Cryptoregiochemistry of the Δ^{11}-Myristoyl-CoA Desaturase Involved in the Biosynthesis of *Spodoptera littoralis* Sex Pheromone[†]

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ABSTRACT: Many moth species biosynthesize their sex pheromones by the action of unique desaturases. These membrane-bound family of enzymes are especially interesting, since some of them produce (*E*)-unsaturated fatty acids either exclusively or along with the (*Z*)-isomer. In this article we present the first mechanistic study on one of these enzymes, namely, the Δ^{11}-myristoyl-CoA desaturase of the moth *Spodoptera littoralis*. Intermolecular primary isotope effect determinations were performed in competition experiments. The unusual use of odd-number fatty acids, tridecanoic acid and deuterium-labeled tridecanoic acid, in these experiments showed the existence of a large isotope effect for the carbon−hydrogen bond cleavage at C11, but no isotope discrimination occurred in the removal of C12−H. The results of the competitive experiments are consistent with the hypothesis that this Δ^{11}-desaturase involves a first slow, isotope-sensitive C11−H bond cleavage, with probable formation of an unstable intermediate, followed by a second fast C12−H bond removal. We suggest that a single enzyme may be responsible for the formation of both (*Z*)- and (*E*)-11-tetradecenoic acids by accommodating both *gauche* and *anti* conformers of the substrate, respectively. It is also possible that two mechanistically identical discrete enzymes are involved in each desaturation. In this case, the geometry of the resulting double bond would result from the different conformation adopted by the acyl substrate at each enzyme active site.

Fatty acyl desaturases are non-heme iron-containing, oxygen-dependent enzymes involved in the regio- and stereoselective introduction of double bonds in fatty acyl aliphatic chains (*1*). Two different types of desaturases with characteristic differences have been identified (*2*). The first type corresponds to the soluble plant enzymes, which utilize the acyl carrier protein derivative of the substrate fatty acid and have a consensus motif consisting of carboxylates and histidines that are thought to act to coordinate an active diiron cluster. The second type of desaturases, present in yeast, mammals, and insects, among others, are membrane-bound enzymes that act on either the acyl coenzyme A or the lipid-esterified derivative of the fatty acid substrate. The integral membrane class of desaturases has a different consensus motif composed of histidines that act as ligands for the active-site diiron cluster.

Many moth species biosynthesize their sex pheromones by the action of unique desaturases. After the pioneering works of Roelofs and Bjostad (*3*), different desaturase systems have been identified in pheromone glands of Lepidoptera. Δ^{11}-Desaturases, described in different moth species (*4*−*7*), are the most widely distributed. This membrane-bound family of enzymes (*8, 9*) is especially interesting, since some of them produce (*E*)-unsaturated fatty acids, either exclusively (*10, 11*) or along with the (*Z*)-isomer (*4, 6, 12*), thereby being excellent models to study these distinct enzymes. Furthermore, in the latter cases, whether both isomers are formed by the action of a single desaturase or two discrete enzymes is still an open question.

The mechanism of enzymatic desaturation of fatty acids is currently under intensive investigation. Several lines of evidence indicate that the desaturation and the biohydroxylation of inactivated aliphatic compounds follow similar reaction mechanisms (*2*). Buist and Marecak (*13*) have proposed a possible mechanistic scheme relating hydroxylation and desaturation. The reaction would begin with an initial hydrogen abstraction step by a hypervalent iron-oxo species to generate a very short-lived intermediate species, which could then give rise to the olefin via a one-electron oxidation/deprotonation (*14*) or simple disproportionation (*15*) pathways. Such a mechanism appears to operate in the fatty acyl desaturases thus far investigated (*16, 17*).

Whereas all the reported mechanistic studies on desaturases have focused on the enzymes that give rise to (*Z*)-unsaturated fatty acids, a single investigation has been published on the enzymes that catalyze the introduction of (*E*) double bonds (*18*). In the moth *Spodoptera littoralis*, myristic acid is converted into both (*E*)-11-tetradecenoic and (*Z*)-11-tetradecenoic acids (*6*). Whereas formation of (*E*)-11-tetradecenoic acid occurs by stereospecific removal of the *pro*-(*R*) C11−H and the *pro*-(*S*) C12−H, in the formation of the (*Z*)-isomer, both *pro*-(*R*) C11−H and C12−H are stereospecifically removed (*18*), in agreement with the previously reported stereospecificities of other (*Z*)-desaturases (*13, 19*−*22*).

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To continue with our studies on (*E*)-fatty acyl desaturases, we report herein on the cryptoregiochemistry[1] of the Δ^{11} desaturation of myristic acid in *S. littoralis* by determination of intermolecular primary isotope effects. The possible mechanisms for the formation of both (*Z*)- and (*E*)-isomers are also discussed.

EXPERIMENTAL PROCEDURES

Materials. All reagents for synthesis, dimethyl sulfoxide, and the odd-number fatty acids were supplied by Sigma−Aldrich Química S.A. (Madrid, Spain). The probes [11,11-$^2H_2$]tridecanoic acid (11,11-$d_2$13:Acid)[2] and [12,12-$^2H_2$]-tridecanoic acid (12,12-$d_2$13:Acid) were prepared as described in the following section. *S. littoralis* specimens were reared as reported elsewhere (*6*).

Instrumentation. Elemental analyses were obtained with a Carlo Erba model 1106. Fourier transform infrared spectra (FT-IR) were recorded in chloroform solutions on a Michelson Bomem MB-120 spectrometer. Proton and carbon nuclear magnetic resonance (^{1}H NMR or ^{13}C NMR) spectra were recorded on a Varian Unity 300 instrument at 300 or 75 MHz for ^{1}H and ^{13}C, respectively. Deuteriochloroform was used as solvent, and chemical shifts are expressed as parts per million downfield from tetramethylsilane. Gas chromatography coupled to mass spectrometry (GC-MS) was performed at 70 eV on a Fisons gas chromatograph (8000 series) coupled to a Fisons MD-800 mass-selective detector. The system was equipped with a nonpolar Hewlett-Packard HP-1 capillary column (30 m × 0.20 mm i.d.) and used the following temperature program: from 120 to 180 °C at 5 °C/min and then to 260 °C at 2 °C/min after an initial delay of 2 min. Specific operation details are described in each experiment.

Synthetic Procedures. [12,12-$^2H_2$]Tridecanoic acid (11,-11-$d_2$13:Acid) and [12,12-$^2H_2$]tridecanoic acid (12,12-$d_2$13:Acid) were prepared as detailed in the Supporting Information. Analytical and spectroscopic data were as follows:

11,11-$d_2$13:Acid. FT-IR: 2921, 2852, 1712, 1465, 1288, 910, and 734 cm^{-1}. ^{1}H NMR: δ 2.5 (t, J = 5.0 Hz, 2 H, C2−H), 1.8 (m, 2 H, C3−H), 1.4 (s, 16 H, C4−H to C11−H), and 1.0 (s, 3 H, C13−H). ^{13}C NMR: δ 180.2 (C1), 34.1 (C2), 31.7 (C11), 29.6, 29.5, 29.4, 29.3, 29.2, 29.1 (C4 to C10), 24.7 (C3), and 13.9 (C13). GC-MS (*m*/*z*, methyl ester): 74 (100%), 87, 187, 199, and 230 (M^+). Anal. Calcd for $C_{13}H_{24}D_2O_2$: C, 77.22; H/D, 12.96. Found: C, 77.24; H/D, 12.94.

12,12-$d_2$13:Acid. FT-IR: 2954, 2920, 2852, 1704, 1411, 1292, 933, and 723 cm^{-1}. ^{1}H NMR: δ 2.4 (t, J = 5.0 Hz, 2 H, C2−H), 1.6 (m, 2 H, C3−H), 1.3 (s, 16 H, C4−H to C10−H and C12−H), and 0.9 (s, 3 H, C13−H). ^{13}C NMR: δ 180.2 (C1), 33.9 (C2), 29.6, 29.5, 29.4, 29.2, 29.1, 29.0 (C4 to C10), 24.7 (C3), 22.5 (C12), and 13.9 (C13). GC-MS (*m*/*z*, methyl ester): 74 (100), 87, 143, 187, 199, and 230 (M^+). Anal. Calcd for $C_{13}H_{24}D_2O_2$: C, 77.22; H/D, 12.96. Found: C, 77.23; H/D, 12.95.

The deuterium contents of the labeled substrates were determined by GC-MS analysis of their respective methyl esters and were found to be as follows: 11,11-$d_2$13:Acid, 90.0% $^2H_2$, 8.9% $^2H_1$, and 1.1% $^2H_0$; 12,12-$d_2$13:Acid, 88.2% $^2H_2$, 8.7% $^2H_1$, and 3.1% $^2H_0$.

Metabolization of Odd-Number Fatty Acids. These experiments were performed as previously reported (*18*). Briefly, 1-day-old virgin *S. littoralis* females were immobilized, their pheromone glands were extruded, and each acid was topically applied to the gland as dimethyl sulfoxide solutions (0.1 μL, 2.5 μg/μL). A total dose of 2 μg was given in eight subsequent 30 min incubations with 0.25 μg. Pheromone glands were dissected 30 min after the last application and the tissues were processed for analysis as described below.

Isotope Effect Determination Experiment. These experiments were performed as indicated above, but a ca. 1:1 mixture of each deuterated substrate and tridecanoic acid was topically applied to the gland (0.1 μL, 10 μg/μL in dimethyl sulfoxide). A total dose of 2 μg of each probe was given in eight subsequent 30 min incubations with 0.25 μL. Some animals were treated with the same doses of the individual probes, 13:Acid, 11,11-$d_2$13:Acid, and 12,12-$d_2$13:Acid.

Preparation of Extracts. Pheromone glands were soaked in chloroform/methanol (2:1) at 25 °C for 1 h. The lipidic extract thus obtained was base-methanolyzed as described elsewhere (*6*) to obtain the fatty acid methyl esters. In some experiments, this solution was derivatized with dimethyl disulfide (DMDS) following reported procedures (*23*). The extracts were analyzed by GC-MS with the equipment mentioned previously and the conditions described in the following.

Analytical Methods. In the metabolization of odd-number fatty acids, fatty acid methyl ester extracts and the DMDS-derivatized samples were prepared from groups of four pheromone glands. Analysis was carried out by GC-MS under the Scan mode.

Intermolecular primary isotope effects were calculated from the ratios of product formed from unlabeled substrate and that produced from the deuterated analogues. These measurements were carried out by GC-MS of extracts from individual glands, under the selected ion monitoring mode (SIM), and were based on the abundance of the respective molecular ions of the various isotopomers of methyl (*Z*)-11-tridecenoate (Z11−13:Me) and methyl (*E*)-11-tridecenoate (E11−13:Me) [*m*/*z* 226 (d_0) and 227 (d_1)]. Isotope effects were corrected for the exact proportion of unlabeled and labeled substrates administered, which was determined by GC-MS analysis of a BF_3·MeOH-derivatized sample of the applied mixture. Corrections were also made for incomplete deuterium incorporation in the substrates and for the natural abundance of carbon and oxygen isotopes in the ions monitored. These latter values were obtained from the GC-MS chromatograms of extracts of glands incubated with the individual probes.

RESULTS

Metabolization of Odd-Number Fatty Acids. The use of the natural substrate of the Δ^{11}-myristoyl-CoA desaturase

[1] The term cryptoregiochemistry in connection with desaturases was defined by Buist (see ref *16*) to describe the site of initial oxidation in this two-step dehydrogenation reaction.

[2] Abbreviations: ^{13}C NMR, carbon nuclear magnetic resonance; DMDS, dimethyl disulfide; GC-MS, gas chromatography coupled to mass spectrometry; FT-IR, Fourier transform infrared spectra; E11−13:Me, methyl (*E*)-11-tridecenoate; Z11−13:Me, methyl (*Z*)-11-tridecenoate; ^{1}H NMR, proton nuclear magnetic resonance; 13:Acid, tridecanoic acid; 11,11-$d_2$13:Acid, [11,11-$^2H_2$]tridecanoic acid; 12,12-$d_2$13:Acid, [12,12-$^2H_2$]tridecanoic acid; SIM, selected ion monitoring.

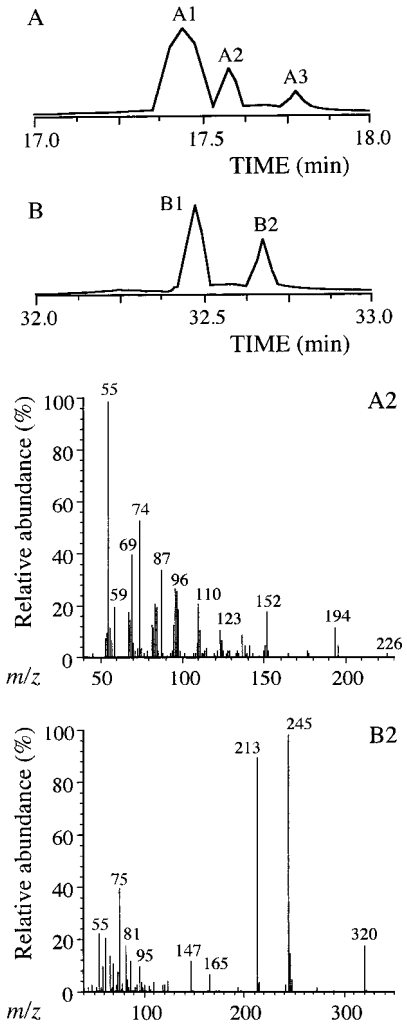
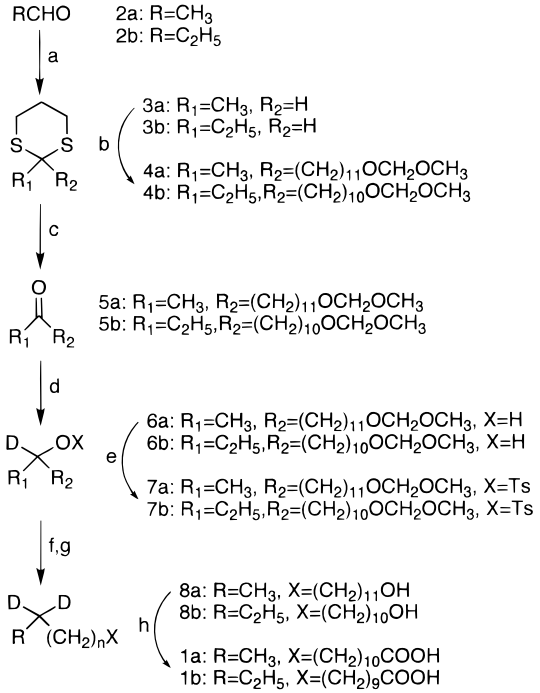


FIGURE 1: Partial GC-MS chromatograms corresponding to (A) base-methanolyzed lipidic extract of pheromone glands treated with 13:Acid and (B) DMDS-derivatized extract of fatty acid methyl esters from pheromone glands treated with 13:Acid. Compounds are as follows: **A1**, methyl tridecanoate; **A2**, methyl (*E*)-11-tridecenoate; **A3**, methyl (*Z*)-11-tridecenoate; **B1**, dimethyl disulfide adduct of methyl (*E*)-11-tridecenoate; and **B2**, dimethyl disulfide adduct of methyl (*Z*)-11-tridecenoate. Mass spectra of compounds **A2** (or **A3**) and **B1** (or **B2**) are also depicted.

studied here, tetradecanoic acid, for the isotope effect determinations required the introduction of additional deuterium atoms, besides those at C11 and C12, to unambiguously identify the unsaturated products formed in the competitive experiments, since the presence of endogenous material would alter the d_1/d_0 ratio of the olefinic products if dideuterated tetradecanoic acid was used as substrate. To avoid the arduous preparation of such a highly deuterated probe, the possibility of using an alternative unnatural substrate of the Δ^{11}-desaturase was initially investigated (*24*). As the simplest option, a series of odd-number fatty acids, namely, tridecanoic, pentadecanoic, and heptadecanoic acids, was first tested. Compounds were topically applied to the pheromone glands as dimethyl sulfoxide solutions and the fatty acid methyl esters were then obtained by base methanolysis of the gland lipidic extracts and analyzed by GC-MS. In these experiments, 13:Acid gave rise to two monoolefinic acids (Figure 1A), which were identified on the basis of their mass spectra fragments (*m*/*z* 55, 152, 194, and 226) (Figure 1). The location of the double bond along the aliphatic chain was determined by GC-MS analysis of the DMDS derivatives (*23*). Two dimethyl disulfide adducts (Figure 1B) were formed that had identical mass spectra (Figure 1) with characteristic fragments at *m*/*z* 75 and 245, indicating the presence of a double bond at C11 in the parent tridecenoic acids. Both dimethyl disulfide adducts were stereoisomers arising from both (*Z*)-11-tridecenoic acid (Z11−13:Acid) and (*E*)-11-tridecenoic acid (E11−13:Acid). Synthetic standards showed that the (*E*)-isomer had a shorter retention time than that of the (*Z*)-isomer in the GC-MS chromatograms. The transformation of 13:Acid into both E11−13:Acid and Z11−13:Acid (*E*/*Z* = 85:15, *n* = 8) was similar to the fate of the natural substrate, tetradecanoic acid (*E*/*Z* = 65:35, *n* = 6), in *S. littoralis* pheromone glands, although the ratios of *E*/*Z* isomers were higher in the first case.

Scheme 1: Synthesis of 11,11-$d_2$13:Acid and 12,12-$d_2$13:Acid[a]



[a] Reagents: (a) propanedithiol/BF_3·EtO_2/CH_3COOH/$CHCl_3$/reflux; (b) *n*-BuLi/THF/−20 °C, then $Br(CH_2)_{11}OCH_2OCH_3$/THF; (c) *n*-bromosuccinimide/acetone/H_2O; (d) $NaBD_4$/MeOD; (e) TsCl/triethylamine/(dimethylamino)pyridine/CH_2Cl_2; (f) $LiAlD_4/Et_2O$; (g) HCl/MeOH 10%; (h) CrO_3/H_2SO_4/acetone.

When the same methodology was applied to pentadecanoic and heptadecanoic acids, GC-MS analysis of the dimethyl disulfide-treated methanolyzed lipidic extracts showed that only the (*Z*)-isomers of the resulting monounsaturated products were formed (data not shown), as it occurs with the natural substrate hexadecanoic acid.

Synthesis of Deuterium-Labeled Substrates. The required deuterium-labeled compounds for the competition experiments, 11,11-$d_2$13:Acid and 12,12-$d_2$13:Acid, were prepared as depicted in Scheme 1, following well-established procedures. Intermediate dithianes **4** were synthesized by reaction of aldehydes **2** with 1,3-propanedithiol in boron trifluoride/etherate (*25*), followed by alkylation of the resulting 1,3-dithianes **3** (*26*) by sequential treatment with *n*-butyllithium and the acetal derivative of the suitable

Table 1: Intermolecular Isotope Effects on the Formation of (*Z*)-11-Tridecenoic Acid and (*E*)-11-Tridecenoic Acid from Tridecanoic Acid[a]

substrate	metabolite[b]	isotope effect
11,11-$d_2$13:Acid	E11-13:Acid	5.12 ± 0.53[c]
11,11-$d_2$13:Acid	Z11-13:Acid	5.49 ± 0.51[c]
12,12-$d_2$13:Acid	E11-13:Acid	1.07 ± 0.03[d]
12,12-$d_2$13:Acid	Z11-13:Acid	1.16 ± 0.04[d]

[a] Assays and intermolecular primary isotope effect calculations were performed as described under Experimental Procedures. Values are the mean ± SD of four groups of five glands. [b] Analyzed as methyl ester. [c] Mean ± SD of isotope effect at C11. [d] Mean ± SD of isotope effect at C12.

bromoalkanol. Dithianes **4** were converted into ketones **5** by treatment with *N*-bromosuccinimide in acetone/H_2O (*27*). Reduction of ketones **5** with $NaBD_4$ (*28*), followed by tosylation (*29*) of the resulting alcohols **6**, reduction of the tosylates **7** with $LiAlD_4$ (*30*), hydrolysis of the protective group (*31*), and final Jones oxidation (*32*) afforded the expected acids **1**.

The presence of two deuterium atoms in both probes was confirmed by GC-MS of the corresponding methyl esters ($M^{\cdot+}$ at *m*/*z* 230), whereas the location of label was confirmed by ^{13}C NMR. Thus, the signals at 31.8 (C11) and 22.5 ppm (C12) in the ^{13}C NMR spectra of tridecanoic acid were not observed in 11,11-$d_2$13:Acid and 12,12-$d_2$13:Acid, respectively, indicating the presence of deuterium atoms at C11 and C12, respectively, in both compounds.

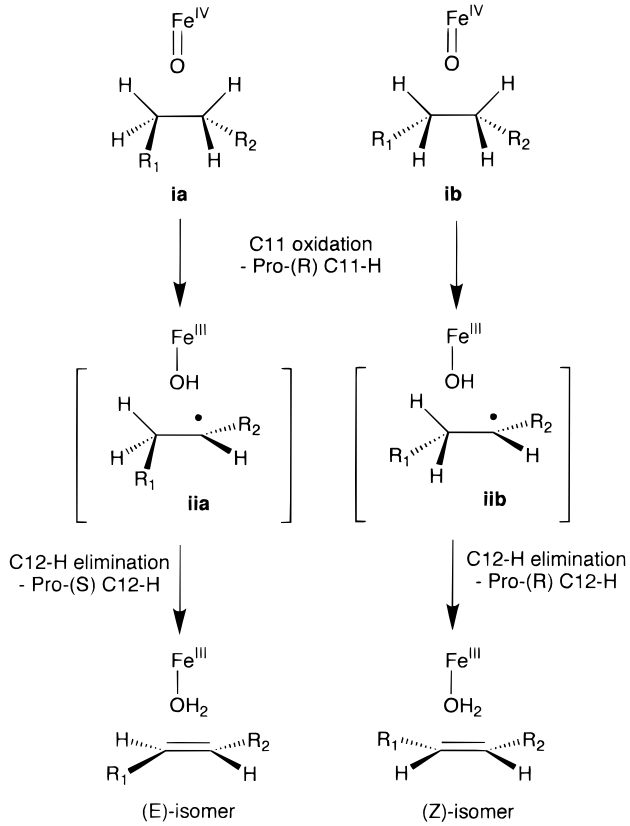
Isotope Effect Experiments. The *in vivo* methodology used in this work was similar to that used in previous studies (*18*). The experimental design (*16*, *17*, *33*) involves comparing the d_1/d_0 ratio in both (*Z*)- and (*E*)-11-tridecenoate products derived from a 1:1 mixture of 11,11-$d_2$13:Acid and 13:Acid with that obtained from a 1:1 mixture of 12,12-$d_2$13:Acid and 13:Acid. The competitive experiments were therefore carried out by administration to the pheromone gland of an approximately 1/1 mixture of 13:Acid and each of the deuterated substrates. After the incubation time, the base-methanolyzed lipidic extract was analyzed by GC-MS under the SIM mode. Areas of the molecular ions were determined and the isotope effects were calculated as mentioned under Experimental Procedures. As shown in Table 1, a large isotope effect was observed for the carbon−hydrogen bond cleavage at C11 in the formation of both isomers, but no isotope discrimination occurred in the removal of C12−H to give either of both isomers.

DISCUSSION

In this article we have applied the determination of isotope effects to shed some light into the cryptoregiochemistry of the Δ^{11}-myristoyl-CoA desaturase. This methodology has been validated for other desaturases (*16*, *17*). As mentioned in the Results section, the transformation of 13:Acid into both E11−13:Acid and Z11−13:Acid, comparable to the fate of the natural substrate, tetradecanoic acid, prompted us to chose tridecanoic acid as substrate for our mechanistic study.

The results of the competitive experiments showed that C11−H removal, but not elimination of C12−H, was sensitive to deuterium substitution. These results are consistent with the hypothesis that this Δ^{11}-desaturase involves a first slow, isotope-sensitive C11−H bond cleavage, with

Scheme 2: Mechanistic Model for the Formation of (*Z*)- and (*E*)-11-Tetradecanoic Acids from Myristic Acid[a]



[a] Assuming that a single enzyme occurs, both conformations, *gauche* (Ia) and *anti* (Ib), would coexist at the enzyme active site. In the case of two discrete enzymes, the gauche conformation (Ia) of the acyl substrate would fit into the (*Z*)-desaturase cavity, whereas the (*E*)-desaturase would accommodate the anti substrate conformer. The stereospecificity of the C11-H and C12-H removed is that previously reported (*18*). The second iron atom present in the enzyme active center cluster is not depicted.

probable formation of an unstable intermediate, followed by a second fast C12−H bond removal (Scheme 2). This result is similar to those found previously in the Δ^9-stearoyl-CoA desaturase from other systems (*16*,*20*), a Δ^{12}-oleoyl-CoA desaturase (*17*), and a Δ^6-desaturase (*34*), as well as in the cytochrome P-450-mediated desaturation of valproic acid (*33*).

It is worth noting that in this study similar isotope effect values were obtained for both (*Z*)- and (*E*)-11 desaturation reactions. This result indicates that should two discrete enzymes catalyze the formation of each isomer, then they would promote the desaturation with identical cryptoregiochemistry. Biological desaturation of fatty acids to the corresponding (*Z*)-isomers is a *syn* elimination reaction (*1*). Assuming that desaturation to the (*E*)-olefin is also a *syn* elimination process, formation of the two isomers through the action of two different enzymes would result from the different conformations adopted by the acyl substrates at each enzyme active site, which might be influenced by different amino acid sequence alignments in the enzyme active center of both (*Z*)- and (*E*)-enzymes.

However, the experimental evidence does not prove that generation of both isomers is not mediated by a distinct desaturase. Inhibition studies with 11,12-methylenehexadec-11-enoic acid, a reported inhibitor of the (Z)-11-palmitoyl-

CoA desaturase (*35*), showing that this compound inhibits the formation of both (*Z*)- and (*E*)-11-tridecenoic acid from tridecanoic acid with similar dose−response curves (data not shown) suggest the involvement of a single enzyme. A possible mechanism involving a single enzyme would imply the existence of two substrate conformers, *gauche* and *anti*, at the enzyme active site, probably prior to initial C11 oxidation (Scheme 2). Although it is possible that the change of conformation occurs after the C-11 oxidation step (*36*), this seems unlikely according to the results of the isotope effects experiments. Thus, the lack of isotope effect in the elimination of C12−H indicates that the rate constant for this reaction is probably very large and any of the intermediate species, **iia** or **iib** (Scheme 2), would not probably have sufficient lifetime to rotate about the C11−C12 bond before C12−H elimination.

The formation of different geometric isomers depending on the substrate chain length does also deserve a comment. Thus, only tridecanoic and tetradecanoic acids afford (*E*)-isomers of the monounsaturated product, along with the (*Z*)-olefin, and the *E*/*Z* ratios were 3 times higher for 11-tridecenoic acid than for 11-tetradecenoic acid. In contrast, only the (*Z*)-isomers of the alkenoic fatty acids result from pentadecanoic, hexadecanoic, and heptadecanoic acids. Again, the existence of diverse enzymes with different specificities depending on the acyl substrate chain length arises as a simple explanation. Regarding this possibility, it has been reported that chain-length recognition by fatty acid desaturases from plants is influenced by the amino acid residues of the enzyme portion that binds to the substrate beyond the point of double-bond insertion (*37*). But, again, these results can be rationalized by considering a single enzyme. In this case, the anti conformation of the longer acyl chain substrates would not fit into the enzyme cavity, whereas both *anti* and *gauche* conformers of tridecanoic and tetradecanoic acids would be accommodated in the enzyme pocket. The finding that the *E*/*Z* ratios were 3 times higher for 11-tridecenoic acid than for 11-tetradecenoic acid may indicate that changing the substrate from tetradecanoic to tridecanoic acid shortens the molecule to the point that the change of conformation of the substrate required to give each isomer is easily achieved, since swapping a hydrogen atom with a methyl group (tridecanoic acid) is easier than swapping with ethyl (tetradecanoic acid) due to lower interactions with a putative active-site channel. In contrast, extensive interactions with the longer chain fatty acids (pentadecanoic and hexadecanoic acids) may be responsible for the exclusive (*Z*) double-bond formation in the reaction products.

For the time being, there is no genetic evidence as to whether a single or two unique enzymes are involved in the formation of geometric isomers of olefinic products through desaturation reactions. The recent cloning and functional expression of the cDNA encoding the Δ^{11}-palmitoyl-CoA desaturase of the cabbage looper moth (*38*) has provided the technical tools for the isolation and characterization of additional pheromone desaturases, which, in conjunction with functional studies, should permit soon the identification of specific mutational events that give rise to additional catalytic specificities. The occurrence of a single desaturase mediating the formation of different geometric isomers from acyl substrates differing in their chain length would be fascinating, since it would illustrate how the biological purpose of generating a unique species-specific semiochemical signal is achieved in the most economical way for the cell.

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SUPPORTING INFORMATION AVAILABLE

Experimental procedures for the synthesis of the deuterium-labeled tridecanoic acids, ^{1}H and ^{13}C NMR, and IR spectroscopic data for the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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