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REACTION OF SINGLET OXYGEN WITH 2-CYCLOPENTEN-1-ONES

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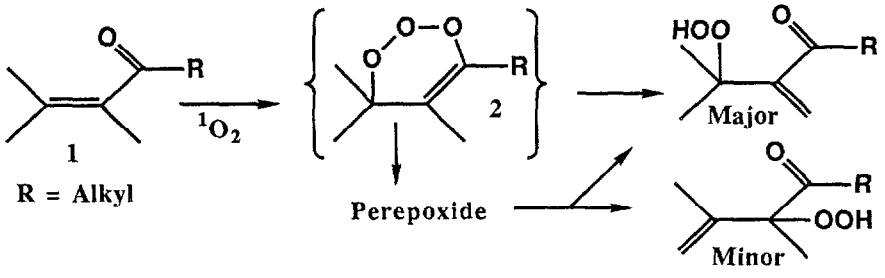
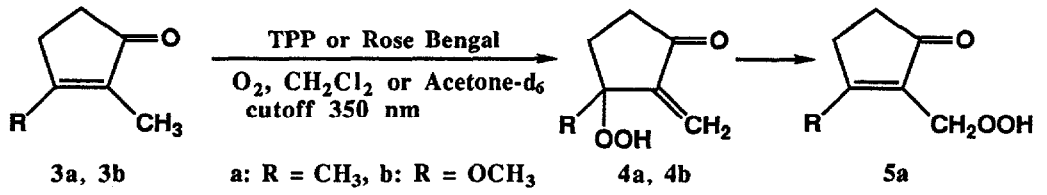
Abstract: The reaction of singlet oxygen with 2-cyclopenten-1-one derivatives is regioselective. Reactivity toward singlet oxygen is not solely determined by the conformation of the carbonyl group relative to the olefinic double bond, since even some s-*trans* derivatives are reasonably reactive.

Although the photosensitized oxygenation of alkenes and enol ethers has been studied extensively,[1] few reactions of α,β-unsaturated ketones have been reported.[2] Since these compounds are electron-poor, reaction with the electrophilic singlet oxygen is often slow. Regioselective reactions of singlet oxygen with α,β-unsaturated cyclic ketones[2] and esters[3] have been reported. In all cases, the entering oxygen preferentially bonds to the carbon remote to the carbonyl. Ensley *et al.* reported that α,β-unsaturated cyclic ketones with an s-*cis* conformation of the conjugated system react much more rapidly with $^1O_2$ than those with the s-*trans* conformation.[2] To explain the reactivity difference and the regioselectivity, they proposed that s-*cis* compounds (**1**) form a trioxene intermediate (**2**), but that the formation of this intermediate is geometrically forbidden in the s-*trans* conformers (**3**).

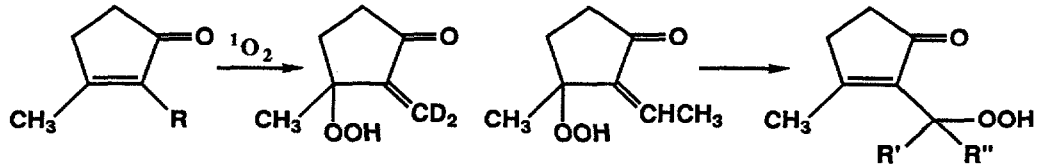


As with the previous compounds, photooxygenation of the 2-cyclopenten-1-one derivatives **3a** and **3b** gives hydroperoxides **4a**[4] and **4b**[5], respectively, by exclusive abstraction of allylic hydrogens from the carbon next to the carbonyl group. Hydroperoxide **4a** readily rearranged to **5a**[4] at room temperature, a well-known reaction that probably goes through a radical mechanism.[6] This allylic rearrangement was not observed with compound **4b**.



3a, 3b **a: R = CH_3, b: R = OCH_3** **4a, 4b** **5a**

Similarly, compounds **3c** and **3d** react with singlet oxygen to give **4c**[7] and **4d**[8] in isolated yield of 70~80%. On standing in solution for about 5 days at room temperature, hydroperoxides **4c** and **4d** are converted to **5c**[7] and **5d**[8], respectively. The rearrangement did not occur in the presence of the radical inhibitor 2,6-di-t-butylphenol (2 x 10^{-3} M).



3c : R = CD_3
3d : R = CH_2CH_3
4c
4d
(*E*- and *Z*-Isomer)
5c: R', R"= D
5d: R'= H, R"= CH_3

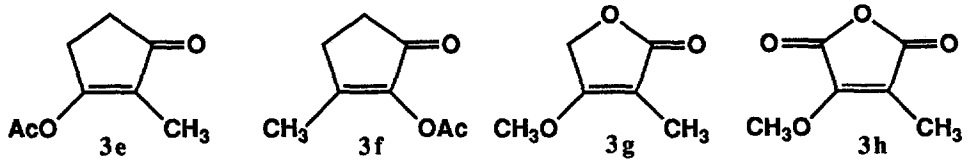
Compounds **3a-d** are limited to the s-*trans* conformation but react with singlet oxygen at a reasonable rate. For example, the reaction of 0.02 M **3a** with $^1O_2$ in acetone-d_6 or CH_2Cl_2 is complete within 6 hours,[4] while **3b** requires about 1.5 hours for 100% reaction. The absolute rates for reaction with singlet oxygen, by quenching of the 1.27 mm luminescence[9] (Table) confirm this reactivity. Compounds **3a,b,** and **d** react at rates near 10^5 M^{-1} s^{-1}. For comparison, $k_q + k_r$ of R-(+)-pulegone (which has the s-*cis*-conformation) is 8 x 10^5 $M^{-1}s^{-1}$ and of some other s-*cis* compounds, reported by Ensley *et al.*[2] is around 5 x 10^5 M^{-1} s^{-1}. It is clear that these compounds react only slightly faster than the s-*trans* compounds studied here.

Table. Singlet oxygen quenching rates.[a]

Compound	$(k_q + k_r)$	Compound	$(k_q + k_r)$
3a	7.8	**3b**	7.5
3d	18.4	**3e**	3.6
3f	2.9		

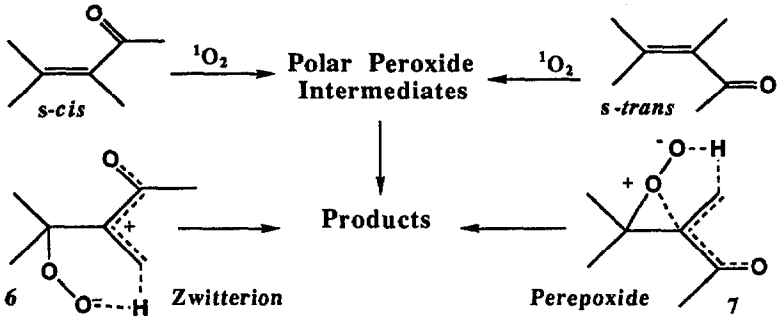
a. X 10^4 $M^{-1}s^{-1}$, acridine as sensitizer in acetone-d_6 at 355 nm.[9]

On the other hand, compounds **3e-h** do not react with $^1O_2$ appreciably during the time required for the above compounds to give preparative reaction, and only starting materials were recovered. The lack of reactivity is also shown by the lower singlet oxygen quenching rates of **3e** and **f**.



Compounds **3e-3h** almost certainly have higher ionization potentials than **3a-d.**[10] The lower reactivity of these compounds shows that electronic effects such as the increased electron-withdrawing ability of an acetoxy group relative to an alkoxy group, or of a lactone relative to a ketone are more important than the conformation around the s-*cis* double bond of the π-system in determining the reactivity of these compounds toward singlet oxygen.

The consistent regioselectivity of all these systems in the ene reaction appears to be independent of the relative arrangement of carbonyl group and alkene, and cannot derive from formation of a cyclic trioxene. It seems more probable that the regioselectivity derives from the properties of a common intermediate such as a zwitterion (**6**) or a perepoxide (**7**). The formation of such intermediates in the ene reaction of alkenes and enol ethers is supported by isotope effects[11] and theoretical calculations[12]. In polar intermediates such as **6**, the C-H bond next to the carbonyl should be weakened and polarized by proximity to the partial or full charge, and should thus be preferentially removed, consistent with both our and Ensley's results.



The reactivity in these systems does not yet present a clear picture. It is clear that, although s-*cis* compounds are generally more reactive with $^1O_2$ than s-*trans* conformers, some s-*trans* compounds are more reactive than previously thought. Theoretical calculations in progress to explain the correlation between the reactivity toward singlet oxygen and the electronic structure of the π system of these compounds will be reported elsewhere.

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References and Notes

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4. Typical procedure: 2 mmoles of **3a** in acetone (5 mL) containing rose bengal as sensitizer was photolyzed at -15 °C with a Varian-Eimac 300 W Xenon lamp and 0.1M K_2CrO_4 or $BiCl_3$ filter solution until no more **3a** was detected by GC. **4a** was obtained as an oil: ^{1}H-NMR ($CDCl_3$, TMS, δ): 9.3 (1H, brd OOH), 6.23 (1H, s), 5.66 (1H, s), 1.8-2.6 (4H, m), 1.55 (3H, s). ^{13}C-NMR ($CDCl_3$, ppm): 206.59 (C=O), 146.30 (s) 121.74 (t), 85.94 (s), 35.31 (t), 31.01 (t), 21.30 (q). Compound **5a**: ^{1}H-NMR ($CDCl_3$, TMS, δ): 10 (1H, brd OOH), 4.67 (2H, s), 2.62 (2H, m), 2.43 (2H, m), 2.19 (3H, s). ^{13}C-NMR ($CDCl_3$, ppm): 209.84 (C=O), 178.23 (s), 135.48 (s), 68.15 (t), 34.47 (t), 32.23 (t), 17.61(q). Exact mass for $C_7H_{10}O_3$: found m/e 142.0615, calcd 142.0630.

5. **4b**: mp 93-94 °C; ^{1}H-NMR ($CDCl_3$, TMS, δ): 9.1 (1H, brd OOH), 6.15 (1H, s), 5.62 (1H, s), 3.3 (3H, s), 2.4-2.1 (4H, m). ^{13}C-NMR ($CDCl_3$, ppm): 203.10 (C=O), 141.89 (s), 124.09 (t), 108.68 (s), 49.3 (q), 35.94(t), 29.58 (t). IR (KBr): 3350 (OOH), 1710 (C=O) cm^{-1}; m/e 158 (M^+). Anal. Calcd for $C_7H_{10}O_4$: C, 53.8, H, 6.34. Found: C, 53.10, H, 6.49.

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7. **3c** was prepared by a literature method (K. Tonari, K. Machiya, I. Ichimoto, and H. Ueda, *Agric Biol. Chem.* **45**, 295 (1981); bp 52-55 °C/20 mm Hg. Exact mass for $C_7H_7D_3O$: found 113.0919 calcd 113.092. Compounds **4c** and **5c** were obtained as an oil and purified by SiO_2 column chromatography. **4c**: ^{1}H-NMR ($CDCl_3$, TMS, δ): 1.8-2.6 (4H, m), 1.5 (3H,s). **5c**: ^{1}H-NMR ($CDCl_3$, TMS, δ): 10.6 (1H, brd OOH), 2.63 (2H, m), 2.42 (2H, m), 2.20 (3H, s). Exact mass for $C_7H_7D_3O_3$: found m/e 144.0742, calcd 144.0755.

8. Product **4d** , an oil, was separated as a mixture of *E*- and *Z*-isomers. *E*-isomer (75%); ^{1}H-NMR ($CDCl_3$, TMS, δ): 8.7 (1H, brd OOH), 6.93 (1H, q, J=6.2Hz), 2.51 (4H, m), 2.06 (3H, d, J=6.4 Hz), 1.66 (3H, s); *Z*-isomer (25%); δ 7.5 (1H, brd), 6.39 (1H, q, J=6.2Hz), 2.51 (4H, m), 2.25 (3H, d, J=6.3Hz), 1.51 (3H, s). These two isomers were converted to **5d** in solution. Compound **5d**: ^{1}H-NMR ($CDCl_3$,TMS, δ): 10.1 (1H, brd OOH), 4.98 (q, 2H, J=6.1Hz), 2.56 (2H, m), 2.43 (2H, m), 2.21 (3H, s), 1.38 (3H, d, J=6.8Hz). ^{13}C-NMR ($CDCl_3$, ppm): 209.59 (C=O), 175.58 (s), 139.13 (s), 75.66 (t), 34.54 (t), 32.26 (t), 17.69 (q), 17.10 (q). Exact mass for $C_8H_{12}O_3$: found m/e 156.0783, calcd 156.0786.

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