Enantioselective Conversion of Linoleate Hydroperoxide to an α, β-Epoxy Alcohol by Niobium Ethoxide

George J. Piazza*, Thomas A. Foglia, and Alberto Nuñez

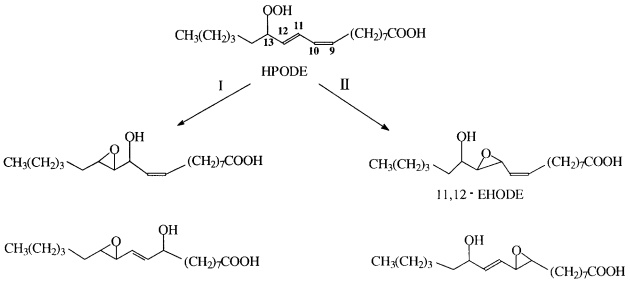
Eastern Regional Research Center, Agricultural Research Service, U.S. Department of Agriculture, Wyndmoor, Pennsylvania 19038

ABSTRACT: Niobium (V) ethoxide [$Nb(OC_2H_5)_5$] catalyzed the rearrangement of methyl 13(*S*)-hydroperoxy-9(*Z*),11(*E*)-octadecadienoate (Me-HPODE) to epoxy hydroxy isomers. At low temperature (5°C) in aprotic solvent, Me-HPODE was converted to the diastereomeric α, β-epoxy alcohols, methyl 11(*R,S*), 12(*R,S*)-epoxy-13(*S*)-hydroxy-9(*Z*)octadecenoate. These products are referred to as oxylipids and structurally resemble those obtained from the vanadium- and epoxygenase-catalyzed rearrangement of Me-HPODE but are distinct from products obtained from ferrous iron-, hematin-, and hemoglobin-catalyzed rearrangements. Because the product of the niobium-catalyzed rearrangement of Me-HPODE was predominantly the *erythro* diastereomer, the rearrangement is distinguished from that produced by a titanium catalyst, in which the *threo* diastereomer [methyl 11(*R*), 12(*R*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate] predominates, and from that produced by a vanadium catalyst, in which both diastereomers are produced in equal proportion. The synthesis of alcohol epoxide by $Nb(OC_2H_5)_5$ was inhibited by traces of water, but inclusion of molecular sieves in the reaction medium did not improve yield, as the alcohol epoxide rearranged to ketonic materials.

JAOCS 75, 939–943 (1998).

KEY WORDS: Epoxide, hydroperoxide, linoleic acid, lipoxygenase, niobium (V) ethoxide.

Soybean lipoxygenase (LOX) catalyzes the addition of oxygen to linoleic acid to form 13(*S*)-hydroperoxy-9(*Z*),11(*E*)-octadecadienoic acid (HPODE, Scheme 1). This hydroperoxide and those of other fatty acids are converted to epoxy alcohols by chemical and biological catalysts. Two major pathways of conversion are known and shown in Scheme 1. Pathway I is promoted by strong acid, ferrous iron, hematin, hemoglobin, and by enzymic catalysts from a variety of sources (1–9). Two of the epoxy alcohols from pathway I have been specially termed "hepoxilins" and have been shown to have biological activity in mammalian systems (7,10). Pathway II is promoted by salts of vanadium, hydroperoxide isomerase, and peroxygenase (11–14). These epoxy alcohols are termed "oxylipids," and some oxylipids



SCHEME 1

and their hydrolysis products are known to have biological activity in plants (14). Prior work showed that vanadium oxyacetylacetonate rearranged the methyl ester of HPODE (Me-HPODE) to methyl 11,12-epoxy-13-hydroxyoctadecadienoate (Me-11,12-EHODE, Scheme 1), with both diastereomers (*erythro* and *threo*) being formed in equal amounts (11). Recently, this laboratory studied the rearrangement of Me-HPODE by titanium (IV) isopropoxide; the predominant methyl ester formed was the *threo* isomer: methyl 11(*R*),12(*R*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate (15). As part of our continuing investigations of metal ion-catalyzed rearrangement of Me-HPODE, we have investigated the effect of niobium (V) ethoxide [$Nb(OC_2H_5)_5$]. Niobium is known to catalyze a wealth of chemical transformations (16). Previous work has shown that niobium complexes can catalyze epoxidation of double bonds with an external oxidant, such as *tert*-butyl hydroperoxide (17). Other work has shown that niobium coordinates with hydrogen peroxide, and it is reasonable to speculate that niobium might also coordinate with the hydroperoxide HPODE, and that such coordination would sufficiently polarize the hydroperoxide to lead to rearrangement (18,19). This study is part of a continuing effort to find novel methods of conversion of common fats and oils to more reactive and polar materials. Increased reactivity allows these materials to chemically interact with other components in a complex mixture, and increased polarity causes these materials to become partially water-soluble, which allows them to be components of water-based formulations with low levels of volatile organics.

*To whom correspondence should be addressed.
E-mail: gpiazza@arserrc.gov

MATERIALS AND METHODS

Materials. Soybean (*Glycine max* L. Merr.) LOX (Lipoxidase, Type 1-B) and linoleic acid were purchased from Sigma (St. Louis, MO). Niobium (V) ethoxide [$Nb(OC_2H_5)_5$], titanium (IV) isopropoxide [Ti(O-*i*-Pr)$_4$], and molecular sieves, 3A, 4-8 mesh, were purchased from Aldrich (Milwaukee, WI). Dichloromethane (Burdick & Jackson, Muskegon, MI) was placed over molecular sieves and was stored under a nitrogen atmosphere. Water was purified to a resistance of 18 mΩ-cm in a Barnstead (Dubuque, IA) NANOpure system. All other reagents were of the highest purity available.

Me-HPODE formation. Linoleic acid (80 mg) was placed in a 125-mL Erlenmeyer flask, along with 80 mL 0.2 M borate buffer, pH 9.0. The flask was packed in ice and stoppered with a rubber septum. The contents were stirred gently for 30 min while oxygen was slowly sparged into the buffer through a metal syringe needle. Four 50-µL aliquots of a LOX solution (32 mg/mL) in borate buffer were added at 30-min intervals during which oxygen sparging was continued. The pH of the reaction medium was lowered to 3 with 1 M HCl, and HPODE was extracted with 2 × 50 mL diethyl ether. The diethyl ether was dried over potassium sulfate, and the diethyl ether was removed under a stream of nitrogen. HPODE was dissolved in 5 mL CH_2Cl_2 and reacted with diazomethane to give Me-HPODE, and the solvent was removed under a stream of nitrogen.

Niobium and titanium treatments. Additions of solvent and catalyst to Me-HPODE were made in a nitrogen glove box. Me-HPODE (19 mg, 58 µmol) was dissolved in 3.95 mL CH_2Cl_2 in a 10-mL Erlenmeyer flask, equipped with a 19/22 ground glass joint. The solution was cooled in dry ice, and 69 µL (34 µmol) $Nb(OC_2H_5)_5$ dissolved in CH_2Cl_2 was added. After tightly stoppering the Erlenmeyer flask, it was removed from the nitrogen atmosphere and was agitated for 4 h at 5°C, unless otherwise indicated. After adding 320 µL water, the reaction mixture was diluted with 25 mL diethyl ether. The organic layer was washed with water (4 × 20 mL) and dried over potassium sulfate, and the ether was removed under a stream of nitrogen.

Me-HPODE (19 mg, 58 µmol) was treated with titanium in a manner identical to the niobium reaction, except that 88 µL (37 µmol) Ti(O-*i*-Pr)$_4$ in CH_2Cl_2 was used, and the reaction mixture was agitated for 1 h at 5°C.

High-performance liquid chromatography (HPLC). Reaction products were separated on a Lichrosorb 5µ diol HPLC column (250 × 10 mm) (Phenomenex, Torrance, CA), installed on a Waters (Milford, MA) LCM1 HPLC instrument. The instrument was equipped with a Waters 996 photodiode array detector in tandem with a Varex evaporative light-scattering detector MK III (Alltech, Deerfield, IL), operated at a temperature of 55°C, and with N_2 as the nebulizing gas at a flow rate of 1.5 L/min. The mobile phase gradient was hexane/isopropanol (98:2) to (96:4) by means of a 28-min linear gradient. The flow rate was 2 mL/min.

Gas chromatography–mass spectrometry (GC–MS). Samples were analyzed before and after treatment with N,O-bis(trimethylsilyl) trifluoroacetamide (BSFTA, Pierce, Rockford, IL). Mass spectra were obtained on a Hewlett-Packard (HP) (Wilmington, DE) 5890 Series II Plus gas chromatograph, equipped with an HP 5972 mass-selective detector, which was set to scan from *m/e* 10 to 600 at 1.2 scans/s. A capillary column (HP-5MS, 30 m × 0.25 mm), coated with 0.25 µm 5% cross-linked phenyl methyl silicone, was used to separate the products. The oven temperature was increased from 80 to 230°C at 10°C per min. The injector port temperature was 230°C, and the detector transfer line temperature was 240°C.

Nuclear magnetic resonance (NMR) spectrometry. Spectra were obtained on a Varian Unity Plus 400 MHz NMR spectrometer in either 99 atom-% *p*-dioxane-d_8 or 99.6 atom-% benzene d_6 (Cambridge Isotope Labs, Woburn, MA). Typical acquisition conditions for the proton spectra were 9,600 data points; 4 kHz spectral width; 2.2 s recycle time. For carbon spectra, typical acquisition conditions were 60,000 data points; 25 kHz spectral width, 21.7 s recycle time. The 90° pulse was measured for both proton and carbon spectra prior to acquisition. All spectra were recorded at 30°C.

RESULTS AND DISCUSSION

Identification of reaction products. Figure 1A shows the HPLC elution profile of Me-HPODE. Figure 1B shows the profile after treating Me-HPODE with $Nb(OC_2H_5)_5$. Major product **a**, isolated by semipreparative HPLC, accounted for approximately 71% of the total product and was determined to be an α, β-epoxy alcohol with an *erythro* configuration. After formation of the $(CH_3)_3Si$ derivative of **a**, its mass spectrum showed ions at *m/z* 383 (M − 15), 327 (M − 71), 270 [M − 128; rearrangement with expulsion of ·CO-CH(O·)-$(CH_2)_4$-CH_3] (12) and 173 [$(CH_3)_3SiO^+$=CH-$(CH_2)_4$-CH_3]. The ultraviolet/visible (UV/VIS) spectrum showed end absorbance below 210 nm. Thus, the data show that compound **a** is a monounsaturated 18-carbon epoxy alcohol methyl ester with the hydroxyl group at C-13.

The neat infrared spectrum of product **a** showed a broad band centered at 3475 cm^{-1} (hydrogen-bonded hydroxyl), 1739 cm^{-1} (ester carbonyl), and 892 cm^{-1} (*trans* epoxide). No absorption band appeared in the region of 900–1000 cm^{-1}, excluding the presence of *trans* double bond(s) (20).

Important signals in the decoupled ^{13}C NMR (C_6D_6, 100 MHz) spectrum of product **a** are δ 51.4 (C-12), 51.6 (OCH_3), 63.1 (C-11), 69.5 (C-13), and 174.1 [$\underline{C}(O)OCH_3$]. The solvent signal partially obscured those from the double-bond carbons. Thus, the ^{13}C NMR spectrum was also obtained in $C_4D_8O_2$ to obtain the carbon signals for the double bond: δ 129.5 (C-10) and 137.5 (C-9). Because there are only two signals for the epoxide carbons, two signals for the double bond carbons, and one signal for the alcoholic carbon, product **a** is predominantly one structural isomer.

As shown in Table 1, important signals in the ^1H NMR (C_6D_6, 400 MHz) spectrum of product **a** are δ 2.97 (*t*, *J* = 3.0

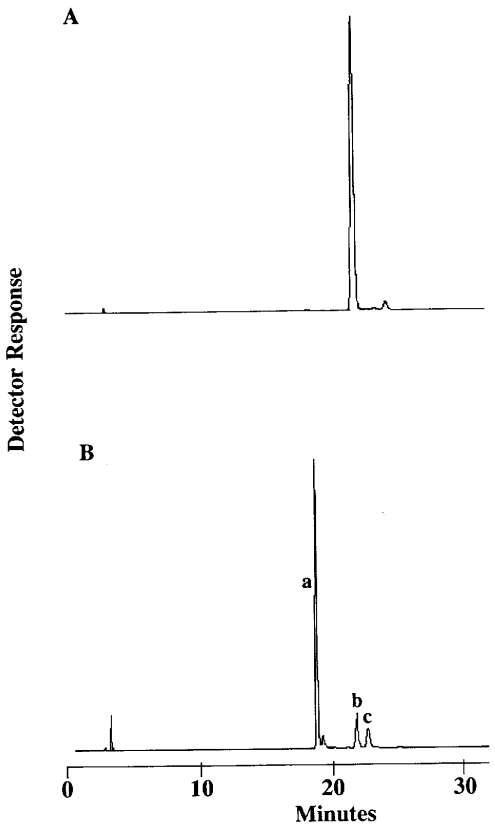


FIG. 1. Normal-phase high-performance liquid chromatography (HPLC) analyses of the action of $Nb(OC_2H_5)_5$ on methyl 13(*S*)-hydroperoxy-9(*Z*),11(*E*)-octadecadienoate (Me-HPODE). (A) Me-HPODE prior to reaction. (B) Reaction products; **a**, methyl 11(*S*),12(*S*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate (*erythro* Me-11,12-EHODE); **b**, Me-HPODE; **c**, methyl 11(*R*),12(*R*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate (*threo* Me-11,12-EHODE).

Hz, 1H, H-12), 3.84 (*br s*, 1H, H-13), 4.02 (*dd*, *J* = 1.6, 8.8 Hz, 1H, H-11), 5.44 (*dd*, *J* = 9.9, 10.0 Hz, 1H, H-10), 5.80 (*dt*, *J* = 7.7, 11.2, 1H, H-9). The coupling constant $J_{9–10}$ was 10.0–11.2 Hz, indicating that the double bond is in the *cis* configuration: *J* = 5–14 Hz for *cis* protons and 12–18 Hz for *trans* protons (21). The coupling constant $J_{11–12}$ was 1.6–3.0 Hz, establishing that the configuration of the epoxide group is *trans*: *J* = 4.3 Hz for *cis* and 2.1–2.4 for *trans* (21). The coupling constant $J_{12–13}$ is 3.0 Hz, indicating that the relationship between the adjacent protons of the alcohol and the epoxide is *erythro*: *J* = 5 Hz for *threo* and 3.25 Hz for *erythro* (22). In support of the *erythro* assignment, H-13 resonates at 3.84 ppm: 3.8 ± 1 ppm for *erythro* and 3.5 ± 1 ppm for *threo* (23).

Based on all data, we concluded that the stereochemical structure of product **a** is *erythro* Me-11,12-EHODE (Scheme 1): methyl 11(*S*),12(*S*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate.

Peak **b** in Figure 1 was determined to be unreacted Me-HPODE and had the characteristic absorbance maximum at 234 nm.

Minor product **c** accounted for 9% of the total product and was determined to be an α, β-epoxy alcohol with a *threo* configuration. The mass spectrum and neat infrared spectrum of product **c** were identical to those given by product **a**.

Important signals in the decoupled ^{13}C NMR (C_6D_6, 100 MHz) spectrum of product **c** are δ 51.6 (OCH_3), 52.8 (C-12), 63.7 (C-11), 71.6 (C-13), and 174.0 [$\underline{C}(O)OCH_3$]. The solvent signal partially obscured those from the double bond carbons. Thus, the ^{13}C NMR spectrum was also obtained in $C_4D_8O_2$ to give the signals for the double bond: δ 129.4 (C-10) and 137.5 (C-9). Because there are only two signals for the epoxide carbons, two signals for the double bond carbons, and one signal for the alcoholic carbon, product **c** is predominantly one structural isomer.

As shown in Table 1, important signals in the decoupled ^1H NMR (C_6D_6, 400 MHz) spectrum of product **c** are δ 2.97 (*dd*, *J* = 2.0, 4.2 Hz, 1H, H-12), 3.60 (*br s*, 1H, H-13), 3.89 (*dd*, *J* = 2.4, 8.8 Hz, 1H, H-11), 5.39 (*dd*, *J* = 9.0, 10.9 Hz, 1H, H-10), 5.80 (*dt*, *J* = 7.7, 10.8 Hz, 1H, H-9). The coupling constant $J_{9–10}$ was 10.8–10.9 Hz, demonstrating that the double bond is in the *cis* configuration: *J* = 5–14 Hz for *cis* protons and 12–18 Hz for *trans* protons (20). The coupling constant $J_{11–12}$ was 2.0–2.4 Hz, demonstrating that the configuration of the epoxide group is *trans*: *J* = 4.3 Hz for *cis* and 2.1–2.4 Hz for *trans* (21). The coupling constant $J_{12–13}$ is 4.2 Hz, indicating that the relationship between the adjacent protons of the alcohol and the epoxide is *threo*: *J* = 5 Hz for *threo* and 3.25 Hz for *erythro* (22). An analogous coupling constant reported for the *threo* derivative of an alcoholic epoxide de-

TABLE 1
Diagnostic ^1H Nuclear Magnetic Resonance Chemical Shifts and Coupling Constants of Products a and c

Chemical shift (δ)	Number of protons	Appearance	Assignment	Coupling constant (Hz)
Product **a**				
2.97	1H	*t*	H-12	$J_{11–12,\ 12–13}$ = 3.0
3.84	1H	*br s*	H-13	
4.02	1H	*dd*	H-11	$J_{10–11}$ = 8.8, $J_{11–12}$ = 1.6
5.44	1H	*dd*	H-10	$J_{9–10}$ = 10.0, $J_{10–11}$ = 9.9
5.80	1H	*dt*	H-9	$J_{8–9}$ = 7.7, $J_{9–10}$ = 11.2
Product **c**				
2.97	1H	*dd*	H-12	$J_{11–10}$ = 2.0, $J_{12–13}$ = 4.2
3.60	1H	*br s*	H-13	
3.89	1H	*dd*	H-11	$J_{10–11}$ = 8.8, $J_{11–12}$ = 2.4
5.39	1H	*dd*	H-10	$J_{9–10}$ = 10.9, $J_{10–11}$ = 9.0
5.80	1H	*dt*	H-9	$J_{8–9}$ = 7.7, $J_{9–10}$ = 10.8

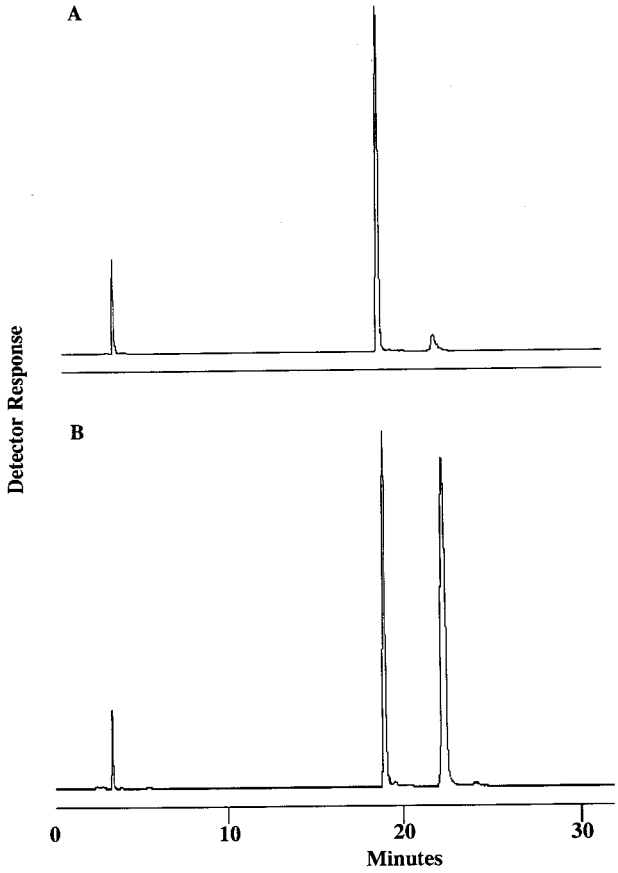


FIG. 2. Normal-phase HPLC analyses to compare the products obtained with $Nb(OC_2H_5)_5$ and Ti(O-*i*-Pr)$_4$. (A) Major product from $Nb(OC_2H_5)_5$, methyl 11(*S*),12(*S*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate (*erythro* Me-11,12-EHODE); (B) major product from titanium (IV) isopropoxide [Ti(O-*i*-Pr)$_4$], methyl 11(*R*),12(*R*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate (*threo* Me-11,12-EHODE).

rived from the action of the fungus *Saprolegnia parasitica* upon arachidonic acid was 4.5 Hz (24). In support of the *threo* assignment, H-13 resonates at 3.60 ppm: 3.8 ± 1 ppm for *erythro* and 3.5 ± 1 ppm for *threo* (23).

Based on all data, we concluded that the stereochemical structure of product **c** is *threo* Me-11,12-EHODE (Fig. 1): methyl 11(*R*),12(*R*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate.

Comparison of niobium and titanium catalysts. Shown in Figure 2 is a comparison of the reaction products from reactions of $Nb(OC_2H_5)_5$ and Ti(O-*i*-Pr)$_4$ on Me-HPODE. Both reactions were conducted at the same time with the same batch of Me-HPODE. As before, $Nb(OC_2H_5)_5$ produced mostly *erythro* Me-11,12-EHODE (Fig. 3A). Although the major peak given by Ti(O-*i*-Pr)$_4$ eluted at a position nearly identical to Me-HPODE (Fig. 3B), the product was easily distinguished from Me-HPODE by the lack of absorbance at 234 nm. This product was determined to be *threo* Me-11,12-EHODE and had spectral characteristics as described earlier (15).

Influence of water on product formation. Epoxy alcohol formation by $Nb(OC_2H_5)_5$ was found to be more sensitive to the presence of trace amounts of water than formation by

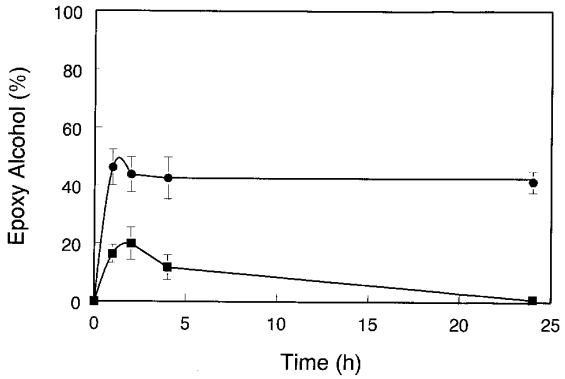


FIG. 3. Time course of stability of methyl 11(*S*),12(*S*)-epoxy-13(*S*)-hydroxy-9(*Z*)-octadecenoate *(erythro* Me-11,12-EHODE), formed by $Nb(OC_2H_5)_5$ in the absence (●) and presence (■) of 3A molecular sieves (0.6 g). The data are the means of three and four determinations, respectively.

Ti(O-*i*-Pr)$_4$. As was shown previously with Ti(O-*i*-Pr)$_4$ as a catalyst, alcohol epoxide formed even in the presence of water (15). However, when sufficient water was present, only triol product was detected, demonstrating that the epoxide group was hydrolyzed after its formation. With $Nb(OC_2H_5)_5$ as catalyst and trace amounts of water present, either no reaction occurred or Me-HPODE was reduced to form the corresponding alcohol without concomitant epoxide formation. Several steps were taken to overcome this problem: Water was removed from CH_2Cl_2 by placing it over activated molecular sieves, Me-HPODE was dried as outlined in Materials and Methods, CH_2Cl_2 and catalyst solutions were stored in a nitrogen dry box, and reaction mixtures were prepared under nitrogen. When these precautions were taken, failure of alcohol epoxide formation was usually caused by traces of water that remained in the Me-HPODE preparation, and it was sometimes necessary to measure out an aliquot of a solution of Me-HPODE and redry it under a stream of nitrogen.

The addition of molecular sieves to the reaction mixture as a precaution against contamination by water was tested. As shown in Figure 3, rather than enhancing conversion, the presence of molecular sieves in the reaction medium promoted the loss of *erythro* Me-11,12-EHODE; it decomposed to materials that eluted close to the solvent front in HPLC. These materials have not been completely characterized, but UV/VIS absorbance spectra and mass spectra indicate that these materials are fatty ketones. Also shown in Figure 3 is the time course of reactions conducted without molecular sieves; over the time of the experiment, *erythro* Me-11,12-EHODE alcohol epoxide was stable, and almost no loss of this product was observed.

In conclusion, it is now possible to prepare both conformations of the Me-11,12-EHODE from Me-HPODE (Scheme 1, pathway II). The *threo* diastereomer is given by Ti(O-*i*-Pr)$_4$, and $Nb(OC_2H_5)_5$ produces predominantly the *erythro* diastereomer. Treatment of Me-HPODE with $VO(acac)_2$ gives a racemic mixture.

ACKNOWLEDGMENT

The authors thank C.F. Fox for technical assistance.

REFERENCES

1. Gardner, H.W., Oxygen Radical Chemistry of Polyunsaturated Fatty Acids, *Free Radical Biol. Med. 7*:65–86 (1989).
2. Hamberg, M., Decomposition of Unsaturated Fatty Acid Hydroperoxides by Hemoglobin: Structures of Major Products of 13L-Hydroperoxy-9,11-octadecadienoic Acid, *Lipids 10*:87–92 (1975).
3. Song, W.C., S.W. Baertschi, W.E. Boeglin, T.M. Harris, and A.R. Brash, Formation of Epoxyalcohols by a Purified Allene Oxide Synthase, *J. Biol. Chem. 268*:6293–6298 (1993).
4. Garssen, G.J., G.A. Veldink, J.F.G. Vliegenthart, and J. Boldingh, The Formation of *threo*-11-Hydroxy-*trans*-12:13-epoxy-9-*cis*, 11-*trans*-octadecadienoic Acid by Soybean Lipoxygenase-1, *Eur. J. Biochem. 62*:33–36 (1976).
5. Weiss, R.H., J.L. Arnold, and R.W. Estabrook, Transformation of an Arachidonic Acid Hydroperoxide into Epoxyhydroxy and Trihydroxy Fatty Acids by Liver Microsomal Cytochrome P-450, *Arch. Biochem. Biophys. 252*:334–338 (1987).
6. Galliard, T., D.R. Phillips, and J.A. Matthew, Enzymic Reactions of Fatty Acid Hydroperoxides in Extracts of Potato Tuber. II. Conversion of 9- and 13-Hydroperoxy-octadecadienoic Acids to Monohydroxydienoic Acid, Epoxyhydroxy- and Trihydroxymonoenoic Acid Derivatives, *Biochim. Biophys. Acta 409*:157–171 (1975).
7. Reynaud, D., P. Demin, and C.R. Pace-Asciak, Hepoxilin A_3 Formation in the Rat Pineal Gland Selectively Utilized (12*S*)-Hydroperoxyeicosatetraenoic Acid (HPETE), but Not (12*R*)-HPETE, *J. Biol. Chem. 269*:23976–23980 (1994).
8. Chang, M.S., W.E. Boeglin, F.P. Guengerich, and A.R. Brash, Cytochrome P450-Dependent Transformations of 15*R*- and 15*S*-Hydroperoxyeicosatetraenoic Acids—Stereoselective Formation of Epoxy Alcohol Products, *Biochemistry 35*:464–471 (1996).
9. Dix, T.A., and L.J. Marnett, Conversion of Linoleic Acid Hydroperoxide to Hydroxy, Keto, Epoxyhydroxy, and Trihydroxy Fatty Acids by Hematin, *J. Biol. Chem. 260*:5351–5357 (1985).
10. Pace-Asciak, C.R., D. Reynaud, and P.M. Demin, Hepoxilins: A Review on Their Enzymatic Formation, Metabolism and Chemical Synthesis, *Lipids 30*:107–114 (1995).
11. Hamberg, M., Vanadium-Catalyzed Transformation of 13(*S*)-Hydroperoxy-9(*Z*),11(*E*)-octadecadienoic Acid: Structural Studies on Epoxy Alcohols and Trihydroxy Acids, *Chem. Phys. Lipids 43*:55–67 (1987).
12. Gardner, H.W. Recent Investigations into the Lipoxygenase Pathway of Plants, *Biochim. Biophys. Acta 1084*:221–239 (1991).
13. Hamberg, M., C.A. Herman, and R.P. Herman, Novel Biological Transformation of 15-L_S-Hydroperoxy-5,8,11,13-eicosatetraenoic Acid, *Biochim. Biophys. Acta 877*:447–457 (1986).
14. Blée, E., Phytooxylipins: The Peroxygenase Pathway, in *Lipoxygenase and Lipoxygenase Pathway Enzymes,* edited by George J. Piazza, AOCS Press, Champaign, 1996, pp. 138–161.
15. Piazza, G.J., T.A. Foglia, and A. Nuñez, Enantioselective Formation of an α, β-Epoxy Alcohol by Reaction of Methyl 13(*S*)-Hydroperoxy-9(*Z*),11(*E*)-octadecadienoate with Titanium Isopropoxide, *J. Am. Oil Chem. Soc. 74*:1385–1390 (1997).
16. Tanabe, K., and S. Okazaki, Various Reactions Catalyzed by Niobium Compounds and Materials, *Appl. Catal. A: Gen. 133*:191–218 (1995).
17. Jørgensen, K.A., Transition-Metal-Catalyzed Epoxidations, *Chem. Rev. 89*:431–458 (1989).
18. Mathern, G., R. Weiss, and R. Rohmer, The Crystal Structures of Potassium Triperoxo-(*o*-phenanthroline)niobiate Trihydrate and Its Hydrogen Peroxide Adduct, *Chem. Comm.*:153–154 (1970).
19. Gardner, H.W., Lipoxygenase as a Versatile Biocatalyst, *J. Am. Oil Chem. Soc. 73*:1347–1357 (1996).
20. Pretsch, E., J. Seibl, and W. Simon, in *Tables of Spectral Data for Structure Determination of Organic Compounds*, Springer-Verlag, Berlin, 1981, p. B25.
21. Pierre, J.-L., P. Chautemps, and P. Arnaud, Résonance Magnétique Nucléaire des Petits Cycles. IV. Étude d'α-Époxy-Alcools, *Chim. Anal. 50*:494–500 (1968).
22. Mercier, J., and B. Agoh, Comportement d'Hydroperoxydes Allyliques à Longue Chaine en Presence de Complexes de Certains Metaux de Transition. II. Structure des Époxy-Alcools Formés à Partir d'Hydroperoxydes d'Octadécène-9 Oates de Méthyle *Cis* et *Trans* en Présence d'Acétylacétonate de Vanadyle, *Chem. Phys. Lipids 12*:239–248 (1974).
23. Mihelich, E.D., Vanadium-Catalyzed Epoxidations. I. A New Selectivity Pattern for Acyclic Alcohols, *Tetrahedron Lett. 49*:4729–4732 (1979).
24. Hamberg, M., R.P. Herman, and U. Jacobsson, Stereochemistry of Two Epoxy Alcohols from *Saprolegnia parasitica*, *Biochim. Biophys. Acta 879*:410–418 (1986).

[Received October 6, 1997; accepted March 2, 1998]