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THE HBr CATALYSED AROMATIZATION OF SOME STEROIDAL ENE-DIOLS AND TRIOLS

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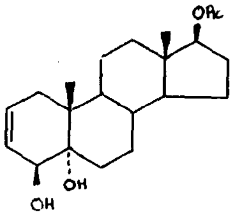
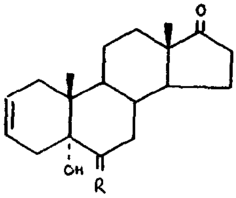
There has recently been some interest in the aromatization of steroids through spiro-cationic intermediates produced from substrates containing three potential sites of unsaturation in rings A and B.[1,2] When the ene-diols (1 - 3)[3] were heated with HBr in glacial acetic acid under reflux for 10 - 15 min., the corresponding 4-methyl-oestra-1,3,5(10)-trienes (4 and 5 respectively) were formed in 25 - 30% yield.

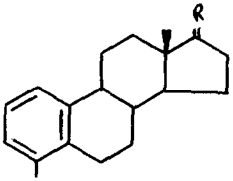


(1)



(2) R = H, OH

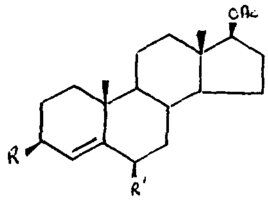
(3) R = OH, H



(4) R = OAc, H

(5) R = O

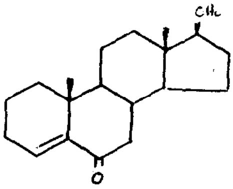
However the acetoxy-alcohol (6) gave predominantly the unsaturated ketone (7) with only a trace of aromatic product. The isomeric acetoxy-alcohol (8) gave the aromatic steroid (4) and a smaller amount of testosterone acetate. However the diacetate (9) gave the aromatic steroid (4) in 40% yield. The following triols were also examined. Both (10) and (11), epimeric at C-4, gave the 4-methyloestra-1,3,5(10)-triene (4) in 30 -40% yield together with a trace of testosterone acetate. **Whilst** the 5α-hydroxy-6β-acetate (12) gave the 4-methyloestra-1,3,5(10)-triene (4) in 35% yield, its C-6 epimer, the 5α-hydroxy-6α-acetate(13) gave the 3β,17β-diacetoxy-6-ketone (14) in 40% yield.



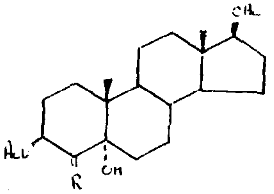
(6) R = OAc; R' = OH

(8) R = OH, R' = OAc

(9) R = R' = OAc

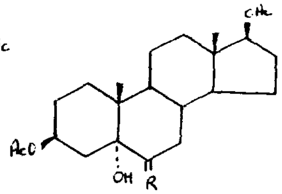


(7)



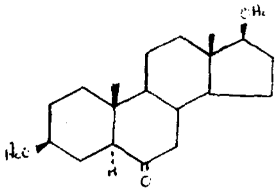
(10) R = ◀OH ··H

(11) R = ◀H ··OH



(12) R = ◀OAc ··H

(13) R = ◀H ··OAc



(14)

Hence the aromatization of steroids, presumably through a spiro-diene cation, may occur with ene-diols and triols which contain these substituents at C-3 - C-6. Although some potential sites of unsaturation may lie on ring B, with HBr in glacial acetic acid, the major aromatic steroid is the 4-methyloestra-1,3,5(10)-triene rather than the anthrasteroid.

REFERENCES

1. For a recent review see:- D.N.Kirk in 'Terpenoids and Steroids' Specialist Periodical Reports, The Chemical Society, London. Vol.1(1971), p.376; Vol.2(1972), p.309.
2. J.Libman and Y.Mazur, Chem.Comm., 1971, 729.
   J.R.Hanson, Chem.Comm., 1971, 1119; 1343.
3. The preparation of the steroidal substrates will be detailed in our full paper.

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