The Photochemical Oxidation, Ozonization, and Rearrangement of Cholesta-3,5-dieno[3,4-*b*]-1,4-oxathian

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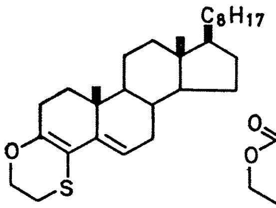
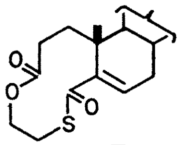
Summary Photochemical oxidation and ozonization of cholesta-3,5-dieno[3,4-*b*]-1,4-oxathian proceed *via* the selective addition of reagents to the 3-eno-group.

OUR interest in the delocalized *p*-electron system in the oxathiano-ring (λ_{max} 223—227 nm) of cholesta-3,5-dieno-[3,4-*b*]-1,4-oxathian (I)[1] prompted our investigation of photo-oxidation and ozonization of (I) to examine if the Δ^3 double bond group in the 3,5-diene system reacts specifically toward electrophilic reagents such as oxygen and ozone. We report that the photo-oxidation and ozonization proceed *via* the selective addition of reagents to the Δ^3 double bond, possibly from the α-side, followed by rearrangement of the Δ^5 double bond and a preferential β or axial attack at C-6 (stereoelectronic requirements[2]) of a suitable nucleophile in the reaction mixture.


(I)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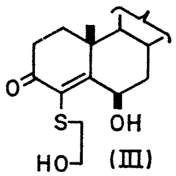
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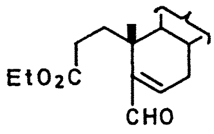
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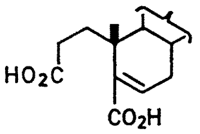
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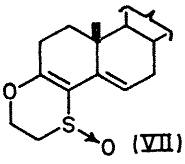
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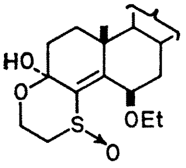
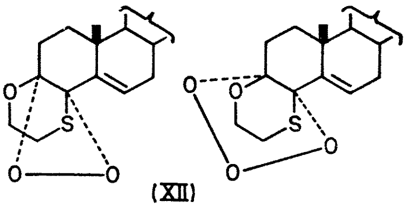

(XI)


(XII)

Exposure of a 1% solution of (I) in 4 : 1 acetone–ether to sunlight in the presence of oxygen resulted in the formation of the 3,4-seco-3,4-dioxo-compound (II), m.p. 133—134·5°, $[\alpha]_D$ ($CHCl_3$) +26°, λ_{max} 238 nm, ν_{max} 3020, 1740, 1645, and 1620 cm^{-1}, τ ($CDCl_3$) 3·37 (6-H), 5·04—5·24 and 6·16—6·39 ($\cdot O\cdot CH_2\cdot$), 6·51—6·76 and 6·94—7·18 ($\cdot S\cdot CH_2\cdot$), 8·69 (19-H), 9·30 (18-H) (37% yield), and a trace of 6β-hydroxy-4-(β-hydroxyethylthio)cholest-4-en-3-one (III) m.p. 163—183°, $[\alpha]_D$ ($CHCl_3$) +31°, λ_{max} 247 and 320 nm, ν_{max} 3400, 1675, and 1550 cm^{-1}, τ ($CDCl_3$) 4·20 (6α-H), 6·10—6·35 (OH, $\cdot O\cdot CH_2\cdot$), 7·18—7·60 (OH, $\cdot S\cdot CH_2\cdot$), 8·60 (19-H), 9·26 (18-H). When (I) was irradiated in wet ether, the formation of (III) (40% yield) was favoured as compared with that of (II) (7%). The n.m.r. spectrum of (III) exhibits the 19-H_3 peak at τ 8·60, establishing the β-configuration of the 6-hydroxy-group.[3] The equatorial character of the 6α-hydrogen in (III) was supported by the fact that the peak due to this proton appeared at τ 4·20, because of the deshielding effect of the thio-function attached to C-4 in the 4-en-3-oxo system.[4] Desulphurization of (II) and (III) with Raney nickel afforded the aldehydo-ester (IV) (identified as 2,4-dinitrophenylhydrazone, m.p. 160—162·5°) and 6β-hydroxycholestenone (V)[5] (mixed m.p. determination) in high yields, respectively. Air oxidation of (IV), followed by alkaline hydrolysis, gave the dicarboxylic acid (VI)[6] (mixed m.p. determination).

Irradiation of (I) with a high-pressure mercury lamp gave similar results. However, when the irradiation (with either sunlight or the mercury lamp) was carried out under nitrogen, no reaction took place. Peroxy-acid or hydrogen peroxide oxidation of (I) did not give (II) or (III) but only the corresponding sulphoxide (VII).

3-Ethoxy-4-ethanethiocholesta-3,5-diene (VIII)[7] on photo-oxidation in wet ether gave 6β-hydroxy-4-ethanethio-cholest-4-en-3-one (IX), m.p. 154·5—155·5°, as the only isolable product in low yield (19%). The oxidation of cholesta-3,5-diene (X)[8] was non-selective; there was no isolable product.

Ozonization of (I) in chloroform also gave (III) and (IV). When ozonization was carried out in 4 : 1 $CHCl_3$–EtOH, another rearranged product characterized as (XI) could be isolated. Ozonization of (X) was non-specific, as was the case with photo-oxidation.

The results suggest that both photo-oxidation and ozonization reactions described may proceed *via* selective adducts (XII) of oxygen or ozone to the Δ^3 double bond as the key intermediate, the formation of (XII) being favoured by the mesomeric effect of thio- and oxygen functions in the conformationally rather rigid oxathiano-3-ene ring system.

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