Loss of a Methyl Group in a Modified Baeyer–Villiger Oxidation of 4,4-Dimethylcholestan-3-one

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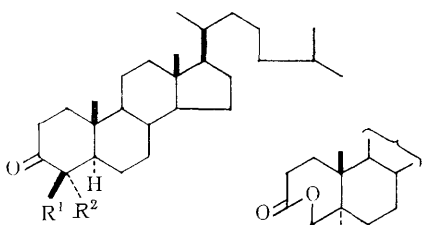
IN a recent publication[1] it has been shown that oxidation of 4α- (I) and 4β-methylcholestan-3-one (II) with *m*-chloroperbenzoic acid in chloroform gave 4-oxa-4aα-methyl-(IV) and 4-oxa-4aβ-methyl-A-homocholestan-3-one (V) respectively.

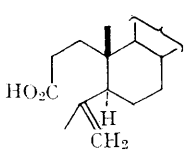
We have now shown that oxidation of 4,4-dimethylcholestan-3-one (III) (500 mg.) with *m*-chloroperbenzoic acid (700 mg.) in methylene chloride (17 ml.) and 10% sulphuric acid in acetic acid (3·0 ml.) for 90 hours at room temperature gives the monomethyl lactone (IV) (320 mg.) This interesting modification of the Baeyer–Villiger oxidation which involves the loss of a methyl group from C-4 of (III), does not appear to have any parallels in the literature.

Although our investigations on the scope and mechanism of the above reaction are not yet complete, we believe that 4a,4a-dimethyl-4-oxa-A-homocholestan-3-one (VI) and 3,4-seco-4-methyl-4-methylenecholestan-3-oic acid (VII) are both intermediates in the acid-catalysed Baeyer–Villiger reaction. Thus, we have shown that, (i) both compounds (VI) and (VII) are converted into the monomethyl lactone (IV) under the same conditions as compound (III) and, (ii) the dimethyl lactone (VI) is quantitatively converted into the unsaturated acid (VII) with 10% sulphuric acid in

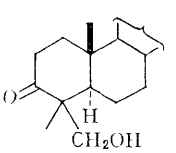


(I); $R^1 = H$, $R^2 = Me$
(II); $R^1 = Me$, $R^2 = H$
(III); $R^1 = R^2 = Me$

(IV); $R^1 = H$, $R^2 = Me$
(V); $R^1 = Me$, $R^2 = H$
(VI); $R^1 = R^2 = Me$



(VII)



(VIII)

[1] D. Rosenthal, A. O. Niedermeyer, and J. Fried, *J. Org. Chem.*, 1965, **30**, 510.

acetic acid at room temperature. It has previously been shown that the dimethyl lactone (VI), (which is formed from 4,4-dimethylcholestan-3-one by oxidation with peracid in the absence of mineral acid[1]), is converted to the unsaturated acid (VII) under pyrolytic conditions.[1]

In our studies on the acid catalysed Baeyer–Villiger oxidation of 4,4-dimethylcholestan-3-one we have been seeking a possible analogy for the loss of methyl groups at C-4 in the biogenetic conversion of lanosterol into cholesterol. We argued originally that an unsaturated acid of type (VII) formed as an intermediate in the acid-catalysed reaction, might cyclise to a β-ketol type (VIII) which would give the monomethyl ketone (I) by loss of formaldehyde. Although it is now clear that the unsaturated acid (VII) does not cyclise under acid conditions, we believe that there is an alterntive probable mechanism for the formation of the monomethyl ketone (I) from the unsaturated acid (VII) in the presence of peracid and mineral acid. Furthermore, it seems likely that (I) is the immediate precursor of (IV). Thus, the present work may well have biogenetic significance. This aspect and a more detailed mechanistic approach will be developed fully elsewhere.

The physical constants for all the compounds discussed in this communication agree satisfactorily with those reported elsewhere.[1]

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