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A NOVEL RING CONTRACTION: 3β-METHYL-A-NOR-5β-CHOLESTAN-5-OL-6-ONE FROM 3β-TOSYLOXY-5α-CHOLESTANE-5,6β-DIOL THROUGH AN ENE REACTION OF AN UNSATURATED ACYLOIN

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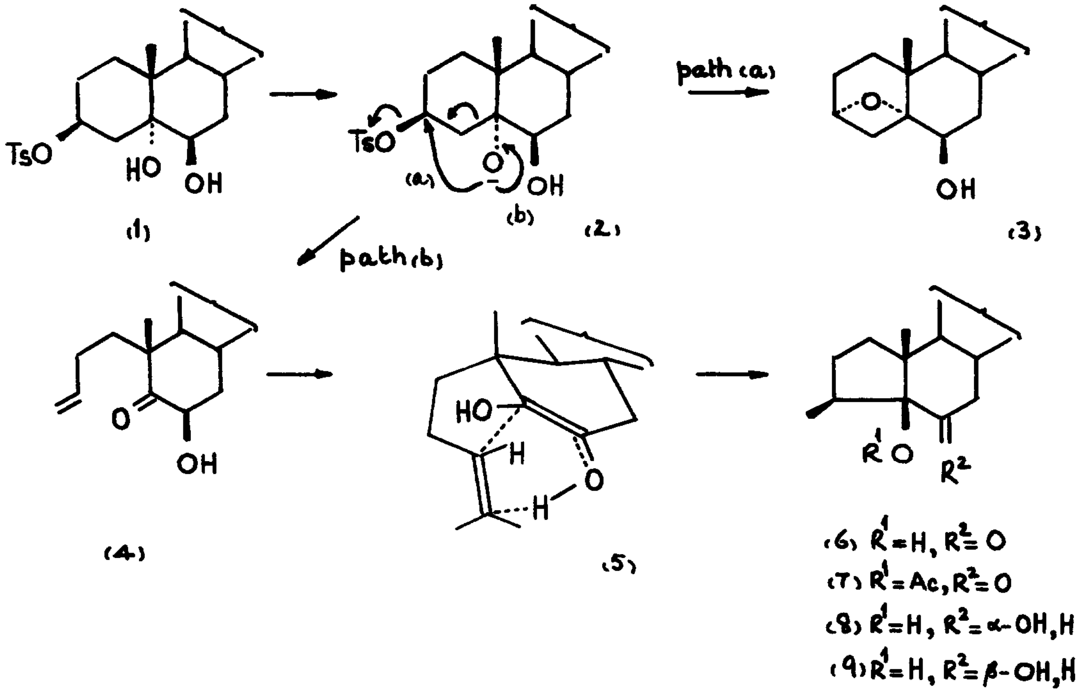
Summary A by-product of the reaction of 3β-tosyloxy-5α-cholestane-5,6β-diol with Bu^tOK/Bu^tOH, 3β-methyl-A-nor-5β-cholestan-5-ol-6-one, is believed to arise from the intramolecular ene reaction of 4,5-seco-cholest-3-en-6β-ol-5-one.

We have recently reported[1] the preparation of the oxetane (3) by reaction (path a) of 3β-tosyloxy-5α-cholestane-5,6β-diol (1) with Bu^tOK/Bu^tOH at 30°. We report here the structure (6) of a by-product (up to 25%) of this reaction which appears to arise through an ene reaction of the intermediate unsaturated acyloin (4).



(6) R¹=H, R²=O
(7) R¹=Ac, R²=O
(8) R¹=H, R²=α-OH,H
(9) R¹=H, R²=β-OH,H

The assignment of the structure (6) was supported by the i.r. spectrum which showed bands at 3480 (H-bonded O-H) and 1695 (H-bonded C=O) cm^{-1}. The hydrogen bonding appeared to be intramolecular as the solution i.r. spectrum did not change on dilution. This was further supported by the observation that the O-H signal (S, $\delta 3.8$) in the ^1H n.m.r. spectrum disappeared only slowly as a result of shaking with D_2O. The intramolecular nature of the hydrogen bonding suggested the 5β-configuration. The presence of an extra methyl group (at C-3) was indicated by a doublet (J ∿7Hz) at $\delta 0.79$* in the ^1H n.m.r. spectrum and a singlet at $\delta 13.0$ in the noise-decoupled ^{13}C n.m.r. spectrum (quartet in the off-resonance decoupled spectrum). Further support for the structure (6) was provided by its acid-catalysed acetylation to the acetate (7) and its lithium aluminium hydride reduction to give the 5β,6α-diol (8) and the 5β,6β-diol (9). The diols (8) and (9) were identified from the 6-H signals in their ^1H n.m.r. spectra ($W_{1/2}$ 18 and 6Hz respectively) and the 6β-configuration was confirmed for the diol (9) by the low-field position ($\delta 1.03$) of the signal for the 10-methyl group. The 3-methyl doublet in the ^1H n.m.r. spectrum of the diols (8) and (9) appeared at $\delta 1.08$ and 0.90 respectively. It was not possible to determine the configuration at C-3 unequivocally from these data since the observed downfield shift in converting the 6-oxo-group to the 6α-hydroxy-group could arise in both the 3α- and 3β-methyl compounds.

Final proof of the structure (6), including the establishment of the 3β,5β-configuration, was achieved through X-ray crystallography. Direct methods were employed using MULTAN[2] and the present conventional R is 0.089 for the 1459 observed reflexions (diffractometer data). The full details will be published elsewhere.

It is believed that the A-nor-hydroxy-ketone (6) arises from the ene reaction of the intermediate unsaturated acyloin (4) which is formed by a fragmentation (path b) of the alkoxide (2). Similar fragmentation has been observed[3] in the reaction of 3β-tosyloxy-5α-cholestan-5-ol with $Bu^{t}OK/Bu^{t}OH$. The most favourable transition state (5) for the ene reaction would lead to the observed stereochemistry. Although cyclisation of unsaturated ketones through ene reactions are relatively common,[4,5] there appear to be no reports of similar reactions of unsaturated acyloins. Furthermore, the reaction reported here proceeds under very mild conditions relative to those required for the unsaturated ketones and, in general, only very few ene reactions proceed at relatively low temperature.[6]

Thus far, attempts to isolate the intermediate (4) have failed but work is in progress to synthesise it by an alternative route and to investigate the generality of this reaction.

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1. R. W. G. Foster and B. A. Marples, Tetrahedron Letters, 1979, 2071.
2. G. Germain, P. Main, and M. M. Woolfson, Acta. Cryst., 1971, A27, 368.
3. R. B. Clayton, H. B. Henbest, and M. Smith, J. Chem. Soc., 1957, 1982.
4. W. Oppolzer and V. Snieckus, Angew. Chem. Internat. Edn., 1978, 17, 476.
5. J. M. Conia and P. Le Perchec, Synthesis, 1975, 1.
6. cf. E. Vedejs and G. P. Meier, Tetrahedron Letters, 1979, 4185.

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* This doublet is clearly resolved in the 300MHz spectrum but only the up-field branch is resolved in the 90MHz spectrum.

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