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REACTION OF SINGLET OXYGEN WITH β-ALKOXYENONES

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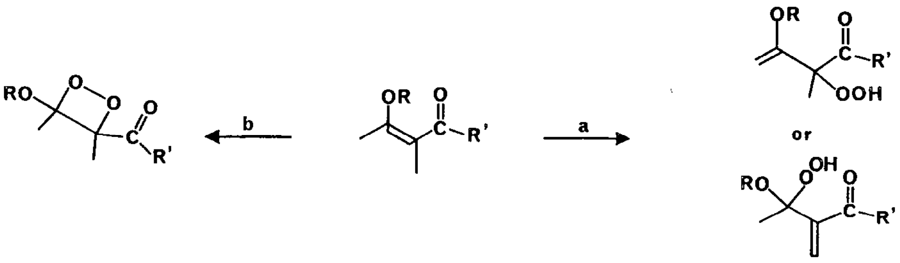
Summary: Singlet oxygen reacts with 1-acetyl-2-methoxycyclopentene (1a) to give the unsaturated hemiperketal 3a. 3a decomposes by an intermolecular oxygen atom transfer to give the epoxy-β-diketone 2a. Several β-alkoxyenones which are held in the s-*trans* conformation failed to react with singlet oxygen.

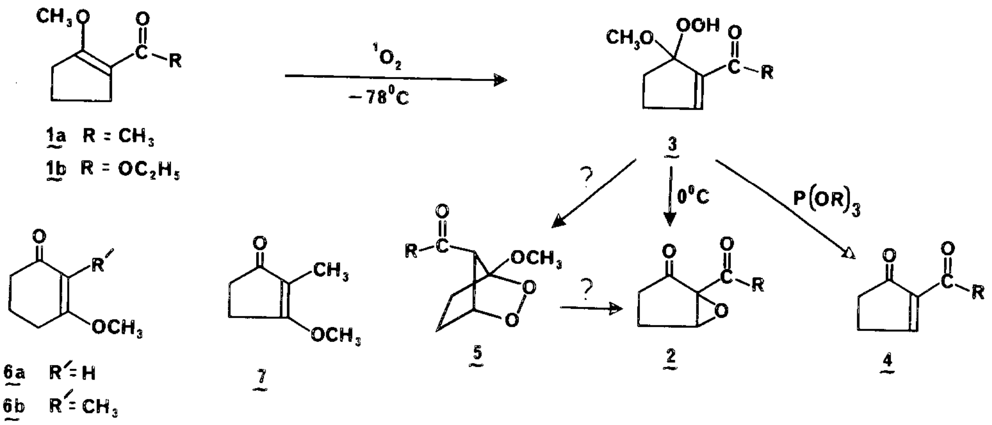
As part of our continuing interest in the reactions of enophiles with α,β-unsaturated carbonyl compounds,[1a] we have investigated the reaction of singlet oxygen with several compounds possessing the β-alkoxyenone subunit. Of the two expected reaction modes, ene reaction (Scheme I, path a) and dioxetane formation (path b), only the ene reaction was observed.[1b] Furthermore, the ene reaction occurred only with β-alkoxyenones capable of adopting the s-*cis* geometry. This geometry preference for the reaction of enophiles with α,β-unsaturated carbonyl compounds has been noted previously.[1a,2]

Scheme I



The photooxygenation[3] of 1-acetyl-2-methoxycyclopentene (1a) at 10°C gave essentially complete conversion (NMR) to 2-acetyl-2,3-oxidocyclopentenone (2a)[4] (Scheme II). Flash chromatography[5] (10% EtOAc - pet ether) of the reaction mixture (after concentration at reduced pressure) afforded 2a in 40% yield. The low yield of purified material reflects considerable on-column decomposition. When the photooxygenation[3] was conducted at -78°C, 1a was converted quantitatively (NMR, -40°C) to 1-acetyl-5-hydroperoxy-5-methoxycyclopentene (3a).[6] On warming to 0°C, the NMR signals attributed to the allylic hydroperoxide 3a disappeared completely, and 2a[7] was produced as the only detectable product.

Scheme II



The decomposition of 3a to 2a could proceed by way of an intramolecular epoxidation or by an intermolecular process. The facility with which the decomposition occurs suggested the possibility of an intramolecular process involving 5a as an intermediate. That this is not the case was demonstrated by performing the photooxygenation of 1a using a 1:3 mixture of $^{16}O_2$ and $^{18}O_2$. Assuming negligible isotope effects,[8] the 2a produced by an intramolecular decomposition of 3a should be 75% $^{18}O_2$ labeled (m/e 144), and none of the singly ^{18}O labeled material (m/e 142) should be observed. If 2a were produced by intermolecular epoxidation, the ratio of unlabeled 2a: ^{18}O labeled 2a: $^{18}O_2$ labeled 2a should be 6:38:56, respectively. The observed ratio of m/e 140:142:144 was 14:41:45, which is in fair agreement with that expected for an intermolecular process.[9,10]

Treatment of 3a with 1.5 equivalents of triethyl phosphite at -40°C gave 50% conversion to 2-acetylcyclopent-2-enone (4a), identified by spectral comparison to 4a prepared by a separate route.[11] Conducting the reduction at higher temperatures or in the presence of a larger excess of triethyl phosphite led to a complex mixture of products.

Ethyl 2-methoxycyclopentene carboxylate (1b) reacts with singlet oxygen[3] in a similar fashion (at -40°C) to give 3b;[12] however, the conversion was not as clean as that with 1a. After approximately 50% conversion of 1b to 3b the rate of the intermolecular decomposition of 3b becomes appreciable. The decomposition of 3b leads not only to 2b (*ca.* 40%), but also to several unidentified products.

The three β-alkoxyenones 6a,[13] 6b and 7,[13] which are structurally confined to the s-*trans* conformation, fail to react with singlet oxygen at -78°C or at 20°C.[14] Mechanistic arguments about the possible basis for the difference in reactivity of s-*cis* and s-*trans* enones toward singlet oxygen have previously been suggested;[1] however, this is still under investigation.

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References

1a. H. E. Ensley, R. V. C. Carr, R. S. Martin and T. E. Pearce, *J. Amer. Chem. Soc.*, 102, 2836 (1980).

1b. These results should be contrasted with the results of the reaction with singlet oxygen with enaminoketones which result in carbon-carbon double bond scission. See H. H. Wasserman and J. L. Ives, *J. Amer. Chem. Soc.*, 98, 7868, 1966.

2. T. R. Hoye, K. J. Bottorff, A. J. Caruso, and J. F. Dellaria, *J. Org. Chem.*, 45, 4287 (1980).

3. Photooxygenation conditions: 200 mg substrate, 10 mg rose bengal or methylene blue in 5 ml CD_3OD; irradiated with a 750 watt DDB-DDW tungsten-halogen lamp for 4 hours under an oxygen atmosphere.

4. Compound 2a had previously been isolated as a by-product in the oxidation of 2-acetyl-2-methylselenenylcyclopentanone using excess H_2O_2. See ref. 10.
5. W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 43, 2923 (1978).
6. For 3a: ^1H NMR (CD_3OD, -20°C) δ 7.06 (t, J = 1.5 Hz, 1H, vinyl), 3.40 (s, 3H, OCH_3), 2.1 - 2.7 (m, 4H, CH_2CH_2), 2.3 (s, 3H, CH_3); ^{13}C NMR (CD_3OD, -35°C) δ 199.0, 150.2, 144.7, 117.9, 51.0, 34.2, 29.3 (two carbons).
7. For 2a: ^1H NMR ($CDCl_3$) δ 4.17 (bs, 1H, epoxy), 2.25 (s, 3H, CH_3), 2.0 - 2.6 (m, 4H, CH_2CH_2); ^{13}C NMR ($CDCl_3$) δ 204.5, 199.2, 65.6, 63.6, 32.4, 27.9, 22.3.
8. Oxygen isotope effects are usually in the range of 1.0 to 1.1.
9. A technical difficulty with this experiment is the rapidity with which the carbonyl oxygen of 2a exchanges with atmospheric moisture. See D. Samuel and B. L. Silver, *Adv. Phys. Org. Chem.*, 3, 123 (1965); R. P. Bell, *ibid.*, 4, 1 (1966). After two hours exposure to the atmosphere the observed ratio of m/e 140:142:144 was 19:46:35.
10. An alternative explanation for this result is the possibility that the $^{16}O_2$: $^{18}O_2$ mixture is undergoing label scrambling (*via* an intermolecular, excited-state reaction) faster than reaction with 1a. However, the generation of singlet oxygen from a 1:1 mixture of $^{16}O_2$ and $^{18}O_2$ in the absence of a substrate indicated no detectable scrambling after 4 hrs. irradiation. The singlet oxygen generation was performed in CH_3OH (m/e 32) rather than CD_3OD (m/e 36). The m/e 34 and m/e 36 ratio was monitored by GCMS and remained constant during the 4 hr period of irradiation.
11. D. Liotta, M. Saindane, C. Barnum, H. Ensley, and P. Balakrishnan, *Tetrahedron Lett.*, 3043 (1981).
12. For 3b: ^1H NMR ($CDCl_3$, -10°C) δ 8.1 (bs, 1H, OOH), 7.16 (t, J = 1.5 Hz, 1H, vinyl), 4.23 (q, J = 7 Hz, 2H, OCH_2), 3.5 (s, 3H, OCH_3), 2.1 - 2.8 (m, 4H, CH_2CH_2), 1.33 (t, J = 7 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, -35°C) δ 165.2, 150.2, 135.8, 116.5, 61.1, 50.9, 32.3, 28.2, 14.0.
13. D. J. Crispin, A.E. Vanstone, and J. S. Whitehurst, *J. Chem. Soc. (C)*, 10 (1970).
14. This observation should be contrasted to the fluoride-catalyzed reaction of singlet oxygen with α- and β-hydroxyenones. See H. H. Wasserman and J. E. Pickett, *J. Amer. Chem. Soc.*, 104, 4695 (1982).

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