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REARRANGEMENTS OF 10β-ETHENYL STEROIDS

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Homoallylic participation of the 5,6-double bond in the solvolyses of 3- and 19-toluene-*p*-sulphonyloxy-steroids is believed to give intermediate non-classical carbonium ions from which the various products are derived.[1] The acid-catalysed rearrangements of 5,6-epoxy- and 5α-hydroxy-steroids proceed, at least formally, through C(5)-carbonium ions, though the degree of rearrangement is variable (backbone- or Westphalen-type).[2] In continuation of our studies of the detailed factors which control these rearrangements,[3] we have examined the boron-trifluoride-catalysed rearrangement of the 10β-ethenyl-5α,6α-epoxide (1),[4] and the sulphuric acid-catalysed rearrangement of the 10β-ethenyl-5α-hydroxy-compound (3). Both compounds (1) and (3) could in principle lead to non-classical ions of the type (6) (or the equivalent bicyclobutonium ions)[5] by homoallylic participation of the double bond. The epoxide (1) reacts in a similar manner to 3β-acetoxy-5α,6α-epoxycholestane[6] and gives a reasonable yield of the fluorohydrin (7) (47%) and some backbone rearranged dimer (8) (26%). In contrast, and in an analogous manner to 3β,6β-diacetoxy-5α-hydroxycholestane,[7] the hydroxy-compound (3) rearranges to the 5β-ethenyl-Δ^9-compound (9) (58%). Thus, surprisingly the 19-methylene group appears to have little effect on the product distribution, suggesting that homoallylic participation of the double bond leading to stabilised non-classical carbonium ion intermediates is not important in these reactions. In support of this, compound (3) appears to rearrange through the intermediate classical ions (11) and/or (12) and (13) since scrambling of the deuterium label in the vinyl group is observed during rearrangement.

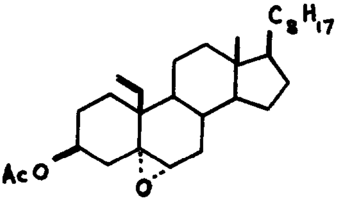
The crude product from the brief reaction (5 min.) of the epoxide (1)[4] (in 5% benzene solution) with boron trifluoride-ether complex was separated into its components by t.l.c. The fluorohydrin (7) was readily identified from its ^{1}H n.m.r. spectrum which showed diagnostic peaks at τ 5.7 (doublet of multiplets, J *ca*. 50 Hz, 6-H) and 6.6 (singlet, exchanged with D_2O, 5-OH). The backbone-rearranged dimer (8) was also identified from its ^{1}H n.m.r. spectrum (100 MHz) in which the 20-Me doublet (τ 9.06) collapsed to a singlet (τ 9.06) on double irradiation at -144 Hz.[6] Other important multiplets appeared at τ 2.8 - 4.2 (α-vinyl-2H), 4.5 - 5.4 (β-vinyl-4H, 3-2H), and 6.66 and 6.76 (6-2H). Some epoxide (1) (18%) was recovered from the reaction mixture; the quoted yields allow for this.

Compound (3) was prepared from the epoxide (1) *via* the diol (2) by the usual procedures.[8] The usual conditions[7] were employed for the rearrangement of compound (3), and the product was purified by t.l.c. The 5β-ethenyl-Δ^9-compound (9), the major product, was identified from its ^{1}H n.m.r. spectrum which showed a characteristic 13-Me signal (τ 9.2),[7] and multiplets at τ 4.0 - 4.6 (α-vinyl-H) and 4.6 - 5.5 (β-vinyl-2H, 3-H, 6-H). The ^{1}H n.m.r. spectrum of the hydrolysed derivative (10) showed characteristic signals for the 3-H (τ 6.1, m, $W_{\frac{1}{2}}$ *ca.* 10 Hz) and the 6-H (τ 6.55, m, $W_{\frac{1}{2}}$ *ca.* 16 Hz).

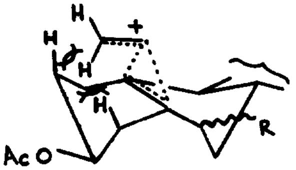
The rearrangement of a mixture of compounds (3) (11.0%), (4) (38.4%), and (5) (50.6%) has allowed some elucidation of the details of the reaction path from compound (3) to compound (9). The mixture was prepared by the usual route[4] using trideuteriomethyltriphenylphosphonium iodide in the Wittig reaction, and its composition was determined by mass spectrometric measurements on the M-60 peak. Similar analysis of the product mixture showed that no proton exchange with solvent occurred (d_0 9.5%, d_1 37.5%, d_2 53.0%). In the ^{1}H n.m.r. spectrum, the ratio of the area of the α-vinyl proton multiplet to that of the combined β-vinyl protons and the 3-H and 6-H changed from *ca.* 1:2.5 in the starting materials to *ca.* 1:3.4 in the products. This scrambling could occur by 1,2-hydride shifts in the classical ions (11) and (12) but seems unlikely to occur in non-classical ions of the type (6).[9] Overlap of the π-electrons of the double bond with the developing (or fully developed) positive charge at C(5) could lead directly to the ions (11) and (12). The product (9) could be formed from the ion (11) but not directly from the ion (12). However, rearrangement of the ions (11) or (12) would give ion (13) which could in turn give the product (9). At present, we are unable to specify which of these classical ions are involved.

In the reaction of the epoxide (1), it appears that participation of the double bond at C(5) does not compete very favourably with attack of fluoride at C(6). Thus, although no direct evidence is available regarding the ionic intermediates from epoxide (1), it does seem unlikely that non-classical ions of the type (6) are particularly energetically favourable.[10]

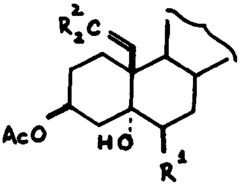
Steric interaction between one of the methylene hydrogen atoms and the hydrogen atoms



(1)



(6)



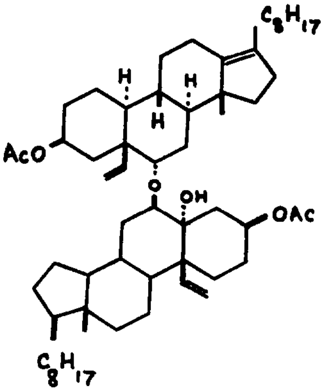
(2) $R^1 = OH$, $R^2 = H$

(3) $R^1 = OAc$, $R^2 = H$

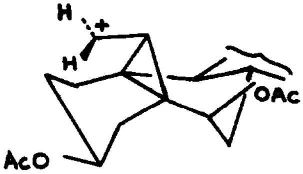
(4) $R^1 = OAc$, $R^2_2 = DH$

(5) $R^1 = OAc$, $R^2 = D$

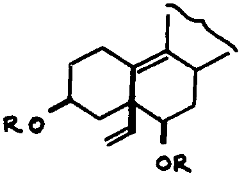
(7) $R^1 = F$, $R^2 = H$



(8)

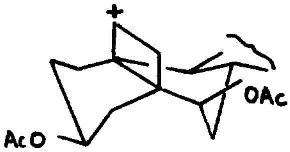


(11)

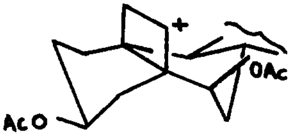


(9) R = Ac

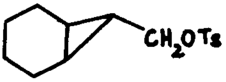
(10) R = H



(12)



(13)



(14)

at C(2) and C(4) may be a factor in destabilising ions of the type (6).[5] Such interactions can be avoided in the classical ion (11), and would not be present in the intermediate non-classical bicyclobutonium ion through which compound (14) is assumed to rearrange.[11]

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