Photo-oxygenation of βγ-Unsaturated Ketones

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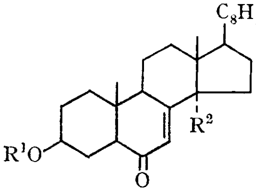
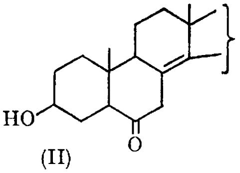
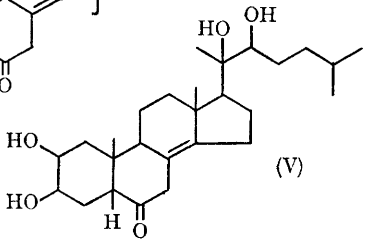
THE mechanism of photosensitized oxygenation of isolated olefins has been greatly clarified in recent years.[1] Participation of the excited singlet-state oxygen is now generally accepted,[2] and a concerted cycloaddition of oxygen to olefins containing allylic hydrogens is favoured.[3] We have investigated the photosensitized oxidations of $\beta\gamma$-unsaturated ketones, and preliminary data indicate that also in these systems, which contain more labile allylic hydrogens, a concerted cycloaddition is favoured over a step-wise ionic addition.[4]



(I) R^1=Ac, R^2=H
(III) R^1=H, R^2=OOH
(IV) R^1=H, R^2=OH



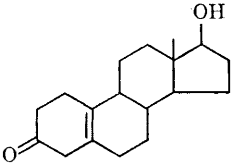
(II)



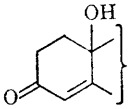
(V)

3β-Acetoxycholest-7-en-6-one (I)[5] was converted into (II) upon brief treatment with Bu^{t}OK–Bu^{t}OH[6] followed by rapid neutralization with acetic acid. Irradiation of (II) in pyridine with a 250 w tungsten lamp in the presence of Rose Bengal under oxygen gave the hydroperoxide (III), which upon reduction with NaI–AcOH yielded the authentic 14α-hydroxy-enone (IV),[5] the yield of (IV) from (I) being *ca.* 70%. Similarly, the $\beta\gamma$-unsaturated ketone (V) yielded ponasterone A[7] (14α-hydroxy-7-en-6-one) *via* the hydroperoxide in almost quantitative yield, and hence this photo-oxygenation provides an alternative method[8] for making the 14α-hydroxy-7-en-6-one moiety present in all ecdysones discovered to date (about twenty).

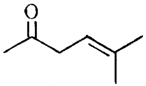
Photosensitized oxidation of 17β-hydroxy-19-norandrost-5,10-en-3-one (VI), prepared from oestradiol[5] by Birch reduction, was also transformed into 10β-hydroxy-19-nortestosterone (VII)[9] *via* the hydroperoxide in 45% overall yield. Likewise, 5-methylhex-4-en-2-one (VIII)[10] was quantitatively oxidized to the hydroperoxide (IX).†



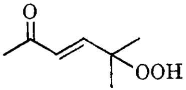
(VI)



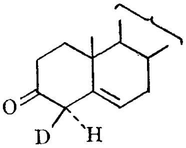
(VII)



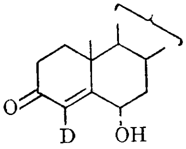
(VIII)



(IX)

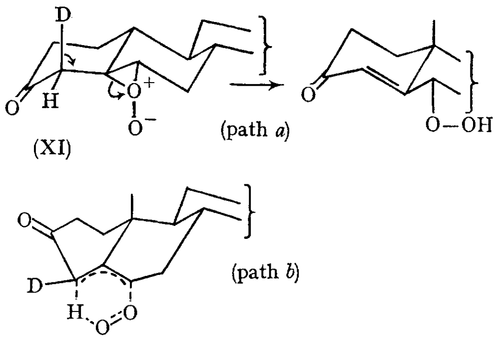


(X)
90% ^{2}H



(XII)
85% ^{2}H

The cyclic nature of olefin photo-oxygenation has been elegantly proven with [7-^{2}H]cholesterol molecules.[3a] $\beta\gamma$-Unsaturated ketones, in which the hydrogen(s) flanked by the carbonyl group and



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† Structure proven by spectroscopic data.

double bond dissociate readily, are suitable systems for studying the participation of an ionic step-wise mechanism. 4β-Deuteriocholest-5-ene (X)[11] (90% deuterium content according to mass and n.m.r. spectroscopy) was therefore synthesized and submitted to the photosensitized oxygenation. If a step-wise mechanism going through an intermediate such as (XI) (or its equivalent) were operating, most of the deuterium should be lost (path *a*). In contrast, path *b* should retain the deuterium. The hydroperoxide was reduced to 6α-hydroxycholest-4-en-3-one (XII), and the deuterium content at C-4 was measured from the n.m.r. curve, taking the 6β-proton as reference for integration. This showed that the product (XII) contained 85% deuterium at C-4, and hence it is very likely that the photo-oxygenation of βγ-unsaturated ketones is a concerted cycloaddition.

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[1] For leading references, see K. Gollnick and G. O. Schenck, in "1,4-Cycloaddition Reactions; the Diels-Alder Reaction in Heterocyclic Syntheses", ed. J. Hamer, Academic Press, New York, **1967**, ch. X, p. 255; see also K. Gollnick, Internat. Oxid. Symp., San Francisco, Abstract II, **1967**, p. 383; A. U. Khan and D. R. Kearns, *ibid.*, p. 633; R. Higgins, C. S. Foote, and H. Cheng, *ibid.*, p. 672.

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[5] We are grateful to Dr. T. Wada, Teikoku Hormone Company, for the generous gifts of (I), (VI), and authentic (IV).

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