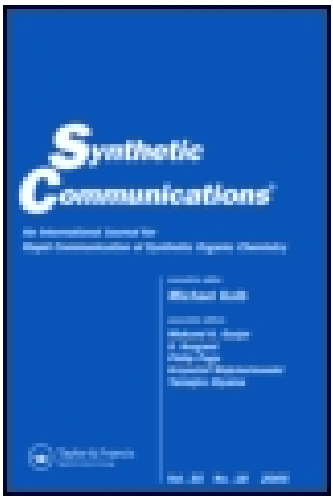


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Regioselective Formation of Cyclic and Allylic Hydroperoxides

Manolis Stratakis [a] & Michael Orfanopoulos [a]
[a] Department of Chemistry , University of Crete , 71110, Iraklion, Crete, Greece
Published online: 23 Sep 2006.

To cite this article: Manolis Stratakis & Michael Orfanopoulos (1993) Regioselective Formation of Cyclic and Allylic Hydroperoxides, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 23:4, 425-430, DOI: 10.1080/00397919308009797

To link to this article: http://dx.doi.org/10.1080/00397919308009797

SYNTHETIC COMMUNICATIONS, 23(4), 425-430 (1993)

REGIOSELECTIVE FORMATION OF CYCLIC AND ALLYLIC HYDROPEROXIDES

Manolis Stratakis and Michael Orfanopoulos*

Department of Chemistry, University of Crete
71110 Iraklion, Crete, Greece.

Abstract: A regioselective photosensitized oxygenation is reported for the preparation of cyclic and allylic hydroperoxides.

The formation of allylic hydroperoxides via the *ene* reaction of singlet oxygen with alkenes has not only biological, enviromental and mechanistic interest but also is synthetically useful as an oxygen functionalization of unsaturated hydrocarbons.[1,2]

Recently, it has been shown that the *ene* addition of singlet oxygen to unsymmetrical *cis* and *trans* alkenes is regioselective.[3] The new double bond is formed preferentially next to the larger group. Furthermore in the reaction of $^1O_2$ with tri- and tetra-substituted alkenes the major product has the double bond geminal to the larger substituent of the olefin.[4] These regioselectivities were explained by the energy difference of isomeric transition states in the product determining step. The energy difference arises from the repulsive non bonded interactions of the incoming oxygen with the alkyl substituent of the double bond.[4b]

---

*To whom correspondence should be addressed.

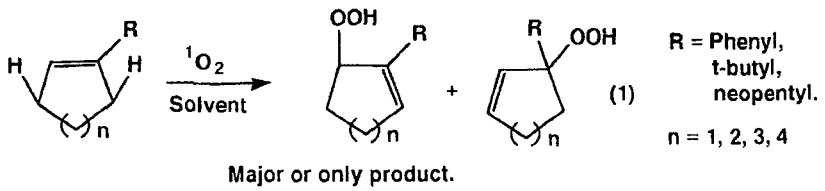
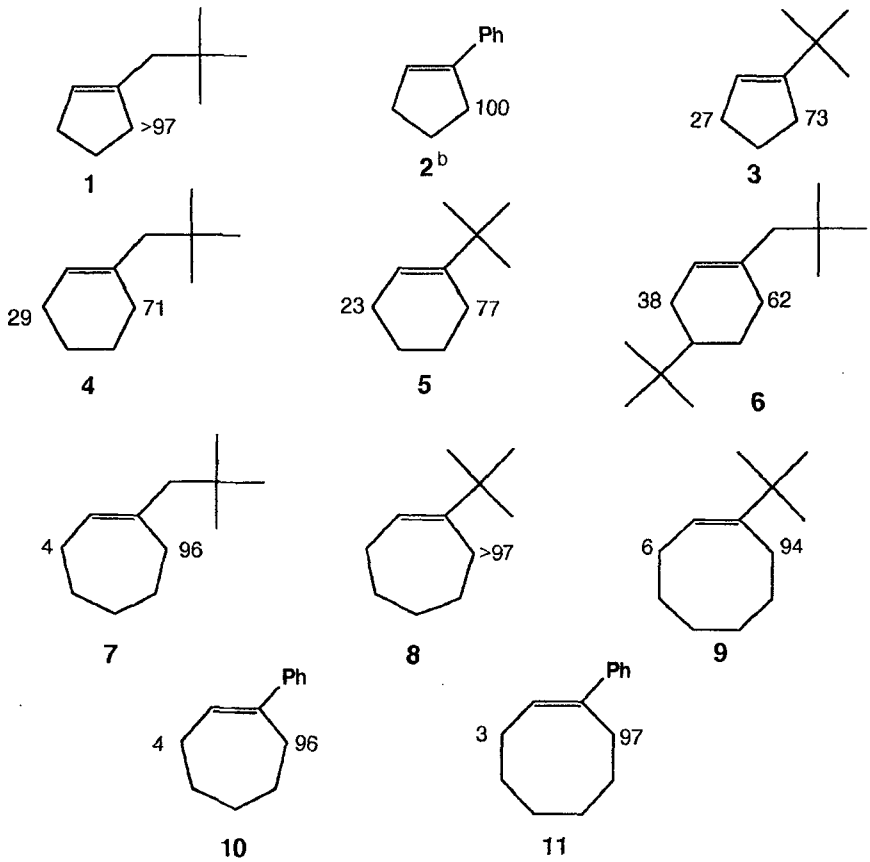


Chart 1. Regioselective Formation of Allylic Hydroperoxides in the Ene Reaction of $^1O_2$ with Alkyl and Aryl substituted Cycloalkenes.[a]



[a]The product ratio was determined by NMR integration and after reduction, by GC. Numerical values represent percent of hydrogen abstraction.[b]From the literature[6]

We now report here that unlike the *syn* selectivity of singlet oxygen with 1-methyl-1-cycloalkenes,[5] alkyl or aryl substituted cycloalkenes show general preference for hydrogen abstraction from the methylene group that is geminal to the alkyl or aryl substituent of the cycloalkene. This highly regioselective reaction in cycloalkenes, has not been previously recognized and produces allylic hydroperoxides according to the equation (**1**).

This reaction is synthetically useful since allylic hydroperoxides can be easily transformed by reduction to the corresponding allylic alcohols. These results are summarized in Chart 1. Photooxygenation of a series of alkyl- and phenyl-substituted cycloalkenes **1-11**, show a strong preference for hydrogen abstraction on the methylene group that is geminal to the alkyl or phenyl substituent of the double bond. The presence of a phenyl substituent does not alter the geminal selectivity.This is demostrated with substrates **2**, **10** and **11** where the formation of the allylic hydroperoxide is highly regioselective.

Experimental Section

Structure and purities of compounds were determined by NMR (FT-80A Varian), Gas Chromatography (Varian 3700) and Infrared spectroscopy (Perkin-Elmer 598). The progress of photooxidation was monitored by GC (SE-30, 10ft x 1/8'' column). Purification of olefins (where necessary) was accomplished by flash column chromatography[7] (silica gel 60, 230-400 mesh) using hexane as eluant, or by preparative Gas Chromatography (OV-275, 10'x3/8'' and SE-30, 6'x1/4''). 1-Alkylcycloalkenes were prepared by the addition of the proper organolithium or organomagnesium reagent to the corresponding cycloketones, followed by dehydration of the carbinols. The organometallic reagents were tert-butylithium, phenyl magnesium bromide and neopentyl magnesium bromide. In some cases, due to enolizable character of ketones, substantial amount of unreacted cycloketone was observed and removed by flash column chromatography.

Dehydration was carried out with catalytic amounts of p-toluenesulfonic acid, either at 110°C without solvent or in refluxing benzene. The only olefinic product from dehydration was the desired cycloalkene. The ratio of the photooxygenation products was determined by NMR integration of the proper peaks and by Gas Chromatography.

General photooxidation procedure

All photooxidations were carried out at 0°C or 25°C in acetone or carbon tetrachloride as solvents. The apparatus for preparative scale photooxidation experiments is equipped with oxygen inlet, thermometer , moisture protecting tube and cooling jacket. The temperature was controlled by continuous water flow. The irradiation with a 300W sun lump or 650W tungsten-halogen lamp was external through the bottom of this equipment.

For small scale (<1mmol) photooxidation, oxygen was bubbled continiously by a syringe in a suitable cell containing 2ml of 10^{-4} M tetraphenyl porphyrin or methylene blue solutions.

In a preparative scale photooxidation of 1.35g (9.76 mmol) 1-tert-butyl-1-cyclohexene (Aldrich Co.)were dissolved in 100ml solution of acetone with 10^{-4} mmol methylene blue as the sensitizer. Oxygen was bubbled continuously through the solution. After 18h, GC analysis showed that starting material was completely consumed. The solution was concentrated to 25ml and one equivalent of dimethyl sulfide was added at -78°C. The reaction mixture was stirred at room temperature for one hour and was poured into water. The product was exctracted with 2x50 ml diethylether. The combined organic layers were washed with water and dried over $MgSO_4$. Evaporation of the solvent afforded 1.36g of allylic alcohols in 90% yield.

1-neopentyl-1-cyclopentene (1) Purified on SE-30 6'x1/4'' preparative column. ^{1}H NMR (DMSO-d_6) δ 5.34 (m, 1H), 2.15 (m, 4H), 2.15 (br. s, 2H), 1.7 (m, 2H), 0.88 (s, 9H).

^{t}butyl-1-cyclopentene (3). Purified on a 10'x3/8'' OV-270 preparative column (T=90°C) ^{1}H NMR (acetone-d_6) δ 5.32 (m, 1H), 2.25 (m, 4H), 1.70 (m, 2H), 1.04 (s, 9H).

1-neopentyl-1-cyclohexene (4). Purified on a SE-30 6'x1/4'' preparative column (T=110°C) ^{1}H NMR (DMSO-d_6) δ 5.32 (m, 1H), 1.96 (m, 6H), 1.40 (m, 4H), 0.87 (s, 9H).

1-^{t}butyl-1-cyclohexene (5). Comercialy available from Aldrich Co.

1-neopentyl-4-tbutyl-1-cyclohexene (6). Purified on a 10'x3/8'' OV-270 preparative column (T=140^{0}C) ^{1}H NMR (DMSO-d$_6$) δ 5.34 (m, 1H), 1.95 (m,4H), 1.60 (m, 3H), 0.86 (s, 9H), 0.84 (s, 9H).

1-neopentyl-1-cycloheptene (7). Purified on a SE-30 6'x1/4'' preparative column (T=120^{0}C) ^{1}H NMR (DMSO-d$_6$) δ 5.47 (t, 1H J=6Hz), 2.00 (m, 2H), 1.40 (m, 6H), 0.86 (s, 9H).

1-^{t}butyl-1-cycloheptene (8). Purified on a 10'x3/8'' OV-270 preparative column (T=130^{0}C) ^{1}H NMR (acetone-d$_6$) δ 5.64 (t, J=6.8 Hz 1H), 1.95-2.20 (m, 4H), 1.35-1, 55 (m, 6H), 1.00 (s, 9H)

1-^{t}butyl-1-cyclooctene (9). Purified on a 10'x3/8'' OV-270 preparative column (T=140^{0}C) ^{1}H NMR (acetone-d$_6$) δ 5.45 (t, J=8Hz, 1H), 2.10 (m, 4H), 1.47 (m, 8H), 1.04 (s, 9H).

1-Phenyl-1-cycloheptene (10). ^{1}H NMR ($CDCl_3$) δ 7.29 (br. s, 5H), 6.11 (br. m, 2H), 2.60 (br. m, 2H), 2.30 (br. m, 2H) 1.50 (br. m, 6H).

1-Phenyl-1-cyclooctene (11) ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 5H), 5.99 (t, 1H), 2.58 (br. m, 2H), 2.29 (br. m, 2H), 1.54 (br. s, 6H).

Acknowledgments. We thank M. and S. Hourdakis SA, and NATO Grand No 880120 for financial support. We also thank Y. Xidianakis for some experimental work.

References

1. (a) Singlet Oxygen; Wasserman, H. H., Murray, R. W., Eds.; Academic Press: New York, 1979.

2. Wasserman, H. H.; Ives, J. L. *Tetrahedron* (Report #109) 1981, **37**, 1825.

3. Orfanopoulos, M.; Stratakis, M.; Elemes, Y. *Tetrahedron Lett.* 1989, 6903.

4. (a) Clennan, E. L.; Chen, X.; Koola, J. J. *J. Am. Chem. Soc*. 1990, **112**, 5193 (b) Orfanopoulos, M.; Stratakis, M.; Elemes, Y *J. Am. Chem. Soc.* 1990, **112**, 6417 (c) Ensley, H. E.; Carr, R. V. C.; Martin, R. S.; Pierce, T. E. *J. Am. Chem. Soc*. 1980, **102**, 2836. (d) Adam, W.; Griesbeck, A. *Synthesis* 1986, 1050. (e) Orfanopoulos, M.; Foote, C. S. *Tetrahedron Lett.* 1985, 5991 (f) Akasaka, T.; Misawa, Y.; Goto, M.; Ando, W. *Tetrahedron* 1989, **45**, 6657. (g) Clennan, E. L.; Chen, X. *J. Org. Chem*. 1988, **53** , 3124.

5. Schulte-Elte, K. H; Rautenstrach Y. *J. Amer. Chem.* Soc. 1980, **102**, 1738

6. Jefford, C. W; Rimbault, C. G. *Tetrahedron Lett.* 1976, 2479.

7. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem*. 1978, **43**, 2923.

(Received in UK 15 July, 1992)