A Mechanistic Study of Oleate Autoxidation: Competing Peroxyl H-Atom Abstraction and Rearrangement

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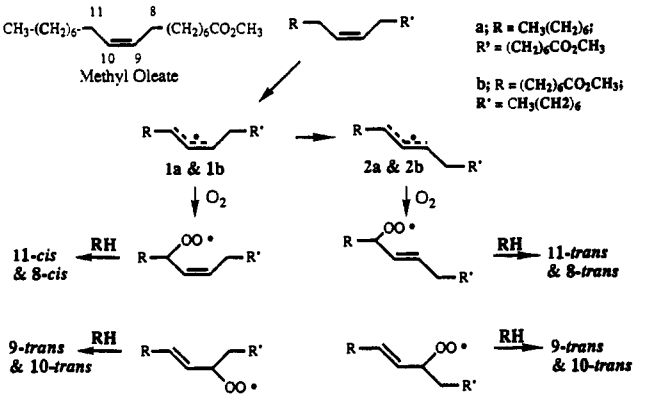
Abstract: The mechanism of methyl oleate autoxidation was investigated. HPLC techniques were developed to analyze the products of autoxidation (hydroperoxides and the corresponding alcohols). The alcohols could be completely resolved by normal-phase chromatography, six products being characterized having oxygen substitution and double position as follows: 11-OOH-*trans*-Δ_{9-10}, 11-OOH-*cis*-Δ_{9-10}, 10-OOH-*trans*-Δ_{8-9}, 9-OOH-*trans*-Δ_{10-11}, 8-OOH-*trans*-Δ_{9-10}, 8-OOH-*cis*-Δ_{9-10} As the hydrogen atom donor concentration of the medium of autoxidation is increased, increased 11-*cis*, 8-*cis*, 9-*trans*, and 10-*trans* hydroperoxides and decreased 11-*trans* and 8-*trans* hydroperoxides were obtained, consistent with a mechanism in which peroxyl H-atom abstraction and [2,3] allylperoxyl rearrangement are in competition. An iterative computer kinetic analysis was developed which modeled the oleate autoxidation mechanism, and rearrangement rate constants were determined. Allylperoxyl radicals undergo rearrangement with different rates depending on the geometry of the allylperoxyl.

Autoxidation, the radical chain reaction of molecular oxygen and organic substrates, results in the formation of hydroperoxides.[1] This reaction has been of interest for many years since it leads to the degradation of natural and synthetic organic materials. Autoxidation of fatty acids and esters in foods leads to rancidity and spoilage, and *in vivo* autoxidation of these same compounds has been suggested in diverse pathologies.[2] Studies of the autoxidation of the methyl ester of oleic acid ((*Z*)-9-octadecenoic acid) date back to 1943 in the work of Farmer and Sutton.[3] These workers suggested that oleate autoxidation products contain a mixture of C_8 and C_{11} oleate hydroperoxides in which the hydroperoxy group is attached to an allylic carbon atom. Later, a free radical chain mechanism was proposed,[4] and it was postulated that there is equal probability for the hydroperoxy group to appear at positions 8, 9, 10, and 11 and for the olefin to remain at the original position (Δ_{9-10}) or appear at the two adjacent C–C bonds (Δ_{8-9} and Δ_{10-11}).

During the period of time 1977–1984, powerful analytical methods such as gas chromatography/mass spectrometry and NMR spectroscopy were applied to the problem of fatty acid autoxidation. By the use of these techniques, Frankel *et al.* reported that autoxidation of methyl oleate occurs symmetrically about the double bond.[5] After autoxidation of methyl oleate at 25 °C, yields of the hydroperoxides were determined by a sequence of thin-layer chromatography, mass spectrometry, and carbon NMR. By this tedious protocol, product distribution was determined to be as follows: 11-*trans*, 12.9%; 11-*cis*, 13.7%; 10-*trans*, 21.7%; 10-*cis*, 1.1%; 9-*trans*, 23.1%; 9-*cis*, 1.1%; 8-*trans*, 12.3%; 8-*cis*, 14.1%.

Scheme 1. Proposed Methyl Oleate Autoxidation Mechanism (1984)



These results were explained upon the basis of the mechanism in Scheme 1. Hydrogen atom abstraction from the oleate 11 position was proposed to lead to delocalized radical **1a**, which isomerizes, particularly at elevated temperatures, to give the isomeric allyl radical **2a**. Subsequent reaction of the allyl radical **1a** with molecular oxygen was suggested to give the 11-*cis* and 9-*trans* oleate hydroperoxides, and reaction of **2a** was proposed to generate the 11-*trans* and 9-*trans* oleate hydroperoxides. According to this mechanism, hydrogen atom abstraction from the 8 position would give delocalized radical **1b**, which would isomerize to allyl radical **2b**. Addition of molecular oxygen to **1b** and **2b** generates the 8-*cis*, 8-*trans*, and 10-*trans* oleate hydroperoxides.

It would appear that the mechanism shown in Scheme 1 is not correct since, under normal oxygen pressures, the allyl radical is trapped with molecular oxygen at or near the diffusion controlled rate, making the allylperoxyl radical the chain carrying radical.[6,7] Allyl radical isomerization[8] thus seems an unlikely competitor with reaction of allyl with oxygen. Indeed, the oleate products

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(1) For reviews on autoxidation, see: (a) Porter, N. A. *Acc. Chem. Res.* **1986**, *19*, 262 (b) Huyser, E. S. *Free Radical Chain Reactions*; Wiley-Interscience: New York, 1970; pp 306–312. (c) Mayo *Acc. Chem. Res.* **1968**, *1*, 193. (c) Porter, N. A. *Membrane Lipid Oxidation*; Vigo-Pelfrey, C., Ed.; CRC Press: Boca Raton, FL.

(2) (a) Frankel, E. N. *Autoxidation in Food and Biological Systems*; Simic, M., Karel, M., Eds.; Plenum: New York, 1980; pp 141–183. (b) Niki, E. *Organic Peroxides*; Ando, W., Ed.; John Wiley & Sons: New York, 1992; pp 763–787.

(3) Farmer, E. H.; Sutton, D. A. *J. Chem. Soc.* **1943**, 119.

(4) (a) Farmer, E. H.; Koch, H. P.; Sutton, D. A. *J. Chem. Soc.* **1949**, 541. (b) Bickford, W. G.; Fisher, G. S.; Kyame, L.; Swift, C. E. *J. Am. Oil Chem. Soc.* **1948**, *24*, 254. (c) Ross, J.; Gebhart, A. I.; Gerecht, J. F. *J. Am. Chem. Soc.* **1946**, *68*, 1373.

(5) (a) Frankel, E. N.; Neff, W. E.; Rohwedder, W. K. *Lipids* **1977**, 901. (b) Frankel, E. N.; Garwood, R. F.; Khambay, B. P.; Moss, G. P.; Weedon, B. C. *J. Chem. Soc., Perkin Trans 1* **1984**, 2233.

(6) Howard, J. A. *Advances in Free Radical Chemistry*, Academic: New York, 1972; Vol. IV, pp 75–138.

(7) We have previously reported in diene autoxidation that dienyl peroxyls, rather the pentadienyl radicals, play a dominant role in determining product distribution, see ref 1a.

(8) Korth, H.-G.; Heinrich, T.; Sustmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4483.

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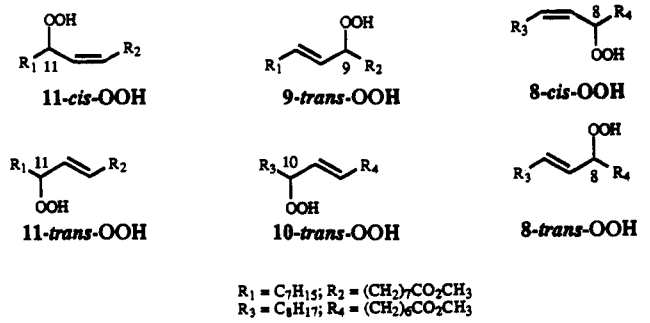


Figure 1. Methyl oleate hydroperoxides formed by autoxidation.

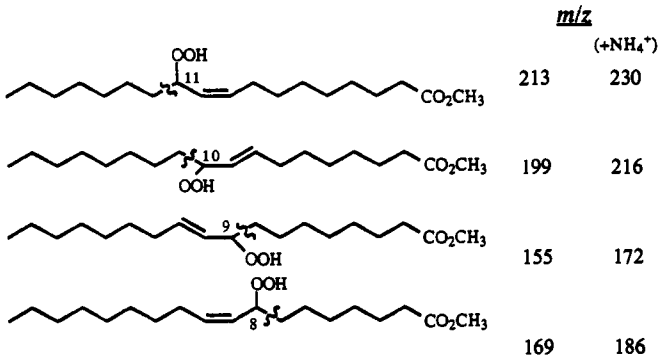


Figure 2. Diagnostic fragmentation ions for oleate hydroperoxides (conditions: CIMS with CH_4/NH_3 (96:4) as the reagent gas).

could be accounted for upon the basis of the anticipated chemistry of intermediate peroxyl radicals,[1a] and we therefore undertook an investigation of oleate autoxidation to address this point. We report here the results of the study.

Results and Discussion

HPLC Analysis of Oleate Hydroperoxides. Methyl oleate was autoxidized in air with 5 mol % of the free radical initiator di-*tert*-butyl hyponitrite (DTBN) at 30 °C. After 4 h, the reaction was quenched with the radical inhibitor tri-*tert* butylphenol (TTBP). The extent of oxidation did not exceed 5% in the cases reported here. Six regioisomeric hydroperoxides that are partially separated by HPLC (UV detection) (Figure 1) are formed in methyl oleate autoxidation. The hydroperoxides were characterized by HPLC–CIMS (chemical ionization mass spectrometry). By this technique, the hydroperoxides could be analyzed directly, avoiding tedious derivatization steps.[6a] The regioisomeric oleate hydroperoxides were identified by diagnostic fragmentation ions that occur *via* scission α to the hydroperoxy group with loss of water (Figure 2). The technique demonstrated sensitivity at microgram to nanogram quantities of hydroperoxide. A typical HPLC chromatogram is presented in the supplementary material.

Chromatography was carried out on 5-μm silica with 0.6% isopropyl alcohol in hexane solvent. The site of hydroperoxy group substitution on the chain was identified by the diagnostic mass spectral fragmentation ions (Figure 2), and olefin geometry was readily assigned by ^{1}H NMR (vinylic vicinal coupling constants J_{trans} = 15.4 Hz and J_{cis} = 11.4 Hz).

The first and second eluting HPLC fractions were identified as the 11-*cis* and 11-*trans* oleate hydroperoxides. The third peak contains both the 10-*trans* and 9-*trans* compounds, and the fifth and sixth eluting fractions were identified as the 8-oleate hydroperoxides, with the 8-*cis* compound eluting before the 8-*trans*. Separation of the hydroperoxides is therefore not complete since the 9- and 10-*trans* compounds coelute on silica.

The methyl oleate used in these experiments contained <1% methyl linoleate impurity. Nevertheless, linoleate hydroperoxides were generated in the autoxidation reactions, and they coelute with the oleate hydroperoxides. Linoleate is substantially more reactive than oleate; thus, linoleate hydroperoxides comprise an even greater contaminant of the oxidation mixture than does linoleate in the starting oleate. Moreover, due to the excellent UV chromophore of the linoleate conjugated diene hydroperoxides, these products create a severe problem when UV–HPLC detection is used, particularly in the analysis of the 8-substituted hydroperoxides. Since methyl linoleate is more oxidizable than oleate, it is gradually removed from oleate through successive autoxidation and quantitative data on oleate products were obtained on methyl oleate that had been recycled through autoxidation more than five times.

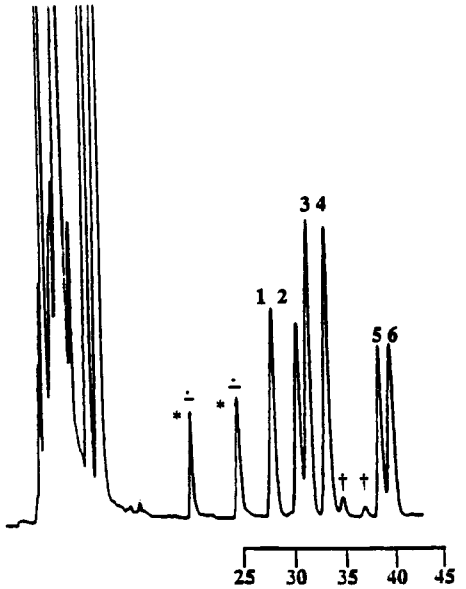


Figure 3. HPLC chromatogram of oleate alcohols. Two 5-μm silica colums are used with 0.6% isopropyl alcohol in hexane solvent and UV detection at 205 nm. Assignments are as follows: **1**, 11-*trans*; **2**, 11-*cis*; **3**, 10-*trans*; **4**, 9-*trans*; **5**, 8-*trans*; **6**, 8-*cis*. Peaks indicated with * are unassigned and represent minor impurities that have relatively large absorbances at 205 nm since sufficient material could not be isolated for characterization from these fractions. Peaks indicated with † are tentatively assigned as 10-*cis* and 9-*cis*.

HPLC Analysis of Oleate Alcohols. Since the oleate hydroperoxide mixture was incompletely resolved by HPLC, the corresponding alcohols were also analyzed. Thus, the hydroperoxide mixture was reduced with 1.5 equiv of PBu_3 in benzene at 0 °C and the reaction mixture was analyzed by analytical normal-phase HPLC–UV. The oleate alcohols were found to separate better than the oleate hydroperoxides, but chemical ionization mass spectrometry failed to produce diagnostic fragmentation ions for the regioisomeric oleate alcohols. Therefore, the oleate alcohols were isolated by HPLC (UV detection) and were reanalyzed by GC–EIMS (electron ionization mass spectrometry). Mass spectrometry using electron ionization was successful in producing diagnostic fragmentation ions, and the regioisomeric oleate alcohols were readily identified by this and by ^{1}H NMR. All of the oleate alcohols separate by silica HPLC, the elution order being 11-*trans*, 11-*cis*, 10-*trans*, 9-*trans*, 10-*cis*, 9-*cis*, 8-*trans*, and 8-*cis*. We find, as did Frankel,[5b] that the 10-*cis* and 9-*cis* products are minor components of the autoxidation mixture, and our assignment here for these two compounds is tentative. A typical HPLC chromatogram of the oleate alcohols is presented in Figure 3. All analyses carried out on the oleate alcohols show that the 11- and 8-*cis* products are formed to extents comparable to those of the 11- and 8-*trans* products and the 9- and 10-*trans* compounds. One expects this upon the basis of the pseudosymmetry of the system. The same symmetry pattern was observed in analyses of hydroperoxides as was seen for alcohols. In most cases reported here, for convenience, the hydroperoxides were analyzed directly and it was assumed that

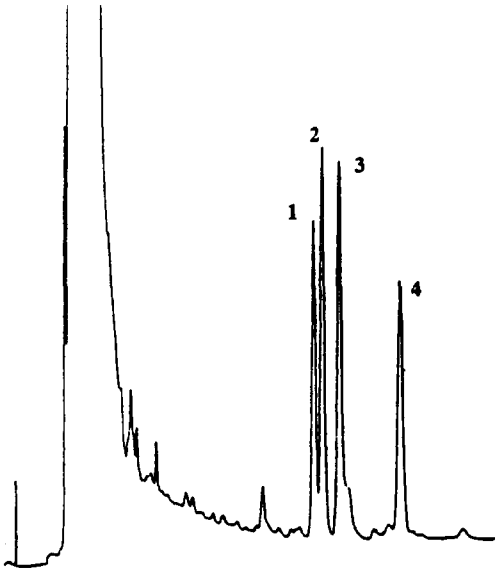


Figure 4. HPLC chromatogram of oleate alcohols formed in *t*-BuOOH cooxidation. HPLC analysis as in Figure 3: **1**, 11-*cis*; **2**, 10-*trans*; **3**, 9-*trans*; **4**, 8-*cis*.

the HPLC fraction consisting of the 9- and 10-*trans* hydroperoxides was an equal mixture of these two compounds. In every case checked by reduction and analysis of the corresponding alcohols, this proved to be the case.

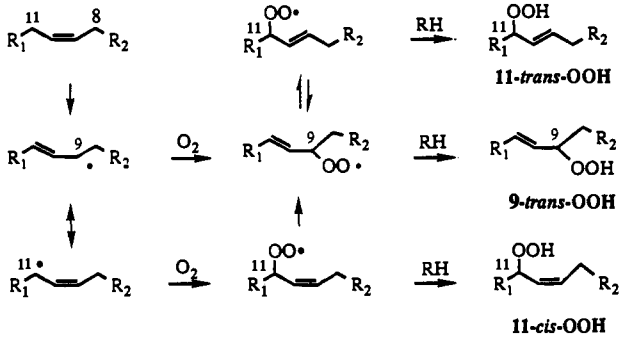
Hydroperoxide Loaded Methyl Oleate Autoxidation. Courtneidge and Bush demonstrated that *tert*-butyl hydroperoxide loaded autoxidation reactions are successful in suppressing rearrangements of allylperoxyls, and we have approached oleate autoxidation using cooxidation as a tool for the study of mechanism.[9] Hydrogen atoms exchange rapidly between peroxyl radicals, and autoxidation of oleate in the presence of excess *tert*-butyl hydroperoxide transfers the chain from oleate peroxyls to *tert*-butyl peroxyls (eq 1).[10]

$$\mathrm{ROO^{\bullet} + (CH_3)_3COOH \xrightarrow{k_p = 2500\ M^{-1}\,s^{-1},\ 30\ ^{\circ}C} ROOH + (CH_3)_3COO^{\bullet}} \quad (1)$$

Cooxidation reactions were performed using methyl oleate and *tert*-butyl hydroperoxide at 30 °C with 5 mol % DTBN initiator. Aliquots were quenched with TTBP and put under vacuum to remove excess *tert*-butyl hydroperoxide. Under conditions of 4.0 M *tert*-butyl hydroperoxide/0.6 M oleate, only the 11-*cis*, 9-*trans*, 10-*trans*, and 8-*cis* oleate hydroperoxides are produced, and no 11- or 8-*trans* hydroperoxides are obtained. The ratio of the 11-*cis*:9-*trans* products is 1:1.2 as is that of the 8-*cis*:10-*trans* compounds. The hydroperoxide loaded oleate autoxidation mixture was reduced under conditions of PBu_3 in benzene at 0 °C. Analysis of the oleate alcohols by HPLC–UV also showed a ratio of 11-*cis*:9-*trans* and 8-*cis*:10-*trans* compounds of 1:1.2 (Figure 4).

The acceleration effect of *tert*-butyl hydroperoxide on oleate autoxidation was demonstrated from the observation that enough oleate hydroperoxide was produced after a reaction time of 15 min to analyze by HPLC–UV. In the absence of *tert*-butyl hydroperoxide, the autoxidation reaction runs approximately 6 h before enough hydroperoxide is produced to analyze by HPLC–UV. The increase in the rate of oxidation is explained by a reduction in the termination rate of chain carrying *tert*-butylperoxyl radicals compared to oleate peroxyls.[11]

Scheme 2. Proposed Mechanism for Formation of the 11-*cis*, 9-*trans* and 11-*trans* Oleate Hydroperoxides[a]



[a] Similar chemistry occurs when hydrogen atom is abstracted at C-8.

These results from the cooxidation of oleate and *tert*-butyl hydroperoxide support the mechanism of oleate autoxidation proposed in Scheme 2. Due to the *pseudo*-symmetry in oleate, only one-half of the hydroperoxide products are presented in the scheme (those obtained from hydrogen atom abstraction from C-11). Indeed, the 11-*trans*-OOH, the 9-*trans*-OOH, and the 11-*cis*-OOH hydroperoxides could be analyzed directly without reduction to the alcohols and autoxidations could be monitored conveniently over time in this way.

According to Scheme 2, the first-formed carbon radical, shown in the scheme as two resonance contributors, has Δ_{9-10} *cisoid* and Δ_{10-11} *transoid* geometries. Addition of oxygen to this radical gives the 11-*cis* and 9-*trans* peroxyl radicals, and if these peroxyls abstract hydrogen, the 11-*cis* and 9-*trans* hydroperoxides result. Similar chemistry after H-atom abstraction at C-8 provides the 8-*cis* and 10-*trans* hydroperoxides. Indeed, these four hydroperoxides are the only products formed in the hydroperoxide loaded autoxidations. Hydroperoxides are excellent hydrogen atom donors, and we suggest that, in the presence of hydroperoxide, the product mixture is a "kinetically controlled" one. The first-formed peroxyls are directed to the kinetic hydroperoxides under these conditions.

By determining the kinetic limit in oleate autoxidation, the partition of oxygen to the ends of the oleate allyl radical is obtained. The ratio of the 11-*cis*: 9-*trans* of 1:1.2 gives evidence that 45% of the oxygen adds to the 11 position of the radical to generate the 11-*cis* allylperoxyl while 55% of the oxygen adds to the 9 position to generate the 9-*trans* allylperoxyl. The partition of oxygen reveals that addition at the *cisoid* terminus of the allyl radical occurs more readily than addition to the *transoid* terminus of the allyl radical.

The allyl radicals derived from methyl oleate and methyl elaidate have been investigated by EPR spectroscopy (Figure 5).[12] For the *cis* allyl radical, the hyperfine coupling constant for the proton α to the *cisoid* allyl terminus (c) is larger than the coupling constant for the proton α to the *transoid* terminus (a). This suggests that the *cisoid* end of the allyl radical has higher spin density than the *transoid* end. Thus, the kinetic limit results are consistent with the argument that molecular oxygen displays a preference for addition to the allyl terminus with higher spin density (*i.e.* the *cisoid* terminus). For the *trans* allyl radical, hyperfine coupling constants for protons α to the *transoid* termini

(9) (a) Courtneidge, J. L.; Bush, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1531. (b) Courtneidge, J. L.; Bush, M.; Loh, L.-S. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1539. (c) Courtneidge, J. L. *J. Chem. Soc., Chem. Commun.* **1992**, 1270.

(10) (a) Howard, J. A.; Schwalm, W. J.; Ingold, K. U. *Adv. Chem. Ser.* **1968**, *75*, 6. (b) For differences in reactivities of primary, secondary, and tertiary peroxyl radicals, see: Middleton, B. S.; Ingold, K. U. *Can. J. Chem.* **1967**, *45*, 191. (c) Chenier, J. H.; Howard, J. A. *Can. J. Chem.* **1975**, *53*, 623. (d) Howard, J. A. *Is. J. Chem.* **1984**, *24*, 33.

(11) (a) Thomas, J. R.; Tolman, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 2079. (b) Thomas, J. R. *J. Am. Chem. Soc.* **1962**, *84*, 4872.

(12) Bascetta, E.; Gunstone, F. D.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* **1983**, 603.

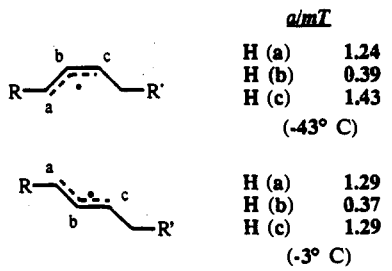
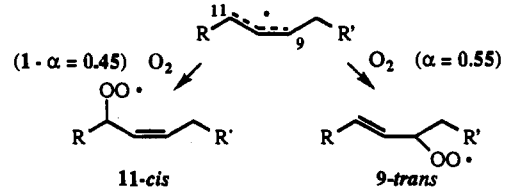


Figure 5. EPR parameters of substituted allyl radicals.

Scheme 3. Partition of Oxygen to the Oleate Radical

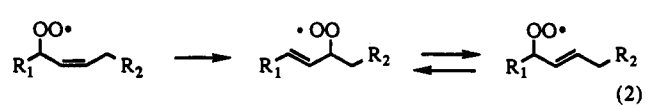


(a and c) are identical, indicating that both *transoid* ends have equivalent spin density.

The kinetic products of oleate autoxidation are formed by trapping the first-formed peroxyl radicals by hydrogen atom transfer. Competing with hydrogen atom abstraction is rearrangement of the allylperoxyls, as shown in Scheme 2, and this rearrangement leads to the 11-*trans* and 8-*trans* hydroperoxides formed in oleate autoxidations. These two hydroperoxides are formed in substantial amount if autoxidation is carried out in the absence of *tert*-butyl hydroperoxide. The analysis of alcohols shown in Figure 3 is a graphic demonstration of this fact, the product distribution for this autoxidation being as follows (on the basis of HPLC integrated peak areas): 11-*trans*, 16%; 11-*cis*, 13%; 10-*trans*, 21%; 10-*cis*, 1%; 9-*trans*, 21%; 9-*cis*, 1%; 8-*trans*, 16%; 8-*cis*, 13%. In the presence of *tert*-butyl hydroperoxide, the 11-*trans*, 10-*cis*, 9-*cis*, and 8-*trans* hydroperoxides are not formed in detectable amounts.

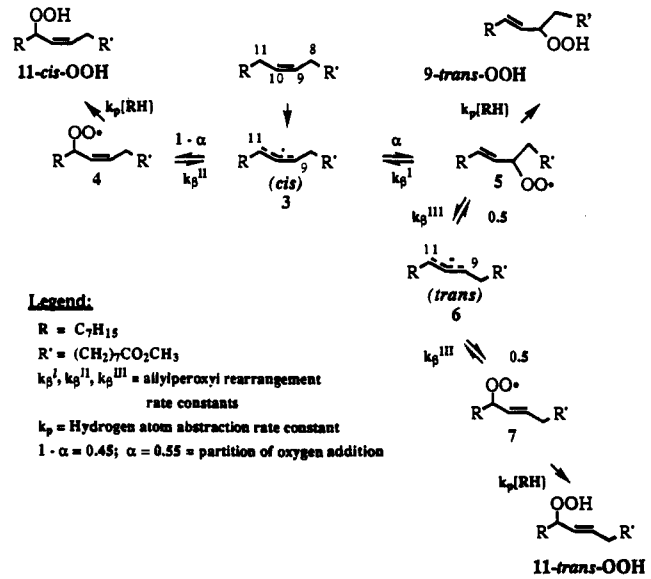
The rearrangement of allylperoxyls has been studied extensively over the years, and the mechanism of this process is still open to debate. A detailed study of the rearrangement is presented in the following article in this issue, but the precise mechanism of the peroxyl rearrangement is not critical to an understanding of product distribution in oleate autoxidation. We assume in subsequent discussions that the rearrangement proceeds by a β-fragmentation–oxygen readdition mechanism as outlined in Scheme 4 based upon work from our laboratories reported elsewhere. The rate of rearrangement is essentially equal to the rate of fragmentation since oxygen addition occurs at or near diffusion control. We note that our oleate autoxidation mechanism requires only that rearrangement compete with hydrogen atom abstraction. Thus, under conditions where good hydrogen atom donors are present, the first-formed peroxyls are trapped and no rearrangement occurs while conditions in which the H-atom donating ability of the medium is low allow the rearrangement to proceed and the "thermodynamic products" are formed.

Previous studies of the rearrangement have shown that *cis* or *trans* allylperoxyls rearrange to give *trans* allyl products but *trans* allylperoxyls do not rearrange to *cis* peroxyls to any significant extent (eq 2). With this as a guide in oleate autoxidation, the 11-*cis* peroxyl rearranges to the 9-*trans* peroxyl radical and the 9-*trans* and 11-*trans* peroxyls are also connected by this rearrangement pathway.



(2)

Scheme 4. Kinetic Scheme for Oleate Autoxidation



Oleate Products vs Medium H-Atom Availability. Additional experiments were carried out to provide further evidence for the mechanism and to obtain rearrangement rate constants. We assume, upon the basis of studies reported in the accompanying article, that rearrangement proceeds by peroxyl fragmentation–oxygen readdition, and three fragmentation rate constants k_β^{I}, k_β^{II} and k_β^{III} are required in the analysis (Scheme 4).[13] Addition of oxygen to either end of the *cis* allyl radical **3** generates the 11-*cis* allylperoxyl **4** or the 9-*trans* allylperoxyl **5**. The partition of oxygen was determined by our *tert*-butyl hydroperoxide loaded autoxidations to be $1 - \alpha = 0.45$ and $\alpha = 0.55$. In a reverse reaction, the 11-*cis* allylperoxyl **4** undergoes β-fragmentation to regenerate the *cis* allyl radical **3** with a rate constant k_β^{II} and the 9-*trans* allylperoxyl radical **5** undergoes β-fragmentation with a rate constant k_β^{I} to regenerate the *cis* allyl radical **3**. The 9-*trans* allylperoxyl radical **5** could also undergo fragmentation to generate the *trans* allyl radical **6**. This new *transoid* allyl radical can now add oxygen at either end to give peroxyl radicals. On the basis of EPR results[12] and 11-*trans* allylperoxyl rearrangement results, there is assumed to be equivalent addition of oxygen to both the 9 and 11 positions of the *trans* allyl radical **6**, giving the 9-*trans* allylperoxyl radical **5** and the 11-*trans* allylperoxyl radical **7**. β-Fragmentation of the 9-*trans* allylperoxyl radical **5** or the 11-*trans* allylperoxyl radical **7** occurs with a rate constant denoted k_β^{III}.

If the mechanism in Scheme 4 is correct, increasing amounts of "kinetic" 11-*cis*-OOH and 9-*trans*-OOH hydroperoxides and decreasing amounts of "thermodynamic" 11-*trans* hydroperoxide will form as the concentration of hydrogen atom donors in the medium is increased. We therefore sought conditions where the distribution of oleate products could be monitored as the H-atom donating ability of the medium of oxidation was changed in a systematic way. Our first experiments to explore this possiblility used *tert*-butyl hydroperoxide as a cooxidant at concentrations less than 1.0 M. At low *tert*-butyl hydroperoxide concentration (*i.e.*, 0.025–0.2 M), the oleate product distribution changes with time. In a typical cooxidation, as time progresses, the relative amounts of the 11- and 8-*trans* hydroperoxides increase and the amounts of the 11- and 8-*cis* and the 9- and 11-*trans* hydroperoxides slightly decrease. This makes the use of a *tert*-butyl hydroperoxide cooxidant inappropriate at concentrations less than

(13) (a) Reference 1c. (b) Mills, K. A.; Caldwell, S. E.; Dubay, G. R.; Porter, N. A. *J. Am. Chem. Soc.* **1992**, *114*, 9690. (c) Boyd, S. L.; Boyd, R. J.; Barclay, R. C.; Porter, N. A. *J. Am. Chem. Soc.* **1993**, *115*, 687. (d) Porter, N. A.; Wujek, D. G. *J. Am. Chem. Soc.* **1984**, *106*, 2626. (e) Porter, N. A.; Mills, K. A.; Caldwell, S. E.; Dubay, G. R. *J. Am. Chem. Soc.*, following article in this issue.

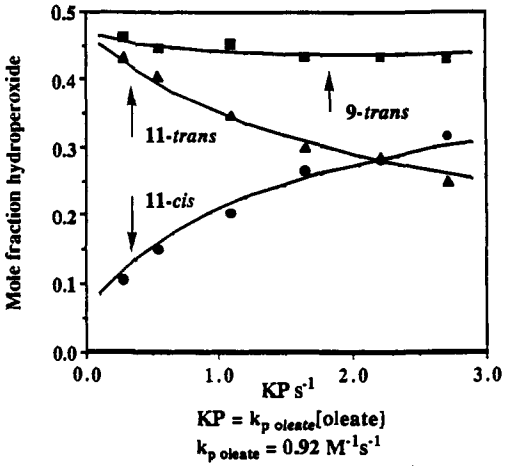


Figure 6. Mole franction of hydroperoxide vs KP, the hydrogen atom availability at 30 °C, [oleate] = 0.3–3.0 M. Similar chemistry occurs for the 8-*cis*, 10-*trans*, and 8-*trans* products. Experimental values are indicated as follows: triangles, 11-OOH-*trans*-Δ_{9-10}; circles, 11-OOH-*cis*-Δ_{9-10}; squares, 9-OOH-*trans*-Δ_{10-11}. Solid lines represent calculated values of products assuming the mechanism shown in Scheme 4 and the values as follows: $k\beta^{I}$ = 0.5 s^{-1}, $k\beta^{II}$ = 3 s^{-1}, $k\beta^{III}$ = 8 s^{-1}.

1.0 M if quantitative information is required since the product distribution changes over the course of an autoxidation in these experiments.

Oleate autoxidation reactions were performed in the absence of *tert*-butyl hydroperoxide at varying concentrations of oleate. Under these conditions of autoxidation, the distribution of oleate autoxidation products does not change significantly with time over 15 h and typically, by 4 h, enough hydroperoxide is generated to analyze by HPLC–UV. If autoxidations are carried out on solutions with starting oleate in the concentration range of 0.3–3.0 M, hydroperoxide product distribution is dependent on the concentration of starting oleate. The results of these studies are presented in Figure 6. At high starting oleate concentration, more of the "kinetic" products are formed, and at low starting oleate concentration, the product mixture contains more "thermodynamic" products. This reveals that hydrogen atom abstraction from oleate by the allylperoxyl radical leading to the "kinetic" 11-*cis* and 9-*trans* hydroperoxides successfully competes with rearrangement of the allylperoxyl radical in this range of concentration. The propagation rate constant for H-atom transfer in oleate autoxidation, k_p, has been reported to be 0.92 M^{-1} s^{-1}.[15a] Therefore, $k\beta^{I}$, $k\beta^{II}$ and $k\beta^{III}$ must be on the order of 0–3 s^{-1}, since the rate of H atom transfer from oleate to oleate peroxyls is (0.92 M^{-1} s^{-1})· [ROO·][oleate] and $k\beta \sim k_p$[oleate]. Indeed, any hydrogen atom donor should similarly affect the distribution of products and kinetic *vs.* thermodynamic control should depend on the overall H-atom donating potential of the medium, defined by KP = Σk_p[H-donor] for all H-donors present.

Computer Model for Oleate Autoxidation. A straightforward iterative kinetic analysis was developed to model the oleate autoxidation mechanism outlined in Scheme 4. By employing this kinetic analysis, the β-fragmentation (or rearrangement) rate constants for the allylperoxyl radicals can be determined. This approach for oleate, based on a similar previous analysis of linoleate autoxidation, allowed for the product distributions of the 11-*cis*, 9-*trans*, and 11-*trans* hydroperoxides to be calculated as a function of the hydrogen atom donating availability of the medium for estimated values of $k\beta^{I}$, $k\beta^{II}$, and $k\beta^{III}$.[13d,14]

The program begins with 100 units of the *cis* allyl radical **3**, and partitions it between 1 - α and α to **4** and **5**. The 11-*cis* allylperoxyl radical **4** (100(1 - α)) can then be trapped by a hydrogen atom donor with a rate proportional to KP to yield 11-*cis* hydroperoxide or undergo β-fragmentation back to **3** with the rate constant $k\beta^{II}$. Similarly, the 9-*trans* allylperoxyl radical **5** (100α) is partitioned between the *cis* allyl radical **3**, the 9-*trans* hydroperoxide product, and the *trans* allyl radical **6** according to rate constants $k\beta^{I}$, KP, and $k\beta^{III}$, respectively. The *trans* allyl radical **6** (100$\alpha k\beta^{III}$) is partitioned equally between **5** and **7**. The 11-*trans* allylperoxyl radical **7** (0.5(100$\alpha k\beta^{III}$)) is partitioned between the *trans* allyl radical **6** and 11-*trans* hydroperoxide according to the rate constants $k\beta^{III}$ and KP, respectively. Thus each radical in the cycle, as generated, is partitioned to neighboring radicals or products. The cycle is continued until the sum of the hydroperoxide products is greater than 99.9 units.

The following assumptions are made in the simulation: (a) the *cis* allyl radical **3** is converted to neighboring 11-*cis* **4** and 9-*trans* **5** allylperoxyl radicals by the factors 1 - α and α where α = 0.55; (b) the *trans* allyl radical **6** is partitioned equally to the 9-*trans* **5** and the 11-*trans* **7** allylperoxyl radicals; (c) allylperoxyl radicals are converted to products 11-*cis*, 9-*trans*, and 11-*trans*-OOH with the rate = k_p[ROO·][R–H] = (0.92 M^{-1} s^{-1})[ROO·][oleate]; (d) trial parameters used in the computation are $k\beta^{I}$, $k\beta^{II}$, and $k\beta^{III}$. A listing of the program used to perform the iterative kinetic analysis is presented in the supplementary material. Subsequent to our analysis, a scheme including exchange of hydrogen in product hydroperoxides was analyzed by Professor Cheves Walling.[15] Inclusion of this exhange process in the analysis gives the same rate constants we determined if exchange is rapid and if all peroxyls abstract hydrogen at the same rate.

The best agreement between the experimental and calculated product ratios is obtained with rate constants of $k\beta^{I}$ = 0.5 ± 0.5 s^{-1}, $k\beta^{II}$ = 3 ± 0.5 s^{-1}, and $k\beta^{III}$ = 8 ± 2 s^{-1} (Scheme 4). The agreement is excellent as indicated by the plot of the mole fraction of hydroperoxide *vs* KP in Figure 6 for the experimental and calculated values (solid lines). In all cases, if values are selected that deviate by more than ±0.5 of the rate constants $k\beta^{I}$ and $k\beta^{II}$ and ±2 of the rate constant $k\beta^{III}$, the fit between the experimental and calculated data is noticeably worse. (It should be noted that the best fit was ascertained by comparing plots within the range KP = 0.1–2.9 s^{-1} rather than comparing the experimental and calculated product ratios for a single value of KP.) Experimentally determined product distributions and computer generated values are presented in tabular form in the supplementary material.

We note that Courtneidge has estimated the rate constant for the [2,3] allylperoxyl rearrangement.[9] In this pioneering study, a tertiary allylic hydroperoxide was used to generate the corresponding allylperoxyl that was constructed such that a 5-*exo* peroxyl cyclization is in competition with the allylperoxyl rearrangement. Applying the "radical clock" concept, Courtneidge's results along with our estimate for 5-*exo* peroxyl radical closure of approximately 8 × 10^2 s^{-1} at 30 °C, suggest that the 6-*exo* cyclization and the [2,3] allylperoxyl rearrangement have rate constants of approximately 10 s^{-1} at 30 °C. There is excellent agreement between Courtneidge's rate constants and the rate constants reported here, and the analyses rely on completely different rate constant standards.

The β-fragmentation rate constants are shown in Scheme 5 with the allylperoxyl radicals represented as Newman projections. Three different fragmentation reactions occur in the oleate system: (1) fragmentation of the 9-*trans* allylperoxyl radical to generate the *cisoid* allyl radical ($k\beta^{I}$); (2) fragmentation of the 11-*cis* allylperoxyl radical to generate a *cisoid* allyl radical ($k\beta^{II}$); (3) fragmentation of the 9-*trans* allylperoxyl radical to generate the *transoid* allyl radical ($k\beta^{III}$).

β-Fragmentation of the 9-*trans* allylperoxyl radical to generate a *cisoid* allyl radical occurs 6 times slower than β-fragmentation of the 11-*cis* allylperoxyl radical to generate a *cisoid* allyl radical. β-Fragmentation of the 9-*trans* allylperoxyl radical leading to a

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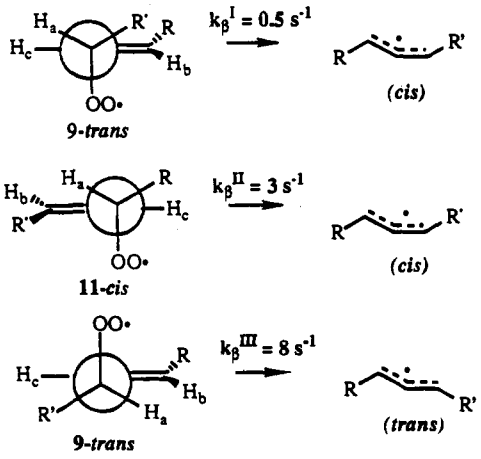
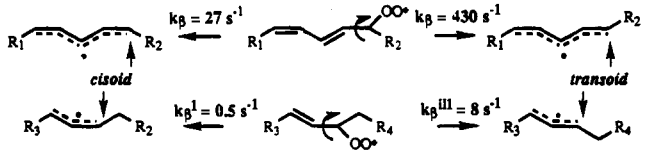
(15) Walling, C. Personal communication. We thank Professor Walling for helpful discussions.

Scheme 5. β-Fragmentation Rate Constants for the Allylperoxyl Rearrangement at 30 °C



R = C_7H_{15}; R' = $(CH_2)_7CO_2CH_3$

Scheme 6. Comparison of β-Fragmentation in Oleate vs Linoleate



transoid allyl radical is 16 times faster than β-fragmentation to a *cisoid* allyl radical.

In the linoleate system studied earlier,[13d] fragmentation to a *transoid* terminus was also found to occur 16 times faster than fragmentation to the *cisoid* terminus (Scheme 6). Substantial allylic 1–3 strain apparently attends fragmentation processes leading to *cisoid* allyls as the sp^3 hybridized carbon bearing the peroxyl oxygen is converted to an sp^2 hybridized atom of the delocalized carbon radical. We suggest that this allylic strain[16] accounts for the rate differences observed for the different fragmentation processes.

Conclusions. Product distribution in oleate autoxidation, as well as for autoxidation of other simple olefins, can be understood upon the basis of competition of H-atom abstraction and fragmentation of intermediate peroxyls. The Frankel mechanism (Scheme 1) involving carbon radical isomerization is not consistent with the observation that product distribution is dependent on the concentration of H-atom donors present during autoxidation. A computer program based upon the mechanism presented in the scheme accurately simulates the kinetics of methyl oleate autoxidation. This allows the determination of the rate constants of β-fragmentation for allylperoxyl radicals as well as the prediction of the oleate hydroperoxide product distribution. The rate constants for β-fragmentation of the oleate allylperoxyl radicals (k_β = 0.5–8 s^{-1}) were found to be on the same order as that for oleate hydrogen atom abstraction of k_p = 0.92 $M^{-1}\ s^{-1}$. In comparing oleate and linoleate systems, β-fragmentation of the oleate allylperoxyl radical was found to be some 70 times slower than β-fragmentation of the linoleate dienylperoxyl radical, and we note that H-atom transfer from oleate to a peroxyl is some 60 times slower than H-atom transfer to a peroxyl from linoleate.[17] This is, perhaps, not surprising since the rate constants for H-atom transfer and peroxyl fragmentation both depend on the stability of the carbon radical generated in the process. For linoleate, both processes generate a pentadienyl radical stabilized by delocalization over five carbons, while for oleate, the corresponding radical generated in both processes is the less stabilized allyl radical.[11]

We also suggest, based upon this study, that the rate constant for oxygen addition to the allyl radical is dependent on the geometry of the allyl terminus. The picture that emerges from the studies is that a *cisoid* center is kinetically more labile toward reaction with oxygen than is a *transoid* center.

Experimental Section

Materials. All autoxidations were run under an atmosphere of air. Methyl oleate (>99%) was purchased from Nu Chek Prep (Elysian, MN). Methyl linoleate (>99%) and tri-*n*-butyl phosphine were purchased from Sigma Chemical Co. (St. Louis, MO). All other reagents were purchased from Aldrich Chemical Co. (Milwaukee, WI). *tert*-Butyl hydroperoxide was purchased as a 5.51 M solution in 2,2,4-trimethylpentane. Sep-pak plus silica cartridges were purchased from Millipore Waters Chromatography (Milford, MA). TLC plates could be visualized for hydroperoxides using a spray of 1.5 g *N*,-*N*'-dimethyl-*p*-phenylenediamine dihydrochloride in 1 mL of HOAc/ 25 mL of H_2O/ 125 mL of CH_3OH. Hydroperoxides gave a pink spot after charring.

Methods. All HPLC was carried out using dual 5-μm silica columns (4.6 mm × 25 cm). All gas chromatography in this section was performed using a 15-m × 0.32-mm i.d. SPB-5 column at 5 psi. The temperature program was 1 min at 220 °C to 250 °C at 5 °C/min to 275 °C at 25 °C/min.

Oleate Autoxidation Procedure. Methyl oleate was purified of any oxidized contaminant prior to reaction *via* flash column chromatography using 15% EtOAc/hexane as the eluant. Typically, 10 g of methyl oleate was purified. The fractions were collected under argon and sealed with parafilm to inhibit oxidation.[16] The purified oleate was concentrated, and the residual solvent was removed *in vacuo*. The oleate was then stored in a sealed flask containing argon at −78 °C.

Autoxidations were performed on 0.7 g of methyl oleate (2.36 mmol) in hexane. To initiate the reaction, 20.8 mg of DTBN (5 mol %) was added. The reaction was stirred at a constant temperature of 3 °C. After 24 hours, the extent of oxidation was determined as follows: A 25-μL aliquot was withdrawn from the reaction mixture and was quenched with a few crystals of TTBP. The following oleate hydroperoxide analysis was performed using analytical NP–HPLC–UV (0.6% *i*-PrOH/hexane, 0.9 mL/min, λ = 254 nm).

Methyl (*Z*)-11-Hydroperoxyoctadec-9-enoate and Methyl (E)-11-Hydroperoxyoctadec-9-enoate are the first and second eluting fractions on HPLC of the oleate hydroperoxides and these compounds have been characterized elsewhere. Only spectral data not reported elsewhere are presented here.

Methyl (*E*)-10-Hydroperoxyoctadec-8-enoate and Methyl (E)-9-Hydroperoxyoctadec-10-enoate. The third HPLC fraction contains coeluting 10- and 9-*trans* hydroperoxides. TLC: R_f 0.17 (15% EtOAc/hexane). Analytical NP–HPLC: t_R 47 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (s, 1H, OOH), 7.69 (s, 1H, OOH), 5.76 (m, 2H, C*H*═CH—CHOOH), 5.36 (dd, J = 15.4, 8.3 Hz, 2H, CH═C*H*—CHOOH), 4.25 (q, J = 7.9 Hz, 2H, C*H*OOH), 3.68 (s, 6H, CO_2CH_3), 2.31 (m, 4H, $CH_2CO_2CH_3$), 2.09 (m, 4H, CH_2C═), 1.71–1.20 (44H), 0.88 (t, J = 7.2 Hz, 6H, terminal CH_3). FTIR ($CHCl_3$): 3690, 3527, 2859, 2257, 1729, 1602, 974 (*trans* alkene) cm^{-1}. MS (CI, CH_4/NH_3): *m/z* 346 (13 M + NH_4^+), 328 (23, M − H_2O + NH_4^+), 312 (50, M − H_2O_2 + NH_4^+), 311 (100, MH^+ − H_2O), 295 (45, MH^+ − H_2O_2), 216 (70), 199(33), 172 (88), 155 (28).[17]

Methyl (*Z*)-8-Hydroperoxyoctadec-9-enoate. The fourth HPLC fraction contains the 8-*cis* compound. TLC R_f 0.17 (15% EtOAc/hexane). Analytical NP–HPLC t_R 51 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (s, 1H, OOH), 5.70 (dt, J = 11.0, 7.5 Hz, 1H, C*H*═CH—CHOOH), 5.27 (dd, J = 10.8, 9.5 Hz, 1H, CH═C*H*—CHOOH), 4.69 (dt, J = 9.1, 6.6 Hz, 1H, C*H*OOH), 3.64 (s, 1H, CO_2CH_3), 2.29 (t, J = 7.2 Hz, 2H, $CH_2CO_2CH_3$), 2.11 (m, 2H, CH_2C═), 1.70–1.15 (22H), 0.88 (t, J = 7.2 Hz, 3H, terminal CH_3). FTIR ($CHCl_3$): 3692, 3605, 2859, 2257, 1730, 1602 cm^{-1}. MS (CI, CH_4/NH_3): *m/z* 346 (15 M + NH_4^+), 328 (20 M − H_2O + NH_4^+), 312 (40, M − H_2O_2 + NH_4^+), 311 (65, MH^+ − H_2O), 295 (35, MH^+ − H_2O_2), 186 (100).

Methyl (*E*)-8-Hydroperoxyoctadec-9-enoate. The fifth eluting HPLC fraction contains the 8-*trans* compound. TLC: R_f 0.17 (15% EtOAc/

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(17) (a) Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1967**, *45*, 793. (b) Barclay, L. R. C.; Baskin, K. A.; Locke, S. J.; Schaefer, T. D. *Can. J. Chem.* **1987**, *65*, 2529. (c) The 9- and 10-*trans* oleate hydroperoxides have been previously characterized by P. Dussault and J. Sullivan Wujek including elemental analysis:Wujek, J. S. Ph.D. Dissertation, Duke University, 1987.

hexane). Analytical NP - HPLC: t_R 53 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (s, 1H, OOH), 5.75 (dt, J = 15.4, 6.6 Hz, 1H, C*H*=CH—CHOOH), 5.34 (dd, J = 15.4, 8.2 Hz, 1H, CH=C*H*—CHOOH), 4.25 (q, J = 8.1 Hz, 1H, C*H*OOH), 3.66 (s, 1H, CO_2CH_3), 2.29 (t, J = 7.2 Hz, 2H, $CH_2CO_2CH_3$), 2.09 (m, 2H, CH_2C=), 1.69–1.15 (22H), 0.88 (t, J = 7.2 Hz, 3H, terminal CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.28 (C=O), 137.25 (CH=CH—CHOOH), 128.37, 86.98 (CHOOH), 51.46, 34.01, 32.32, 31.85, 31.57, 29.39, 29.25, 29.16, 29.09, 29.02, 28.94, 25.09, 24.80, 22.65, 14.09. MS (CI, CH_4/NH_3): m/z 346 (33, M + NH_4^+), 328 (30 M - H_2O + NH_4^+), 312 (40, M - H_2O_2 + NH_4^+), 311 (76, MH^+ - H_2O), 295 (33, MH^+ - H_2O_2), 186 (100).

Synthesis of Oleate Alcohols. A 500-μL aliquot of the oleate autoxidation mixture (~5% oxidation, 0.07 mmol of oleate hydroperoxide) was diluted into 500 μL of benzene and reduced with the addition of 20 μL of tri-*n*-butylphosphine (0.18 mmol). The mixture was stirred at 0 °C for 20 min. The reaction was then diluted with 10 mL of hexane and washed with 3 × 5 mL of H_2O. The solution was dried over Na_2SO_4, and the solvent was removed under reduced pressure. Before performing HPLC analysis, the reaction mixture was purified using a sep-pak plus silica cartridge. The reaction mixture was washed with 8 mL of hexane to remove excess tri-*n*-butylphosphine and methyl oleate followed by 20 mL of EtOAc to elute the oleate alcohols. The EtOAc was removed under reduced pressure.

The following oleate alcohol product analysis was performed using analytical NP-HPLC-UV (0.8% *i*-PrOH/hexane, 1.2 mL/min, λ = 205 nm). Mass spectral analysis was performed on the alcohols and the silyl ethers. Silylations for mass spectral analysis were performed on a mixture of 2 mg of the oleate alcohol (6.7 × 10^{-3} mmol) and 9 mg of bis(trimethylsilyl)trifluoroacetamide (BSTFA, 3.4 × 10^{-2} mmol, ~5 equiv). The mixture was stirred at room temperature for 1 h and submitted directly for GC–MS (EI). Oleate alcohols have been previously characterized by Frankel[5b] and Dussault[17c] and we report here only spectral data not previously published elsewhere.

Methyl (*E*)-11-Hydroxyoctadec-9-enoate. The 11-*trans* alcohol was the first eluting oleate alcohol. TLC R_f 0.06 (15% EtOAc/hexane). Analytical NP-HPLC: t_R 28 min. GC: t_R 6.1 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.61 (dt, J = 15.4, 6.9 Hz, 1H, C*H*=CH—CHOH), 5.43 (dd, J = 15.4, 6.2 Hz, 1H, CH=C*H*—CHOH), 4.01 (m, 1H, C*H*OH), 3.66 (s, 3H, CO_2CH_3), 2.29 (t, J = 7.8 Hz, 2H, $CH_2CO_2CH_3$), 2.00 (m, 2H, CH_2C=), 1.65–1.15 (22H), 0.88 (t, J = 6.9 Hz, 3H, terminal CH_3). MS (CI, CH_4/NH_3): m/z 312 (100, M-H_2O + NH_4^+), 295 (75, MH^+ - H_2O). MS (EI): 213, 285 (trimethylsilyl derivative). HRMS (FAB): calcd for $C_{19}H_{35}O_3$ m/z = 311.2586; found m/z = 311.2579 (-2.4 ppm).

Methyl (*Z*)-11-Hydroxyoctadec-9-enoate. The 11-*cis* alcohol was the second eluting oleate alcohol. Analytical NP-HPLC: t_R 31 min. Full characterization of the 11-*cis* alcohol is provided elsewhere.

Methyl (*E*)-10-Hydroxyoctadec-8-enoate. The third peak contains the 10-*trans* oleate alcohol. TLC: R_f 0.06 (15% EtOAc/hexane). Analytical NP-HPLC: t_R 33 min. GC: t_R 6.1 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.59 (dt, J = 15.3, 6.6 Hz, 1H, C*H*=CH—CHOH), 5.42 (dd, J = 15.6, 6.9 Hz, 1H, CH=C*H*—CHOH), 4.02 (m, 1H, C*H*OH), 3.65 (s, 3H, CO_2CH_3), 2.28 (t, J = 7.8 Hz, 2H, $CH_2CO_2CH_3$), 2.00 (m, 2H, CH_2C=), 1.65–1.15 (22H), 0.86 (t, J = 6.9 Hz, 3H, terminal CH_3). MS (CI, CH_4/NH_3): m/z 312 (100, M - H_2O + NH_4^+), 295 (81, MH^+ - H_2O). MS (EI): 199, 271 (trimethylsilyl derivative).[18]

Methyl (*E*)-9-Hydroxyoctadec-10-enoate. The fourth HPLC fraction contains the 9-*trans* oleate alcohol. TLC: R_f 0.06 (15% EtOAc/hexane). Analytical NP-HPLC: t_R 35 min. GC: t_R 6.1 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.60 (dt, J = 15.3, 6.9 Hz, 1H, C*H*=CH—CHOH), 5.42 (dd, J = 15.2, 7.4 Hz, 1H, CH=C*H*—CHOH), 4.02 (m, 1H, C*H*OH), 3.64 (s, 3H, CO_2CH_3), 2.28 (t, J = 7.8 Hz, 2H, $CH_2CO_2CH_3$), 1.99 (m, 2H, CH_2C=), 1.70–1.12 (22H), 0.86 (t, J = 6.9 Hz, 3H, terminal CH_3). MS (CI, CH_4/NH_3): m/z 312 (100, M - H_2O + NH_4^+), 295 (80, MH^+ - H_2O). MS (EI) 155, 227 (trimethylsilyl derivative).

Methyl (*E*)-8-Hydroxyoctadec-9-enoate. The fifth peak contained the 8-*trans* oleate alcohol. TLC: R_f 0.06 (15% EtOAc/hexane). Analytical NP-HPLC: t_R 41 min. GC: t_R 6.1 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.63 (dt, J = 15.6, 6.6 Hz, 1H, C*H*=CH—CHOH), 5.44 (dd, J = 15.3, 7.2 Hz, 1H, CH=C*H*—CHOH), 4.03 (m, 1H, C*H*OH), 3.67 (s, 3H, CO_2CH_3), 2.30 (t, J = 7.8 Hz, 2H, $CH_2CO_2CH_3$), 2.00 (m, 2H, CH_2C=), 1.70–1.19 (22H), 0.88 (t, J = 6.9 Hz, 3H, terminal CH_3). MS (CI, CH_4/NH_3): m/z 312 (100, M - H_2O + NH_4^+), 295 (58, MH^+ - H_2O). MS (EI): 169, 241 (trimethylsilyl derivative).

Methyl (*Z*)-8-Hydroxyoctadec-9-enoate. The sixth peak contains the 8-*cis* oleate alcohol. TLC: R_f 0.06 (15% EtOAc/hexane). Analytical NP-HPLC: t_R 43 min. GC: t_R 5.8 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.48 (dt, J = 11.1, 7.2 Hz, 1H, C*H*=CH—CHOH), 5.35 (dd, J = 10.8, 9.0 Hz, 1H, CH=C*H*—CHOH), 4.43 (m, 1H, C*H*OH), 3.67 (s, 3H, CO_2CH_3), 2.31 (t, J = 7.8 Hz, 2H, $CH_2CO_2CH_3$), 2.08 (m, 2H, CH_2C=), 1.70–1.18 (22H), 0.88 (t, J = 6.9 Hz, 3H, terminal CH_3). MS (CI, CH_4/NH_3): m/z 312 (100, M - H_2O + NH_4^+), 295 (88, MH^+ - H_2O). MS (EI): 169, 241 (trimethylsilyl derivative).

Cooxidation of Methyl Oleate and *tert*-Butyl Hydroperoxide. To 0.178 g of methyl oleate (0.6 mmol) was added 0.73 mL of *tert*-butyl hydroperoxide (4.0 mmol) and 5.2 mg of DTBN (5 mol % based on methyl oleate). The cooxidation was performed under an atmosphere of air at a constant temperature of 30 °C for 3 h. Aliquots were withdrawn and quenched with TTBP. The reaction mixture was concentrated under reduced pressure, and residual *tert*-butyl hydroperoxide was removed *in vacuo* (bp_{20} = 35 °C). The oleate hydroperoxide product distribution was determined by NP-HPLC-UV (0.5% *i*-PrOH/hexane, 1.0 mL/min, λ = 254 nm): at 15 h, peak 1 (11-*cis*) t_R 45 min; peak 2 (10 and 9-*trans*) t_R 53, 54 min; peak 4 (8-*cis*) t_R 57 min (11-*cis*:9-*trans* = 1:1.2). The cooxidations were repeated with methyl oleate (0.6 mmol) and *tert*-butyl hydroperoxide (0.025–1.0 mmol) with dilutions performed in hexane.

Concentration Study of Autoxidation of Methyl Oleate. To 352 mg of methyl oleate (3.0 M) was added 10.4 mg of DTBN (5 mol %). The autoxidation was run under an atmosphere of air at a constant temperature of 30 °C. Aliquots were withdrawn after 4 h and quenched with TTBP. The reactions were run for 12–15 h. The oleate hydroperoxide product distribution was determined by NP-HPLC (0.6% *i*-PrOH/hexane, 0.9 mL/min, λ = 254 nm). The experiment was repeated with methyl oleate at 0.3, 0.6, 1.2, 1.8, and 2.4 M with dilutions performed in hexane.

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Supplementary Material Available: Figures showing HPLC traces, a listing of the iterative computer program, and tables of experimental and computed values for autoxidation of methyl oleate are presented (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfiche version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(18) The 9- and 10-*trans* oleate fatty acid alcohols have been obtained from the timothy plant fungus *Epichloe typhina*, see: Koshino, H.; Togiya, S.; Yoshihara, T.; Sakamura, S.; Shimanuki, T.; Sato, T.; Tajimi, A. *Tetrahedron Lett.* **1987**, *28*, 73. The 9-*cis* and *trans* oleate alcohols have been previously characterized by Frankel including exact mass measurements, see ref 5b.