Tetrahedron Letters Vol. 22, pp 585 - 586
©Pergamon Press Ltd. 1981. Printed in Great Britain

0040-4039/81/0201-0585$02.00/0

STEREOCHEMISTRY OF THE VINYLOGOUS S_N2' REACTION

William S. Murphy* and Brendan O'Mahony

Chemistry Department

University College

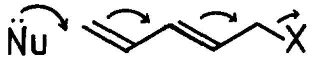
Cork, Ireland

Theoretical treatment indicates that the stereochemistry of both the vinylogous S_N2' and 1,6-conjugate elimination reaction will be opposite to that of the S_N2' and 1,4-conjugate elimination reaction.

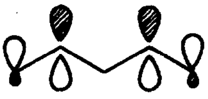
Interest in the S_N2' reaction continues unabated.[1] Attention has centred not alone on the mechanism[2] but also on synthetic[3] and biosynthetic[4] applications. In addition, interest in the related 1,4-conjugate elimination reaction is growing.[4,5]

Most theoretical analyses[6] of the S_N2' reaction have indicated a preference for *syn* attack by the nucleophile. However, the possibility of *anti* stereochemistry has been allowed for in some instances.[6c,e] In practice although *syn* stereochemistry has been most generally observed[2c,7] recent results[2b,8] have diverged from this.

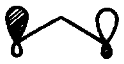
We have now extended orbital symmetry methods[6c] to the vinylogous S_N2' reaction (1).



I



II



III

The LUMO of the pentadienyl cation is ψ_3. In the transition state C-1 and C-5 will be intermediate between sp^3 and p. Mixing the $2s$ and $2p$ AO's of C-1 and C-5 results in the structure (II) for the LUMO of the pentadienyl cation in the transition state. It is immediately apparent that (II) is symmetric relative to a mirror plane through its mid-point. The corresponding allyl transition state, structure (III), is antisymmetric relative to the same symmetry element.

It follows[6c] that when C-1 bond formation is synchronous with C-5 bond cleavage, the attacking nucleophile must enter *syn* to the leaving group. Where C-1 bond formation is concerted but not synchronous with C-5 bond cleavage, the nucleophile must enter *anti* to the leaving group. Hence all things being equal, the conditions which favour *syn*-S_N2' reactions of allyl systems should result in an *anti* S_N2' reaction in pentadienyl systems and *vice versa*.

Extension of this methodology[6c] to 1,6-conjugate elimination by either a concerted or Elcb mechanism shows that an *anti* process is favoured.

The stereochemistry of the vinylogous S_N2' acetolysis of 6β-bromoandrost-4-ene-3,17-dione, a longstanding problem,[9] has now been shown[10] to be at least predominantly *syn*. 1,6-Conjugate elimination is known[10] but is of unknown stereochemistry.

References

1. R.M. Magid, *Tetrahedron*, 1980, 36, 1901, and references therein.

2.(a) F.G. Bordwell, P.F. Wiley and T.G. Mecca, *J. Amer. Chem. Soc.*, 1975, 97, 132;
(b) T. Oritani and K.H. Overton, *J.C.S. Chem. Comm.*, 1978, 454; (c) R.M. Magid and O.S. Fruchey, *J. Amer. Chem. Soc.*, 1979, 101, 2107.

3. N. Ikota and B. Ganem, *J. Amer. Chem. Soc.*, 1978, 100, 351; P.C. Cherry, G.I. Gregory, C.E. Newall, P. Ward and N.S. Watson, *J.C.S. Chem. Comm.*, 1978, 467.

4. K.H. Overton, *Chem. Soc. Rev.*, 1979, 8, 447 and references therein.

5. R.K. Hill and M.G. Bock, *J. Amer. Chem. Soc.*, 1978, 100, 637 and references therein; A. Eschenmoser, paper presented at the RSC International Symposium, St. Andrews, Scotland, 21-25 July 1980.

6.(a) K. Fukui and H. Fujimoto, *Bull. Chem. Soc. Japan*, 1967, 40, 2018; (b) W. Dreuth, *Recl. Trav. Chim. Pays-Bas*, 1967, 86, 318; (c) N.T. Ahn, *J.C.S. Chem. Comm.*, 1968, 1089; (d) J. Mathieu, *Bull. Soc. Chim. Fr.*, 1973, 807; (e) R.L. Yates, N.D. Epiotis and F. Bernardi, *J. Amer. Chem. Soc.*, 1975, 97, 6615; (f) C.L. Liotta, *Tetrahedron Letters*, 1975, 523; (g) E. Toromanoff, *Tetrahedron*, 1978, 34, 1665.

7. G. Stork and W.N. White, *J. Amer. Chem. Soc.*, 1956, 78, 4609.

8. G. Stork and A.F. Kreft, *J. Amer. Chem. Soc.*, 1977, 99, 3850; A.A. Dobbie and K.H. Overton, *J.C.S. Chem. Comm.*, 1977, 722.

9. C. Djerassi, G. Rosenkranz, J. Romo, S. Kaufmann and J. Pataki, *J. Amer. Chem. Soc.*, 1950, 72, 4534.

10. R.D. Burnett and D.N. Kirk, *J.C.S. Perkin 1*, 1973, 1830.

(Received in UK 17 November 1980)