Pergamon

Bioorganic & Medicinal Chemistry, Vol. 4, No. 3, pp 439–443, 1966

0968-0896/96 $15.00 + 0.00

S0968-0896(96)00023-5

Synthesis of [14,14,14-$^2H_3$] 12-Hydroxytetradecanoic Acid and [13,14-$^2H_2$] 11-Hydroxytetradecanoic Acid Useful as Tracers to Study a (11*E*)-Desaturation Reaction in *Spodoptera littoralis*

Isabel Navarro, Gemma Fabriás* and Francisco Camps*

Department of Biological Organic Chemistry, CID-CSIC, Jordi Girona 18–26, 08034-Barcelona, Spain

Abstract.—The synthesis of deuterium labeled 11- and 12-hydroxytetradecanoic acids to study a (11*E*) desaturase in the moth *Spodoptera littoralis* is reported. [14,14,14-$^2H_3$] 12-hydroxytetradecanoic acid was synthesized in four steps from 11-iodo-1-undecene in 49% overall yield. Deuterium was introduced by reaction of an epoxy ester with $(CD_3)_2CuLi$. The preparation of [13,14-$^2H_2$] 11-hydroxytetradecanoic acid was carried out in six steps from 11-bromoundecanoic acid in 55% overall yield. In this case, label was introduced by deuteration of an homoallyl alcohol with D_2, using the Wilkinson catalyst. Incubation of pheromone glands with either of both acids did not lead to the formation of the labeled (11*E*)-tetradecenoic acid. Copyright © 1996 Elsevier Science Ltd

Introduction

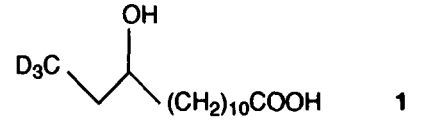
The biochemical pathways that lead to lepidopteran sex pheromones have been elucidated in many species. Among the enzymes involved in these processes, delta-11 desaturases are receiving most attention because of their uniqueness in nature.[1] Although both (11*Z*)- and (11*E*)-monounsaturated fatty acids have been detected in pheromone glands, until now, investigations in this area have concentrated on the formation of the (*Z*) isomer, which takes place by the action of (11*Z*)-desaturases.[1]

In our ongoing project on the study of the action of a (11*E*)-desaturase of tetradecanoic acid involved in the biosynthesis of *Spodoptera littoralis* sex pheromone,[2] we required mass-labeled 11-hydroxytetradecanoic acid and 12-hydroxytetradecanoic acid. These tracers would be used to investigate the possibility that (*E*)-11-tetradecenoic acid might be formed by dehydration of 11- or 12-hydroxytetradecanoic acids. In this article we report facile procedures to prepare [14,14,14-$^2H_3$] 12-hydroxytetradecanoic acid (**1**) and [13,14-$^2H_2$] 11-hydroxytetradecanoic acid (**2**) (Fig. 1), as well as the results of the mass-labeling experiments with both compounds.

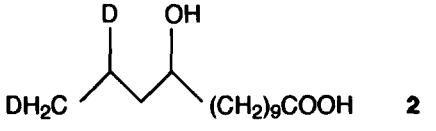
Results and Discussion

The preparation of labeled tracer **1** was accomplished, in four steps, as outlined in Scheme 1. Alkylation of the lithium salt of 2,4,4-trimethyl-2-oxazoline[3] with 11-iodo-1-undecene (**3**) afforded the oxazoline **4**. Treatment of **4** with 10% H_2SO_4:MeOH furnished the expected methyl ester **5**, which upon reaction with *m*-chloroperbenzoic acid gave rise to the epoxy ester **6**. Treatment of this epoxy ester **6** with $(CD_3)_2CuLi$.[4] readily prepared by reaction of CD_3Li with CuI, in Et_2O at 0 °C, followed by hydrolysis of the ester function afforded the expected acid **1** in 49% overall yield. Structural characterization of tracer **1** was carried out by ^1H and ^{13}C NMR and MS. The presence of the trideuteromethyl group was confirmed by the absence of the methyl signal in the ^1H NMR spectrum and by the multiplicity of the signal corresponding to C-14 at δ 8.93 (*hept*, $J = 25$ Hz) in the ^{13}C NMR spectrum. The MS analysis of the trimethylsilyl derivative of the corresponding methyl ester of **1** (**12a**) also revealed the existence of the ω-trideuteromethyl group, as concluded from the diagnostic fragment at *m/z* 134, corresponding to ion A^+ (Fig. 2).[5]

The synthesis of the labeled hydroxy acid **2** was carried out as indicated in Scheme 2. In the first step,



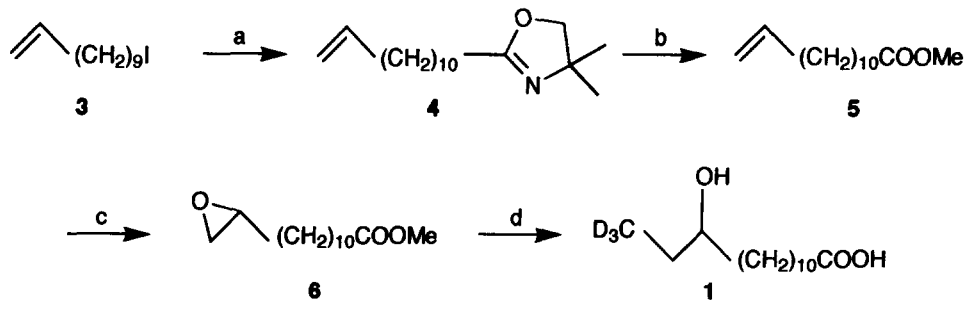
1



2

Figure 1. Mass labeled hydroxytetradecanoic acids synthesized and bioassayed in this study.

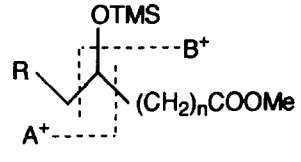
Key words: Sex pheromone, biosynthesis, mass labeling, hydroxyfatty acid, *Spodoptera littoralis*.



Scheme 1. Reagents: a, 2,4,4-trimethyl-2-oxazoline/BuLi/THF/ −78 °C (92%); b, H_2SO_4/MeOH/reflux (71%); c, MCPBA/$CHCl_3$ (92%); d, $(CD_3)_2CuLi/Et_2O$/0 °C, then KOH/MeOH:H_2O (82%).

11-bromoundecanoic acid (**7**) was protected as the oxazoline derivative following the standard sequence of reactions.[6] This usual treatment led, in our case, to a mixture of bromo- and chlorooxazolines (**8a** and **b**), which was directly oxidized with pyridine oxide[7] to afford the aldehyde **9**. Reaction of **9** with allylmagnesium bromide in Et_2O at 0 °C gave the expected homoallyl alcohol **10** in 97% yield. As the homoallyl alcohol group was potentially labile against acids, removal of the oxazoline group of **10** was carried out under basic conditions following the method reported by Meyers et al.[3] Thus, **10** was first treated with MeI to form the *N*-methyl oxazoline salt, which was then hydrolyzed with 1 N NaOH. Finally, deuteration of **11** with D_2 in MeOD:C_6D_6, in the presence of the Wilkinson catalyst,[8] afforded the expected deuterated hydroxy acid **2**. When deuteration of **11** was assayed in MeOD using 10% Pd/C as a catalyst, compound **2** was obtained as a mixture of isotopomers at C-12, C-13 and C-14. Their proportions were determined from the abundances of ions A^+ (Fig. 2)[5] in the MS of the trimethylsilyl derivative **12b**. As expected,[8] a single isotopomer was isolated by using the Wilkinson catalyst in the deuteration reaction, as concluded from the MS spectrum of derivative **12b** (Fig. 2), in which a single ion A^+, at *m/z* 147, was observed.

In the bioassays, incubations of pheromone glands with either **1** or **2** did not result in the formation of the labeled (11*E*)-tetradecenoic acid. Thus, coupled GC–MS analyses (Fig. 3) of extracts prepared from glands treated with either **1** or **2** did not show the presence of ions at *m/z* 243 (treatment with **1**) or 242 (treatment with **2**) at the expected retention times of labeled methyl (11*E*)-tetradecenoate. Labeled methyl (11*E*)-tetradecenoate was observed, however, in extracts arising from glands treated with [14,14,14-$^2H_3$] tetradecanoic acid, which indicated that the bioassay conditions were suitable. These results suggest that the formation of (11*E*)-tetradecenoic acid from tetradecanoic acid does not occur by dehydration of 11- or 12-hydroxytetradecanoic acid. However, since it is



	R	A^+	B^+
12a:	CD_3	134	301
12b:	$CHDCH_2D$	147	287

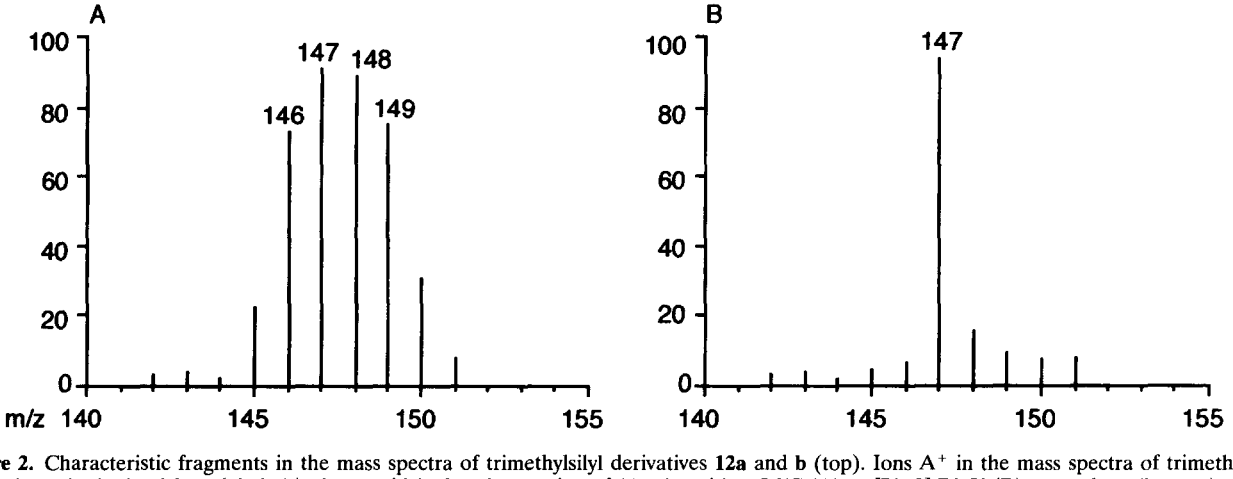
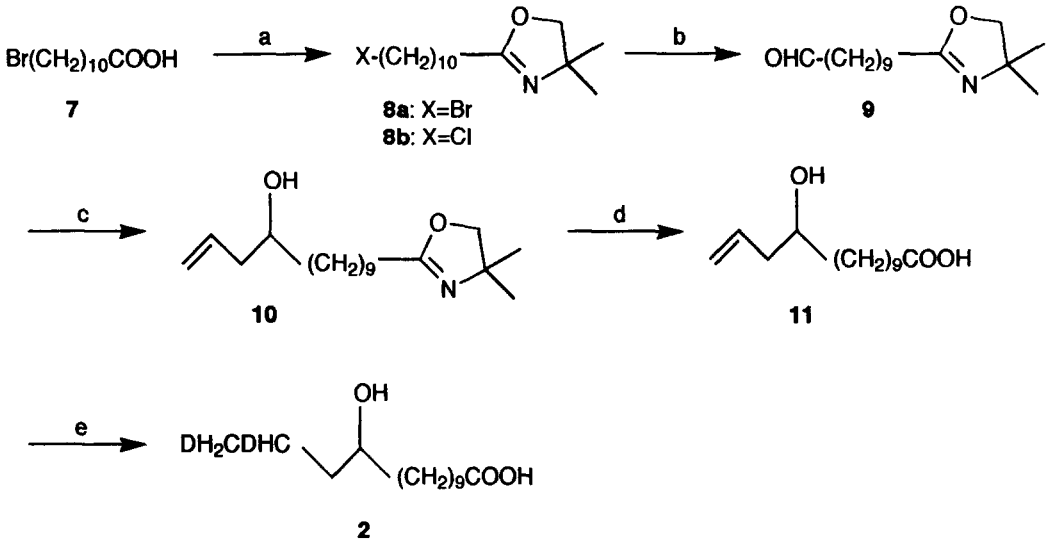


Figure 2. Characteristic fragments in the mass spectra of trimethylsilyl derivatives **12a** and **b** (top). Ions A^+ in the mass spectra of trimethylsilyl derivative **12b** obtained from labeled hydroxy acid **2** after deuteration of **11** using either Pd/C (A) or $[Ph_3P]_3RhCl$ (B) as catalysts (bottom).



Scheme 2. Reagents: a, $Cl_2(CO)_2$, then $H_2NC(CH_3)_2CH_2OH$, then Cl_2SO (82%); b, Pyridine oxide/toluene/120 °C (98%); c, $H_2C=CHCH_2MgBr$/Et_2O/−10 °C (97%); d, MeI, then 1 N NaOH/MeOH (95%); e, D_2/$[Ph_3P]_3RhCl$ (74%).

possible that acids **1** and **2** are not appropriate substrates to be incorporated into the biochemical pathway, a series of other alternative derivatives are now being prepared to pursue these biochemical studies.

Experimental

Microanalyses were performed with a Carlo Erba model 1106 at the Microanalysis Service of CID-CSIC. FT-IR spectra were recorded in film on a Michelson Bomem MB-120 spectrometer. ^1H and ^{13}C NMR spectra were obtained in $CDCl_3$ with either a Varian XL200 or Varian Unity 300 spectrometers at 200 or 300 MHz, respectively, for ^1H and 50 or 75 MHz for ^{13}C, respectively. Low resolution MS were determined on a Hewlett Packard HP 5995 mass spectrometer coupled to a gas chromatograph equipped with a fused silica capillary column HP-1. Isolation of products was accomplished, unless otherwise indicated, by pouring the reaction mixture into ice, extractions with the specified solvent, washing of the combined extracts with 10% HCl and/or satd $NaHCO_3$ if required and then with brine, drying over $MgSO_4$, followed by filtration and then evaporation of the solvent under reduced pressure. To prepare deactivated silica gel, 10% water (v/w) was added and the mixture was shaken and immediately used. Preparation of trimethylsilyl derivatives of hydroxy esters was performed by treatment with bis(trimethylsilyl)trifluoroacetamide according to reported procedures.[9] Methyl esters of hydroxy acids were prepared by treatment with BF_3/MeOH.[10] The bioassays and analyses were performed as previously described.[2]

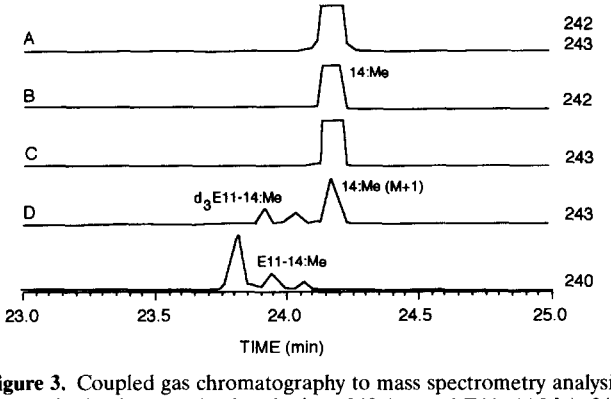


Figure 3. Coupled gas chromatography to mass spectrometry analysis traces obtained by monitoring the ions 240 (natural E11-14:Me), 242 (d_2-E11-14:Me) and 243 (d_3-E11-14:Me) in methanolyzed lipidic extracts of *S. littoralis* pheromone glands treated with A: DMSO; B: hydroxy acid **2**; C: hydroxy acid **1** and D: [14,14,14-$^2H_3$] tetradecanoic acid. Abbreviations are: 14:Me, methyl tetradecanoate; E11-14:Me, methyl (11*E*)-tetradecenoate; d_2-E11-14:Me, methyl (13,14-$^2H_2$) (11*E*)-tetradecenoate; d_3-E11-14:Me, methyl (14,14,14-$^2H_3$) (11*E*)-tetradecenoate.

2-(11-Dodecenyl)-4,4-dimethyl-2-oxazoline (4). To a solution of 2,4,4-trimethyl-2-oxazoline (1.8 g, 16.0 mmol) in 16 mL of anhydrous THF was added, under Ar at −78 °C, 11 mL (5.9 mmol) of a 1.4 M solution of ^{n}BuLi in pentane. After 30 min of stirring was added, at −78 °C, 3 g (0.7 mmol) of 11-iodo-1-undecene (**3**) dissolved in 9 mL of THF. The reaction mixture was stirred at room temperature for 3 h and extracted with hexane. Purification of the crude by flash chromatography using hexane:Et_2O (1:1) as eluent furnished 3.9 g (14.7 mmol, 92%) of pure oxazoline **4**. Calcd for $C_{17}H_{31}NO$: C, 76.98; H, 11.69; N, 5.28. Found: C, 76.93; H, 11.84; N, 5.29. IR: 2964, 2925, 2854, 1668, 1639, 1604, 1461, 1363, 985 cm^{-1}. ^1H NMR (300 MHz): δ 5.81 (*m*, 1H, C11′—H), 4.93 (*m*, 2H, C12′—H), 3.87 (*s*, 2H, C5—H), 2.22 (*t*, J=7.8 Hz, 2H, C1′—H), 2.03 (*m*, 2H, C10′—H), 1.59 (*m*, 2H, C2′—H), 1.24 (*b*, 20H, 2×CH_3, C3′—H to C9′—H). ^{13}C NMR (50 MHz): δ 166.09 (C-2), 139.22 (C-11′), 114.06 (C-12′), 78.83 (C-5), 66.79 (C-4), 33.79 (C-10′), 29.49, 29.43, 29.18,

29.11, 28.90, 28.43, 28.16 (C-1′ to C-9′), 26.04 ($2 \times CH_3$).

Methyl 12-tridecenoate (5). A solution of oxazoline **4** (0.265 g, 1 mmol) in 5% H_2SO_4/MeOH (5 mL) was stirred under reflux for 18 h. After this time, solvent was removed and the residue extracted with hexane, giving 0.16 g (0.7 mmol, 71%) of ester **5**, which was submitted to the next reaction without further purification. IR: 2925, 2854, 1714, 1641, 1436, 1170, 910 cm^{-1}. ^1H NMR (200 MHz): δ 5.82 (*m*, 1H, C12—H), 4.94 (*m*, 2H, C13—H), 3.65 (*s*, 3H, $COOCH_3$), 2.29 (*t*, $J=7.2$ Hz, 2H, C2—H), 2.00 (*m*, 2H, C11—H), 1.60 (*m*, 2H, C3—H), 1.26 (*b*, 14H, C4—H to C10—H). ^{13}C NMR (50 MHz): δ 174.11 (CO), 139.01 (C-12), 113.98 (C-13), 51.24 (OCH_3), 33.97 (C-2), 33.73 (C-11), 29.44, 29.38, 29.35, 29.17, 29.06, 28.85 (C-4 to C-10), 24.86 (C-3).

Methyl 12,13-epoxytridecanoate (6). Ester **5** (1.3 g, 5.8 mmol) dissolved in $CHCl_3$ (17 mL) was treated, at 0 °C, with *m*-chloroperbenzoic acid (2 g, 11.6 mmol). The mixture was stirred at room temperature for 18 h, hydrolyzed with 0.2 M phosphate buffer at pH 7.0 and extracted with $CHCl_3$. Purification of the crude thus obtained by column chromatography using hexane:Et_2O (1:1) as eluent furnished 1.3 g (5.3 mmol, 92%) of pure epoxide **6**. Calcd for $C_{14}H_{26}O_3$: C, 69.42; H, 10.74. Found: C, 69.41; H, 10.88. IR: 2925, 2854, 1739, 1463, 1436, 1253, 1195, 1172, 833 cm^{-1}. ^1H NMR (300 MHz): δ 3.54 (s, 3H, $COOCH_3$), 2.77 (*m*, 1H, C12—H), 2.61 (*dd*, $J=5.1$ and 2.7 Hz, 1H, C13—H), 2.18 (*t*, $J=7.8$ Hz, 2H, C2—H), 1.49 (*m*, 2H, C3—H), 1.17 (*b*, 16H, C4—H to C11—H). ^{13}C NMR (50 MHz): δ173.85 (CO), 52.00 (C-12), 51.24 (OCH_3), 46.71 (C-13), 33.75 (C-2), 32.23 (C-11), 29.26, 29.17, 29.14, 28.98, 28.87 (C-4 to C-9), 25.73 (C-10), 24.68 (C-3).

[14,14,14-$^2H_3$] 12-Hydroxytetradecanoic acid (1). To a suspension of CuI (0.77 g, 4 mmol) in Et_2O (4 mL) was added, under Ar at −0 °C, a 0.5 M solution of CD_3Li–LiI in Et_2O until complete solubilization of the precipitate. Then, 0.163 g (0.67 mmol) of epoxide **6** dissolved in Et_2O (6 mL) was added at 0 °C. Stirring was maintained for 1 h at 0 °C and at room temperature for 2 h. Extraction with hexane furnished a crude that was treated with a solution of KOH (0.04 g, 0.71 mmol) in 1 mL of EtOH:H_2O (75:25) for 24 h. After this time, solvent was removed and the residue was extracted with $CHCl_3$. Purification of the resulting crude by flash chromatography eluting with CH_2Cl_2:MeOH (95:5) gave 0.136 g (0.55 mmol, 82%) of the pure hydroxy acid **1**. Calcd for $C_{14}H_{25}D_3O_3$: C, 68.02; H, 10.12. Found: C, 68.04; H, 10.18. IR: 3388, 2914, 2848, 2213, 1695, 1465, 1122, 906, 720 cm^{-1}. ^1H NMR (200 MHz): δ 3.53 (*m*, 1H, C12—H), 2.29 (*t*, $J=7.6$ Hz, 2H, C2—H), 1.59 (*m*, 2H, C11—H), 1.42, 1.24 (*b*, 18H, C13—H, C3—H to C10—H). ^{13}C NMR (50 MHz): δ 179.25 (CO), 73.37 (C-12), 36.71 (C-11), 34.02 (C-2), 29.63 (C-13), 29.58, 29.46, 29.35, 29.28, 29.10, 28.94 (C-4 to C-9), 25.49 (C-10), 24.64 (C-3), 8.93 (*m*, $J=25$ Hz, C-14).

2-(10-Bromodecyl)-4,4-dimethyl-2-oxazoline (8a). A mixture of 11-bromoundecanoic acid (**7**) (3 g, 11.3 mmol) and oxalyl chloride (1.5 mL, 16.9 mmol) was stirred for 1 h. The crude reaction was then distilled under reduced pressure and the distillate was dissolved in 16 mL of dry CH_2Cl_2 and treated with a solution of 2,2-dimethyl-2-amino-1-ethanol (3 g, 33.6 mmol) in dry CH_2Cl_2 (14 mL). After 2 h, the mixture was filtered and the solvent was evaporated. The resulting crude was treated with 8 mL (113 mmol) of $SOCl_2$ and stirred for 30 min. Extraction with CH_2Cl_2 afforded a crude that was purified by column chromatography on silica gel eluting with hexane:Et_2O (60:40) to obtain 2.14 g of a mixture of **8a** and **b**, 1:1 (82% total yield). IR: 2962, 2927, 2854, 1668, 1461, 644 cm^{-1}. ^1H NMR (200 MHz): δ 3.86 (*s*, 2H, C5—H), 3.52 (*t*, $J=6.8$ Hz, 2H, C9′—H), 3.39 (*t*, $J=6.8$ Hz, 2H, C9′—H), 2.21 (*t*, $J=8.0$ Hz, 2H, C1′—H), 1.82 (*m*, $J=6.8$ Hz, 2H, C8′—H), 1.59 (*m*, 2H, C2′—H), 1.25 (*s*, 6H, $2 \times$ C4—CH_3), 1.23 (*b*, 12H, C3′—H to C7′—H).

2-(9-Formylnonyl)-4,4-dimethyl-2-oxazoline (9). To a solution of 1.5 g of a 1:1 mixture of **8a** and **b** in toluene (7 mL) was added 0.9 g (9.4 mmol) of pyridine *N*-oxide and then 0.8 g (9.5 mmol) of $NaHCO_3$. The mixture was stirred at 140 °C for 4 h, cooled to room temperature and extracted with hexane, affording 1.3 g of crude. Purification by flash chromatography eluting with hexane:Et_2O (1:1) yielded 0.63 g (2.5 mmol, 98%) of aldehyde **9**. Calcd for $C_{15}H_{27}NO_2$: C, 71.10; H, 10.74; N, 5.53. Found: C, 71.23; H, 10.62; N, 5.54. IR: 2964, 2927, 2715, 1724, 1666, 1461, 1363, 993 cm^{-1}. ^1H NMR (200 MHz): δ 9.73 (*t*, $J=1.8$ Hz, 1H, C10′—H), 3.86 (*s*, 2H, C5—H), 2.39 (*dt*, $J=7.2$ and 2.0 Hz, 2H, C9′—H), 2.21 (*t*, $J=8.0$ Hz, 2H, C1′—H), 1.59 (*m*, 2H, C2′—H), 1.26 (*s*, 6H, $2 \times$ C4—CH_3), 1.23 (*b*, 12H, C3′—H to C8′—H). ^{13}C NMR (50 MHz): δ 202.9 (CHO); 166.05 (C-2), 78.84 (C-5), 66.79 (C-4), 43.87 (C-9′), 29.22, 29.19, 29.08, 28.41, 28.11 (C-1′ to C-7′), 25.99 (CH_3), 22.03 (C-8′).

2-(10-Hydroxy-12-tridecenyl)-4,4-dimethyl-2-oxazoline (10). To a 1 M solution of allylmagnesium bromide (3.2 mL, 3.2 mmol) in Et_2O was added, under Ar and at −10 °C, a solution of **9** (0.41 g, 1.6 mmol) in Et_2O (2 mL). After stirring for 8 h at rt, extraction with CH_2Cl_2 furnished a crude that was purified by flash chromatography eluting with CH_2Cl_2:MeOH (95:5). Alcohol **10** (0.466 g, 1.69 mmol) was thus obtained in 97% yield. Calcd for $C_{18}H_{33}NO_2$: C, 73.17; H, 11.26; N, 4.74. Found: C, 73.14; H, 11.34; N, 4.69. IR: 3313, 3088, 2964, 2854, 1664, 1641, 995 cm^{-1}. ^1H NMR (300 MHz): δ 5.80 (*m*, 1H, C12′—H), 5.40 (*m*, 2H, C13′—H), 3.86 (*s*, 2H, C5—H), 3.61 (*m*, 1H, C10′—H), 2.21 (*t*, $J=7.5$ Hz, 2H, C1′—H), 3.13 (*m*, 2H, C11′—H), 1.58 (*m*, 2H, C2′—H), 1.42 (*m*, 2H, C9′—H), 1.25 (*s*, 6H, $2 \times$ C4—CH_3), 1.23 (*b*, 12H, C3′—H to C8′—H). ^{13}C NMR (50 MHz): δ 166.18 (C-2), 134.93 (C-12′), 117.99 (C-13′), 78.84 (C-5), 70.59 (C-10′) 66.76 (C-4), 41.92 (C-11′), 36.77 (C-9′), 29.55, 29.45, 29.32, 29.12, 29.07, 28.4, 28.11 (C-1′ to C-7′), 25.98 (CH_3), 25.60 (C-8′).

11-Hydroxy-13-tetradecenoic acid (11). A mixture of **10** (0.466 g, 1.6 mmol) and MeI (1 mL, 16 mmol) was stirred at room temperature for 48 h. After this time, excess MeI was evaporated and the residue was treated with 3–4 mL of 1 N NaOH in MeOH. Extraction with $CHCl_3$ gave a crude that, after purification by column chromatography on deactivated silica gel eluting with CH_2Cl_2:MeOH (99:1), yielded 0.372 g (1.5 mmol, 95%) of pure **11**. Calcd for $C_{14}H_{26}O_2$: C, 69.32; H, 10.81. Found: C, 69.34; H, 10.98. IR: 3413, 3100, 2927, 2865, 2650, 1708, 1645, 1414, 1226, 908 cm^{-1}. ^1H NMR (200 MHz): δ 5.80 (*m*, 1H, C13—H), 5.14 (*m*, 2H, C14—H), 3.65 (*m*, 1H, C11—H), 2.33 (*t*, $J=7.0$ Hz, 2H, C2—H), 2.15 (*m*, 2H, C12—H), 1.61 (*m*, 2H, C10—H), 1.42 (*m*, 2H, C3—H), 1.27 (*b*, 14H, C4—H to C9—H). ^{13}C NMR (50 MHz): δ 179.10 (COOH), 134.83 (C-13), 118.10 (C-14), 70.72 (C-11), 41.87 (C-12), 36.73 (C-10), 33.93 (C-2), 29.52, 29.44, 29.26, 29.14, 28.98 (C-4 to C-8), 25.58 (C-9), 24.64 (C-3).

[13,14-$^2H_2$] 11-Hydroxytetradecanoic acid (2). A solution of $[Ph_3P]_3RhCl$ (0.032 g, 0.034 mmol) in 2.5 mL of C_6D_6 was stirred under a D_2 atmosphere for 1 h. After this time, 0.11 g (0.45 mmol) of **11** dissolved in 2.5 mL of C_6D_6 was added with a syringe and the resulting solution was stirred at room temperature for 24 h. After this time, the solvent was removed and the residue purified by column chromatography on deactivated silica gel eluting with CH_2Cl_2:MeOH (95:5). Labeled acid **2** (0.081g, 0.33 mmol) was thus isolated in 74% yield. Calcd for $C_{14}H_{26}D_2O_3$: C, 69.36; H, 10.88. Found: C, 69.30; H, 10.96. IR: 3350, 2921, 2848, 1710, 1562, 1463, 1087, 720 cm^{-1}. ^1H NMR (300 MHz): δ 3.57 (*m*, 1H, C11—H), 2.31 (*t*, $J=7.6$ Hz, 2H, C2—H), 1.60 (*m*, $J=7.2$ Hz, 2H, C3—H), 1.43, 1.38, 1.27 (*b*, 16H, C12—H, C4—H to C10—H). ^{13}C NMR (50 MHz): δ 179.34 (CO), 71.78 (C-11), 39.76 (C-12), 37.56 (C-10), 33.95 (C-2), 29.75, 29.62, 29.44, 29.30, 29.15 (C-4 to C-8), 25.73 (C-9), 24.64 (C-3), 18.79 (*t*, $J=25$ Hz, C-14), 14.11 (*t*, $J=25$ Hz, C-13).

(*Received* 31 *July* 1995; *accepted* 8 *September* 1995)

Acknowledgments

Financial support of this work by CICYT (Grants AGF 92–178 and 95–0185), Comissionat per a Universitats i Recerca, Generalitat de Catalunya (Grant GRQ93–8016) and SEDEQ S.A. is gratefully acknowledged.

References

1. Roelofs, W. L.; Bjostad, L. *Bioorg. Chem.* 1984, *12*, 279.

2. Martinez, T.; Fabrias, G.; Camps, F. *J. Biol. Chem.* 1990, *265*, 1381.

3. Meyers, A. I.; Temple, D. L.; Nolen, R. L.; Mihelich, E. D. *J. Org. Chem.* 1974, *39*, 2787.

4. Gorzinski Smith, J. *Synthesis* 1984, 629.

5. Kolattukudy, P. E.; Rogers, L. *Arch. Biochem. Biophys.* 1987, *252*, 121.

6. Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N.; Smith, A. B. *J. Amer. Chem. Soc.* 1986, *108*, 2662.

7. Stowell, J. C. *J. Org. Chem.* 1970, *34*, 244.

8. Rakoff, H. *Prog. Lipid Res.* 1982, *21*, 225.

9. Kolattukudy, P. E.; Walton, T. J. *Biochemistry* 1972, *10*, 1897.

10. Hallas, G. *J. Chem. Soc.* 1965, 5770.