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SYNTHESIS AND MECHANISM OF FORMATION OF STEROIDAL 3-ENO[3,4-b]DITHIANES

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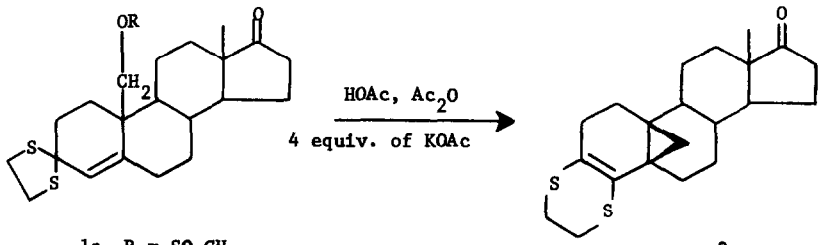
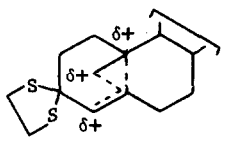
The preparation of several steroidal 3,5-dieno[3,4-b]dithianes have recently been reported.[1-3] We wish to report a convenient synthesis for the first steroidal 3-eno[3,4-b]dithiane (2) via a carbonium ion rearrangement, the mechanism of which is pertinent to the above steroidal dieno[3,4-b]dithiane syntheses.



1a R = SO_2CH_3

1b R = $COCH_3$

2



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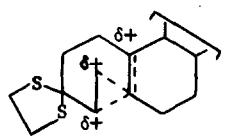

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Acetolysis of 19-methanesulfonoxy-4-androstene-3,17-dione-3-thioketal, 1a, according to the conditions of Tadanier [4] afforded the following results. Refluxing a solution of 1a for 16 hours and using the mildest acetolysis conditions (KOAc, H_2O, CH_3COCH_3) gave no reaction. Using buffered acetolysis conditions (KOAc, HOAc, Ac_2O, 100°, 50 min.) 1a yielded the dithiane 2 (73%), m.p. 157-158°, ν_{max} (KBr) 1730 cm^{-1} (cyclopentanone); nmr ($CDCl_3$) δ3.16 (4H, S, thioketal) 0.89 (3H, S, 4-18) and 0.68 (2H, S, cyclopropyl methylene), mass spec. (70 eV) m/e 360. The addition of a small quantity of lanthanide shift reagent caused the chemical shifts of the cyclopropyl

methylene protons to differ and appear as an AB quartet, J_{AB} = 5.0Hz. In the absence of buffer, the acetolysis (HOAc, 100°, 3 hours) of 1a gave 19-acetoxy-4-androstene-3,17-dione-3-thioketal 1b (65%) as the only product. The structure of 1b was confirmed by comparison (m.p., ir and nmr) with an authentic sample.[5]

These results indicate that only the kinetically formed homoallylic cation 3 is produced.[4] In the case of the buffered acetolysis conditions the carbonium ion 3 is trapped by a sulfur migration before the ion has a chance to rearrange to the carbonium ion 4 which is the precursor of the thermodynamic product.[4a] Loss of a proton following the sulfur migration affords the dithiane 2. There is also ample precedent that the Δ^4-19-acetoxy steriod 1b is also formed via the homoallylic carbonium ion 3, since the Δ^5-19-methanesulfonates have been shown to rearrange under similar conditions via a homoallylic cation.[4]

These results confirm the previously proposed hypothesis that the steroidal 3,5-dieno [3,4-b]dithianes were formed by migration of sulfur to a carbonium at C-6.[3] Furthermore this migration may provide a useful method for intramolecular trapping of carbonium ion intermediates.

Desulfurisation of 2 with Raney-nickel afforded 5β,19-cycloandrost-3-ene-17-one (81% yield), mp 70-71°, ν_{max} (CCl_4) 1640 (olefin) and 1735 cm^{-1} (cyclopentanone), nmr ($CDCl_3$) δ5.80(1H, q, J = 10Hz, H-4) 5.38 (1H, m, H-3) 0.87 (3H, s, H-18) 0.95 (1H, d, J = 5.0Hz) 0.50 (1H, d, J = 5.0Hz, cyclopropyl methylene). This is therefore a convenient method for the synthesis of Δ^3-5β,19-cyclosteroids.

References

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4. a) J. Tadanier, J. Org. Chem., 31, 2124 (1966).
   b) J. Tadanier, ibid., 31, 3204 (1966).
   c) J. Tadanier, R. Hallas, and J. R. Martin, ibid., 34, 3837 (1969).
5. The 19-acetate, 1b was prepared by acetylating 19-hydroxy-4-androstene-3,17-dione-3-thioketal. Satisfactory analyses were obtained for all new compounds reported.