lowest energy minimum. However, the possibility can not be disregarded that electrostatic interaction between an aromatic ring and an allylic oxygen controls delicately conformation of allylic functionality.
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17. The phenomenon suggests that singlet oxygen may be physically quenched to some extent by the allylic oxygen as by amines and sulfides, though quenching of singlet oxygen by alcohols or ethers has scarcely been discussed.[18] Partial quenching of singlet oxygen has been reported not to affect the steering effect by allylic nitrogen in diastereoselective singlet oxygenation of allylic amines.[19]
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