

# Regioselective Cationic 1,2- and 1,4-Additions Forming Carbon–Carbon Bonds to Methyl Santalbate, a Conjugated Enyne

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Lewis acid-induced carbocationic addition reactions to methyl santalbate [methyl (*E*)-octadec-11-en-9-ynoate] [(*E*)-**1**] give products by regioselective formation of a new carbon–carbon bond at C-9 of the molecule chain. The allenic fatty acid derivatives methyl 12-chloro-9-(1-oxoheptyl)-9,10-octadecadienoate (**2**) and methyl 9-isopropyl-9,10-octadecadienoate (**3**) were obtained by Friedel–Crafts acylation

of **1** with heptanoyl chloride and alkylation of **1** with isopropyl chloroformate, respectively. While the reaction between **1** and formaldehyde induced by Me<sub>2</sub>AlCl or Et<sub>3</sub>Al<sub>2</sub>Cl<sub>3</sub> gives a mixture of the conjugated chlorodienes **5a** and **5b**, the corresponding reaction carried out in the presence of AlCl<sub>3</sub> affords the  $\alpha,\beta$ -unsaturated ketone **6**.

## Introduction

Electrophilic addition reactions to conjugated enynes<sup>[1–3]</sup> are well-known to give 1,3-dienes (1,2-addition),<sup>[2]</sup> and allenic compounds (1,4-addition).<sup>[1,3]</sup> Because of the polarisation of the conjugated enyne system, the attack of the electrophile takes place regioselectively at C-1 of the carbon–carbon triple bond.<sup>[1]</sup> In most cases, the reactions have been carried out with polar reagents like hydrochloric and hydrobromic acid and with organolithium compounds.  $\delta$ -Chloro- $\alpha$ -allenyl ketones have been obtained regioselectively from AlCl<sub>3</sub>-mediated acylation reactions of 3-buten-1-yne with acyl chlorides.<sup>[4,5]</sup>

Recently, our interest has been focused on carbon–carbon bond-forming addition reactions to unsaturated fatty compounds, to obtain new branched and/or chain-elongated fatty compounds with possibly interesting properties.<sup>[6]</sup> Up to now, we have carried out electrophilic additions such as Friedel–Crafts acylations,<sup>[7]</sup> Friedel–Crafts alkylations<sup>[8]</sup> and ene additions of formaldehyde<sup>[9]</sup> to mono-unsaturated fatty acids. In all cases we obtained a 1:1 mixture of two regioisomeric addition products, which could not be separated. Thus, a method for a highly regioselective functionalization of the alkyl chain of fatty compounds would be desirable.

Here we describe for the first time highly regioselective carbon–carbon bond-forming additions to unsaturated fatty compounds. Methyl santalbate [(*E*)-**1**] (Figure 1) was used as the substrate for these investigations. Santalbic acid is the main fatty acid of the seed oil of sandalwood [*Santalum album* (Linn.)]. Most of our experiments were carried out with a stereoisomeric mixture of methyl octadec-11-en-9-ynoate [(*E*)-**1**/(*Z*)-**1** = 2:3] that was obtained in an ultra-

sound-assisted five-step reaction sequence from methyl ricinoleate.<sup>[10]</sup>

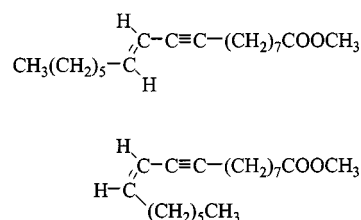
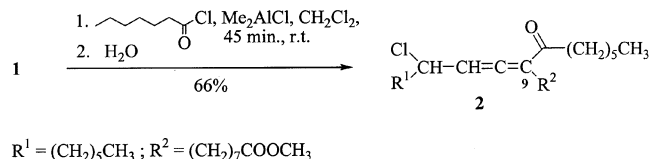


Figure 1. Methyl santalbate [(*E*)-**1**] from the seed oil of sandalwood; a stereoisomeric mixture of methyl octadec-11-en-9-ynoate [(*E*)-**1**/(*Z*)-**1** = 2:3] can be obtained in a five step reaction sequence from methyl ricinoleate<sup>[10]</sup>

## Results and Discussion

### 1,4-Additions: Friedel–Crafts Acylation and Alkylation

The Friedel–Crafts acylation of methyl octadec-11-en-9-ynoate (**1**) with heptanoyl chloride was carried out in the presence of dimethylaluminium chloride (Me<sub>2</sub>AlCl) in CH<sub>2</sub>Cl<sub>2</sub> (Scheme 1). After a reaction time of 45 min. the acylation product **2**, a new allenic fatty compound, was isolated in a yield of 66%. Compound **2** was obtained regioselectively as a diastereomeric mixture in a ratio of approximately 1:1. The same diastereomeric mixture was obtained when using stereoisomerically pure (*E*)-**1**.



R<sup>1</sup> = (CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>; R<sup>2</sup> = (CH<sub>2</sub>)<sub>7</sub>COOCH<sub>3</sub>

Scheme 1. Regioselective acylation of methyl octadec-11-en-9-ynoate (**1**) with heptanoyl chloride, induced by dimethylaluminium chloride

Usually, Friedel–Crafts acylations of unsaturated fatty compounds make use of ethylaluminium dichloride (EtAlCl<sub>2</sub>).<sup>[7]</sup> Our results show that, in the case of the conjug-

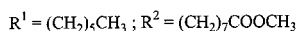
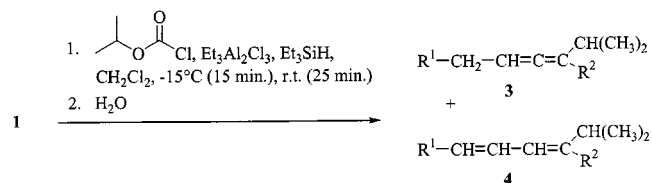
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ated enyne **1**, the milder Lewis acid  $\text{Me}_2\text{AlCl}$  has to be used, because in the presence of  $\text{EtAlCl}_2$  a complex mixture of products was obtained. The mechanism and the regioselectivity of the acylation reaction have been discussed by Santelli-Rouvier et al.<sup>[5]</sup>

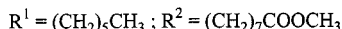
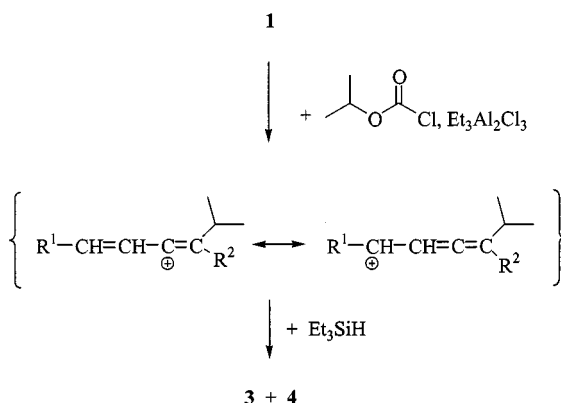
Fatty acid derivatives with an allenic system are known to have interesting properties,<sup>[11]</sup> and in special cases they have been used as substrates in the synthesis of new fatty compounds; one example is as a  $\text{C}_{18}$  keto allenic ester for the synthesis of pyrazole ester derivatives.<sup>[12]</sup>

In analogy to Friedel–Crafts alkylations of alkenes,<sup>[8]</sup> the corresponding reaction of **1** was carried out with isopropyl chloroformate and ethylaluminium sesquichloride ( $\text{Et}_3\text{Al}_2\text{Cl}_3$ ) (Scheme 2). Equimolar amounts of triethylsilane had to be added to the reaction mixture to minimize the formation of dimeric addition products. Isopropylated 1,4- and 1,2-addition products were obtained in 54% yield. The main product was the isopropylated allenic fatty acid methyl ester **3** (60%, GC). A stereoisomeric mixture of conjugated dienes **4** was observed as minor products.



Scheme 2. Regioselective alkylation of methyl octadec-11-en-9-ynoate (**1**) and isopropyl chloroformate in the presence of triethylsilane, induced by ethylaluminium sesquichloride

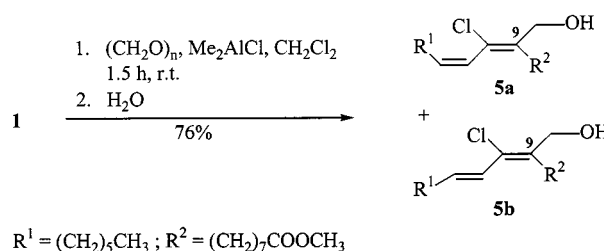
The formation of **3** and **4** can be rationalized assuming regioselective addition of the isopropyl cation, generated from isopropyl chloroformate, to C-9 of **1**, giving the resonance-stabilized intermediate, which can be trapped by hydride transfer from triethylsilane to give **3** as the 1,4-addition product and **4** as minor products by 1,2-addition (Scheme 3).



Scheme 3. Mechanism of the Friedel–Crafts alkylation of methyl octadec-11-en-9-ynoate (**1**)

## 1,2-Additions of Formaldehyde

Reactions induced by alkylaluminium halide between formaldehyde and alkenes give homoallylic alcohols,<sup>[9]</sup> while in the case of formaldehyde and 1-alkynes, mixtures of products, consisting of  $\alpha$ -allenic alcohols and (*Z*)-3-chloroallylic alcohols, are obtained.<sup>[13]</sup> The  $\text{Me}_2\text{AlCl}$ -induced addition of formaldehyde to the enyne **1** afforded the stereoisomeric 10-chloro-9-hydroxymethyl fatty acid esters **5a** and **5b** in 76% yield (Scheme 4). GC analysis indicates that only two of the eight possible regio- and stereoisomers were obtained, in a 1.1 : 1 ratio. Analytical samples of these isomers were obtained by column chromatography on silica, with petroleum ether/ether (6:4 v/v) as eluent.



Scheme 4. Regioselective and stereoselective reaction of methyl octadec-11-en-9-ynoate (**1**) and paraformaldehyde, induced by dimethylaluminium chloride

From  $^1\text{H}$ ,  $^2\text{H}$ -COSY, HMQC and HMBC NMR experiments in  $\text{CDCl}_3$  at room temperature, we were able to assign unambiguously the positions of the hydroxymethyl group at C-9 and the chlorine at C-10 in the major isomer **5a** (Figure 2). Furthermore, we were able to assign the configuration of the conjugated double bonds of **5a** as (*Z*)-9 and (*Z*)-11, by performing selective 1D-NOESY experiments, since no NOEs were measurable between the hydrogens of the hydroxymethyl group and the alkenic H-11 and H-12, whereas a strong NOE was observed between H-11 and the H-8s (Figure 3). However, the NMR spectra obtained from an almost analytically pure sample of the minor isomer **5b** turned out to be only poorly resolved with very broad signals, no matter whether recorded in  $\text{CDCl}_3$  or deuterated methanol, or at ambient temperature or at 0 °C. However, we were able to obtain well-resolved spectra from an 85:15 mixture of **5a**:**5b**. Again,  $^1\text{H}$ ,  $^2\text{H}$ -COSY, HMQC and HMBC NMR experiments in  $\text{CDCl}_3$  at room temperature proved the substitution pattern of the  $\Delta$ -9,10 double bond of **5b** to be the same as in **5a**. Fortunately, the most important signals for H-11, H-12 and the hydrogens of the hydroxymethyl group were also sufficiently well separated to perform selective 1D-NOESY experiments. As for **5a**, no NOEs were observed between the hydrogens of the hydroxymethyl group and H-11 or H-12, but a strong NOE was found between the H-8s and H-11 for **5b**, thus establishing the 9*Z* configuration of the chlorinated double bond. The 11*Z* and 11*E* configurations in **5a** and **5b**, respectively, were further confirmed by analysis of the vicinal coupling constants  $^3J_{11,12}$ , which indicate the assigned *cis* [ $^3J_{11,12}$  (**5a**) =

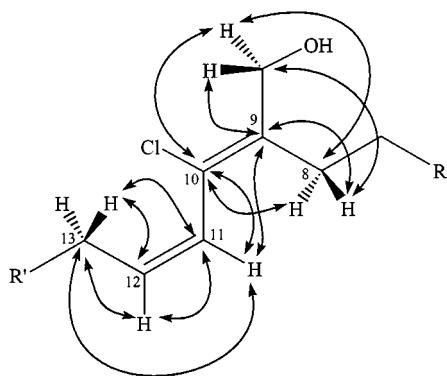


Figure 2. Correlations between hydrogen atoms 8-H, 11-H, 12-H, 13-H, and the hydrogens of the hydroxymethyl group, and carbon atoms C-8–C-13 and the carbon of the hydroxymethyl group, in **5a**, observed in the HMBC experiment

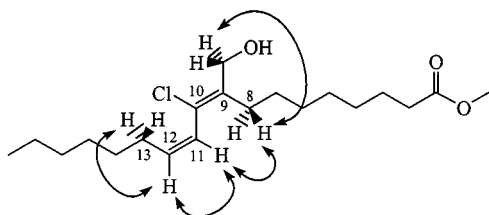
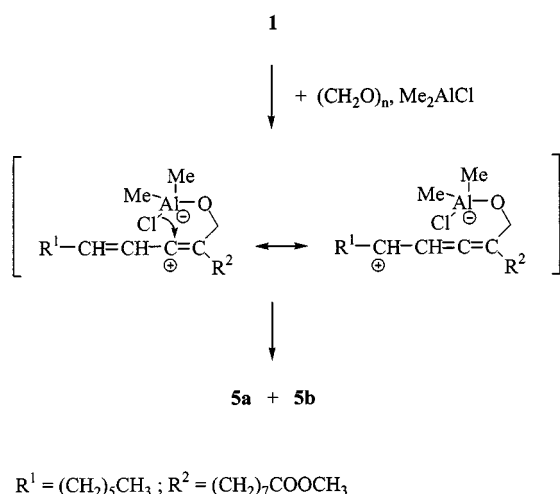


Figure 3. Strong NOEs between the hydrogen atoms 8-H, 11-H, 12-H, 13-H, and the hydrogens of the hydroxymethyl group in **5a** observed in the selective 1D-NOESY experiments

11.0 Hz] and *trans* geometries [ $^3J_{11,12}$  (**5b**) = 14.7 Hz] of the  $\Delta$ -11,12 double bonds.

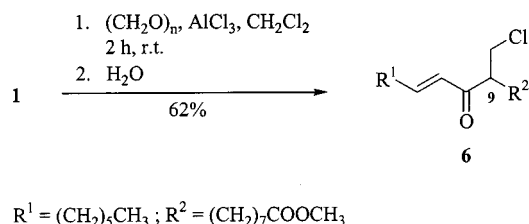
Therefore, we conclude that the  $\text{Me}_2\text{AlCl}$ -induced 1,2-addition reaction of formaldehyde occurs with complete regio- and stereoselectivity (Scheme 5). The stereoselective formation of the *Z*-configured  $\Delta$ -9,10 double bond of **5a** and **5b** is in agreement with the results of Rodini and Snider, who reported on stereoselective intramolecular chloride transfers in reactions induced by alkylaluminum halide between formaldehyde and 1-alkynes, leading exclusively to *Z*-configured double bonds.<sup>[13]</sup> Addition of formaldehyde to stereoisomerically pure (*E*)-**1** afforded pure product **5b**, with 11*E* configuration. The reaction takes place with retention of the stereochemistry of the  $\Delta$ -11,12 double bond.



Scheme 5. Mechanism of the addition of paraformaldehyde to methyl octadec-11-en-9-ynoate (**1**), induced by  $\text{Me}_2\text{AlCl}$

In general, the  $\text{AlCl}_3$ -induced reactions of alkenes and formaldehyde proceed by addition of two equivalents of the aldehyde and elimination of  $\text{H}_2\text{O}$ , to give chlorotetrahydropyran derivatives.<sup>[14]</sup>

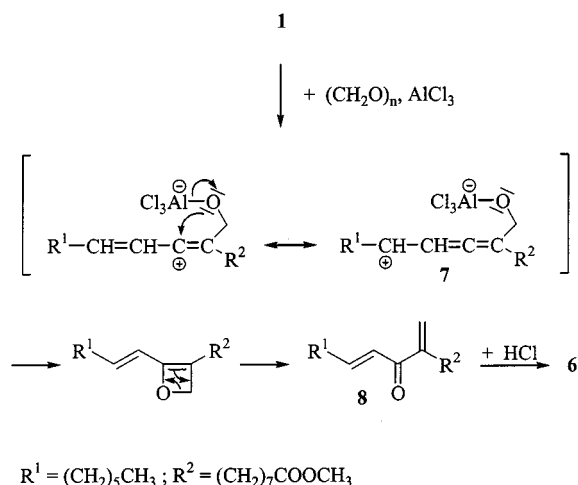
Quite differently, the reaction of enyne **1**, paraformaldehyde and  $\text{AlCl}_3$  in a ratio of 1:4:0.5 gave the  $\alpha,\beta$ -unsaturated  $\beta$ -chloro ketone **6** in 62% yield after a reaction time of 2 h (Scheme 6). To our initial surprise, the product obtained was clearly identified as the unexpected  $\alpha,\beta$ -unsaturated  $\beta$ -chloro ketone **6** by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy and mass spectrometry. The formation of product **6** can be rationalized as follows (Scheme 7): in the first step of the reaction, the formaldehyde/ $\text{AlCl}_3$  complex adds regioselectively to C-9 of the molecule chain of **1** to give a resonance-stabilized intermediate **7**, that could be expected to be trapped by chloride transfer to give compound **5** after hydrolysis, in a manner comparable to that of the  $\text{Me}_2\text{AlCl}$ -induced reaction (see Scheme 5). However, compound **5** is not observed. Therefore, we hypothesize that intermediate **7** is cyclized to give an oxetene derivative. Oxetenes are unstable compounds, which are well-known to undergo electrocyclic ring-opening reactions, yielding  $\alpha,\beta$ -unsaturated ketones.<sup>[15,16]</sup> In our case, nucleophilic addition of  $\text{HCl}$  to the unsaturated ketone **8**, obtained by the oxetene ring opening, followed to give product **6**. The formation of pure (*E*)-**6** – when using a stereoisomeric starting mixture of (*E*)-**1**/*Z*-**1** = 2:3 – can be explained by isomerization of the double bond of the  $\alpha,\beta$ -unsaturated ketone under these reaction conditions to give the more stable product. The  $\alpha,\beta$ -unsaturated ketone **8** was observed only in minor amounts. Using pure (*E*)-**1** as substrate, the same product **6** is obtained.



Scheme 6.  $\text{AlCl}_3$ -induced regioselective and stereoselective reaction of methyl octadec-11-en-9-ynoate (**1**) and paraformaldehyde

## Conclusion

Electrophilic addition reactions, induced by Lewis acids, to the conjugated enyne system of methyl santalbate proceed with high regioselectivity to form a new carbon–carbon bond. New products with an allenic system were obtained by acylation and alkylation reactions by a 1,4-addition. Formaldehyde additions induced by alkylaluminum halides lead, by a 1,2-addition, to 1,3-dienes with an allylic alcohol functionality, while the corresponding reaction in the presence of  $\text{AlCl}_3$  gave an  $\alpha,\beta$ -unsaturated chloro ketone.



Scheme 7. Rationalization of the reaction of methyl octadec-11-en-9-ynoate (**1**) and paraformaldehyde, induced by  $AlCl_3$

## Experimental Section

**General:** A mixture of methyl (*E*)- and methyl (*Z*)-octadec-11-en-9-ynoate (**1**) in a ratio of (*E*)-**1**/*Z*-**1** = 2:3 was prepared as described previously.<sup>[10]</sup> Pure santalbic acid was isolated from the seed oil of sandalwood.<sup>[17]</sup> Heptanoyl chloride (Aldrich), isopropyl chloroformate (BASF),  $Me_2AlCl$  and  $Et_3Al_2Cl_3$  (Witco), paraformaldehyde (Janssen), triethylsilane and  $AlCl_3$  (Fluka) were used without further purification.

**Analytical Equipment:** NMR: Bruker Avance 500,  $^1H$  NMR (500.13 MHz),  $^{13}C$  NMR (125.78 MHz). Chemical shifts are reported in the  $\delta$  scale in ppm relative to residual nondeuterated solvent signals or TMS as internal standard. – MS: Finnigan MAT 95. – Elemental analysis: Mikroanalytisches Labor Beller, D-37004 Göttingen.

**Methyl 12-Chloro-9-(1-oxoheptyl)-9,10-octadecadienoate (Diastereomeric Mixture) (2):** A mixture of **1** (0.29 g, 1 mmol) and heptanoyl chloride (0.15 g, 1 mmol) in  $CH_2Cl_2$  (8 mL) was stirred magnetically under nitrogen (1 bar) for 5 min. at  $-15^\circ C$ . After dropwise addition of  $Me_2AlCl$  (0.19 g, 2 mmol), the sample was stirred for an additional 2 h at room temp.. The reaction was quenched by the addition of  $Et_2O$  (50 mL) and  $H_2O$  (20 mL). 10% HCl was added until the precipitated aluminium salts had dissolved. The organic layer was separated and washed with  $H_2O$  ( $3 \times 20$  mL). The organic layer was dried ( $Na_2SO_4$ ) and the solvent evaporated. The acylation product **2** was purified by column chromatography (28 cm  $\times$  2 cm, silica gel 60, Merck 70–230 mesh) with the eluent petroleum ether/ether = 95:5 and obtained as a colourless oil. Yield: 0.29 g (66%). –  $^1H$  NMR ( $CDCl_3$ ):  $\delta$  = 0.83 (t, 3 H,  $CH_3$ ), 0.85 (t, 3 H,  $CH_3$ ), 1.24 (m, 20H,  $CH_2$ ), 1.39–1.58 (m, 6 H,  $CH_2$ ), 1.85 (m, 2 H, 8-H), 2.15 (m, 2 H,  $COCH_2$ ), 2.25 (t, 2 H, 2-H), 2.57 (m, 2 H, 13-H), 3.62 (s, 3 H,  $OCH_3$ ), 4.43 (m, 1 H, 12-H), 5.68 (dt,  $J$  = 8.4, 2.3 Hz, 1 H, 11-H), 5.74 (dt,  $J$  = 7.7, 2.3 Hz, 1 H, 11-H). –  $^{13}C$  NMR ( $CDCl_3$ ):  $\delta$  = 13.9 ( $2 \times CH_3$ ), 22.4, 22.5, 24.8, 24.9, 25.0, 26.5, 26.65, 26.69, 27.7, 27.8, 28.7, 28.6, 28.9, 29.0, 31.5, 31.6, 34.0 (C-2), 38.6, 38.9, 39.6, 39.7, 51.3 ( $OCH_3$ ), 58.7, 59.3 (C-12), 98.6, 98.7 (C-11), 111.1, 111.6 (C-9), 174.1, 174.1 (C-1), 200.4, 200.7 (C-10), 211.4, 211.5 (CO). – MS/CI (isobutane);  $m/z$  (%): 441 (100)/443 (32) [ $MH^+$ ], 405 (35) [ $MH^+ - HCl$ ]. – IR (neat):  $\nu$  = 1940  $cm^{-1}$  (m, C=C=C). –  $C_{26}H_{45}ClO_3$  (440.31): calcd. C 70.80, H 10.28; found C 70.76, H 10.18.

**Methyl 9-Isopropyl-9,10-octadecadienoate (3):** A mixture of **1** (0.29 g, 1 mmol) and isopropyl chloroformate (0.14 g, 1 mmol) in  $CH_2Cl_2$  (2 mL) was stirred magnetically under nitrogen (1 bar) for 5 min. at  $-15^\circ C$ . Then a mixture of triethylsilane (0.12 g, 1 mmol) and  $Et_3Al_2Cl_3$  (0.33 g, 1.3 mmol) was added dropwise over 15 min. at  $-15^\circ C$ . The sample was stirred for an additional 30 min. at room temp. and was then quenched by addition of  $Et_2O$  (50 mL) and  $H_2O$  (20 mL). 10% HCl was added to dissolve precipitated aluminium salts. The organic layer was separated and washed with  $H_2O$  ( $3 \times 20$  mL). The organic layer was dried ( $Na_2SO_4$ ) and the solvent evaporated. The product (0.18 g, 54%; GC: 60% **3**, 40% stereoisomeric mixture of **4**) was obtained by kugelrohr distillation ( $1.5 \times 10^{-2}$  mbar,  $95^\circ C$ ). – **3**: (from the mixture of **3** and **4**)  $^1H$  NMR ( $CDCl_3$ ):  $\delta$  = 0.81 (t, 3 H,  $CH_3$ ), 0.92 (d, 3 H,  $CH_3CH$ ), 0.93 (d, 3 H,  $CH_3CH$ ), 1.21 (m, 18 H,  $CH_2$ ), 1.57 (m, 2 H, 3-H), 1.84 (dt,  $J$  = 3.0, 8.0 Hz, 2 H, 8-H), 1.88 (dt,  $J$  = 7.4, 6.7 Hz, 2 H, 12-H), 1.99 (m, 1 H,  $CH(CH_3)_2$ ), 2.23 (t, 2 H, 2-H), 3.59 (s, 3 H,  $OCH_3$ ), 5.03 ( $2 \times$  t,  $J$  = 6.5 Hz and 5.8 Hz, 1 H, 11-H). –  $^{13}C$  NMR ( $CDCl_3$ ):  $\delta$  = 14.1 (C-18), 21.8 ( $CH_3$ ), 22.0 ( $CH_3$ ), 22.7, 25.0, 27.9, 29.0, 29.2, 29.20, 29.24, 29.4, 29.5, 29.6, 30.8, 31.0 [ $CH(CH_3)_2$ ], 31.9, 34.1 (C-2), 51.4 ( $OCH_3$ ), 93.1 (C-11), 110.6 (C-9), 174.3 (C-1), 199.6 (C-10).

**Methyl (9*Z*,11*Z*)-10-Chloro-9-hydroxymethyl-9,11-octadecadienoate (5a) and Methyl (9*Z*,11*E*)-10-Chloro-9-hydroxymethyl-9,11-octadecadienoate (5b):** A mixture of **1** (0.29 g, 1 mmol) and paraformaldehyde (0.03 g, 1 mmol) in  $CH_2Cl_2$  (5 mL) was stirred magnetically under an  $N_2$  atmosphere for 5 min. at  $-15^\circ C$ . After dropwise addition of  $Me_2AlCl$  (0.3 g, 3 mmol) or  $Et_3Al_2Cl_3$  (0.33 g, 1.3 mmol), the sample was stirred for an additional 2 h at room temp. The reaction was quenched by addition of  $Et_2O$  (50 mL) and  $H_2O$  (20 mL). 10% HCl was added until the precipitated aluminium salts were dissolved. The organic layer was separated and the aqueous layer extracted with  $Et_2O$  ( $3 \times 20$  mL). The combined organic layers were dried ( $Na_2SO_4$ ) and evaporated. Product **7** was purified by column chromatography (28 cm  $\times$  2 cm) on silica gel 60 (Merck, 70–230 mesh) with petroleum ether/ $Et_2O$  (6:4) as eluent.

Fractions containing the product were collected and the residue dried at  $20^\circ C/0.01$  mbar. – Yield: 0.27 g (76%). – **5a**:  $^1H$  NMR ( $CDCl_3$ , 300 K):  $\delta$  = 0.88 (t, 3 H,  $^3J_{17,18}$  = 6.6 Hz, 18-H), 1.29 (m, 12 H, 4-H – 6-H, 15-H – 17-H), 1.36–1.45 (m, 4 H,  $^3J_{7,8}$  = 7.7 Hz,  $^3J_{13,14}$  = 7.0 Hz, 7-H, 14-H), 1.61 (m, 2 H,  $^3J_{2,3}$  = 7.3 Hz, 3-H), 2.13 (m, 2 H,  $^3J_{12,13}$  = 7.3 Hz, 13-H), 2.19 (m, 2 H, 8-H), 2.29 (t, 2 H, 2-H), 3.66 (s, 3 H,  $CH_3O-$ ), 4.34 (s, 2 H,  $-CH_2OH$ ), 5.61 (dt, 1 H,  $^3J_{11,12}$  = 11.0 Hz, 12-H), 5.94 (d, 1 H, 11-H). –  $^{13}C$  NMR ( $CDCl_3$ , 300 K):  $\delta$  = 14.0 (C-18), 22.6 (C-17), 24.8 (C-3), 27.7 (C-7), 28.9, 28.9, 29.0, 29.3 (C-4 – C-6, C-13 – C-15), 31.6, 31.7 (C-8, C-16), 34.0 (C-2), 51.4 ( $CH_3O-$ ), 62.2 ( $-CH_2OH$ ), 124.7 (C-11), 125.3 (C-10), 136.5 (C-12), 137.7 (C-9), 174.2 (C-1). **5b**: (from a 85:15 mixture of **5a**:**5b**)  $^1H$  NMR ( $CDCl_3$ , 300 K):  $\delta$  = 0.88\* (t, 3 H, 18-H), 1.28\* (m, 12 H, 4-H – 6-H, 15-H – 17-H), 1.37–1.43\* (m, 4 H, 7-H, 14-H), 1.60\* (m, 2 H, 3-H), 2.13\* (m, 2 H,  $^3J_{12,13}$  = 7.3 Hz, 13-H), 2.18\* (m, 2 H, 8-H), 2.29\* (t, 2 H, 2-H), 3.66\* (s, 3 H,  $CH_3O-$ ), 4.36 (s, 2 H,  $-CH_2OH$ ), 6.20 (dt, 1 H,  $^3J_{11,12}$  = 14.7 Hz, 12-H), 6.35 (d, 1 H, 11-H). –  $^{13}C$  NMR ( $CDCl_3$ , 300 K):  $\delta$  = 14.0\* (C-18), 22.6\* (C-17), 24.8\* (C-3), 27.7 (C-7), 28.7, 28.8, 28.9, 28.9, 29.0, 29.1, 29.3\* (C-4 – C-6, C-13 – C-15), 30.9 (C-8), 31.5 or 31.6\* (C-16), 34.0\* (C-2), 51.4\* ( $CH_3O-$ ), 63.6 ( $-CH_2OH$ ), 123.4 (C-11), 128.6 (C-10), 136.2, 136.3 (C-9, C-12), 174.2\* (C-1) (\* signal crowding due to overlapping signals of **5a**; no individual assignment for **5b** possible) –  $C_{20}H_{35}ClO_3$  (358.95): calcd. C 66.92, H 9.83; found C 66.12, H 9.50.



**Methyl (*E*)-9-Chloromethyl-10-oxo-11-octadecenoate (6):** A mixture of **1** (0.29 g, 1 mmol) and paraformaldehyde (0.12 g, 4 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was stirred magnetically under an N<sub>2</sub> atmosphere for 5 min. at –15 °C. After addition of AlCl<sub>3</sub> (0.07 g, 0.5 mmol), the sample was stirred for an additional 1.5 h at room temp.. The reaction was quenched by addition of Et<sub>2</sub>O (50 mL) and H<sub>2</sub>O (20 mL). 10% HCl was added until the precipitated aluminium salts dissolved. The organic layer was separated and the aqueous layer extracted with Et<sub>2</sub>O (3 × 20 mL). The combined organic extracts were dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The product was purified by column chromatography (20 cm × 2 cm) on silica gel 60 (Merck 70–230 mesh), with petroleum ether/ether (6:4) as eluent. Fractions containing the product were collected, the solvent evaporated and the residue dried at 20 °C/0.01 mbar. – Yield: 0.22 g (62%). – <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 0.82 (t, 3 H, CH<sub>3</sub>), 1.22 (m, 14 H, CH<sub>2</sub>), 1.42 (m, 3 H), 1.53 (m, 2 H, 3-H), 1.58 (m, 1 H, 8-H<sub>a</sub>), 2.17 (dt, *J* = 6.9, 6.9 Hz, 2 H, 13-H), 2.22 (t, 2 H, 2-H), 3.05 (m, 1 H, 9-H), 3.46 (dd, *J* = 10.7, 5.6 Hz, 1 H, CH<sub>a</sub>Cl), 3.59 (s, 3 H, OCH<sub>3</sub>), 3.68 (dd, *J* = 10.7, 8.2 Hz, 1 H, CH<sub>b</sub>Cl), 6.12 (dt, *J* = 15.8, 1.5 Hz, 1 H, 11-H), 6.85 (dt, *J* = 15.8, 6.9 Hz, 1 H, 12-H). – <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 14.0, 22.5, 24.8, 26.7, 28.0, 28.8, 28.9, 29.0, 29.4, 30.5, 31.5, 32.6, 34.0 (C-2), 44.4 (CH<sub>2</sub>Cl), 51.22 (C-9), 51.4 (OCH<sub>3</sub>), 129.8 (C-11), 149.0 (C-12), 174.1 (C-1), 200.6 (C-10). – MS (70 eV); *m/z* (%): 358 (1) [M<sup>+</sup>], 327 (3), 291 (2), 211 (2), 202 (6), 167 (17), 139 (100). – HR-MS/EI C<sub>20</sub>H<sub>35</sub>ClO<sub>3</sub>: calcd. 358.2275; found 358.2258.

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