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_2AlCl or $Et_3Al_2Cl_3$ gives a mixture of the conjugated chlorodienes **5a** and **5b,** the corresponding reaction carried out in the presence of $AlCl_3$ affords the α,β-unsaturated ketone **6**.

Introduction

Electrophilic addition reactions to conjugated enynes[1−3] are well-known to give 1,3-dienes (1,2-addition),[2] and allenic compounds (1,4-addition).[1,3] 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.[1] In most cases, the reactions have been carried out with polar reagents like hydrochloric and hydrobromic acid and with organolithium compounds. δ-Chloro-α-allenyl ketones have been obtained regioselectively from $AlCl_3$-mediated acylation reactions of 3-buten-1-ynes with acyl chlorides.[4,5]

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.[6] Up to now, we have carried out electrophilic additions such as Friedel−Crafts acylations,[7] Friedel−Crafts alkylations[8] and ene additions of formaldehyde[9] 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 ultrasound-assisted five-step reaction sequence from methyl ricinoleate.[10]

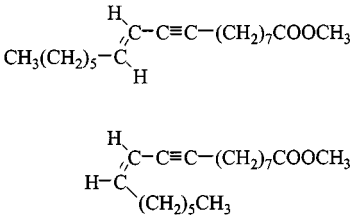
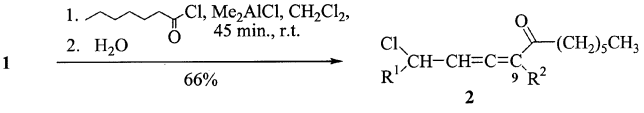


Figure 1. Methyl santalbate [(*E*)-**1**] from the seed oil of sandalwood; a stereoisomeric mixture of methyl octadec-11-en-9-ynoate [(*E*)-**1**/(*Z*)-**1** = 2:3] can be obtained in a five step reaction sequence from methyl ricinoleate[10]

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_2AlCl) in CH_2Cl_2 (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**.



$R^1 = (CH_2)_5CH_3$; $R^2 = (CH_2)_7COOCH_3$

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 ($EtAlCl_2$).[7] Our results show that, in the case of the conjug-

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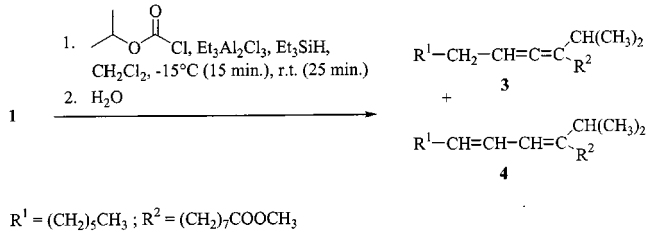
ated enyne **1**, the milder Lewis acid Me_2AlCl has to be used, because in the presence of $EtAlCl_2$ a complex mixture of products was obtained. The mechanism and the regioselectivity of the acylation reaction have been discussed by Santelli-Rouvier et al.[5]

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

In analogy to Friedel–Crafts alkylations of alkenes,[8] the corresponding reaction of **1** was carried out with isopropyl chloroformate and ethylaluminium sesquichloride ($Et_3Al_2Cl_3$) (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.



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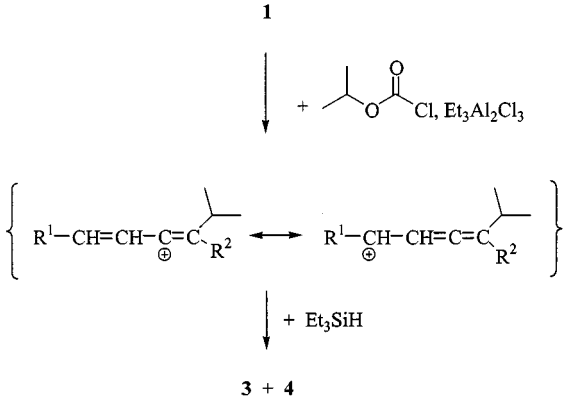
Scheme 2. Regioselective alkylation of methyl octadec-11-en-9-ynoate (**1**) and isopropyl chloroformate in the presence of triethylsilane, induced by ethylaluminium sesquichloride

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).

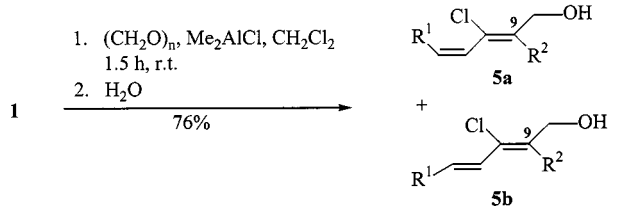


$R^1 = (CH_2)_5CH_3$; $R^2 = (CH_2)_7COOCH_3$

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,[9] while in the case of formaldehyde and 1-alkynes, mixtures of products, consisting of α-allenic alcohols and (*Z*)-3-chloroallylic alcohols, are obtained.[13] The Me_2AlCl-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.



$R^1 = (CH_2)_5CH_3$; $R^2 = (CH_2)_7COOCH_3$

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

From H,H-COSY, HMQC and HMBC NMR experiments in $CDCl_3$ 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 $CDCl_3$ 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, H,H-COSY, HMQC and HMBC NMR experiments in $CDCl_3$ at room temperature proved the substitution pattern of the Δ-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**) =

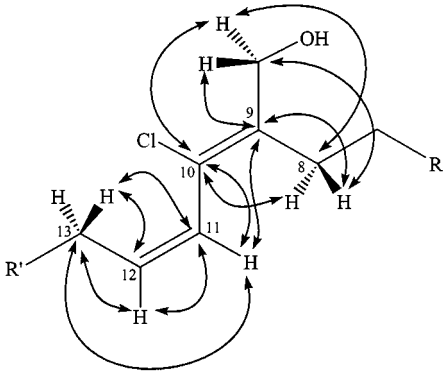


Figure 2. Correlations between hydrogen atoms 8-H, 11-H, 12-H, 13-H, and the hydrogens of the hydroxymethyl group, and carbon atoms C-8−C-13 and the carbon of the hydroxymethyl group, in **5a**, observed in the HMBC experiment

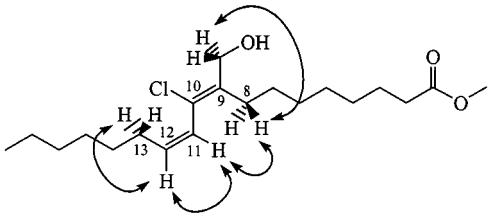
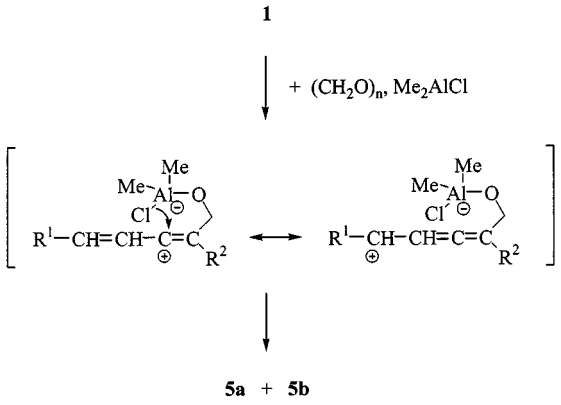


Figure 3. Strong NOEs between the hydrogen atoms 8-H, 11-H, 12-H, 13-H, and the hydrogens of the hydroxymethyl group in **5a** observed in the selective 1D-NOESY experiments

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

Therefore, we conclude that the Me_2AlCl-induced 1,2-addition reaction of formaldehyde occurs with complete regio- and stereoselectivity (Scheme 5). The stereoselective formation of the *Z*-configured Δ-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 alkylaluminium halide between formaldehyde and 1-alkynes, leading exclusively to *Z*-configured double bonds.[13] 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 Δ-11,12 double bond.

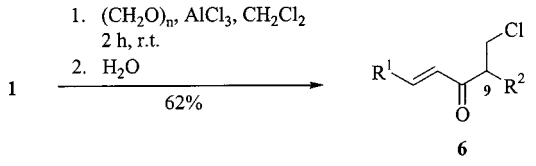


$R^1 = (CH_2)_5CH_3$; $R^2 = (CH_2)_7COOCH_3$

Scheme 5. Mechanism of the addition of paraformaldehyde to methyl octadec-11-en-9-ynoate (**1**), induced by Me_2AlCl

In general, the $AlCl_3$-induced reactions of alkenes and formaldehyde proceed by addition of two equivalents of the aldehyde and elimination of H_2O, to give chlorotetrahydropyran derivatives.[14]

Quite differently, the reaction of enyne **1**, paraformaldehyde and $AlCl_3$ in a ratio of 1:4:0.5 gave the α,β-unsaturated β-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 α,ß-unsaturated β-chloro ketone **6** by ^1H and ^{13}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/$AlCl_3$ 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 Me_2AlCl-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 α,β-unsaturated ketones.[15,16] In our case, nucleophilic addition of 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 α,ß-unsaturated ketone under these reaction conditions to give the more stable product. The α,ß-unsaturated ketone **8** was observed only in minor amounts. Using pure (*E*)-**1** as substrate, the same product **6** is obtained.

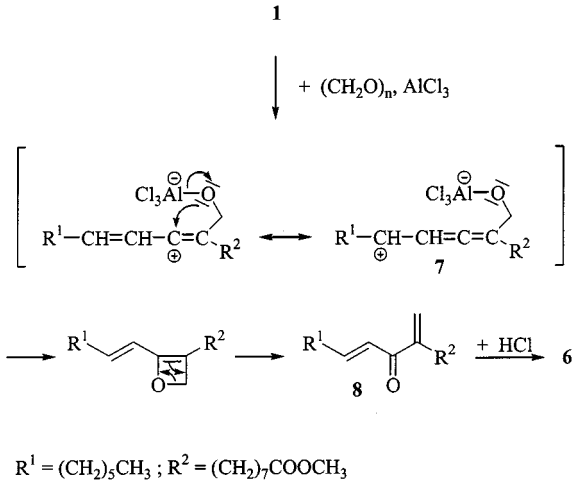


$R^1 = (CH_2)_5CH_3$; $R^2 = (CH_2)_7COOCH_3$

Scheme 6. $AlCl_3$-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 alkylaluminium halides lead, by a 1,2-addition, to 1,3-dienes with an allylic alcohol functionality, while the corresponding reaction in the presence of $AlCl_3$ gave an α,β-unsaturated chloro ketone.



$R^1 = (CH_2)_5CH_3$; $R^2 = (CH_2)_7COOCH_3$

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.[10] Pure santalbic acid was isolated from the seed oil of sandalwood.[17] 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 δ 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 °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 × 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 × 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 ($CDCl_3$): δ = 0.83 (t, 3 H, CH_3), 0.85 (t, 3 H, CH_3), 1.24 (m, 2OH, 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 ($CDCl_3$): δ = 13.9 (2 × 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): $\tilde{\nu}$ = 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 °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 °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 × 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 × 10^{-2} mbar, 95 °C). − **3:** (from the mixture of **3** and **4**) ^1H NMR ($CDCl_3$): δ = 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 × t, *J* = 6.5 Hz and 5.8 Hz, 1 H, 11-H). − ^{13}C NMR ($CDCl_3$): δ = 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 °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 × 20 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. Product **7** was purified by column chromatography (28 cm × 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 °C/0.01 mbar. − Yield: 0.27 g (76%). − **5a:** ^1H NMR ($CDCl_3$, 300 K): δ = 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): δ = 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): δ = 0.88* (t, 3 H, H-18), 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): δ = 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_2Cl_2 (10 mL) was stirred magnetically under an N_2 atmosphere for 5 min. at −15 °C. After addition of $AlCl_3$ (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_2O (50 mL) and H_2O (20 mL). 10% HCl was added until the precipitated aluminium salts dissolved. The organic layer was separated and the aqueous layer extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) 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%). − ^{1}H NMR ($CDCl_3$): δ = 0.82 (t, 3 H, CH_3), 1.22 (m, 14 H, CH_2), 1.42 (m, 3 H), 1.53 (m, 2 H, 3-H), 1.58 (m, 1 H, 8-H_a), 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_aCl), 3.59 (s, 3 H, OCH_3), 3.68 (dd, *J* = 10.7, 8.2 Hz, 1 H, CH_bCl), 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). − ^{13}C NMR ($CDCl_3$): 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_2Cl), 51.22 (C-9), 51.4 (OCH_3), 129.8 (C-11), 149.0 (C-12), 174.1 (C-1), 200.6 (C-10). − MS (70 eV); *m*/*z* (%): 358 (1) [M^+], 327 (3), 291 (2), 211 (2), 202 (6), 167 (17), 139 (100). − HR-MS/EI $C_{20}H_{35}ClO_3$: calcd. 358.2275; found 358.2258.

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[1] M. Murray, *Methoden Org. Chem.* (Houben-Weyl), 4th ed. **1977**, vol. 5/2a, p. 963−1076, here p. 1024.
[2] M. Cais, in *The Chemistry of Alkenes* (Ed.: S. Patai), Wiley & Sons Ltd., London, **1964**, p. 955−1023, here p. 967.
[3] H. Hopf, in *The Chemistry of Ketenes, Allenes and Related Compounds,* vol. 2, (Ed.: S. Patai), Wiley & Sons, Ltd., London, **1980**, 779−901, here 784.
[4] C. Santelli-Rouvier, S. Lefrere, M. Mamai, M. Santelli, *Tetrahedron Lett.* **1995**, *36*, 2459−2460.
[5] C. Santelli-Rouvier, S. Lefrere, M. Santelli, *J. Org. Chem.* **1996**, *61*, 6678−6684.
[6] U. Biermann, W. Friedt, S. Lang, W. Lühs, G. Machmüller, J. O. Metzger, M. Rüsch gen. Klaas, H. J. Schäfer, M. P. Scheider, *Angew. Chem*. **2000**, in press.
[7] J. O. Metzger, U. Biermann, *Liebigs Ann.* **1993**, 645−650.
[8] U. Biermann, J. O. Metzger, *Angew. Chem.* **1999**, *111*, 3874−3876; *Angew. Chem. Int. Ed.* **1999**, *38*, 3675−3677.
[9] J. O. Metzger, U. Biermann, *Synthesis* **1992**, *5*, 463−465.
[10] M. S. F. Lie Ken Jie, M. K. Pasha, F. Ahmad, *Lipids* **1996**, *31*, 1083−1089.
[11] M. S. F. Lie Ken Jie, *Prog. Lipid Res.* **1993**, *32*, 151−194.
[12] M. S. F. Lie Ken Jie, M. M. L. Lau, *Chem. Phys. Lipids* **1999**, *101*, 237−242.
[13] D. J. Rodini, B. B. Snider, *Tetrahedron Lett*. **1980**, *21*, 3857−3860.
[14] J. O. Metzger, U. Biermann, *Bull. Soc. Chim. Belg.* **1994**, *103*, 393−397.
[15] S. Searles, in *Comprehensive Heterocyclic Chemistry*, vol. 7, (Ed.: W. Lwowski), Pergamon Press Ltd., Oxford, **1984**, p. 363−402, here p. 375.
[16] H. Yu, W.-T. Chan, J. D. Goddard, *J. Am. Chem. Soc.* **1990**, *112*, 7529−7537.
[17] M. K. Pasha, F. Ahmad, *Lipids* **1993**, *28*, 1027−1031.

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