

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

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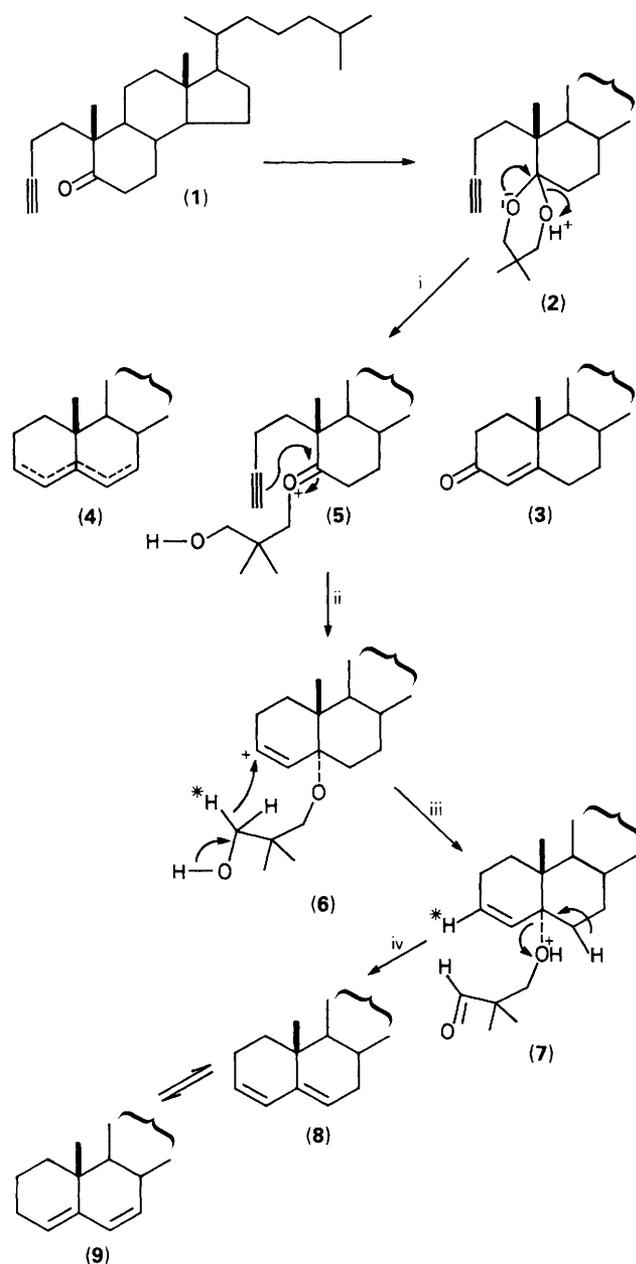
The acetylenic acetal (**2**) is converted in 90% yield to a mixture of cholesta-3,5- and 4,6-dienes on reflux in toluene containing toluene-*p*-sulphonic acid.

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 (\pm)-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



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 $[\alpha]_D -71^\circ$ (CCl₄), and was shown to be a mixture (4 : 1) of cholesta-3,5- and 4,6-dienes, as follows: ¹³C NMR, GC-MS⁸ (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 ¹³C 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.

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 spiro-acetals 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-[²H₄]propane-1,4-diol¹³ furnished a diene mixture, m.p. 70–78 °C, $[\alpha]_D -73^\circ$ (CCl₄), ν_{\max} 2160 and 2240 cm⁻¹; *m/z* 22% D₀, 48% D₁, 30% D₂. 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 cation¹⁴ 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 cholesta-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 CH₃C₆H₄SO₃H·H₂O).

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References

- M. Hanack, J. Haffner, and I. Herterich, *Tetrahedron Lett.*, 1965, 875; M. Hanack and I. Herterich, *ibid.*, 1966, 3847; M. Hanack, I. Herterich, and V. Vott, *ibid.*, 1967, 3871.
- (a) P. E. Peterson and R. J. Kamat, *J. Am. Chem. Soc.*, 1966, **88**, 3152; (b) *ibid.*, 1969, **91**, 4521.
- W. S. Johnson, *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 9; P. T. Lansbury, T. R. Demmin, G. E. duBois, and V. R. Haddon, *J. Am. Chem. Soc.*, 1975, **97**, 394, and references cited therein.
- W. S. Johnson, M. B. Gravestock, and B. E. McCarry, *J. Am. Chem. Soc.*, 1971, **93**, 4332.
- P. J. Stang, *Prog. Phys. Org. Chem.*, 1973, **10**, 205.
- P. J. Stang, Z. Rappoport, M. Hanack, and L. R. Subramanian, 'Vinyl Cations,' Academic Press, New York, 1979.
- S. K. Pradhan and V. M. Girijavallabhan, *Steroids*, 1969, **13**, 11.
- E. Homberg and B. Bielefeld, *J. Chromatogr.*, 1979, **180**, 83.
- C. E. Harding and M. Hanack, *Tetrahedron Lett.*, 1971, 1253.
- H. L. Holland and S. R. Khan, *Can. J. Chem.*, 1985, **63**, 2763.
- J. C. Eck, R. L. van Peurse, and E. W. Hollingsworth, *J. Am. Chem. Soc.*, 1939, **61**, 171.
- R. B. Woodward, F. Sondheimer, and Y. Mazur, *J. Am. Chem. Soc.*, 1958, **80**, 6693; P. Deslongchamps, D. D. Rowan, and N. Pothier, *Can. J. Chem.*, 1981, **59**, 2787.
- G. Wood, R. M. Srivastava, and B. Adlam, *Can. J. Chem.*, 1973, **51**, 1200.
- W. D. Pfeifer, C. A. Bahn, P. v. R. Schleyer, S. Bocher, C. E. Harding, K. Hummel, M. Hanack, and P. J. Stang, *J. Am. Chem. Soc.*, 1971, **93**, 1513; W. S. Johnson, M. B. Gravestock, R. J. Parry, and D. A. Okorie, *ibid.*, 1972, **94**, 8604.

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