SYN REGIOSELECTIVITY OF THE HYDROPEROXIDATION OF CYCLO-ALKENES WITH SINGLET OXYGEN

Charles W. Jefford and Christian G. Rimbault

Department of Organic Chemistry, University of Geneva, 1211 Geneva 4, Switzerland.

Summary. The regioselectivity of hydroperoxidation of 1-alkylcycloalkenes is rationalized in terms of the formation of a zwitterionic peroxide.

We have recently pointed out that the *syn* regioselectivity of allylic hydroperoxidation of trisubstituted mono-olefins by singlet oxygen is largely independent of the nature of the reference or non-geminal substituent.[1,2] Furthermore, we have ascribed the selectivity to conformational changes occurring on bond formation by oxygen at the mono-substituted vinyl carbon atom. We now show that our zwitterionic peroxide model is equally valid for the case of cyclo-alkenes which are mono-substituted at the C-1 atom.[2]

The 1-*t*-butyl and methyl derivatives of cyclobutene, cyclopentene and cyclohexene, together with the 1-methyl derivatives of cyclopropene, cycloheptene and cyclooctene were photo-oxygenated in acetonitrile at 0° using methylene blue as sensitizer.[3] After reduction of the resulting mixture of hydroperoxides, three allylic alcohols were obtained (Table 1). They reflect the different modes of attack by singlet oxygen on the allylic fragment. Three patterns can be discerned. Firstly, it is evident that the bulky *t*-butyl group behaves like the methyl group, as the ratio of endocyclic olefinic secondary to tertiary alcohols is essentially the same. Secondly, 1-methylcyclopropene is inert towards singlet oxygen, whereas the rates of photo-oxygenation for the other olefins bearing *t*-butyl and methyl substituents are similar, but showing, even so, small differences indicative of ring size, with cyclohexenes being character-istically the least reactive. Thirdly, for 1-methyl olefins, endocyclic olefinic products pre-dominate (mode b); exocyclic products (mode a) only become important for 1-methylcyclohexene and, to a lesser extent, for 1-methylcyclooctene. In other words, abstraction of the allylic

hydrogen substituent occurs usually on the more substituted side of the trisubstituted double bond, demonstrating *syn* regioselectivity.[4]

The best rationalization of these results, we believe, is in terms of a zwitterionic peroxide or a two-stage dipolar transition state.[5] The rate-determining step is attack by oxygen on the face of the double bond to create a carbon-oxygen bond with its attendant configurational and polar consequences, followed by conformational adjustments which permit the end of the peroxide group to reach the abstractable hydrogen substituent. Discrimination between the modes b and c leading to secondary and tertiary endocyclic allylic hydroperoxides is determined by electronic differences ascribable to the corresponding secondary and tertiary carbocations. Consideration of Dreiding models of the cyclobutene (10) and cyclohexene (13) rings respectively shows the C-1 substituent to be without conformational effect on the resulting secondary and tertiary carbocations; in both cases the ring hydrogen substituent is abstracted with equal ease (*cf.* sequences 10 → 11 → 12 with 10 → 13 → 14 and *cf.* 15 → 16 → 17 with 15 → 18 → 19)

Table 1. Kinetic and Modal Analysis of the Photo-oxygenation of some 1-Alkylcyclo-alkenes

Compound No	Ring size	R	k_{rel}	Modes: a	b	c
1	2	Me	0			
2	4	Me	9.3	0%	86.5%	14.5%
3	4	t-Bu	5.8	-	80.0	20.0
4	5	Me	17.4	5.6	64.6	29.8
5	5	t-Bu	14.3	-	71.0	29.0
6	6	Me	2.3	42.6	12.2	45.2
7	6	t-Bu	1.0	-	79.0	21.0
8	7	Me	17.4	5.5	58.8	35.7
9	8	Me	4.7	28.4	51.0	20.6
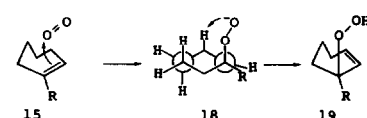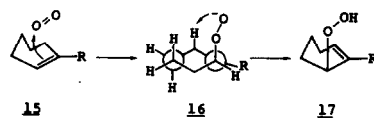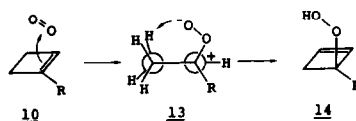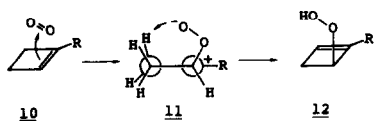
A similar comparison between the endocyclic and exocyclic modes leading to secondary hydro-peroxides uncovers a subtle intramolecular feature which explains the regioselectivity of hydrogen abstraction. Attack at C-2 in 1-methylcyclobutene generates the zwitterionic peroxide which could abstract hydrogen from methylene or m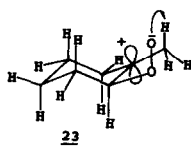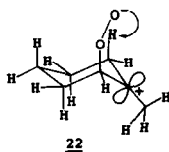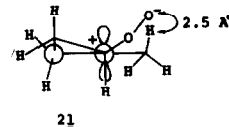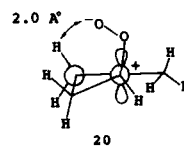ethyl groups. However, in order to be abstractable the hydrogen substituent must not only align its bond with the empty P_z orbital on the cationic center, but also be close to the terminal peroxide atom for reaction. Only the ring substituent satisfies this condition, the appropriate interatomic distance being ∿2.0 Å (20). The corresponding methyl proton is out of reach at ∿2.5 Å (21). For the pair of corresponding conformations of the methylcyclopentyl peroxides, the proximity difference is less marked, thereby accounting for the formation of some exocyclic hydroperoxide.

1-Methylcyclohexene gives products in keeping with the properties of the chair conformation. The incipient zwitterionic (22), formed by attack of oxygen at the developing axial position,[6] is awkwardly disposed on two counts. The mobile methyl group is out of range of the peroxide grouping, while the axial hydrogen substituent has poor sigma-P_z overlap with the cationic center (22). Nevertheless, some abstraction or the ring substituent occurs. However, the easy expedient of conformational inversion places the peroxide group in the equatorial

Table 2.
Photo-oxygenation of Methylidenecyclo-alkanes. Relative Rates & Ionization Potentials.

k_{rel}	0	0	150	1	62
IP^a	9.50	9.19	9.16		
e.v.^{b}		9.15	8.93	8.98	

^{a}Ref. 8. ^{b}Ref. 9

20

21

22   23   24   25
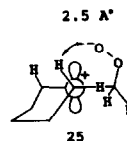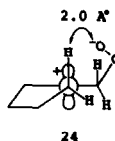
position (<u>23</u>) where it is now conveniently close for reaction with the methyl group, hence the preponderance of exocyclic methylidene product.

The validity of the zwitterionic model is re-inforced by the trends observed on photo-oxygenation of the methylidene derivatives of cyclopropane, butane, pentane, hexane & heptane (Table 2). The inertness of the small ring olefins could well be due to their low-lying HOMO's as attested by the ionization potentials.[7] However, the sizable rate difference between the 5- and 6-membered rings, despite their similar IP's, is due, we maintain, to the α-carbon-hydrogen bond having better sigma-P_z overlap with the cationic center and greater accessibility to the peroxide group in the cyclopentyl zwitterion. The smallest interatomic gaps for hydrogen abstraction in the most favourable conformations are 2.0 and 2.5 Å for the cyclopentyl and cyclohexyl zwitterions respectively (<u>24</u> and <u>25</u>).

Lastly, we reiterate that the demands of the initial configurational change, hyper-conjugation, conformational adjustment, and propinquity for abstraction, are all operative in determining the course of the reaction, no matter whether it involves a real zwitterionic intermediate or whether it passes through a two-stage transition state.

BIBLIOGRAPHY AND NOTES

1) C.W. Jefford, Tetrahedron Letters <u>1979</u>, 985.

2) For the case of the 1-phenyl derivatives see: C.W. Jefford & G.C. Rimbault, Tetrahedron Letters <u>1976</u>, 2479.

3) Solutions 0.1 mMolar in sensitizer (1 ml) containing 1 mmol of substrate were photo-oxygenated according to our procedure (C.W. Jefford & A.F. Boschung, Helv. Chim. Acta <u>57</u>, 2242 (1974).

4) For other examples see K.H. Schulte-Elte & V. Rautenstrauch, J. Am. Chem. Soc. <u>102</u>, 1738 (1980).

5) For a recent review on possible mechanisms see: A.A. Frimer, Chem. Rev. <u>79</u>, 359 (1979).

6) The stereoelectronic considerations will be the same as those which operate for the bromination of cyclohexanone (H.O. House, Modern Synthetic Reactions, 2nd Ed., W.A. Benjamin, Inc., Menlo Park, California, pp. 468-474).

7) C.W. Jefford & C.G. Rimbault, J. Org. Chem. <u>43</u>, 1908 (1978).

8) D.W. Turner, Molecular Photoelectron Spectroscopy, Wiley-Interscience, New York, 1970.

9) D.A. Demeo & A.J. Yencha, J. Chem. Phys. <u>53</u>, 4536 (1970).