Allylic Hydroxy Fatty Compounds with Δ5-, Δ7-, Δ8-, and Δ10-Unsaturation

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ABSTRACT: Several novel allylic mono- and dihydroxy fatty compounds were synthesized from Δ5, Δ7-, Δ8-, and Δ10-monounsaturated fatty acids with the selenium dioxide/*tert*-butylhydroperoxide. Chainlengths were C_{19} for Δ7 and Δ10, and C_{20} for Δ5 and Δ8 compounds. With a full range of Δ5- to Δ11-unsaturated allylic monohydroxy fatty compounds available, position-dependent effects in the ^{13}C-nuclear magnetic resonance spectra of these compounds are discussed. The olefinic carbon shift differences in monohydroxy compounds, where the OH group is located between the double bond and the terminal methyl group, were plotted as a function of double-bond distance from C_1. This plot is presumably a rational function. During SeO_2-based hydroxylation, lactonization of the hydroxy groups, located between the double-bond and the carboxyl group, also occurs for Δ5 unsaturation.
JAOCS 72, 703–706 (1995).

KEY WORDS: Allylic hydroxylation, hydroxy fatty acids, lactonization, NMR.

Recently, we reported numerous novel allylic mono- and dihydroxy fatty compounds that had been synthesized from monounsaturated fatty compounds with the selenium dioxide/*tert*-butylhydroperoxide (TBHP) system (1,2). Chainlengths included C_{16}, C_{18}, C_{20}, and C_{22}. The positions of unsaturation were Δ_6, Δ_9, Δ_{11}, and Δ_{13}. We now synthesized analogous hydroxy compounds with unsaturation at Δ5, Δ7, Δ8, and Δ10 from the corresponding unsubstituted fatty acids. Thus a series of allylic mono- and dihydroxy compounds are now available to compare nuclear magnetic resonance (NMR) chemical shifts. The dihydroxy products were again obtained as *erythro/threo* diastereomers (1,2).

NMR characterization of fatty compounds is of special interest, and many of them have been investigated by this method (3–25). Among the products of allylic hydroxylation, the monohydroxy compounds with the hydroxy group between the double-bond and the terminal methyl group (referred to in the following text as position-II compounds; the monohydroxy products with the OH group between the double bond and C_1 will be referred to as position-I compounds) are of particular interest (2) because the allylic hydroxy group and the functional group at C_1 both exert their influence. Previous NMR characterization of allylic hydroxy compounds in the literature (1,2) was extended by the present compounds.

Products such as those presented here are surface-active (26). Particularly the allylic monohydroxy compounds are good surfactants. The compounds may therefore be suitable as additives in products such as biodiesel, lubricants, greases, and cosmetics.

EXPERIMENTAL PROCEDURES

All starting materials [5(*Z*)-eicosenoic acid, 7(*Z*)-nonadecenoic acid, 8(*Z*)-eicosenoic acid, and 10(*Z*)-nonadecenoic acid] were obtained from Nu-Chek-Prep, Inc. (Elysian, MN). 7(*Z*)-Octadecenoic acid was obtained from Sigma Chemical Co. (St. Louis, MO). Selenium dioxide and 90% TBHP solution, containing 5% water and 5% *tert*-butyl alcohol, were purchased from Aldrich Chemical Co. (Milwaukee, WI). Solvents were obtained from EM Science (Gibbstown, NJ). Melting points are uncorrected.

All equipment used in this work, experimental procedures, and some compounds mentioned in this work were described previously (1,2). Hydroxylation reactions were conducted here on a 3-g scale with the amounts of all other reactants calculated accordingly. This scale proved to be advantageous for the separation of monohydroxy compounds on the high-performance liquid chromatography (HPLC) system compared to other amounts used previously (1,2) because less coelution occurred. Methyl esters were prepared by a standard procedure with diazomethane.

RESULTS AND DISCUSSION

Figure 1 depicts the hydroxylated products obtained in this work. Yields of hydroxy products after HPLC purification are given in Table 1. Characterization of the new compounds by mass spectrometry [MS; electron ionization (EI) mode], NMR, and infrared (IR) spectroscopy coincides with that of the previously synthesized materials (1,2).

The reaction products and the characteristic MS ions for their silylated derivatives (trimethylsilyl ether trimethylsilyl esters) are: 7-hydroxy-5(*E*)-eicosenoic acid, *m/z* 287; 6-hydroxy-7(*E*)-nonadecenoic acid, *m/z* 283; 9-hydroxy-7(*E*)-

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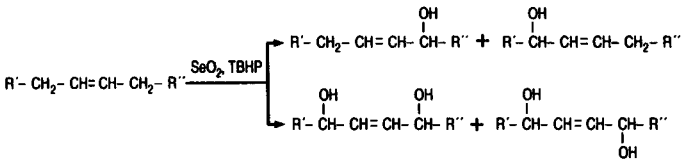

FIG. 1. Reaction procedure and hydroxy products.

TABLE 1
Yields of Monohydroxy and Dihydroxy Compounds in the Reaction of Isolated Double Bonds in Straight-Chain Fatty Acids with SeO_2/TBHP[a]

	Yields (%)			
	Monohydroxy products		Dihydroxy products	
Starting material[b]	Position-I	Position-II	*erythro*	*threo*
19,Δ7*Z*,CO_2H	25	24	12	16
19,Δ10*Z*,CO_2H	24	22	10	18
20,Δ5*Z*,CO_2H[c]	—	17	—	—
20,Δ8*Z*,CO_2H	27	24	11	20

[a]The yields given in this table were obtained by gas chromatography mass spectrometry (GC/MS) analysis of the crude mixture and GC/MS and gravimetry of high-performance liquid chromatography (HPLC) fractions. Total yields obtained after HPLC purification reported previously from similar reactions (Refs. 1,2) are lower. Yield determination of monohydroxy compounds: The relative amounts of each compound were determined by comparing peak intensities of the major fragments and relating them to the weight of the fraction. The ratio of compounds was then related to the GC/MS of the crude mixture. yield determination of the dihydroxy compounds: The weight ratios of the HPLC fractions of the diastereomers were related to the GC/MS of the crude mixture; TBHP, *tert*-butylhydroperoxide.

[b]The starting materials are coded as in the following example: 5(*Z*)-eicosenoic acid is 20,Δ5*Z*,CO_2H. First, the number of carbon atoms in the chain is given, followed by location and geometry of the double bond and finally by the functional group at C_1.

[c]No position-I monohydroxy and dihydroxy compounds were obtained due to lactonization (see text). Yield of γ-lactone 24%.

TABLE 2
Melting Points of Monounsaturated Allylic Monohydroxy Compounds and ^{13}C Nuclear Magnetic Resonance Signals (solvent: $CDCl_3$) of Olefinic Carbon Atoms in Monounsaturated Allylic Hydroxy Fatty Compounds

Compound[a]	m.p. (°C)	^{13}C (ppm; olefinic carbons)[b]
19,Δ7,CO_2H,6-OH	56–57	132.61 (7), 132.53 (8)
19,Δ7,CO_2H,9-OH	55–55.5	133.22 (8), 131.76 (7)
19,Δ10,CO_2H,9-OH	45.5–52.5	132.78 (10), 132.38 (11)
19,Δ10,CO_2H,12-OH	54.5–55	132.86 (11), 132.23 (10)
20,Δ5, CO_2H, 7-OH	61–63	134.14 (6), 130.46 (5)
20,Δ8, CO_2H, 7-OH	56.5–58	132.66 (8), 132.51 (9)
20,Δ8,CO_2H, 10-OH	60.5–61.5	133.07 (9), 132.00 (8)
19,Δ7,CO_2CH_3,6-OH	Liquid	132.74 (7), 132.40 (8)
19,Δ7, CO_2CH_3,9-OH	Liquid	133.13 (8), 131.53 (7)
19,Δ10,CO_2CH_3,9-OH	Liquid	132.94 (10), 132.29 (11)
19,Δ10, CO_2CH_3,12-OH	Liquid	133.05 (11), 132.13 (10)
20,Δ5,CO_2CH_3,7-OH	Liquid	134.20 (6), 130.41 (5)
20,Δ8,CO_2CH_3, 7-OH	Liquid	132.84 (7), 132.32 (8)
20,Δ8,CO_2CH_3,10-OH	Liquid	133.18 (8), 131.93 (7)

[a]The compounds are coded as in Table 1. However, here the location of the hydroxy group is also indicated.

[b]The numbers in parentheses indicate the carbon atom assigned to the signal.

nonadecenoic acid, *m/z* 315; 7-hydroxy-8(*E*)-eicosenoic acid, *m/z* 283; 10-hydroxy-8(*E*)-eicosenoic acid, *m/z* 329; 9-hydroxy-10(*E*)-nonadecenoic acid, *m/z* 241; 12-hydroxy-10(*E*)-nonadecenoic acid, *m/z* 357; *erythro-* and *threo*-6,9-dihydroxy-7(*E*)-nonadecenoic acid, *m/z* 243, 275, 281, 313, 371, 403, 529; *erythro-* and *threo*-7,10-dihydroxy-8(*E*)-eicosenoic acid, *m/z* 243, 281, 289, 327, 371, 417; *erythro-* and *threo*-9,12-dihydroxy-10(*E*)-nonadecenoic acid, *m/z* 201, 239, 317, 329, 355, 445. These ions arise from the cleavage pattern discussed previously (Refs. 1,2, and references therein). As discussed below, the hydroxylation of 5(*Z*)-eicosenoic acid gave only one hydroxy product due to lactonization.

Melting points and characteristic NMR signals are given in Tables 2–4. The ^{13}C NMR spectra of the present products show the effects discussed previously (2), which are: (i) distinguishing position-I and position-II monohydroxy compounds by the differences of the olefinic carbon signals; (ii) decreasing olefinic shift differences in position-II compounds with increasing chainlength; (iii) dependence of the differences on the functional group at C_1 (the differences are greater for methyl esters than for acids; the more-polar alcohol and acid groups have similar effects); and (iv) discerning *erythro/threo* diastereomers of the dihydroxy products (downfield shifts of the olefinic and α carbons in the *threo* diastereomers compared to the *erythro* diasteromers). Also, ^1H NMR can distinguish the allylic dihydroxy diastereomers by the shifts of the olefinic protons (2).

^{13}C NMR and ^1H NMR characterization of long-chain fatty compounds has been described extensively by other researchers (3–24; for a review of ^{13}C NMR, see Ref. 25). Of particular interest are the shifts of unsaturated carbons and their neighboring carbons when the double bond continuously moves down the chain. This has been described for monoenoic (5–10,15,16,20), polyenoic (5-7,9,15,16,20,22), and acetylenic (5–7,14,15,20) fatty acids as well as for some substituted monoenoic (1,2,12,21) fatty acids. NMR effects, similar to those mentioned above for the present allylic hydroxy acids, are also discussed in many of these papers.

Table 5 lists the differences in the ^{13}C NMR shifts of the olefinic carbons of position-II monohydroxy fatty acids and esters. Further insight into these differences can be gained when the values are plotted (Fig. 2). This plot shows that the differences in the shifts for olefinic carbons of position-II allylic monohydroxy compounds are presumably a rational function, thus confirming earlier discussion of this observation (2). Previous evaluations of NMR spectra had focused only on determing additive or substractive increments by which the shifts differ in comparison to a selected standard (4,6,7,9,10,12,14). The ^{13}C NMR spectra of other fatty compounds discussed in the literature can be evaluated in a similar fashion. Detailed calculations on this novel evaluation of ^{13}C NMR spectra of unsaturated fatty compounds have now been conducted (27).

It is permissible to compare the position-II monohydroxy compounds despite their varying chainlengths (especially

TABLE 3
Melting Points and Selected ^{13}C Nuclear Magnetic Resonance (NMR) Signals (solvent: $CDCl_3$) of Monounsaturated *Allylic* Dihydroxy Acids

Compounds[a]	m.p. (°C)	^{13}C-NMR signals (ppm)	
		Olefinic[b]	Hydroxy-bearing
19,Δ7,CO_2H,*e*-6,9-diOH	97–97.5	133.28, 132.80	71.68, 71.35
19,Δ7,CO_2H,*t*-6,9-diOH	65–67	133.87,133.48	72.31, 71.91
19,Δ10,CO_2H,*e*-9,12-diOH	90–91	133.25, 133.14	71.84, 71.81
19,Δ10,CO_2H,*t*-9,12-diOH	71–73.5	133.84, 133.76	72.34, 72.29
20,Δ8,CO_2H,*e*-7,10-diOH[c]	89.5–95	133.14, 132.88	71.66, 71.49
20,Δ8,CO_2H,*t*-7,10-diOH	75–76.5	133.87, 133.62	72.30, 72.11

[a]The compounds are coded as in the preceding tables. *Erythro* and *threo* are abbreviated *e* and *t*, respectively.
[b]The ^{13}C signals of the olefinic carbons of the dihydroxy compounds could not be assigned.
[c]NMR spectrum obtained with CD_3OD as cosolvent.

TABLE 4
Selected ^1H NMR Signals (solvent: $CDCl_3$) of Allylic Dihydroxy Compounds

Compounds[a]	^1H NMR signals (ppm)	
	CH=*CH*	CH_2 at C_2 (triplet)[b]
19,Δ7,CO_2H,*e*-6,9-diOH	5.51	2.18
19,Δ7,CO_2H,*t*-6,9-diOH	5.59	2.29
19,Δ10,CO_2H,*e*-9,12-diOH	5.57	2.21
19,Δ10,CO_2H,*t*-9,12-diOH	5.53	2.23
20,Δ8,CO_2H,*e*-7,10-diOH[c]	5.48	2.14
20,Δ8,CO_2H,*t*-7,10-diOH	5.52	2.23

[a]The compounds are coded as in the preceding tables. See Table 3 for abbreviations.
[b]Signals of these protons chosen as standard to compare the different shifts of the *erythro* and *threo* diastereomers (2). The differences between δ(C*H*=C*H*) and δ(CH_2 at C_2) are greater for *erythro* than for *threo* diastereomers.
[c]NMR spectrum obtained with CD_3OD as cosolvent.

TABLE 5
Resonance Shift Differences of Olefinic Carbon Atoms in the ^{13}C NMR Spectra of Position-II Allylic Monohydroxy Fatty Acids and Esters

Compound[a]	^{13}C NMR resonance differences of olefinic carbons (ppm)	
	CO_2H	CO_2CH_3
20,Δ5,7-OH[b]	3.68	3.79
18,Δ6,8-OH[c]	2.20	2.37
19,Δ7,9-OH[b]	1.46	1.60
20,Δ8,10-OH[b]	1.07	1.25
16,Δ9,11-OH[c]	0.89	1.22
18,Δ9,11-OH[c]	1.00	1.29
19,Δ10,12-OH[b]	0.63	0.92
18,Δ11,13-OH[c]	0.74	0.93
20,Δ11,13-OH[c]	0.74	1.05
22,Δ13,15-OH[c]	0.65	0.92

[a]The compounds are coded analogous to the preceding tables. The functional group at C_1, however, is given in the columns for resonance differences. The compounds are arranged in order of increasing distance of the double bond from C_1.
[b]NMR spectrum reported in Table 2 of this paper.
[c]NMR spectrum reported in Reference 2.

with regard to the length of the hydrocarbon chain on the side of the terminal methyl group), because a comparison of literature values (7,9,14) shows that the distal hydrocarbon moiety does not significantly affect the resonances until the double bond is within four to five carbons of the terminal methyl group. The present compounds contain no double bonds that close to the terminal methyl group. For example, we also synthesized 9-hydroxy-7(*E*)-octadecenoic acid and found a difference of the olefinic carbons of 1.48 ppm (133.24 and 131.76 ppm), which is virtually identical to the values for 9-hydroxy-7(*E*)-nonadecenoic acid (see Tables 2 and 5). The second monohydroxy and the dihydroxy products obtained from 7(Z)-octadecenoic acid also closely resembled the products from the other homologues and are therefore not included in the data.

Neither position-I monohydroxy nor dihydroxy products were found for 5(*Z*)-eicosenoic acid as starting material. This is due to spontaneous cyclization of the product with a position-I hydroxy group to give the corresponding γ-lactone. Lactonization was also found in the SeO_2/TBHP-based hydroxylation of fatty compounds with Δ6-unsaturation (2). No lactonization occurred with the Δ7 starting material. Lactonization in SeO_2-based hydroxylations thus occurs for double bonds up to C_6 in position-I hydroxy compounds.

The melting point of the present γ-lactone, [4-(1(*E*)-tetradecenyl)-4-butanolide], is 49.5–50°C. The δ-lactone obtained previously is a liquid at room temperature (2). The carbonyl absorption in the IR spectrum of the present γ-lactone was found at 1783 cm^{-1} compared to 1730 cm^{-1} of the δ-lactone (2). ^{13}C NMR signals were found at 177.10 (C_1), 135.79 (C_5), 127.25 (C_6), 81.18 (C_4), 32.09, 31.90, 29.64, 29.55, 29.42, 29.34, 29.10, 28.83, 28.74, 22.67, 14.11 (C_{18}), which correspond to the spectra reported elsewhere for lactones (28,29). ^1H NMR resonances were at 5.83-5.76 (*m*, 1H, C_5), 5.50–5.44 (*dd*, J = 15.4 Hz, 1H, C_6), 4.91–4.85 (*q*, 1H, C_4), 2.55–2.50 (*t*, C_2), 2.40–2.31 (*m*, 1H, C_3), 2.07–2.01 (2H, C_2), 1.99–1.94

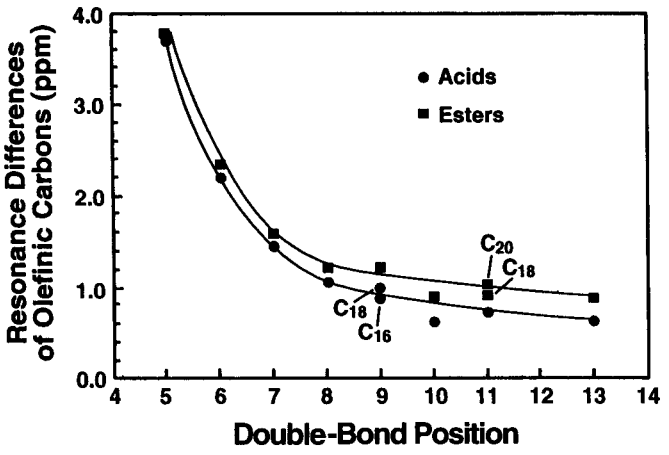

FIG. 2. Plots of the olefinic carbon shift separation of position-II fatty acids and esters in ^{13}C nuclear magnetic resonance vs. the position of the double bond. The values used for these plots are given in Table 5.

(*m*, 1H, C_3), 1.38–1.24 (*m*, CH_2), and 0.88–0.85 (*t*, 3H at C_{18}). EI–MS: 41 (100%), 43 (81%), 55 (67%), 111 (65%), 57 (35%), 81 (33%).

In conclusion, an extensive range of monounsaturated fatty acids with allylic hyroxy groups is now available. The olefinic shift differences in the ^{13}C NMR spectra of position-II compounds can be plotted as rational functions. Lactonization occurs with Δ5 and Δ6 position-I hydroxy compounds.

ACKNOWLEDGMENT

We thank Dale W. Ehmke and Scott P. Blomberg for excellent technical assistance.

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[Received August 12, 1994; accepted March 28, 1995]