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1,5-Hydrogen Shift and Other Isomerization Reactions of Certain Ethyl Octadecatrienoates

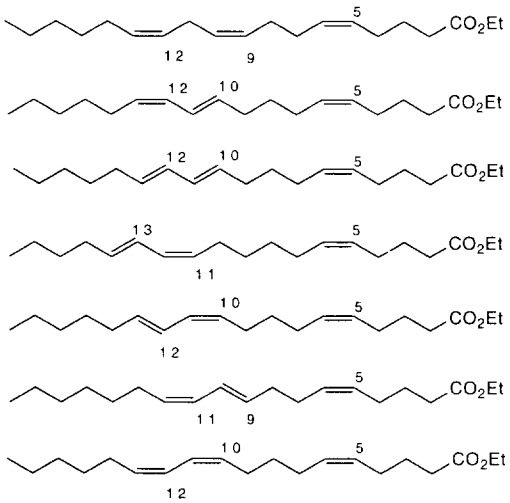
Jorma Matikainen, Seppo Kaltia, Markku Hämäläinen and Tapio Hase*

Laboratory of Organic Chemistry, Department of Chemistry, University of Helsinki
P.O. Box. 55, 00014 UNIVERSITY, Finland

Abstract: Four new octadecatrienoic acid ethyl esters (**4** - **7**) were synthesized. On heating these undergo cyclization, *via* an intramolecular Diels-Alder (IMDA) reaction, mainly to stereoisomers of ethyl 4-(5-pentyl-1,2,3,3a,4,5,7a-hexahydroindenyl)-butanoate (CP-1, CP-2, CP-3, CP-4 and CP-5) and 3-(6-pentyl-1,2,3,4,4a,5,6,8a-octahydronaphthyl)propanoate. 1,5-Sigmatropic hydrogen shift reactions of the trienoic esters **4**-**7**, all possessing a conjugated *Z,E* structure, precede the IMDA reactions. The 1,5-hydrogen shift reaction occurs in *Z,E* dienoic structures at a lower temperature than the *Z,E* to *E,E* isomerization. © 1997 Elsevier Science Ltd.

We have described earlier the synthesis and IMDA cyclization of ethyl 5*Z*,10*E*,12*Z*-octadecatrienoate (**2**) and 5*Z*,10*E*,12*E*-octadecatrienoate (**3**)[1] in the course of our studies concerning intramolecular Diels-Alder (IMDA) reactions of pinolenic acid (5*Z*,9*Z*,12*Z*-octadecatrienoic acid **1**) found in tall oil. These cyclization reactions lead to hexahydroindenylcarboxylic acids such as CP-1 and CP-2 (cyclopinolenic acids).

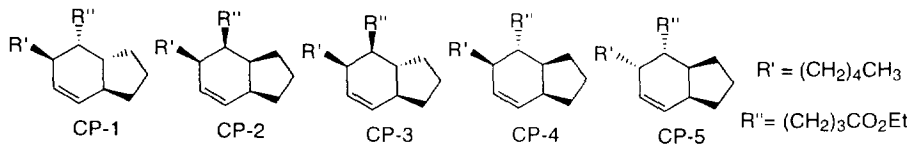
In order to cyclize to hexahydroindenoic compounds, pinolenic acid must first undergo regioisomerization whereby the $(CH_2)_2$ bridge between the dienophilic and enophilic moieties is expanded to $(CH_2)_3$ while the 9,12-dienoic system is converted to the conjugated 10,12-diene.[2-4] Presumably this happens in the alkaline pulping process as was indicated[5] by the treatment of pinolenic acid with sodium hydroxide in hot glycerol, producing the 5*Z*,10*E*,12*Z*-triene **2**. This is the inititial isomerization product in the sequence of reactions leading from pinolenic acid to bicyclic compounds.



In a previous article[1] we reported preliminary results on the isomerization reactions of the triene **2**. This gave, on heating, first a new straight chain isomer **X** as an intermediate product and not directly the bicyclic compounds. On prolonged heating the new isomer gradually disappeared and cyclopinolenoate esters were formed. It was suggested that the new trienoic compound **X** is the 5*Z*,11*Z*,13*E*-triene **4**, a 1,5-sigmatropic hydrogen shift product. We have now verified by proton and carbon NMR, and by GC using an authentic synthetic sample of **4** for comparison, that the unknown new intermediate

is indeed the isomer **4**. Another alternative, the *Z,E*-isomerized product **5**, was excluded by comparison with a synthetic sample.

We report here the stereocontrolled synthesis of ethyl 5*Z*,11*Z*,13*E*-octadecatrienoate (**4**) and ethyl 5*Z*,10*Z*,12*E*-octadecatrienoate (**5**). Furthermore, in view of the random isomerizations that are possible at the high temperatures of tall oil distillation, the less expected isomers **6** (5*Z*,9*E*,11*Z*-octadecatrienoate) and **7** (5*Z*,10*Z*,12*Z*-octadecatrienoate) were synthesized as well. In addition, we show that their IMDA cyclization leads to mixtures of cyclic compounds where the cyclopinolenoate esters CP-1 and CP-2 predominate. Three new pentylhexahydroindenylbutanoates (CP-3, CP-4 and CP-5) are also shown to be constituents in some of the reaction products.

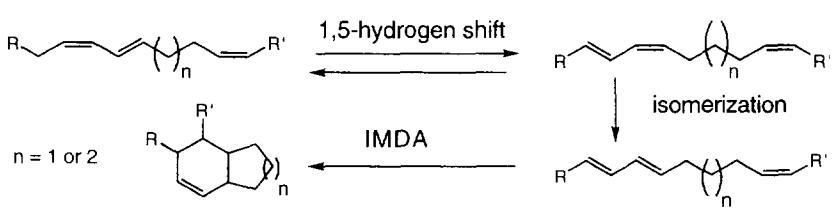


There is no mention in the literature of previous work on thermal 1,5-sigmatropic hydrogen shift reactions in unbranched acyclic trienoic systems, although thermal *E,Z*-isomerization reactions of methyl pinolenoate were reported very recently.[6] However, there are papers[7] from the early 1970's concerning the chemical behaviour of linseed oil on heating under alkaline conditions. Although 1,5-hydrogen shift reactions were not mentioned in those articles, the fact that hexahydroindenoic structures were assigned to some of the reaction products by mass spectrometry suggests the intermediacy of 1,5-shift reactions. We have studied in detail the thermal behaviour of alkali-isomerized methyl linolenoate but will report separately on those results later.

Results and discussion

The above pre-IMDA trienes (**4-7**) are regioisomerized reversibly by way of 1,5-sigmatropic hydrogen shift reactions[8] (Scheme 1). Subsequent heat-induced isomerization of the *Z,E*-dienoic structures to the *E,E* configuration facilitates the formation of hexahydroindenic or octahydronaphthalenic structures. This is because the IMDA reaction is more favoured for the *EE* than for the *ZE* dienoic system.[9]

SCHEME 1



If the diene system has a 10*Z* structure, as in the ester **5**, the IMDA reaction should lead, in an ideal situation, to the new hexahydroindenoic product CP-5 *via* the *anti* transition state.[10] Indeed, CP-5 appears to be one of the main cyclization products of **5**, judging by its NMR and mass spectra and GC characteristics. The methine signals in the ^{13}C-spectrum of this compound are very close to those of CP-2 but clearly different from those of CP-1. On this basis and for mechanistic reasons we tentatively propose the 3aα,4α,5α,7aα-

stereochemistry for this new compound. The fact that major quantities of CP-1 and CP-2 are also formed tells that isomerizations in the diene system are taking place prior to cyclization. The IMDA reactions seem to be very sensitive to alterations in reaction conditions but it remains to be established how the isomer distribution depends on the cyclization temperature and pressure and on the solvent used. Heating the compound **4** gives the cyclopinolenoate esters CP-1 and CP-2 as the main products, but in reversed relative proportions compared to the reaction of the isomers **2**, **3**, **5** and **6** (for an as yet unclear reason). A notable amount of the compound **4** is also cyclized to octahydronaphthalenic structures,[11] a reaction that probably goes by prior isomerization to the 5*Z*,11*E*,13*E*-triene.

The dienophilic moiety (*i.e.*, the C-5 *Z* double bond) is considerably more resistant to geometrical isomerization than a conjugated diene system. Isomerization may nevertheless occur to some extent and the resulting all-*E* 5,10,12-octadecatrienoic ester should then cyclize to two further hexahydroindenoates (CP-3 and CP-4). We have established the presence of minor quantities of such structures, and have verified their structures[12] by the X-ray analysis[13] of anilide derivatives of analogous compounds, correlated chemically to CP-3 and CP-4. Thus in all there are five hexahydroindenoic structures found in the isomerized pinolenic acid but some additional hexahydroindenoic and octahydroindenoic isomers of unknown structure appear to be also present.

For an IMDA reaction there should be optimally 3 or 4 methylene groups between the enophilic and dienophilic parts of the molecule. If 1,5-hydrogen shift reactions operate to bring the entire double bond system into conjugation, the resulting conjugated trienoic ester may be cyclized to a cyclohexadienoic structure. In this connection it is interesting to note that tall oil distillates contain[2,3] small quantities of various ω-(o-alkylphenyl)alkanoic acids, which could have been formed by aromatization of the corresponding cyclohexadienoic species. Another isomerization route from pinolenic acid may lead to the conjugated 5*Z*,9*Z*,11*E*-structure, and further to the 5*Z*,8*E*,10*Z*-isomer *via* a 1,5-hydrogen shift reaction. This compound has only one methylene group between the dienophilic and enophilic sections and thus cannot undergo the IMDA reaction to bicyclic products. If the system becomes fully conjugated, the cyclohexadienoic pathway will again play a role. We have also evidence that dimers are formed to some extent by way of an intermolecular Diels-Alder reaction.

The synthetic 5*Z*,9*E*,11*Z*-triene (**6**) also gave on heating cyclopinolenoate isomers as the main products. GC monitoring revealed that **6** reverts to **5** prior to cyclization, in analogy with the **2** → **4** isomerization. The least probable isomerization product of pinolenic acid is the all-*Z* 5,10,12-isomer (**7**). A synthetic sample of **7**, heated at 240 °C, gave the isomers **2**, **4**, **5** and **6** in an approximately equal ratio (Fig. 1) as shown by GC monitoring. On further heating cyclopinolenoate esters appeared as the main products.

On the basis of the above results, it may be stated that a conjugated *Z*,*E*-dienoic structure embedded in a methylene chain undergoes a 1,5-hydrogen shift reaction much more easily than an isomerization to the conjugated *E*,*E*-dienoic structure.

SYNTHESIS

The stereoselective synthesis of the trienoic carboxylates **4** - **7** (Scheme 2, 3 and 4) relied mainly on the Wittig reaction. The reactions of the hydroxyphosphonium salts (Scheme 2) with α,β–unsaturated aldehydes gave ca. 1:1 mixtures of the *Z*,*E*- (**8**, **9**) and *E*,*E*-dienoic alcohols. The former were readily obtained in a pure state by removing the *E*,*E*-isomers by argentation chromatography or simply by cold precipitation in pentane or hexane.

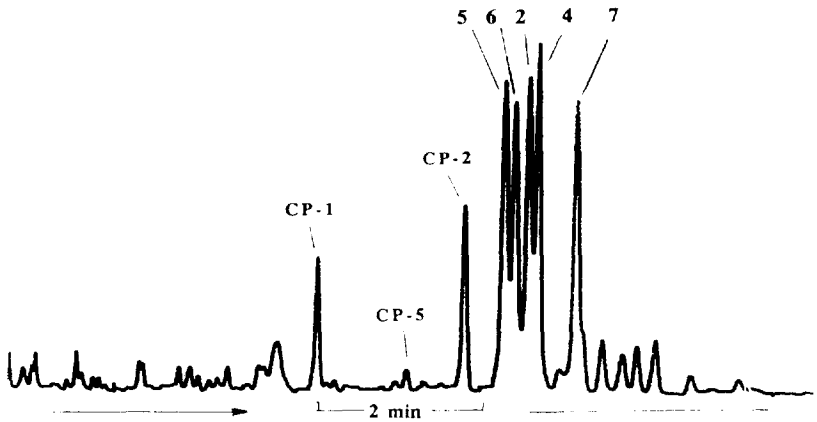
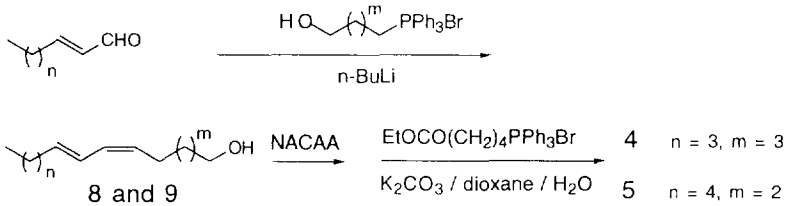
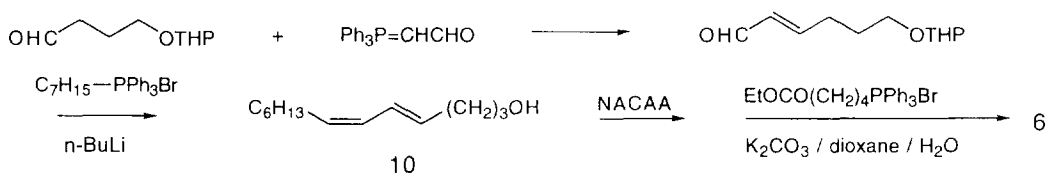


Fig.1. Partial chromatogram of the isomerization of ethyl 5Z,10Z,12Z-octadecatrienoate (**7**). Column: BDS, 45m, 0.32mm, 0.15 μm. Conditions: 50-200 °C, 20 °/min, He 1.5 bar.

SCHEME 2



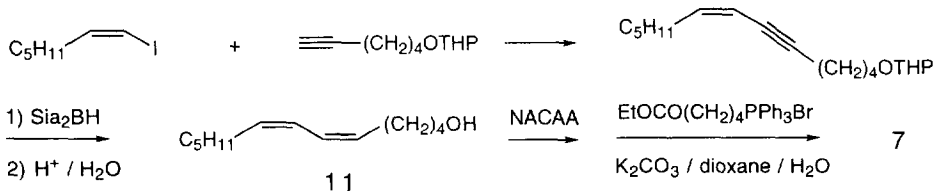
SCHEME 3



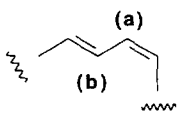
The inverse *Z,E*-dienoic structure of **10** (Scheme 3) was constructed by starting with the Wittig reaction of 4-tetrahydropyranyloxybutenal with Ph_3P=CHCHO. The *Z,Z*-dienoic alcohol **11** (Scheme 4) was obtained in high geometrical purity by the palladium catalyzed coupling of an iodoolefin with the THP-protected acetylenic alcohol followed by the reduction of the triple bond by disiamylborane.[14] The sensitive dienoic alcohols (**8-11**) were then oxidized to the corresponding aldehydes using the NACAA reagent[15] (nicotinic - chromic mixed anhydride betaine). For the remaining Wittig step, in the presence of the ω-carbethoxy functional group, the K_2CO_3-catalyzed phase transfer modification[16] worked very well and gave an *E/Z*-selectivity of about 1:9. The final purification was done by argentation chromatography.

The structure and purity of the products were established by ^1H and ^{13}C NMR techniques. The limited

SCHEME 4



previous literature data[17] on the *E,Z*-diene substructure appears to be partly in error. The highest upfield ^{13}C signal at δ 128.6 ppm in these structures does not correspond to the inner *Z* carbon (a) as claimed but to the inner *E* carbon (b). This assignment is based on the analysis of the 300 MHz ^{1}H NMR olefinic coupling pattern where the *E*-signals are clearly recognizable. The related carbon signals can then be found by heteronuclear correlation techniques such as HETCOR or HMQC. This assignment was further corroborated by TOCSY 1D spectra of the tridecadienols with sufficiently long mixing times (80 -120 ms). Excitation of the alcoholic methylene group shows correlation to one end of the diene system and excitation of the chain end methyl to the other end.



EXPERIMENTAL PROCEDURES

Chromatography

GLC analysis was performed with an Orion-Analytica Micromat HRGC chromatograph using a BDS (butanediol succinate) column (silica tubular, 45 m, 0.32 mm, 0.15 μm), He gas as carrier (1.5 bar) and a temperature program (50 - 200 °C, 20 °C/min). For argentation chromatography, silica gel (60 g; Kieselgel 60, E. Merck, Darmstadt, no. 9385, 230-400 mesh ASTM; kept overnight in an oven at 120 °C) was treated with 100 ml of a 10% solution of $AgNO_3$ in acetonitrile, predried over 3 Å molecular sieves. After the removal of acetonitrile under vacuum in a rotary evaporator at 70 °C, the impregnated silica was used to fill a glass chromatography column (23x2.5 cm).

Spectroscopy

NMR spectra were run on a Varian Gemini 200 or Varian Innova 300 spectrometer (200 MHz or 300 MHz for ^{1}H; $CDCl_3$ solvent, and referenced to solvent δ ^{1}H = 7.29 ppm and ^{13}C = 77.30 ppm). HRMS were run on a JEOL JMS-SX102 instrument.

5*Z*,7*E*-Tridecadien-1-ol (9): Butyllithium (4.7 mL of 1.2 M solution in hexane, 5.6 mmol) was added to suspension of 5-hydroxypentyl triphenylphosphonium salt[18] (1.2 g, 2.8 mmol) in THF (20 mL) and after stirring under Ar at room temperature for 20 min, 2*E*-octenal (0.42 mL, 2.8 mmol) was added slowly. After 30 min, water (2.0 mL) was added, the organic phase separated and THF removed under vacuum. Flash chromatography of the crude products in a silica gel column (elution with 5:95 EtOAc:CH_2Cl_2) gave 0.38 g (70 %) of crude **9**, in about 1:1 mixture with 5*E*,7*E*-tridecadien-1-ol. The *ZE* isomer was obtained in a pure state by removing the *EE* isomer at -60 °C in pentane. ^{1}H NMR δ 0.92 (t, *J* = 6.9 Hz, 3H, H-13), 1.31 (m, 4H, H-11 and H-12), 1.39 (m, 2H, H-10), 1.48 (m, 2H, H-3), 1.62 (m, 3H, H-2 and -OH), 2.10 (q, "*J*" = 7.1 Hz, 2H, H-9), 2.31 (q, "*J*" = 7.3 Hz, 2H, H-4), 3.67 (t, *J* = 6.4 Hz, 2H, H-1), 5.30 (dt, *J* = 10.9 and 7.5 Hz, 1H, H-5), 5.68 (dt, *J* = 15.0 and 7.2 Hz, 1H, H-8), 5.78 (t, *J* = 10.9 Hz, 1H, H-6), 6.31 (dd, *J* = 15.3 and 10.9 Hz, 1H, H-7); ^{13}C NMR δ 14.8 (C-13), 22.8 (C-12), 25.7 and 26.1 (C-4 and C-3), 29.3 (C-10), 31.7, 32.5 and 32.9 (C-11, C-2 and C-9), 63.0 (C-1), 125.7 (C-7), 129.3 (C-6), 133.0 (C-5), 135.3 (C-8).

5*Z*,7*E*-Tridecadienal (12): The alcohol **9** (0.20 g, 1.0 mmol) was added to a suspension of NACAA[15] (0.56 g, 2.5 mmol) in CH_2Cl_2 (8 mL) and pyridine (1.6 mL). After stirring at ambient temperature for 20 min, the reaction mixture was filtered through a pad of silica gel (70-230 mesh). The eluate was monitored by tlc and the fractions containing the product collected to give 0.15 g (75 %) of **12** as an oil.

Ethyl 5*Z*,10*Z*,12*E*-octadecatrienoate (5): The phosphonium salt of ethyl 5-bromopentanoate (0.47 g, 1.0 mmol), K_2CO_3[16] (0.14 g), the aldehyde **12** (0.14 g, 0.71 mmol), 1,4-dioxane (1.5 mL) and H_2O (0.02 mL) were stirred overnight at 95 °C under argon. The solvent was evaporated under reduced pressure, and the residue extracted several times with hexane. Flash chromatography of the concentrate in a silica gel column (elution with CH_2Cl_2) yielded 0.12 g (55%) of crude **5**, consisting of the 5*Z*,10*Z*,12*E* isomer (85-90%) and the 5*E*,10*Z*,12*E* isomer (10-15%). The main product was isolated in a pure state by argentation chromatography. ^{1}H NMR δ 0.92 (t, *J* = 6.7 Hz, 3H, H-18), 1.24 (t, *J* = 7.1 Hz, 3H, H-2'), 1.31 (m, 6H, H-15, H-16 and H-17), 1.45 (quintet, "*J*"= 7.5 Hz, 2H, H-8), 1.70 (quintet, "*J*"= 7.2 Hz, 2H, H-3), 2.10 (m, 8H, H-4, H-7, H-9 and H-14), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 4.13 (q, *J* = 7.1 Hz, 2H, H-1'), 5.28 (m, 1H, H-10), 5.40 (m, 2H, H-5 and H-6), 5.67 (dt, *J* = 15.7 and 7Hz, 1H, H-13), 5.97 (t, *J* = 10 Hz, 1H, H-11), 6.31 (dd, *J* = 15 and 10 Hz, 1H, H-12); ^{13}C NMR δ 14.3 (C-18), 14.5 (C-2'), 22.8 (C-17), 25.2 (C-3), 26.9 (C-4), 27.1 (C-7), 27.6 (C-9), 29.4 (C-15), 30.0 (C-8), 31.8 (C-16), 33.1 (C-14), 34.0 (C-2), 60.5 (C-1'), 125.8 (C-12), 129.1 and 129.2 (C-5 and C-11), 129.8 (C-10), 130.9 (C-6), 135.1 (C-13), 174.0 (C-1). HRMS: $C_{20}H_{34}O_2$ requires 306.2559, found 306.2554.

6*Z*,8*E*-Tridecadien-1-ol (8) was prepared as described for the alcohol **9**, using 6-hydroxyhexyltriphenylphosphonium bromide (prepared from 6-bromo-1-hexanol)[19] and 2-heptenal as the starting materials. ^{1}H NMR δ 0.93 (t, *J* = 7.0 Hz, 3H, H-13), 1.40 (m, 9H, H-3, H-4, H-11, H-12 and OH), 1.61 (quintet, "*J*"= 6.6 Hz, 2H, H-2), 2.10 (q, "*J*"= 7.2 Hz, 2H, H-10), 2.32 (q, "*J*"= 7.2 Hz, 2H, H-5), 3.67 (t, *J* = 6.5 Hz, 2H, H-1), 5.32 (dt, *J* = 10.7 and 7.7 Hz, 1H, H-6), 5.45 (dt, *J* = 15.0 and 7.2 Hz, 1H, H-9), 5.98 (t, *J* = 11.0 Hz, 1H, H-7), 6.32 (dd, *J* = 15.0 and 10.9 Hz, 1H, H-8); ^{13}C NMR δ 14.2 (C-13), 22.6 (C-12), 25.6 (C-3), 27.9 (C-5), 29.7 (C-4), 31.8 (C-11), 32.9 (C-10), 33.0 (C-2), 63.3 (C-1), 125.8 (C-8), 129.1 (C-7), 129.9 (C-6), 135.2 (C-9).

Ethyl 5*Z*,11*Z*,13*E*-octadecatrienoate (4): NACAA oxidation of **8** and the subsequent Wittig reaction were conducted as described above for the synthesis of ethyl 5*Z*,10*Z*,12*E*-octadecatrienoate (**5**). ^{1}H NMR δ 0.93 (t, *J* = 7.0 Hz, 3H, H-18), 1.28 (t, *J* = 7.1 Hz, 3H, H2'), 1.41 (m, 8H, H-17, H-8, H-16 and H-9), 1.70 (quintet, "*J*"=7.2 Hz, 2H, H-3), 2.12 (m, 8H, H-7, H-4, H-15 and H-10), 2.33 (t, *J* = 7.5 Hz, 2H, H-2), 4.13 (q, *J* = 7.1 Hz, 2H, H-1'), 5.34 (m, 1H, H-11), 5.38 (m, 1H, H-5), 5.44 (m, 1H, H-6), 5.67 (dt, *J* = 15.1 and 7.1 Hz, 1H, H-14), 5.96 (t, *J* = 11 Hz, 1H, H-12), 6.31 (ddq, *J* = 15.1, 11.0 and 1.1 Hz, 1H, H-13); ^{13}C NMR δ 14.2 (C-18), 14.5 (C-2'), 22.6 (C-17), 25.2 (C-3), 26.8 (C-4), 27.4 (C-7), 27.8 (C-10), 29.5 and 29.6 (C-8 and C-9), 31.8 (C-16), 32.9 (C-15), 34.0 (C-2), 60.5 (C-1'), 125.8 (C-13), 128.8 (C-5), 129.0 (C-12), 130.1 (C-11), 131.1 (C-6), 135.0 (C-14), 174.0 (C-1); HRMS: $C_{20}H_{34}O_2$ requires 306.2559, found 306.2553.

4*E*,6*Z*-Tridecadien-1-ol (10): Ph_3P=CHCHO (4.5 g, 14.8 mmol) and 4-tetrahydropyranyloxybutanal (2.6 g, 15.1 mmol) were refluxed in benzene (100 mL) under Ar.[20] After 45 h, benzene was evaporated and the residue extracted with ether:hexane (1:5, 250 mL). The removal of solvent gave 1.2 g (41 %) of 6-tetrahydropyranyloxy-2*E*-hexenal. The next Wittig reaction was by a procedure similar to that in the case of alcohol **9**, using heptyl triphenylphosphonium salt as the starting compound. The hydrolysis of the protecting

group with 60 mL of THF, 20 mL of H_2O and a few drops of conc. H_2SO_4 at 50 °C for 5 h gave 0.89 g (75%) of crude **10**. The *EE*-isomer was removed by cooling to -60 °C in pentane (repeated twice). ^{1}H NMR δ 0.93 (t, 3H, H-13), 1.2-2.3 (m, 15H, H-2, H-3, H-8-H-12 and OH), 3.69 (t, *J* = 6.5 Hz, 2H, H-1), 5.30 (dt, *J* = 15 and 7 Hz, 1H, H-7), 5.70 (dt, *J* =15 and 11 Hz, 1H, H-4), 5.99 (t, *J* = 11 Hz, 1H, H-6), 6.29 (dd, *J* = 15 and 11 Hz, 1H, H-5); ^{13}C NMR δ 14.3 (C-13), 22.9 (C-12), 28.0 (C-8), 29.2, 29.4 and 30.0 (C-10, C-3 and C-9), 32.0 and 32.5 (C-11 and C-2), 62.6 (C-1), 126.5 (C-5), 128.5 (C-6), 130.6 (C-7), 133.9 (C-4).

Ethyl 5*Z*,9*E*,11*Z*-octadecatrienoate (**6**): NACAA oxidation of **10** and the subsequent Wittig reaction were conducted as described above for the synthesis of ethyl 5*Z*,10*Z*,12*E*-octadecatrienoate (**5**). ^{1}H NMR δ 0.91 (t, *J* = 6.7 Hz, 3H, H-18), 1.28 (t, *J* = 7.1 Hz, 3H, H-2'), 1.32 (m, 8H, H-14, H-15, H-16 and H-17), 1.71 ("quintet", "*J*"= 7.2 Hz, 2H, H-3), 2.12 ("q", "*J*"= 6.7 Hz, 2H, H-13), 2.17 (m, 6H, H-4, H-7 and H-8), 2.33 (t, *J* = 7.4 Hz, 2H, H-2), 4.13 (q, *J* = 7.1 Hz, 2H, H-1'), 5.34 (dt, *J* = 10.8 and 7.3 Hz, 1H, H-12), 5.41 (m, 2H, H-5 and H-6), 5.67 (dt, *J* = 15.1 and 6.7 Hz, 1H, H-9), 5.96 (t, *J* = 10.9 Hz, 1H, H-11), 6.34 (dd, *J* = 15.2 and 10.9 Hz, 1H, H-10); ^{13}C NMR δ 14.4 (C-18), 14.5 (C-2'), 22.9 (C-17), 25.9 (C-3), 26.9 (C-13), 27.4 and 28.0 (C-4 and C-7), 29.2 and 30.0 (C-15 and C-14), 32.0 (C-16), 33.2 (C-8), 34.0 (C-2), 60.5 (C-1'), 126.3 (C-10), 128.7 (C-11), 129.3 and 130.3 (C-5 and C-6), 130.8 (C-12), 133.9 (C-9), 174.0 (C-1). HRMS: $C_{20}H_{34}O_2$ requires 306.2559, found 306.2552.

5*Z*,7*Z*-Tridecadien-1-ol (**11**)[14]: ^{1}H NMR δ 0.90 (t, *J* = 6.6 Hz, 3H, H-13), 1.34 (m, 4H, H-11 and H-12), 1.40-1.78 (m, 6H, H-10, H-3 and H-2), 1.48 (brs, 1H, OH), 2.21 quintet, "*J*"= 7.3 Hz, 4H, H-4 and H-9), 3.64 (t, *J* = 6.4 Hz, 2H, H-1), 5.48 (m, 2H, H-5 and H-8), 6.28 (m, 2H, H-6 and H-7); ^{13}C NMR δ 14.3 (C-13), 22.8 (C-12), 26.0 (C-3), 27.7 and 27.9 (C-4 and C-9), 29.6 (C-10), 31.8 (C-11), 32.6 (C-2), 63.1 (C-1), 123.6 and 124.3 (C-6 and C-7), 131.6 and 132.7 (C-5 and C-8).

Ethyl 5*Z*,10*Z*,12*Z*-octadecatrienoate (**7**): NACAA oxidation of **11** and the subsequent Wittig reaction were conducted as described above for the synthesis of ethyl 5*Z*,10*Z*,12*E*-octadecatrienoate (**5**). ^{1}H NMR δ 0.92 (t, *J* = 6.5 Hz, 3H, H-18), 1.29 (t, *J* = 7.2 Hz, 3H, H-2'), 1.35 (m, 6H, H-15, H-16, H-17), 1.47 (quintet, *J* = 7.5 Hz, 2H, H-3), 1.71 (quintet, *J* = 7.2 Hz, 2H, H-8), 2.08 ("quintet", "*J*"=6.6 Hz, 4H, H-9 and H-14), 2.20 (m, 4H, H-4 and H-7), 2.32 (t, *J* = 7.6 Hz, 2H, H-2), 4.16 (q, *J* = 7.1 Hz, 2H, H-1'), 5.52 (m, 2H, H-5 and H-6), 6.47 (m, 2H, H-10 and H-13), 6.48 (m, 2H, H-11 and H-12); ^{13}C NMR δ 14.3 (C-18), 14.6 (C-2'), 22.8 (C-17), 25.2 (C-3), 26.9 (C-4), 27.1 (C-7), 27.4 (C-14), 27.7 (C-9), 29.6 (C-15), 29.9 (C-8), 31.7 (C-16), 34.1 (C-2), 60.5 (C-1'), 123.8 and 124.2 (C-11 and C-12), 129.2 and 130.8 (C-5 and C-6), 131.8 and 132.6 (C-10 and C-13), 174.0 (C-1). HRMS: $C_{20}H_{34}O_2$ requires 306.2559, found 306.2560.

CP-5 ^{1}H NMR δ 0.90 (t, *J* = 6.8 Hz, 3H, H-5"), 1.10-1.90 [broad multiplets (23H), including H-6' (1.27 (t, *J* = 7.1 Hz), H-4 (1.47 m), and H-5 (1.74 m)], 2.19 (m, 1H, H-3a), 2.32 (m, 2H, H-2'), 2.50 (tm, *J* = 10 Hz, 1H, H-7a), 4.16 (q, *J* = 7.1 Hz, 2H, H-6'), 5.38 (dtd, *J* = 10.1, 2.2 and 0.7 Hz, 1H, H-7), 5.53 (dt, *J* = 10.1 and 2.2 Hz, 1H, H-6); ^{13}C NMR δ 14.4 (C-5"), 14.6 (C-6'), 23.0 (C-4"), 23.1 and 23.2 (C-1 and C-3), 23.5 (C-1'), 26.1 (C-2), 31.5 (C-2'), 32.1 (C-2"), 32.7 (C-3"), 33.1 (C-1"), 35.0 (C-3'), 36.1 (C-5), 38.6 (C-4), 40.1 (C-7a), 40.2 (C-3a), 60.5 (C-5'), 130.6 (C-6), 131.3 (C-7), 174.1 (C-4'). HRMS: $C_{20}H_{34}O_2$ requires 306.2559, found 306.2563.

Isomerization experiments, general procedure: The ethyl octadecatrienoates **2-7**, in about 5% solution in decalin under Ar, were heated for 16 h in a sealed ampoule at 260 °C. The reaction product was then chromatographed over silica (elution with dichloromethane:hexane 1:1). The cyclopinolenoate esters were

isolated by argentation chromatography (elution with 5% ethyl acetate in dichloromethane or alternatively 5-10 % diethyl ether in hexane).

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