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Unexpected Cyclisation of an Acetylenic Acetal: Vinyl Cation Capture by Internally transferred Hydride

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The acetylenic acetal (**2**) is converted in 90% yield to a mixture of cholesta-3,5- and 4,6-dienes on reflux in toluene containing toluene-*p*-sulphonic acid.

Sulphonate ester solvolysis with triple bond participation can result in the formation of three-,[1] four-,[1] five-,[2] and six-membered rings.[2] Johnson has incorporated this chemistry into an extension of his spectacular biogenetic-type cyclisations,[3] culminating in a synthesis of (±)-progesterone.[4] In turn, this has helped to clarify the nature and fate of the intermediate vinyl cations.[5,6] We have unexpectedly observed and now report the mechanistically related cyclisation of a steroidal acetylenic acetal, which has several noteworthy features.

Attempts to convert the acetylenic ketone (**1**)[7] into the acetal (**2**) under standard conditions† led to (**2**) (60%), cholest-4-en-3-one (**3**)‡ (35%), and a non-polar minor product (**4**) (5%). When the reaction was run with a tenfold increase of

† (**1**) 200 mg, toluene-*p*-sulphonic acid 7.5 mg, toluene, reflux, 16 h.

‡ Detected (TLC) in the total product before aqueous work-up; the cyclisation of acetylenic ketones to cyclohexenones has precedent.[9]

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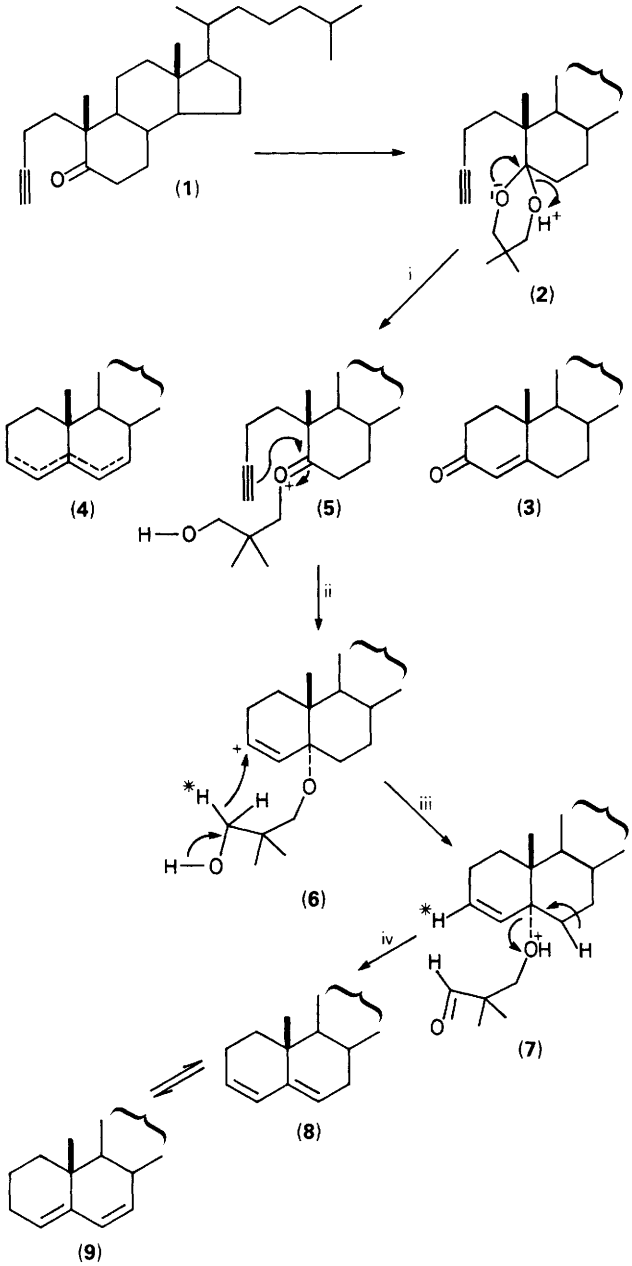

Scheme 1. i, Acetal cleavage; ii, cyclisation; iii, internal hydride transfer; iv, elimination.

toluene-*p*-sulphonic acid,§ the yield of (**4**) increased to around 90%. Product (**4**), obtained by solvent extraction and filtration through silica gel, crystallised spontaneously on solvent removal, had m.p. 70—76 °C and $[\alpha]_D$ −71° (CCl_4), and was shown to be a mixture (4 : 1) of cholesta-3,5- and 4,6-dienes, as follows: ^{13}C NMR, GC–MS[8] (OV1 capillary, 60°), IR, and UV of the mixture identified the major component as cholesta-3,5-diene (comparison with authentic sample) and the minor almost certainly as cholesta-4,6-diene. All the peak positions in the ^{13}C NMR spectrum of the mixture matched those of a mixture (different proportions) of these dienes obtained by a different method.[10] The observed $[\alpha]_D$ of the mixture corresponds to the calculated $[\alpha]_D$[11] of a 4 : 1 mixture of cholesta-3,5- and 4,6-dienes.

§ (**1**) 200 mg, toluene-*p*-sulphonic acid 75 mg, toluene, reflux, 16 h.

The same mixture was obtained§ in comparable yield when either propane-1,3-diol replaced 2,2-dimethylpropane-1,3-diol or ketal (**2**) was substituted for ketone (**1**) plus the propane diol. Ethylene glycol in place of the propane diols gave the corresponding ketal but none of the diene mixture. Butane-1,4-diol or benzyl alcohol did not react.

The formation of cholesta-3,5-diene can be rationalised as shown in Scheme 1. Models, incorporating a rather naive view of transition state geometry,[2b] suggest that the *A*/*B trans*-fused vinyl cation (**6**) may be rather well set up for internal hydride delivery to the vacant p orbital at C-3. Models, and the failure of ethane-1,2- or butane-1,4-diol to generate diene also suggest that the propane diols possess uniquely the required geometry. Mechanistically analogous but simpler cases of hydride transfer following acid-catalysed cleavage of spiroacetals have been reported.[12] The minor amount of 4,6-diene (**9**) obtained is clearly accessible by acid-catalysed isomerisation of the initially formed 3,5-diene. Reaction§ of (**1**) with 1,1,3,3-[$^2H_4$]propane-1,4-diol[13] furnished a diene mixture, m.p. 70—78 °C, $[\alpha]_D$ −73° (CCl_4), $\nu_{max.}$ 2160 and 2240 cm^{-1}; *m*/*z* 22% D_0, 48% D_1, 30% D_2. The ^2H NMR spectrum at 55 MHz showed signals at δ 5.41 (H-4), 5.60 (H-3), and 5.93 (H-6), the largest being at δ 5.60, as well as signals at δ 1.67 and 2.05 (allylic hydrogens), indicating extensive scrambling of deuterium, initially at C-3, *via* the solvent.

Several interesting points emerge: (i) the cationic centre that interacts with the triple bond is generated by acid-catalysed acetal opening; (ii) triple bond participation occurs readily in toluene; (iii) reaction must occur *via* a 'bent' vinyl cation[14] since the alternative 'straight' cation (5-ring) would be primary; (iv) the vinyl cation is captured by internally transferred hydride; (v) in the formation of cholest-4-ene-3-one cyclisation is initiated by the protonated carbonyl group of (**1**) and the cyclic vinyl cation [as (**6**)] is captured by a water molecule (presumably from $CH_3C_6H_4SO_3H{\cdot}H_2O$).

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