Oxidative Acetoxylation of Methyl Oleate with Palladium Catalysts[1]

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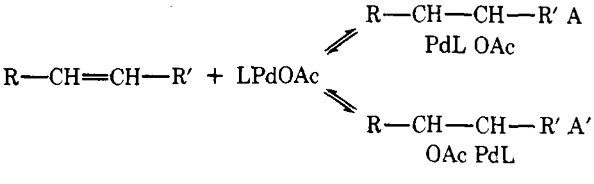
Catalytic acetoxylation of methyl oleate in acetic acid produces allylic acetoxy fatty esters in high yield. These derivatives are related to products of autoxidation. Useful catalyst systems include $PdCl_2 + CuCl_2 + NaOAc$, $PdCl_2$ or $Pd(OAc)_2 + LiNO_3$, Pd/Al_2O_3 or $Pd/C + LiNO_3$, and Pd/C. Esters produced in 50–97% conversion at 70–120° and O_2 at 1 atm pressure or 20–45 psig include acetoxy (20–63%) and diacetoxy (20–47%) octadecenoate. Monooxygenated products characterized by GC–MS of the silyl ether derivatives were mainly a mixture of 8-acetoxy-9(*cis/trans*)-, 10-acetoxy-8(*cis/trans*)-, 9-acetoxy-10(*cis/trans*)-, and 11-acetoxy-9(*cis/trans*)-octadecenoate. Dioxygenated products had both 1,2- and 1,4-diacetoxy allylic structures: –CH(OAc)CH(OAc)CH=CH– and –CH(OAc)CH=CHCH(OAc)–. 1,3-Disubstituted isomers were ruled out by NMR. The Pd–$LiNO_3$ catalyst system proved to be highly selective for the allylic acetoxylation of methyl oleate. A mechanism involving allylic $Pd(Cl/OAc)_x$ complex intermediates explains the formation of allylic acetoxy esters. For diacetoxylation a direct pathway from oleate is invoked that involves interconversion of σ-oxypalladation, π olefin, and π-allyl complex intermediates.

The Pd(II)-catalyzed oxidation of ethylene to acetaldehyde in aqueous solution is the basis for the commercial Wacker process.[2] When the aqueous reaction medium in this process is replaced by acetic acid, olefins are acetoxylated. Unsaturated esters are made commercially by this method.[3] Lower olefins are converted to vinyl acetates when the double bond is terminal and to allyl acetates mainly when the double bond is internal. With higher olefins, the products become quite complicated.[4]

Although acetoxylation processes have been studied in considerable detail, results are conflicting, especially with higher olefins. Much care is needed in interpreting some of the results in the literature because of the complexity of the Pd(II) catalyst systems.[4] The course of catalytic acetoxylation depends on reaction parameters (ligand, solvents, presence of oxygen) and the structure of olefinic substrates.[4,5] Cu(II) salts[6a] and other oxidants, such as nitrates,[7] have been used as redox couples to make the acetoxylation catalytic in Pd(II). The presence of these oxidants and other reagents, such as acetates, affects significantly product distribution from higher olefins, and their mechanism of action is not too clear.[4] The oxidation of *cis*- and *trans*-2-butene in the presence of $CuCl_2$ in acetic acid produces 2,3- and 1,3-diacetates and chloroacetates, in addition to the unsaturated acetates formed in the absence of $CuCl_2$.[6a,b]

A mechanism involving the formation of oxypalladation complexes (A, A′) has been generally accepted for the oxidation of 1- and 2-butenes and pentenes[6,8] (eq 1).



$$R{-}CH{=}CH{-}R' + LPdOAc \rightleftharpoons \begin{cases} \underset{PdL\quad OAc}{R{-}CH{-}CH{-}R'}\ A \\ \underset{OAc\quad PdL}{R{-}CH{-}CH{-}R'}\ A' \end{cases} \qquad (1)$$

The allylic products obtained with internal olefins have been explained by β-elimination of HPdL from the oxypalladation complexes. Isomerization of these complexes before reaction with Cu(II) has been suggested to explain the disubstituted products from butenes.[6] Olefinic and allylic isomerization may also complicate the interpretation of isomeric product distribution. With 1-hexene a high selectivity for primary monoacetates was observed, together with the formation of 1,2-diol mono- and diacetates.[9] The greater amount of 2 than 3 substitution observed with 2-hexene was considered larger than expected from an oxypalladation mechanism. A two-carbon insertion pathway was postulated to explain 2-substitution products and 1,2-diol mono- and diesters, and a one-carbon insertion pathway to explain 1-substitution products and 1,1-diacetates from olefins.[9] No direct evidence was presented, however, for 1,1-disubstitution products.

The intervention of π-allyl intermediates has been discounted because product distribution from 1- and 2-butene was different even though they were expected to give similar π-allyl complexes.[6] However, with cyclohexene-d_4, π-allylic routes have been supported by evidence based on deuterium distribution in the allylic acetate product.[10a] Oxypalladation was considered a minor competing reaction producing mainly homoallylic acetate. Further solvolysis studies with different organopalladium compounds showed that a π-allyl palladium chloride complex can be an intermediate in the allylic oxidation of cyclohexene but the corresponding π-allyl palladium acetate cannot.[10b] The formation of 90% secondary acetate by neutral solvolysis of π-crotyl and π-cinnamyl palladium acetate in acetic acid was explained by neutral depalladation of σ-allyl intermediates.[11]

Much attention has been given to the allylic oxidation of methyl oleate with mercuric salts and selenium,[12] but none with palladium salts. The contrasting mechanisms of allylic oxidation of short-chain olefins with mercuric and palladium acetate[8] stimulated our interest in studying the palladium salt oxidation of methyl oleate. We found that the catalytic acetoxylation of methyl oleate with Pd compounds leads to allylic acetoxy fatty esters related to products of autoxidation. In light of the mechanisms proposed for Pd(II) oxidation of higher olefins, we postulate possible reaction pathways for mono- and diacetoxylation.

Results

Methyl oleate was catalytically acetoxylated with various Pd-containing systems in acetic acid solution made anhydrous with acetic anhydride.[13] Data in Table I are from runs carried out in the presence of O_2 at either 1 atm pressure or 20–45 psi in the temperature range of 70–120°. Among catalyst systems tried the most useful include $PdCl_2 + CuCl_2 + NaOAc$, $PdCl_2$ or $Pd(OAc)_2 + LiNO_3$, and Pd/Al_2O_3 or $Pd/C + LiNO_3$. Analysis by GLC shows conversion of methyl oleate into acetoxy and diacetoxy fatty esters of 50–97%. Significant amounts of diacetoxy esters were formed during the initial stages, and their proportion increased at longer reaction times. With the $PdCl_2$–

Table I
Catalytic Acetoxylation of Methyl Oleate (0.1 Mol)

Run no.	Apparatus[a]	Catalyst	Oxidants and other reagents (0.1 mol)	Temp, °C	Time, hr	Acetate,[b] % Mono-	Di-	Total
1	P	$PdCl_2$	$CuCl_2$, NaOAc	100	24	35.2	44.8	80.0
2	P	$PdCl_2$	$CuCl_2$, NaOAc	120	18	30.4	30.4	60.8
3	P	$PdCl_2$	$LiNO_3$	100	24	19.8	32.1	51.9
4	P	$PdCl_2$	$LiNO_3$, NaOAc	100	24	31.3	19.5	50.8
5	P	$PdCl_2$	$LiNO_3$	80	6	45.8	26.6	72.4
					12	55.9	38.4	94.3
6	F	$PdCl_2$	$CuCl_2$, NaOAc	80	6	17.6	19.9	37.5
					24	29.6	32.8	62.4
7	F	$PdCl_2$	$LiNO_3$	70	6	41.1	12.0	53.1
					24	60.2	27.0	87.2
8[c]	F	$PdCl_2$	$LiNO_3$	80	24	46.9	43.3	90.2
9	F	$PdCl_2$	$LiNO_3$	90	6	52.5	31.7	84.2
					24	45.9	39.0	84.9
10	F	$PdCl_2$	$LiNO_3$, LiOAc	80	6	56.8	23.5	80.3
					24	54.2	29.2	83.4
11	F	$Pd(OAc)_2$	$LiNO_3$, LiCl	80	6	54.4	28.5	82.9
					24	54.9	29.6	84.5
12	F	$Pd(OAc)_2$	$LiNO_3$	80	6	63.2	16.8	80.0
					24	62.9	25.1	88.0
13	F	Pd/Al_2O_3	$LiNO_3$	80	6	45.0	24.9	69.9
					24	46.0	47.0	93.0
14[c]	F	Pd/C	$LiNO_3$	80	24	60.5	36.6	97.1
15	F	Pd	$LiNO_3$	80	6	15.8	17.7	33.5
					24	26.9	26.5	53.4

[a] P = pressure reactions, 20-45 psi O_2, Parr hydrogenation apparatus, 90 ml HOAc + 10 ml Ac_2O + 0.002 mol catalyst (runs 1-4) and 0.005 mol catalyst for run 5; F = open flask reactions, 1 atm pressure, O_2 bubbling, 125 ml HOAc + 10 ml OAc_2 + 0.005 mol catalyst (runs 13-14: 0.53 g Pd). [b] Analyses made by GLC on crude filtered and solvent stripped samples before work up. Percents based on 96% purity of starting material. [c] See rate curves in Figure 1.

$CuCl_2$ system little or no conversions were obtained (less than 10%) without NaOAc. In contrast, with the $PdCl_2$–$LiNO_3$ system, conversions of more than 90% were obtained without acetate; addition of acetate to this system increased the relative proportion of monoacetates (compare runs 3 and 4, 8 and 10). Optimum reaction temperature with this system was 80°. $Pd(OAc)_2$ with or without added chloride was as effective as $PdCl_2$ (runs 11 and 12). Pd supported on either Al_2O_3 or C provided one of the most effective catalyst systems (runs 13 and 14). Unlike the supported catalysts, Pd metal + $LiNO_3$ was practically inactive (run 15).

Although $LiNO_3$ was an effective oxidant, significant amounts of nitrate esters formed with it, as previously observed with olefins.[14] Ir analyses showed varying absorptions at 1630 ($RONO_2$), 1550 and 1520 (α,β-unsaturated RNO_2), and 855 cm^{-1} (NO_3^-).[15] These nitrate esters could be removed readily by hydrogenolysis.

The course of acetoxylation was studied further by sequential analyses of reaction mixtures. Kinetic runs with $PdCl_2$–$LiNO_3$ and Pd/C–$LiNO_3$ at 80° were plotted (Figure 1). Analysis by GLC shows that the disappearance of methyl oleate is followed by rapid monoacetoxylation and diacetoxylation. With $PdCl_2$ + $LiNO_3$ (run 8) monoacetoxy esters peak around 12 hr and decrease at later stages of the reaction. With Pd/C + $LiNO_3$ (run 14), the monoacetoxy esters reach a higher concentration and level off at 12 hr. With both catalytic systems acetoxylation is slowed down markedly after 6 hr and the formation of diacetoxy esters levels off at 24 hr. Initial rapid formation of diacetoxy products indicates a direct diacetoxylation path from oleate. The decrease of monoacetoxy products observed at later stages of the reaction suggests also secondary oxidation of mono- to diacetates. This decrease of monoacetates

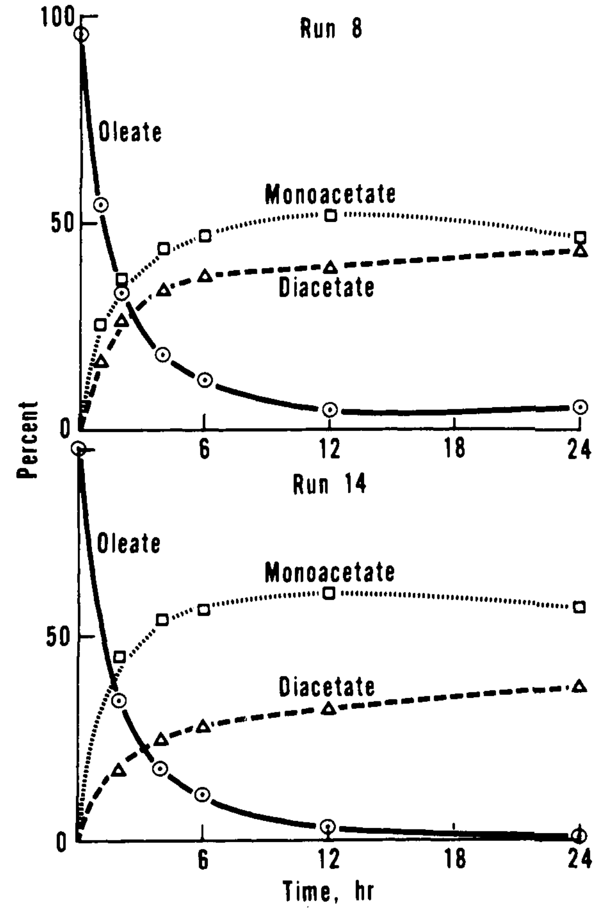


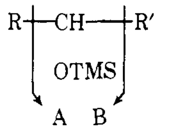
Figure 1. Catalytic acetoxylation of methyl oleate with $PdCl_2$ + $LiNO_3$ (run 8, Table I) and with Pd/C + $LiNO_3$ (run 14, Table I).

Table II

Isomer Distribution of Monohydroxy Derivatives by GC-MS of Silyl Ethers

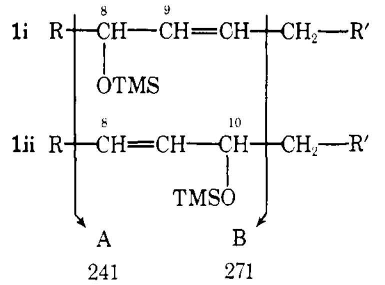
		Before hydrogenation[a]					After hydrogenation[a]			
		Allylic, %[b]					Saturated, %			
Run	Time, hr	8-OH Δ^9 (1i)	9-OH Δ^{10} (1iii)	10-OH Δ^8 (1ii)	11-OH Δ^9 (1iv)	Nonallylic,[c] %	8-OH	9-OH	10-OH	11-OH
1	24	3.6	14.0	14.6	6.3	61.5	12.6	28.4	39.7	19.3
6	6	10.0	27.6	27.6	13.0	21.8	12.6	35.1	37.4	14.9
	24	7.2	23.6	18.3	8.7	42.2	12.2	35.4	38.0	14.4
7	24	17.7	19.2	20.0	19.6	23.5	23.1	24.8	27.2	25.0
8	1	18.8	21.2	22.5	24.2	13.3	21.6	24.8	26.8	26.8
	2	18.2	21.3	21.6	23.3	15.6	21.4	25.3	26.8	26.5
	6	17.4	20.8	22.4	23.5	15.9	20.9	24.8	27.3	27.0
	24	17.1	19.6	21.8	23.4	18.1	20.8	24.0	27.8	27.4
13	24	18.9	20.9	23.5	26.3	10.4	21.3	24.0	26.7	28.0
14	24	24.2	25.5	26.4	23.9	0	24.2	25.5	26.4	23.9

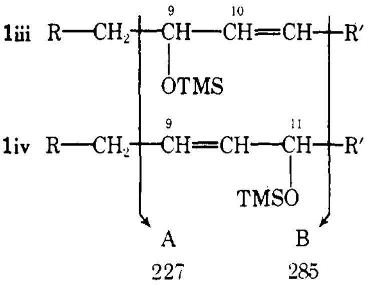
[a] With Pd/C-HOAc, room temperature at 50 psi H_2. Fragment type



	A	B
8-OH	243	245
9-OH	229	259
10-OH	215	273
11-OH	201	287

[b] Based on MS analyses before and after double bond hydrogenation. Fragment type

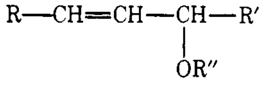




[c] Calculated: total saturated OH ester (100%) − allylic OH esters. [d] See Table I and Figure 1: relative percent, assuming that relative intensities of mass fragments are independent of position of OTMS (silyl ether) substituent in the fatty chain.

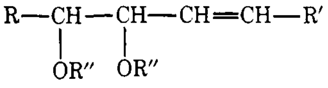
may not be as great as would be expected from stepwise oxidation because the catalyst may be partially inactivated after 6–12 hr.

The longer reaction times that increase conversions also permit more accurate product distribution to be determined. Distilled products were isolated chromatographically as either the acetoxy or free hydroxy derivatives. The main products were characterized chemically and spectrally as acetoxy- (**1a**) and allyl diacetoxy- (**2a, 3a**) octadecenoates.[16] The double bond is approximately 50% trans in both products (ir analysis). Mass spectrometry (MS),[16] as well as other evidence, also indicated varying amounts of nonallylic unsaturated acetoxy products.



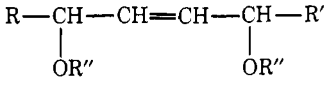
$$R{-}CH{=}CH{-}\underset{OR''}{\underset{|}{CH}}{-}R'$$

1, R″ = H
1a, R″ = Ac
1b, dihydro derivative of **1a**



$$R{-}\underset{OR''}{\underset{|}{CH}}{-}\underset{OR''}{\underset{|}{CH}}{-}CH{=}CH{-}R'$$

2, R″ = H
2a, R″ = Ac
2b, dihydro derivative of **2a**



$$R{-}\underset{OR''}{\underset{|}{CH}}{-}CH{=}CH{-}\underset{OR''}{\underset{|}{CH}}{-}R'$$

3, R″ = H
3a, R″ = Ac
3b, dihydro derivative of **3a**

R/R′ = $CH_3(CH_2)_x$—/—$(CH_2)_yCOOCH_3$
$x + y = 13$ in **1a**
12 in **2a**, **3a**

GC-MS of silyl ethers (OTMS) gave the most detailed structural analysis of the hydroxy ester derivatives. By this procedure the four possible allylic hydroxy isomers from methyl oleate were characterized clearly by their allylic fragmentation (Table II). This type of fragmentation was reported for naturally occurring allyl alcohols[17] but was unrecognized for the corresponding oleate hydroperoxide derivatives.[18] The expected mixture of 8-, 9-, 10-, and 11-acetoxyoctadecanoates (**1b**) was produced by hydrogenation of **1a**. This isomeric distribution corresponds to that determined directly on the saturated acetoxy derivatives.[16] The allylic hydroxy esters estimated from MS analyses before and after hydrogenation include 8-OH, Δ^9 (4–24%); 9-OH, Δ^{10} (14–28%); 10-OH, Δ^8 (15–28%); and 11-OH, Δ^9 (6–26%) octadecenoate (Table II). The total allylic hydroxy esters (**1**) varied from 38.5% with the $PdCl_2$-$CuCl_2$-NaOAc catalyst system to 100% with the Pd/C-$LiNO_3$ catalyst system (runs 1 and 14, Table II). With both catalyst systems the positional distribution of the acetoxy isomers (between C-8 and C-11) does not change significantly during the reaction. However, the proportion of allylic hydroxy isomers to the total hydroxy esters decreases significantly during the reaction with the $PdCl_2$-$CuCl_2$-NaOAc system but not with the Pd/C-$LiNO_3$ system (runs 6 and 8, Table II). Evidently the supported Pd-$LiNO_3$ catalyst system is highly selective for allylic acetoxylation of methyl oleate.

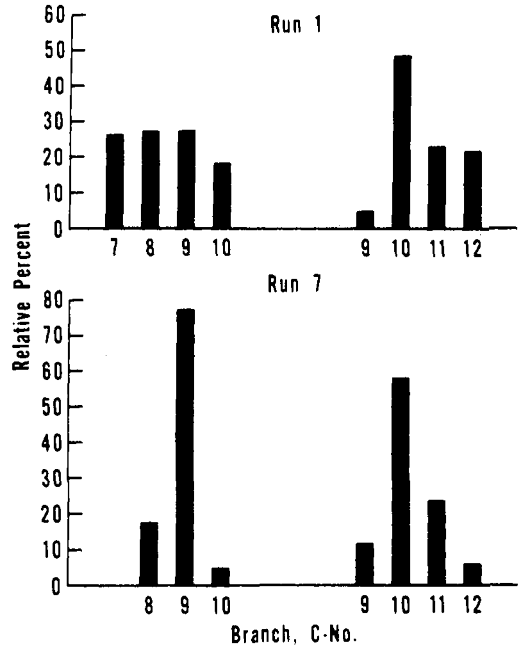


Figure 2. Isomeric distribution by mass spectrometry of dihydroxyoctadecanoate derivatives (**2b** + **3b**): $PdCl_2$ + $CuCl_2$ + NaOAc (run 1, Table I); $PdCl_2$ + $LiNO_3$ (run 7, Table I).

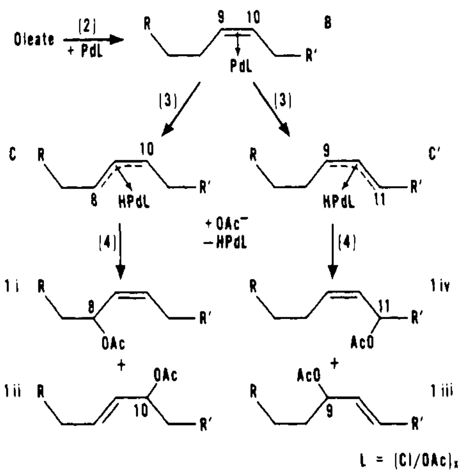
Mass spectra[16] of silyl ethers of dihydroxy derivatives (**2** + **3**) are quite complex. Fragmentation schemes are based on the spectra of allyl monohydroxy esters. Evidence for allylic fragmentation supports the structure of dihydroxy ester **2**. The mass spectra of saturated diOTMS derivatives (of **2b** + **3b**) are more straightforward and simpler than those of corresponding unsaturated derivatives. Quantitative analyses of saturated diOTMS ethers were based on data involving two reference compounds (9,10- and 10,12-dihydroxyoctadecanoate). Analyses of two acetoxylation samples show that one hydroxy substituent is scattered between C-7 and C-10 and the other hydroxy between C-9 and C-12 (Figure 2). Since 1,3-disubstituted isomers were ruled out by NMR,[16] the MS analyses are consistent with the saturated 1,2 isomers (**2b**) being mixtures of 8,9-, 9,10-, and 10,11-dihydroxyoctadecanoate and the 1,4 isomers (**3b**) being mixtures of 7,10-, 8,11-, and 9,12-dihydroxyoctadecanoate.

Discussion

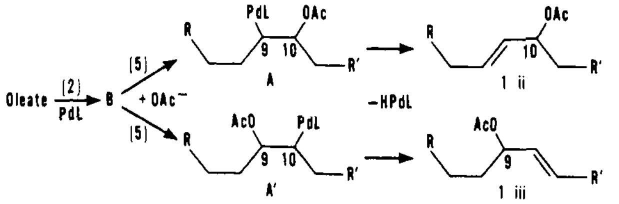
In earlier studies with short-chain acyclic olefins π-allyl routes were ruled out in favor of oxypalladation–dehydropalladation.[6,8] Although there is evidence for π-allyl PdCl complex formation during Pd(II)-catalyzed oxidation of 1-hexene, the function of this complex is uncertain.[9] Under mild conditions (25°, 1 atm O_2), reaction of both 1- and *cis*-2-hexene with $Pd_3(OAc)_6$ formed allylic complexes $Pd_3(1,2,3\text{-}H^3C_6H_{11})_2(OAc)_4$ and $Pd_2(1,2,3\text{-}H^3\text{-}C_6H_{11})_2(OAc)_2$.[19] However, because the oxidation of 2-hexene was extremely slow (4% conversion after 7 days), the addition–elimination mechanism was considered improbable and an alternative free-radical route was supported by the kinetic data.

In contrast to short-chain olefins, methyl oleate undergoes allylic acetoxylation and diacetoxylation preferentially without saturated mono- and disubstituted products being formed. Monosubstitution was limited to carbons 8, 9, 10, and 11 (Table II) and disubstitution to carbons 7 to 10 on one hand and carbons 9 to 12 on the other (Figure 2). Why only the four possible allylic acetoxy esters from methyl oleate are formed can best be explained in terms of olefinic–PdL and allylic HPdL intermediates (eq 2 and 3, Scheme I). Allyl complex C acetoxylates on either carbon 8 or carbon 10 to give 8-acetoxy-*cis*-9-octadecenoate (**1i**) and 10-acetoxy-*trans*-8-octadecenoate (**1ii**). In the same way complex C′ gives 9-acetoxy-*trans*-10-octadecenoate (**1iii**) and 11-acetoxy-*cis*-9-octadecenoate (**1iv**).

Scheme I



Scheme II



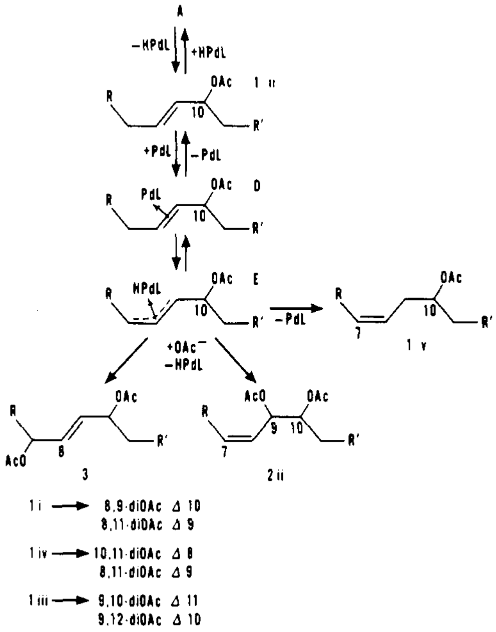
The alternate oxypalladation mechanism would be expected to produce two allylic acetoxy esters with oleate (**1ii** and **1iii**) (eq 5, Scheme II). Since substitution on carbons 9 and 10 was greater with $CuCl_2$ than with $LiNO_3$ (68–73% vs. 51–52% saturated 9-OH and 10-OH esters, Table II), oxypalladation may become important with the former oxidant. However, the stereochemistry of HPdL elimination would not be completely opposite to that of the oxypalladation step, as reported for cyclohexene,[20] because the products observed are 50% in the trans configuration.

The problem of distinguishing between olefinic and allylic isomerization has been discussed previously.[9] Although the relative amount of allylic unsaturation varied with catalysts and conditions (Table II), the positional distribution of acetoxy isomers was narrow (between C-8 and C-11). This positional specificity would be lower if allylic ester isomerization occurred during acetoxylation. Therefore, nonallylic monooxygenated isomers must form from double bond isomerization after acetoxylation and must not involve the acetoxy substituent. A reasonable pathway involves dissociation of complexes D and E (Scheme III) to produce a mixture of allylic (**1ii**) and homoallylic (10-acetoxy-*cis*-7) esters (**1v**).

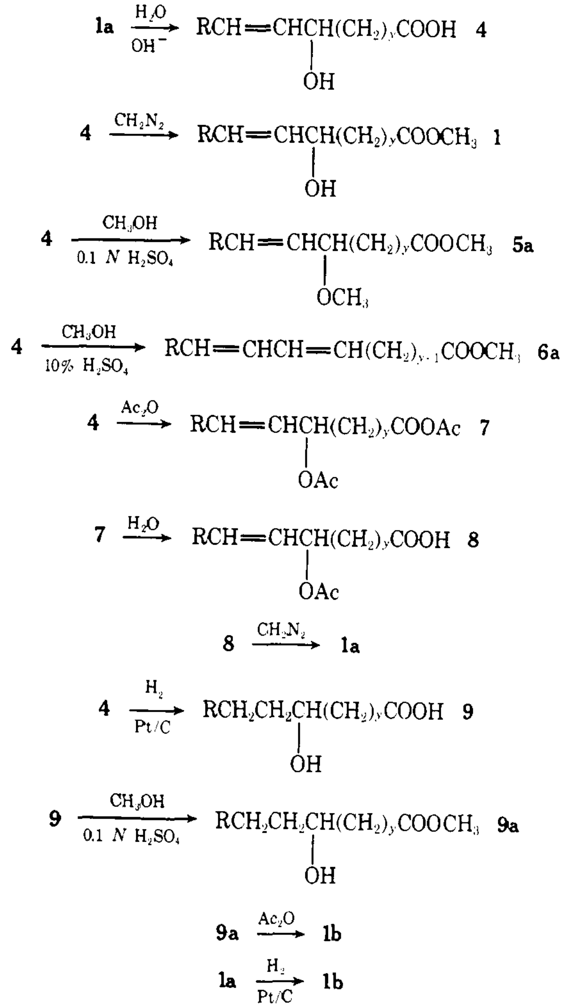
Alternatively, interconversion of the σ-oxypalladation complex A with a π-allyl complex of type E through the intermediacy of a π-olefin complex D (Scheme III) would also produce a mixture of allylic and homoallylic acetoxy esters. The lower proportion of allylic acetates obtained with $CuCl_2$ than with $LiNO_3$ may be attributed to the easier formation of complexes D and E from the trans-unsaturated 9- and 10-acetoxy esters (**1ii** and **1iii**) than from the corresponding cis-unsaturated 8- and 11-aeetoxy esters (**1i** and **1iv**).

For diacetoxylation, the data in Figure 1 indicate a direct pathway from oleate and a mechanism may be operative

Scheme III



Scheme IV



$$\mathbf{1a} \xrightarrow[\mathrm{OH^-}]{\mathrm{H_2O}} \mathrm{RCH{=}CH\underset{\underset{\displaystyle OH}{|}}{C}H(CH_2)_yCOOH} \quad \mathbf{4}$$

$$\mathbf{4} \xrightarrow{\mathrm{CH_2N_2}} \mathrm{RCH{=}CH\underset{\underset{\displaystyle OH}{|}}{C}H(CH_2)_yCOOCH_3} \quad \mathbf{1}$$

$$\mathbf{4} \xrightarrow[0.1\ N\ \mathrm{H_2SO_4}]{\mathrm{CH_3OH}} \mathrm{RCH{=}CH\underset{\underset{\displaystyle OCH_3}{|}}{C}H(CH_2)_yCOOCH_3} \quad \mathbf{5a}$$

$$\mathbf{4} \xrightarrow[10\%\ \mathrm{H_2SO_4}]{\mathrm{CH_3OH}} \mathrm{RCH{=}CHCH{=}CH(CH_2)_{y-1}COOCH_3} \quad \mathbf{6a}$$

$$\mathbf{4} \xrightarrow{\mathrm{Ac_2O}} \mathrm{RCH{=}CH\underset{\underset{\displaystyle OAc}{|}}{C}H(CH_2)_yCOOAc} \quad \mathbf{7}$$

$$\mathbf{7} \xrightarrow{\mathrm{H_2O}} \mathrm{RCH{=}CH\underset{\underset{\displaystyle OAc}{|}}{C}H(CH_2)_yCOOH} \quad \mathbf{8}$$

$$\mathbf{8} \xrightarrow{\mathrm{CH_2N_2}} \mathbf{1a}$$

$$\mathbf{4} \xrightarrow[\mathrm{Pt/C}]{\mathrm{H_2}} \mathrm{RCH_2CH_2\underset{\underset{\displaystyle OH}{|}}{C}H(CH_2)_yCOOH} \quad \mathbf{9}$$

$$\mathbf{9} \xrightarrow[0.1\ N\ \mathrm{H_2SO_4}]{\mathrm{CH_3OH}} \mathrm{RCH_2CH_2\underset{\underset{\displaystyle OH}{|}}{C}H(CH_2)_yCOOCH_3} \quad \mathbf{9a}$$

$$\mathbf{9a} \xrightarrow{\mathrm{Ac_2O}} \mathbf{1b}$$

$$\mathbf{1a} \xrightarrow[\mathrm{Pt/C}]{\mathrm{H_2}} \mathbf{1b}$$

different from that for monoacetoxylation. If oxypalladation is postulated as an initial step (eq 5, Scheme II), then our results can be explained by assuming the same path as isomerization (Scheme III). 1,3-Acetoxylation of the π-allyl system in complex E would produce a mixture of 1,2- (mainly 9,10-) and 1,4-diacetoxy *cis*- and *trans*-octadecenoate consistent with the results of Figure 2.[16] Consecutive oxidation of mono- to diacetoxy esters is apparently another pathway (Figure 1). This reaction (1ii ⇌ D) can also involve intermediate π-olefin and π-allyl complexes of type D and E undergoing 1,3-acetoxylation as above (Scheme III). This secondary oxidation of allylic acetoxy esters does not involve acetylated oxypalladation intermediates because a mixture of allylic 1,2- and vinylic 1,3-diacetoxy esters would then be produced and no 1,4 isomers. This work showed no evidence of either vinylic or 1,3-diacetoxy esters. A study of the Pd(II)-catalyzed reaction of isolated monoacetate intermediates would shed more light on the mechanism of diacetoxylation.

A free-radical mechanism[19] may also account for the high selectivity toward allylic acetoxy esters produced with Pd–$LiNO_3$. However, before this possibility can be considered seriously, a study is needed on the influence of typical free-radical initiators and inhibitors in the polar acetic acid solvent medium.

Interestingly, the allylic products from methyl oleate are similar to corresponding derivatives from hydroperoxides formed by autoxidation,[18] as well as by allylic oxidation with mercuric salts or selenium.[12] Pd-catalyzed acetoxylation provides not only a more efficient route to these allylic oxidation products, but also high yields of diacetoxy esters. Our work suggests that similar allylic dioxygenated products may also be formed under certain conditions during autoxidation of methyl oleate. Consequently, catalytic acetoxylation should provide a useful synthetic route for model compounds needed for the characterization of secondary autoxidation products of unsaturated fatty esters.

Experimental Section

Materials. The catalysts—$PdCl_2$ (Fisher Scientific Co.),[1] palladium(II) acetate (Strem Chemicals, Inc.), Pd on alumina or Pd (10%) on carbon (Engelhardt Industries), Pd black (Matheson Coleman and Bell)—and other reagents—$CuCl_2$, $LiNO_3$, NaOAc, HOAc, Ac_2O, and LiCl (Baker reagents)—were used as purchased. Methyl oleate was redistilled from esterified commercial oleic acid (Pamolyn-100, Hercules, Inc.) and analyzed 96% by GLC (impurities included 2.4% stearate and 1.6% linoleate).

Acetoxylations. A. Pressure Reaction (Run 1, Table I). Methyl oleate (0.1 mol), $PdCl_2$ (0.002 mol), $CuCl_2$ (0.1 mol), NaOAc (0.1 mol), HOAc (90 ml), and Ac_2O (10 ml) were placed in a 500-ml pressure bottle. The contents were pressurized with O_2 at 20 psi in a Parr hydrogenation apparatus and heated to 100° under thermostatic control. The pressure was maintained between 20 and 45 psi during the course of the reaction. After oxidation, the cooled mixture was filtered, concentrated by removing most of the HOAc on a rotating evaporator, poured into water saturated with Na_2CO_3, and extracted with petroleum ether. The ether extract was washed three times with Na_2CO_3 (each wash was extracted with petroleum ether) and then with water. The solution was dried (Na_2SO_4), the solvent was removed in vacuo, and after the dark brown residue (26.5 g) was molecularly distilled at 120–210° (0.02 mm), it gave 22.0 g (83%) of a yellow material containing 36% monoacetoxy and 40.5% diacetoxy esters (by GLC on a JXR silicone column[21] programmed from 180 to 260° at 4°/min): ir (neat) 1740 (C=O), 1235 ($OCOCH_3$), 1015 (C–O), and 960 cm^{-1} (trans C=C).

B. Open-Flask Reactions (Run 7, Table I). $PdCl_2$ (0.005 mol), $LiNO_3$ (0.1 mol), HOAc (125 ml), and Ac_2O (10 ml) were placed in a three-necked 250-ml flask provided with an O_2 inlet, attached to an HOAc trap and a bubbler, and with a reflux condenser, attached to a water trap. The solution, stirred magnetically, was first bubbled with O_2 saturated with HOAc and then heated. When the temperature reached 60°, methyl oleate (0.1 mol) was added through the reflux condenser. After an exothermic rise of 10° occurred, the temperature was controlled at 70°. Acetoxylation was followed by sequential GLC analysis. The cooled and filtered product was worked up as in run 1 (34 g). A 20-g fraction was molecularly distilled to give 18.2 g (91%) of a pale yellow material containing 59.9% monoacetoxy and 22.9% diacetoxy esters by GLC: ir on distillate 1740 (C=O), 1620 ($RONO_2$), 1550, 1520 (RNO_2), 1235 ($OCOCH_3$), 1010 (C–O), 960 (trans C=C), 855 cm^{-1} (ionic NO_3^-); distillation residue same ir spectrum except additional bands at

3440 (OH), 1690 (COOH), and no trans band at 960 cm^{-1}. Another sample of crude product was reactylated by refluxing with excess Ac_2O. The product was molecularly distilled, but the yield increased little (92.9%). Apparently some thermolysis of acetoxy products occurs during distillation.

Run 14 (Table I). This reaction was carried out the same way as run 7, except that 5.3 g of 10% Pd/C was the catalyst and the reaction temperature was 80°. A portion of the HOAc solution of crude product was transferred unfiltered into a pressure bottle and hydrogenated in a Parr apparatus at room temperature and 20 psi H_2 until no uptake was observed (3 hr). Analysis by GLC before hydrogenation gave 58.1% monoacetoxy and 35.1% diacetoxy esters; after hydrogenation saturates increased from 2.5 to 13.2% and acetoxy esters (42.3% mono- and 38.6% diacetoxy) decreased correspondingly. Hydrogenolysis of acetoxy esters is also accompanied by hydrogenolysis of nitrate esters as shown by ir: 3440 (OH^-) and no bands at 1630 ($RONO_2$) and 860 cm^{-1} (NO_3^-).

Product Separations. Distilled products (runs 1 and 7, Table I) were fractionated by silicic acid chromatography.[22] Mono- and diacetoxy esters were isolated in 90–97% purity by eluting successively with mixtures of 5:95 and 10:90 diethyl ether–petroleum ether. The free hydroxy esters could also be separated chromatographically, but the allylic components were easily dehydrated with silicic acid, and useful separations could only be achieved with the saturated hydroxy derivatives.

Methyl Acetoxyoctadecenoate. Compound **1a** was characterized by comparing chromatographic behavior (GLC and TLC) with that of methyl acetyl ricinoleate and by other spectral characteristics.[16] Quantitative analyses by ir (CS_2) showed isolated trans (960 cm^{-1}) estimated as 53.9%, if methyl elaidate is the reference and if difference in molecular weight is corrected.

Anal. Calcd for $C_{21}H_{38}O_4$: C, 71.14, H, 10.80. Found: C, 70.58, H, 11.00.

Methyl Acetoxyoctadecanoate. Compound **1b** was isolated chromatographically after catalytic hydrogenation of crude acetoxylation products with 5% Pt/C in hexane at room temperature and 50 psi for 1 hr. Spectral and chromatographic data are given in the supplementary material.[16] Analyses by ir showed no trans unsaturation (965 cm^{-1}).

Anal. Calcd for $C_{21}H_{40}O_4$: C, 70.74; H, 11.31. Found: C, 71.20; H, 11.36.

Methyl Diacetoxyoctadecenoate (2a + 3a). Although several GLC peaks were obtained for **2a** + **3a**, the principal one from **2b** + **3b** (hydrogenated **2a** + **3a**) corresponded to that of 9,10-diacetoxyoctadecanoate (Table III). No suitable solvent systems proved useful for TLC separation of diacetoxy ester components. Because only saturated reference compounds were available, other functional characterizations were based on data obtained before and after double bond hydrogenation.[16] Quantitative analyses by ir (CS_2) gave a value for isolated trans (960 cm^{-1}) of 53.6% (run 1, Table I).

Anal. Calcd for $C_{23}H_{40}O_6$: C, 66.96; H, 9.77. Found: C, 67.06; H, 10.34.

Methyl Diacetoxyoctadecanoate (2b + 3b). Functional characterization data are given in the supplementary material.[16]

Anal. Calcd for $C_{23}H_{42}O_6$: C, 66.63, H, 10.21. Found: C, 66.70; H, 10.26.

Characterization by Proton NMR.[16] Mono- and diacetoxy fractions showed signals due to OAc (δ 1.98–2.04) and CHOAc (δ 4.82–5.15). Monoacetoxy fractions showed absorptions due to olefinic protons (δ 5.4–5.6) as established by a double resonance experiment; diacetoxy fractions also showed absorptions in this region (δ 5.3–5.6). When used as reference, acetyl ricinoleate (methyl 12-acetoxy-*cis*-9-octadecenoate) gave similar signals as **1a** but a double resonance experiment established that the triplet at δ 2.26 (4 H) is due to both methylenes α to ester carbonyl (on C-2) and α to the double bond (on C-11). With both the monoacetoxy ester **1a** and diacetoxy esters (**2a** + **3a**), the absorption at δ 2.28 (2 H) is due only to the methylene α to the ester carbonyl (C-2). The methylene protons α to the double bond would absorb at about δ 2.0, in the same place as the acetoxymethyl protons. The allylic acetoxy structures of **1a**, **2a**, and **3a** are thus confirmed.

The two reference compounds 9,10- and 10,12-diacetoxyoctadecanoate were distinguished by the quartet in the latter at δ 1.8 due to the methylene on C-11 flanked by two methine protons ($AcOCHCH_2CHOAc$) as established by a double resonance experiment. The absence of this allylic methylene signal at δ 1.8 in **2b** and **3b** (hydrogenated **2a** and **3a**) rules out the presence of 1,3-diacetoxy isomers in the acetoxylation products. Although the two signals in the olefinic proton region may be due to the different allylic structures of **2a** and **3a**, no suitable reference compounds were available to confirm this assignment.

Chemical Characterization. Reactions in Scheme IV were carried out on crude (1 g) and chromatographically purified (30–50 mg) acetoxy esters from runs 1, 13, and 14 (Table I). Characterization data are given in the supplementary material.[16]

Acetoxy esters **1a** were saponified by refluxing for 1 hr in a 95% ethanol solution containing 5% KOH. The isolated hydroxy acids (**4**) from runs 13 and 14 were free of nitrate esters (as shown by ir). The allyl hydroxy acid **4** from **1a** could only be esterified to **1** with diazomethane. The allylic methoxy esters (**5a**) were obtained by treating **4** with weakly acidic methanol (refluxing 1.5 hr in methanol containing 0.1 N H_2SO_4, by allowing a methanol solution to stand at room temperature for 2 hr either in the presence of 1% trimethyl orthoformate and 1% HCl (w/v) or 50% dimethoxypropane (v/v) and 1% *p*-toluenesulfonic acid). Under mildly acidic conditions, the etherification of related conjugated dienols and allylic alcohols takes place readily.[23] On refluxing **4** with methanol containing 10% H_2SO_4, partial dehydration occurred as shown by formation of 16% conjugated diene **6a** (by GLC). Refluxing in benzene containing *p*-toluenesulfonic acid resulted in more efficient dehydration.[24]

After dehydration, conjugated fatty esters from purified monohydroxy (**1**) ester fractions were separated from nonallylic hydroxy components by column chromatography.[25] Fatty esters from monohydroxy esters of run 1 and 13 contained, respectively, 76.7 and 89.1% conjugated diene (by GLC on a DEGS column operated isothermally at 200°; mainly cis,trans and trans,trans and a little cis,cis). Analyses by uv (isooctane) gave ϵ values at 230 nm of 18105, and 21030, respectively. Smaller amounts of enol (about 5% in run 13, Table I, and 20% in run 1, as estimated by GLC) were neither converted to the ether **5a** nor dehydrated, and were therefore considered nonallylic.

Acetylation of hydroxy acids **4** by refluxing for 1 hr in neat acetic anhydride gave the mixed anhydride **7**, which was readily hydrolyzed to the acetoxy acid **8** by refluxing in acetone solution containing 20% (v/v) water. The acetoxy esters **1a** were regenerated by treating an ether solution of the acetoxy acid **8** with excess diazomethane.

Compound **4** was catalytically hydrogenated with 5% Pt/C in methanol or Pd/C in HOAc in a Parr apparatus at room temperature and 50 psi H_2 for 1 hr. Adams catalyst (PtO_2 in methanol) caused excessive hydrogenolysis of **4** to methyl oleate and stearate. Esterification of the saturated hydroxy acid **9** by refluxing with methanol containing 0.1 N H_2SO_4 gave the corresponding hydroxy ester **9a** but no ether. Therefore, formation of the allyl methoxy ester **5a** is due to the special reactivity of the allyl hydroxy function in **4a**. Acetylation of hydroxy ester **9a** with neat Ac_2O gave the same saturated acetoxy ester **1b** as that from catalytic hydrogenation (Pt/C) of the starting allylic acetoxy ester **1a**.

When the diacetoxy components (**2a** + **3a**) were subjected to the reactions in Scheme IV, the same chemical transformations were observed by ir; e.g., saponification, etherification, acetylation, and double bond hydrogenation. However, dehydration of the dihydroxy derivatives (**2** + **3**) formed conjugated trienes. Fatty esters from dehydrated dihydroxy esters of run 1 contained 15.6% conjugated triene (ϵ at 268 nm, 9516). This formation can be attributed to the 1,4-dihydroxy allyl ester **3** since the 1,2-dihydroxy compound **2** should not dehydrate.

Mass Spectral Analyses.[16] Isomeric analysis of **1a** shows prominent peaks due to saturated C-8 and C-9 ester fragments and much less intense peaks due to unsaturated C-10 and C-11. After double bond hydrogenation, isomeric analysis by MS becomes more definitive, and **1b** is shown to be a mixture of 8-, 9-, 10-, and 11-acetoxyoctadecanoate. With diacetoxy components it was possible to determine the position of the first acetoxy substituent (between C-7 and C-11 and mostly at C-9) but not the position of either the second acetoxy substituent or of the double bond.

Isomer Analysis by GC–MS. Ester samples were separated through a gas chromatograph (Packard Model 740 with a 6 ft × $^3\!/_{16}$ in. glass column packed with 3% JXR on Gas-Chrom Q 100/120 mesh, Applied Science) attached to a mass spectrometer (Nuclide 12-90-DF) with a direct valve connection to allow a portion of GLC effluents to enter directly into the ionization chamber. The spectrometer was set to scan every 9 sec from m/e 10 to 450. Output of the MS detector was electrically connected to a computer magnetic tape system. Later processing provided total ion plots and mass spectra of individual scans. Hydroxy ester derivatives (**1** and **2** + **3**) were silylated with bis(trimethylsilyl)trifluoroacetamide (Regis Chemical Co.). The data in Table II and Figure 2[16] were based on analyses before and after double bond hydrogenation, comparisons with reference compounds [methyl 9(10)- and 12-hydroxy-9-octadecenoate, 12-hydroxyoctadecanoate, and 9,10- and 10,12-dihydroxyoctadecanoate] and reported fragmentation schemes.[17,18,26] The 9,10-dihydroxy (threo) compound is derived from methyl oleate; the 10,12-dihydroxy (threo) compound, from methyl ricinoleate (by microbial hydration[27]).

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Registry No.—*cis*-**1a** 8-OAc, Δ^9, 56437-68-4; *trans*-**1a** 8-OAc, Δ^9, 56437-69-5; *cis*-**1a** 10-OAc, Δ^8, 56437-70-8; *trans*-**1a** 10-OAc, Δ^8, 56437-71-9; *cis*-**1a** 9-OAc, Δ^{10}, 56437-72-0; *trans*-**1a** 9-OAc, Δ^{10}, 56437-73-1; *cis*-**1a** 11-OAc, Δ^9, 56437-74-2; *trans*-**1a** 11-OAc, Δ^9, 56437-75-3; **1b** 8-OAc, 2379-99-9; **1b** 9-OAc, 2380-00-9; **1b** 10-OAc, 2380-02-1; **1b** 11-OAc, 2380-04-3; **2a**, 8,9-dihydroxy, 56437-76-4; **2a**, 9,10-dihydroxy, 56437-77-5; **2a**, 10,11-dihydroxy, 56437-78-6; **2b**, 8,9-dihydroxy, 56437-79-7; **2b**, 9,10-dihydroxy, 56437-80-0; **2b**, 10,11-dihydroxy, 56437-81-1; **3a**, 7,10-dihydroxy, 56437-82-2; **3a**, 8,11-dihydroxy, 56437-83-3; **3a**, 9,12-dihydroxy, 56437-84-4; **3b**, 7,10-dihydroxy, 56437-85-5; **3b**, 8,11-dihydroxy, 56437-86-6; **3b**, 9,12-dihydroxy, 56437-87-7; methyl oleate, 112-62-9; $PdCl_2$, 7647-10-1; $Pd(OAc)_2$, 3375-31-3; Pd, 7440-05-3.

Supplementary Material Available. Characterization data by ir, GLC, TLC, NMR, MS, and GC–MS will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Business Office, Books and Journals Division, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for \$4.00 for photocopy or \$2.50 for microfiche, referring to code number JOC-75-3247.

References and Notes

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α Anions. VII. Direct Oxidation of Enolate Anions to 2-Hydroperoxy- and 2-Hydroxycarboxylic Acids and Esters[1]

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2-Hydroperoxy acids were obtained by direct low-temperature oxygenation of enolate dianions of straight-chain and branched-chain aliphatic carboxylic acids. Esters of 2-hydroperoxy acids were similarly obtained from ester enolate anions or by diazomethane reaction with 2-hydroperoxy acids. Alternatively, 2-hydroxy acids are formed directly and nearly quantitatively by dianion oxygenation at ambient temperatures. Stabilities, decompositions, and products of decomposition of the hydroperoxy acids and their esters are described.

Although 2-hydroperoxy esters of aliphatic[3] and araliphatic[4] acids were prepared a decade ago, attempts to derive the parent 2-hydroperoxycarboxylic acids through hydrolysis of the 2-hydroperoxycarboxylic esters[5,6] or by free-radical autoxidation of fatty acids were ineffective.[7] In the course of our studies on enolate dianions,[8a] we indicated the reactivity of the dianions to oxygen and subsequently presented the reaction as a route to 2-hydroperoxy- and 2-hydroxycarboxylic acids.[1] The present paper describes the details of the oxygenation reaction and further provides a facile preparation of 2-hydroperoxycarboxylic esters which has advantages in scope and convenience over those previously reported.[3,4] The decomposition of several hydroperoxycarboxylic acids and esters were also examined.

Simultaneously with our presentation of this work,[1] Adam and Liu[5] reported two methods for deriving 2-hydroperoxy acids. The photodecarboxylation of an ether solution of di-*n*-butylmalonoyl peroxide in the presence of hydrogen peroxide gave 2-butyl-2-hydroperoxyhexanoic acid, which resisted purification. Their more successful alternate method employed the enolate dianion of 3,3-dimethylbutyric acid, which on silylation, oxygenation, and hydrolysis in methanol gave the desired 2-hydroperoxy acid. Although quantitative yields of hydroperoxy acid were reported for