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INTRAMOLECULAR EPOXIDATION WITH THE H_2O_2/ORTHO ESTER SYSTEM

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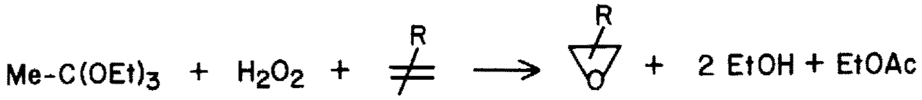
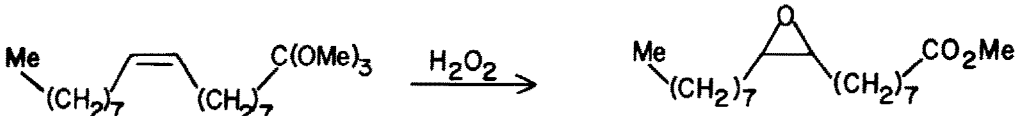
SUMMARY: Intramolecular epoxidation is shown to occur when trimethyl ortho oleate is treated with H_2O_2.

We recently reported[1] that the action of H_2O_2 on ortho esters generates intermediates capable of olefin epoxidation (eq. 1). When the ortho ester[2] of oleic acid 1 is treated with H_2O_2 in rapidly-stirred CH_2Cl_2, a 40% yield of the epoxide 2 can be obtained. On the examination of molecular models it appeared to us that this reaction could proceed in either inter- or intramolecular fashion. Since the latter type of epoxidation is exceedingly rare[3], we undertook competition studies as a means of distinction.

(eq 1)



$$\mathrm{Me\text{-}C(OEt)_3 + H_2O_2 + \overset{R}{\neq} \longrightarrow \overset{R}{\triangledown} + 2\,EtOH + EtOAc}$$



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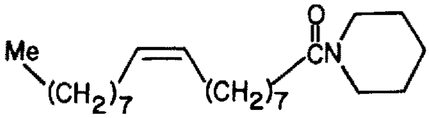

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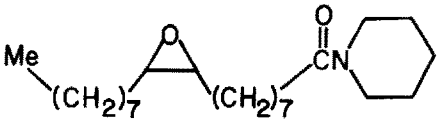

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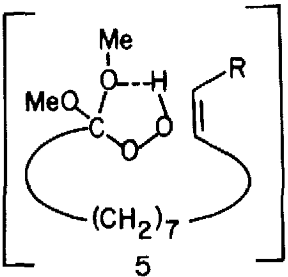
A number of epoxidizing agents failed to show selectivity between methyl oleate and its amide 3 in competition experiments. However, when equimolar amounts of 1 and 3 in THF were treated with H_2O_2, 2 was the major product. Moreover, successive dilution with THF resulted in a greater disparity in the epoxide products.[4] (Table).

Table

$$1 + 3 + H_2O_2 \xrightarrow{THF} 2 + 4$$

Initial Conc. [1] = [3]	Epoxide Ratio [2]/[4]
1 M	7
0.5	12
0.25	27

SCHEME



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$$\xrightarrow{k_{intra}} 2 \qquad \xrightarrow{k_2[1]} 2 \qquad \xrightarrow{k_2'[3]} 4$$

$$\frac{d[2]}{d[4]} = \frac{k_2[1] + k_{intra}}{k_2'[3]} \approx 1 + \frac{k_{intra}}{k_2'[3]}$$

A plot of the epoxide ratio vs. 1/[3] gives a slope of 7 M. Since the competition experiments indicate $k_2 \approx k_2'$, this figure indicates that only at concentrations > 7 M will the intermolecular component compete favorably with intramolecular one (Scheme). Thus it may be concluded that the epoxidation under the present conditions occurs predominately by an intramolecular reaction.

The intermediate, presumably 5 in the case at hand, has only seven connective atoms between the hydroperoxy and olefin functions. Whether intramolecular epoxidation can be accommodated with fewer connective atoms remains to be established.[5]

Acknowledgement - We are grateful to the National Institutes of Health for financial support.

References and Notes

1. J. Rebek and R. McCready, Tetrahedron Lett., 1001 (1979).

2. Prepared from the nitrile by Pinner synthesis: R. H. DeWolf, "Carboxylic Ortho Acid Derivatives", Academic Press, New York, 1970.

3. E. J. Corey, H. Niwa and J. R. Falck, J. Am. Chem. Soc., 101, 1586 (1979).

4. Reaction solutions were treated a limited amount of 90% H_2O_2 at 25°C and allowed to proceed to 5-10% completion (24 h). After the addition of H_2O, epoxide products were determined by HPLC against authentic samples: epoxide 2: T. Findlay, D. Swern and J. Scanlon, J. Am. Chem. Soc., 67, 412 (1945); amide 3 and epoxide 4: E. Skau, R. Mod and F. Magne, Chem. Abstr., 64, 3498c and 3779f (1966), respectively. Methyl oleate and methanol were the only other products detected after work-up.

5. While transition state geometry for these reagents is unknown, peracid epoxidations have been described with structures not dissimilar to 5. For a discussion with leading references see: K. B. Sharpless and T. R. Verhoeven, Aldrichimica Acta., 12, 63 (1979), and ref. 3.

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