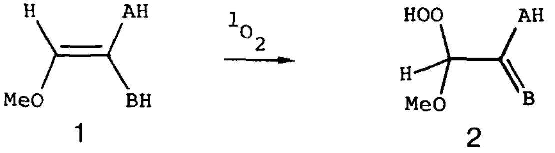
Tetrahedron Letters No. 11, pp 985 - 988.
©Pergamon Press Ltd. 1979. Printed in Great Britain.
0040-4039/79/0308-0985$02.00/0

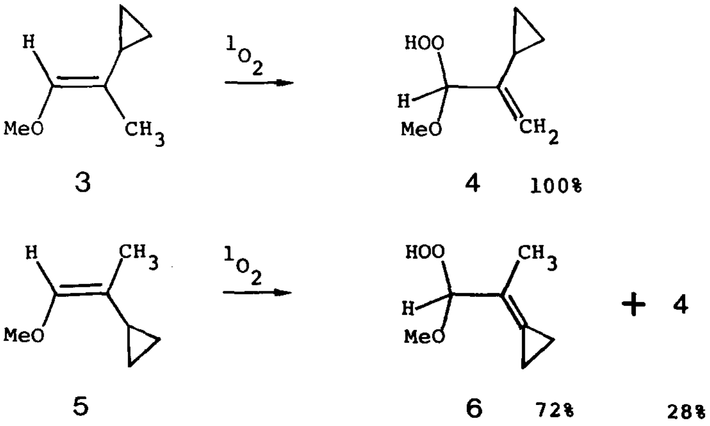
THE ROLE OF ZWITTERIONIC PEROXIDES IN CONTROLLING HYDROPEROXIDATION

Charles W. Jefford,
Department of Organic Chemistry, University of Geneva
1211 Geneva 4, Switzerland

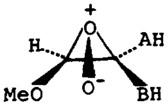
A remarkable directing effect has been recently detected in the reaction of methyl enol ethers of disubstituted acetaldehydes (1) with singlet oxygen.[1,2] Hydroperoxidation takes place to greatly favour the product which arises by allylic shift towards the substituent *cis* to the methoxy group (2).[3] Examples are many, but a typical result is the photo-oxygenation



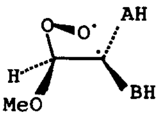
of the isomeric 1-methoxy-2-cyclopropylpropenes (3 and 5). The E isomer 3 gives exclusively the methylene hydroperoxide 4, whereas the Z isomer 5 yields mainly the cyclopropylidene derivative 6 together with a small amount of 4.[1] The reason for this selectivity



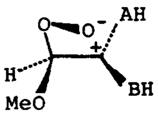
has been variously rationalized. The influence of secondary orbital interactions has been invoked to explain the preferential formation of the perepoxide which has the anionic oxygen atom placed *syn* to the methoxy group (7).[4] Another, ingenious, argument calls for the successive interplay of the lone pairs on both the methoxy substituent and the dioxygen fragment through the operation of anomeric effects to favour the creation of a stiff peroxy diradical where the distal oxygen radical once again is *syn*-disposed (8).[5] A recent variant[6] retains the interaction of lone pairs on the peroxy and methoxy substituents to account for the *cis*-directivity but, following our suggestion,[7] formulates the intermediate as a zwitterionic peroxide (9). Indeed, our evidence obtained from the photo-oxygenation of 2-methylnorbornenes has revealed that the transition state for hydroperoxidation is largely dipolar since the one-point attachment of oxygen to the vinyl carbon of the allylic fragment precedes abstraction of the allylic hydrogen substituent.[8] When similar olefins bear an alkoxy or siloxy substituent, but lack allylic hydrogen atoms, then actual zwitterionic peroxides are formed.[7,9]



7

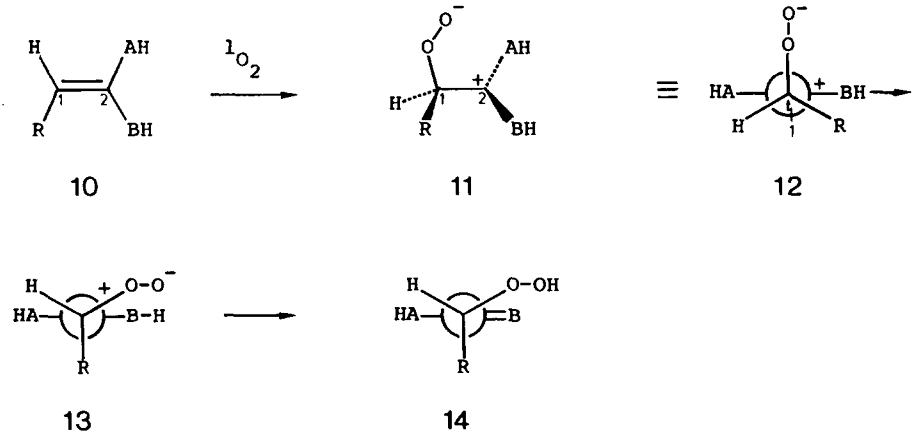


8



9

We now propose that the regioselectivity of hydroperoxidation of acyclic trisubstituted olefins, typified by 10, can be adequately rationalized in terms of the intermediacy of a short-lived zwitterionic peroxide in which conformational adjustment to achieve contiguity of the distal peroxide ion and the allylic hydrogen atom is determinative. For example, electrophilic addition of singlet oxygen to the double bond of 10 generates the zwitterionic peroxide 11. Initially, the formation of the C1-oxygen bond creates the staggered conformation (12) where the peroxide anion portion is not only equidistant from both C2 substituents, but is too far away for hydrogen abstraction. Next, rotation about the C1-C2 axis minimizes the gauche interaction between the R and BH groups leading to the new staggered conformation (13) which now places the peroxide grouping close enough to the BH group to be able to remove a proton.[10] The essence of this mechanism is that the rehydridization of C1 is accompanied or immediately followed by the conformational change (12 → 13) according to the principle of least motion[11] and that reaction to give the product 14 is equally rapid.



Although it is difficult to distinguish between a polar transition state and a short-lived zwitterionic peroxide, the latter nevertheless serves as a useful model of predictive value. The most important feature of this model is that the nature of the group R on C1 is not critical. As the aforementioned anomeric effects are no longer necessary, a methyl or alkyl group would do just as well in directing hydroperoxidation to the *cis* side.[12] A corollary is that the use of solvents, other than aprotic ones, would be expected to diminish the regioselectivity. Photo-oxygenation in methanol, for example, would give external protonation of the peroxide grouping a chance to compete with intramolecular proton transfer.[13]

REFERENCES AND NOTES

1) G. Rousseau, P. Le Perchec, J.M. Conia, Tetrahedron Letters, 2517 (1977); Tetrahedron, in press.

2) D. Lerdal and C.S. Foote, Tetrahedron Letters, 3227 (1978).

3) The symbols AH and BH designate groups which can react in allylic fashion.

4) S. Inagaki, H. Fujimoto and K. Fukui, Chem. Letters, 749 (1976).

5) L.B. Harding and W.A. Goddard, III, Tetrahedron Letters, 747 (1978).

6) G. Rousseau, A. Lechevallier, F. Huet and J.M. Conia, Tetrahedron Letters, 3287 (1978).

7) C.W. Jefford, C.G. Rimbault, Tetrahedron Letters, 2375 (1977); J. Am. Chem. Soc., 100, 295 (1978).

8) C.W. Jefford and A.F. Boschung, Helv., 57, 2242 (1974); C.W. Jefford and C.G. Rimbault, J. Org. Chem., 43, 1908 (1978).

9) C.W. Jefford and C.G. Rimbault, J. Am. Chem. Soc., 100, 6437 (1978).

10) If calculations on the β-hydroxyethyl cation are a reliable guide, the rotational barrier in 11 should be small (∿8.0 kcal/mole). Moreover, conformation 12 should be less stable than 13 on account of the unfavourable eclipsing of the C1-O bond and the empty p_z orbital on C2 (Y. Apeloig, P.v.R. Schleyer and J.A. Pople, J. Am. Chem. Soc., 99, 5901 (1977)).

11) O.S. Tee, J. Am. Chem. Soc., 91, 7144 (1969).

12) This is found to be the case as exemplified by the behaviour of E and Z isomers of trisubstituted ethylenes (K.H. Schulte-Elte, B.L. Muller and V. Rautenstrauch, Helv., 61, 2777 (1978), and M. Orfanopoulos, M. Bellarmine Grdina and L.M. Stephenson, private communication).

13) This would account for the uncoupling of the enantiomeric and isotopic ratios in the hydroperoxides formed from R-(-)-*cis*-2-deuterio-5-methyl-3-hexene on photo-oxygenation in methanol (L.M. Stephenson, D.E. McClure and P.K. Sysak, J. Am. Chem. Soc., 95, 7888 (1973)).

(Received in UK 2 January 1979)