Alkylaluminium Dichloride Induced Friedel-Crafts Acylation of Unsaturated Carboxylic Acids and Alcohols

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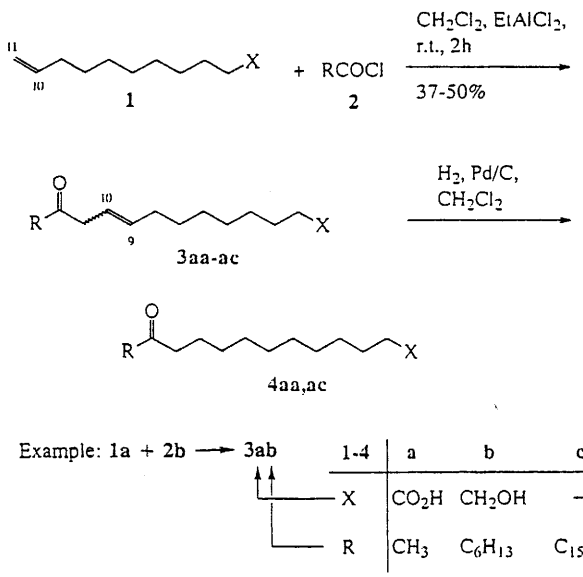
The ethylaluminium dichloride induced Friedel-Crafts acylation of unsaturated carboxylic acids, for example 10-undecenoic acid (**1a**) and oleic acid (**5a**), and of the respective alcohols **1b** and **5b** with acyl chlorides and cyclic acyl anhydrides gave the corresponding long-chain β,γ-unsaturated ketones **3**, **6/7**, **11** and **13/14** with ω-carboxy and ω-hydroxy functions, respectively. The intramolecular cyclization of petroselinic acid chloride (**17**) yielded (*E*)-2-dodecylidenecyclohexanone (**18**). Catalytic hydrogenation gave the respective saturated ketones **4**, **8/9**, **12**, **15/16** and **19**.

The Lewis acid induced Friedel-Crafts acylation of alkenes is a well-known reaction[1–3]. Induced by Lewis acids, for example $AlCl_3$, $SnCl_4$ or $ZnCl_2$, the acylation often leads to a mixture of β,γ-unsaturated ketones, α,β-unsaturated ketones and β-chloro ketones[4]. Snider and Jackson[5] have reported recently, that the Friedel-Crafts acylation of cyclic and aliphatic alkenes with carboxylic acid chlorides and carboxylic acid anhydrides can be induced by ethylaluminium dichloride ($EtAlCl_2$) in equivalent amounts to give the corresponding β,γ-unsaturated ketones in yields of 53–73% with only β-chloro ketones as minor products. Lewis acid ($AlCl_3$, $SnCl_4$) induced Friedel-Crafts cyclizations of unsaturated carboxylic acid chlorides to give five-, six- and seven-membered carbocyclic ketones have been reported as well[2].



There are only very few examples of the acylation of alkenes with functional groups[1–3] and especially the preparatively interesting $EtAlCl_2$ induced acylation has been applied exclusively to simple alkenes[5]. We have been interested in Lewis acid induced C,C-bond forming reactions of unsaturated fatty compounds[6], for example 10-undecenoic acid (**1a**), oleic acid (**5a**), and the respective alcohols **1b** and **5b**, which are of interest as renewable raw materials[7]. Friedel-Crafts acylation of these alkenes should give interesting linear and branched products with potentially interesting properties. There are known many interesting natural products which may be synthesized by conversion of (*E*)-3-oxoalkenes obtained by acylation of the corresponding unsaturated fatty compounds, for example (*E*)-12-hydroxyoctadec-8-enoic acid (ricinelaidic acid), or (*E*)-9-hydroxyoctadec-10-enoic acid and (*E*)-10-hydroxyoctadec-8-enoic acid, respectively, "self-defense substances" of many plants[8], or (*R*)-patulolide A, an antifungal and antibacterial agent[9].

Acylation with Acyl Chlorides 2

The acylation of 10-undecenoic acid (**1a**) with acyl chlorides **2** in the presence of $EtAlCl_2$ in a molar ratio of 1:1:2 gave after a reaction time of 2 h the corresponding β,γ-unsaturated keto carboxylic acids **3aa**, **3ab** and **3ac**. **3aa** was obtained after column chromatography as (*E*)/(*Z*) mixture (2.9:1, GC) in an isolated yield of 50%. Recrystallization of the raw products **3ab** and **3ac** gave the pure (*E*)-products in isolated yields of 48% and 37%, respectively. Catalytic hydrogenation of the unsaturated ketones **3aa** and **3ac** gave the saturated ketones **4aa** and **4ac**, respectively, in quantitative yields. Reduction of the carbonyl group of (*E*)-**3ab** with $NaBH_4$ gave the racemate of (*E*)-12-hydroxy-9-octadecenoic acid (ricinelaidic acid), a natural product. The synthesis of ricinelaidic acid was also performed by $EtAlCl_2$-induced ene reaction of 10-undecenoic acid and heptanal[10].

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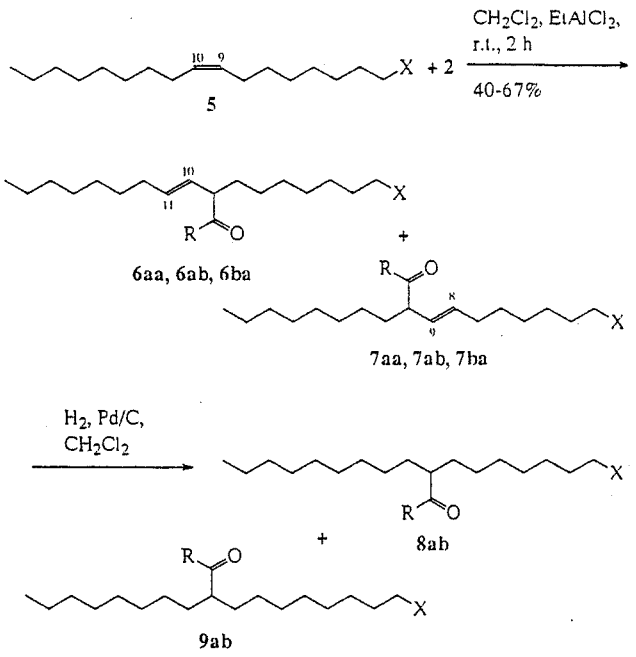


2, 5-9	a	b
X	CO_2H	CH_2OH
R	CH_3	C_6H_{13}

The alkylaluminium chloride induced acylation of **1a** takes place regioselectively at the terminal carbon atom. The ratios of the (*E*)- and (*Z*)-addition products are approximately 3:1. Pure (*E*)-isomers could be isolated by recrystallization in the case of **3ab** and **3ac**.

The acylation of oleic acid (**5a**) and oleyl alcohol (**5b**) with acyl chlorides **2** in the presence of $EtAlCl_2$ in a molar ratio of 1:1:2 gave after a reaction time of 2 h the corresponding β,γ-unsaturated keto carboxylic acids **6aa/7aa** (55%) and **6ab/7ab** (40%) and the corresponding β,γ-unsaturated ketone with ω-hydroxy functionality **6ba/7ba** (62%).

Preliminary results have been obtained with $EtAlCl_2$-induced reactions of unsaturated fatty compounds with unsaturated acyl chlorides, e.g. acrylic acid chloride or crotonic acid chloride, to give the corresponding vinyl allyl ketones. These compounds can be cyclized by the Nazarov reaction[11] to give cyclopentenone derivatives. We carried out the Nazarov cyclization with the acylation product of oleic acid and crotonic acid chloride.

Catalytic hydrogenation of **6ab/7ab** gave the saturated ketones **8ab/9ab** in quantitative yield. The acylation of **5a** and **5b** with acyl chlorides **2** gave approximately equal amounts of the 9- and 10-regioisomers as (*E*)-adducts. The stereochemistry was identified as the (*E*)-configuration by a comparison of their ^{13}C-NMR data with those reported in the literature[12] and the vicinal coupling constants of the olefinic protons in the ^1H-NMR spectra. (*Z*)-isomers were detected neither in the ^1H-NMR nor in the ^{13}C-NMR spectra.

Snider and Phillips[10] observed the formation of pure (*E*)-adducts in related ene reactions of *cis*-alkenes. This is in agreement with our results on ene reactions of formaldehyde with *cis*-unsaturated carboxylic acids, esters and alcohols[6]. The regioisomers **6/7** and **8/9** could not be separated. They were distinguished by their ^1H-NMR and ^{13}C-NMR spectra but they could not be assigned unambiguously to the respective products.

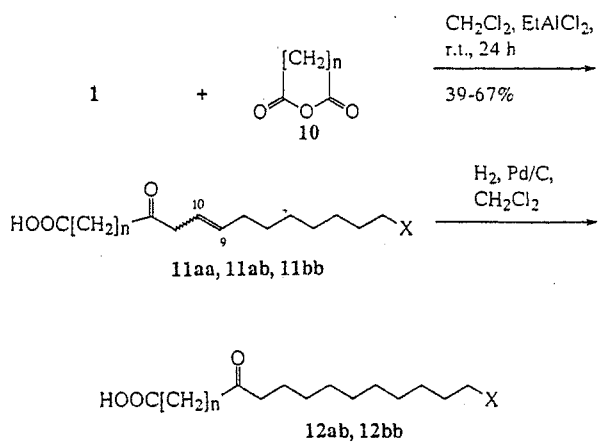
In contrast to the results of Snider and Jackson[5] the formation of chloro ketones was observed only in yields of 1–4% (GC). The formation of α,β-unsaturated ketones (2–9%) was, however, observed. The acylation of **1a** and **5a** could be carried out also with ethylaluminium sesquichloride ($Et_3Al_2Cl_3$), a milder Lewis acid. The reaction time, however, was about 24 h.

Acylation with Cyclic Anhydrides 10

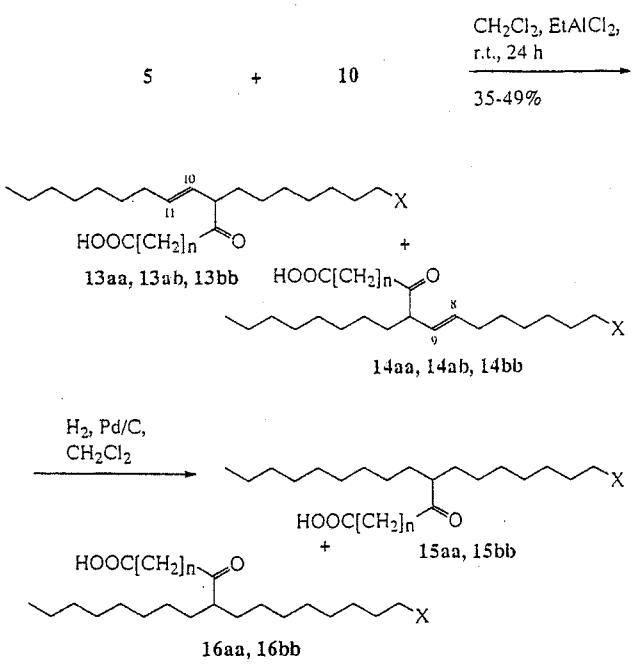
β,γ-Unsaturated keto dicarboxylic acids **11aa** and **11ab** were obtained by acylation of 10-undecenoic acid (**1a**) with cyclic anhydrides **10**. After recrystallization the isolated yields of the pure (*E*)-products were 50% and 67%, respectively. In the case of the acylation of **1a** with **10b** 18% of the corresponding α,β-unsaturated product were formed. Catalytic hydrogenation of **11ab** gave the respective saturated product **12ab**.

The $EtAlCl_2$-induced acylation of 10-undecenol (**1b**) with glutaric anhydride (**10b**) yielded the corresponding β,γ-unsaturated keto carboxylic acid with ω-hydroxy functionality **11bb** (74%).

The acylation of oleic acid (**5a**) with cyclic anhydrides **10** gave the corresponding branched β,γ-unsaturated keto dicarboxylic acids **13aa/14aa** and **13ab/14ab** in isolated yields of 40% and 49%, respectively. Catalytic hydrogenation of **13aa/14aa** gave the saturated product **15aa/16aa**. The addition of glutaric anhydride (**10b**) to oleyl alcohol



10-12	a	b
X	CO_2H	CH_2OH
n	1	2



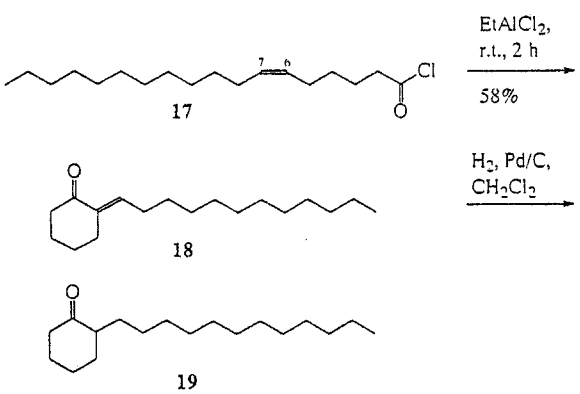
13-16	a	b
X	CO_2H	CH_2OH
n	1	2

(**5b**) yielded the β,γ-unsaturated keto carboxylic acid **13bb/14bb** (35%).

Regarding the stereochemistry and the regioselectivity the results were identical with those obtained in the acylations with acyl chlorides.

Intramolecular Cyclization of Petroselinic Acid (17)

Petroselinic acid (**17**) is a new fatty acid with a content of up to 80% in the seed oil of *Coriandrum sativum* and is of interest as a renewable raw material as well. We have been reported on the free-radical cyclization of **17** to give cyclopentane derivatives[13] and thought that the intramolecular Friedel-Crafts acylation should give easily 2-dodecylcyclohexanone (**19**).



The $EtAlCl_2$-induced intramolecular acylation of petroselinic acid chloride (**17**) gave the cyclization product **18** with an exocyclic double bond in a yield of 58% as (*E*)-product. The stereochemistry at the alkylidene part was assigned as *E* by comparison of the ^{1}H-NMR and ^{13}C-NMR data with those reported in the literature[14]. The ring closure took place regioselectively at C-6. The regioselectivity is in agreement with the results of Moon and Kolesar[15] who carried out the $SnCl_4$-induced intramolecular acylation of 4-cycloocten-1-yl acetyl chloride. The product obtained by the formation of a six-membered ring was the corresponding bicyclic chloro ketone. 2-Alkylidencyclohexanones were synthesized by cross-aldol condensation of cyclohexanone with the appropriate aldehyde in good to moderate yields[16]. The unsaturated ketone **18** could be easily hydrogenated to give 2-dodecylcyclohexanone (**19**).

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Experimental

Melting points (uncorrected): Leitz Laborlux 12. – Refractive indices n_D: Zeiss-Abbé-Refraktometer. – Elemental analysis: Fa. Beller, Göttingen. – ^{1}H and ^{13}C NMR: Bruker AM 300, TMS as internal standard; selected data are given. Full ^{1}H- and ^{13}C-NMR data are available from the authors on request. The signals of the regioisomers of **6/7**, **8/9**, **13/14** and **15/16** were distinguishable in the ^{1}H- and ^{13}C-NMR spectra but they could not be assigned unambiguously to the respective products. – Analytical GC: Carlo Erba GC 6000 Vega Series 2 with a FID (DB 1-column, 30 m). – Mass spectra: Finnegan MAT 212 mass spectrometer. – Oleic acid (new sun flower, 82% oleic acid, 3.5% palmitic acid, 0.6% stearic acid, 12% $C_{18:2}$), oleyl alcohol (new sun flower, 85.5% olelyl alcohol, 6.8% octadecanol, 3.1% hexadecanol, 0.5% $C_{18:2}$) and petroselinic acid (81.3% petroselinic acid, 3.3% palmitic acid, 0.4% stearic acid, 13.5% $C_{18:2}$) were obtained from Henkel KGaA. – The amounts of the starting olefins used in the reactions were calculated based on 100% purity. – Petroselinic acid chloride was prepared in the usual manner with thionyl chloride. – 10-Undecenoic acid (Atochem), 10-undecenol (Aldrich), $EtAlCl_2$ and $Et_3Al_2Cl_3$ (Schering AG), heptanoyl chloride, hexadecanoyl chloride, succinic anhydride and glutaric anhydride (Aldrich) were used without further purification. – Acetyl chloride (Merck) was used after distillation. – All reactions were run under N_2.

Acylation of Unsaturated Carboxylic Acids with Acyl Chlorides or Cyclic Anhydrides. – General Procedure: A mixture of the appropriate unsaturated carboxylic acid **1a** (5 mmol) of **5a** (4.2 mmol) and the acylating agent [acetyl chloride (**2a**), heptanoyl chloride (**2b**), hexadecanoyl chloride (**2c**), succinic anhydride (**10a**), glutaric anhydride (**10b**), 5 mmol] in CH_2Cl_2 was stirred magnetically under nitrogen (1 bar) for 5 min at −15°C. After dropwise addition of $EtAlCl_2$ (1 M in hexane, 10 ml, 10 mmol) the sample was stirred for an additional 2 h (with acyl chlorides) or 24 h (with cyclic anhydrides) at room temp. The reaction was quenched by the addition of Et_2O (100 ml) and H_2O (40 ml). 10% HCl was added until the precipitated aluminium salts had dissolved. The organic layer was separated and washed with H_2O (3 × 30 ml). The organic

layer was dried (Na_2SO_4) and the solvent evaporated. The acylation products were purified by column chromatography in the case of **3aa**, **6aa/7aa**, **6ab/7ab**, **13aa/14aa**, **13ab/14ab** or by recrystallization **3ab**, **3ac**, **11aa**, **11ab**. Column chromatography: 28 cm × 2 cm, silica gel 60 (Merck, 70–230 mesh) with the eluent petroleum ether/EtOAc (9:1, 250 ml) for **3aa**, **6aa/7aa** and **6ab/7ab** and (9:1, 250 ml) and (6:4, 250 ml) for **13aa/14aa** and **13ab/14ab** as eluent. Fractions containing the acylation product were collected, the solvent was evaporated and the residue dried at 20°C/0.01 mbar. – Catalytic hydrogenation of the acylation products **3aa**, **3ac**, **6ab/7ab**, **11ab** and **13aa/14aa** was carried out with Pd/C in CH_2Cl_2 at 2 bar. The reaction time was 24 h at room temp. – The reduction of the carbonyl group of (*E*)-**3ab** was carried out with $NaBH_4$ in the usual manner. (*E*)-12-Hydroxy-9-octadecenoic acid was obtained in a yield of 85%.

12-Oxotridec-9-enoic Acid (**3aa**) [(*E*):(*Z*) = 2.9:1, GC]: Yield 0.56 g (50%), $n_D^{21} = 1.4775$. – ^1H NMR (C_6D_6) of (*E*)-**3aa**: δ = 5.47 (dtt, *J* = 15.3, 6.7, 0.8 Hz, 1H, 10-H), 5.33 (dtt, *J* = 15.3, 6.5, 1.0 Hz, 1 H, 9-H), 2.73 (d, *J* = 6.7 Hz, 2H, 11-H), 1.69 (s, 3H, 13-H). – ^{13}C NMR ($CDCl_3$): δ = 207.9 (C=O), 179.7 (C-1), 135.2 [C-9, (*E*)], 133.7 [C-9, (*Z*)], 121.6 [C-10, (*E*)], 120.6 [C-10, (*Z*)], 47.5 (C-11). – MS (70 eV): *m/z* (%) = 226 (0.2) [M^+], 224 (1), 208 (1), 181 (1), 152 (10), 98 (32), 97 (40), 58 (33), 43 (100). – $C_{13}H_{22}O_3 \times H^+$: calcd. 227.1647, found 227.1649 (MS/CI).

12-Oxotridecanoic Acid (**4aa**): *Catalytic hydrogenation of* **3aa** (0.45 g) gave 0.44 g (96%) of **4aa**, m.p. 70°C (ref.[17] 71–72°C). – ^1H NMR ($CDCl_3$): δ = 2.42 (t, *J* = 7.4 Hz, 2H, 11-H), 2.14 (s, 3H, 13-H), 1.61 (m, 2 × 2H, 3-H and 10-H). – ^{13}C NMR ($CDCl_3$): δ = 209.6 (C=O), 179.8 (C-1), 43.8 (C-11). – MS (70 eV): *m/z* (%) = 228 (1) [M^+], 210 (3), 170 (4), 152 (14), 58 (90), 43 (100). – MS/CI (isobutane): *m/z* (%) = 229 (100) [MH^+], 211 (82).

(E)-12-Oxooctadec-9-enoic Acid (**3ab**): Yield 0.71 g (48%), obtained by recrystallization of the (*E*)/(*Z*) mixture (2.7:1, GC) from hexane, m.p. 72°C (ref.[18] 72–72.5°C). – ^1H NMR (C_6D_6): δ = 5.66 (dtt, *J* = 15.3, 6.8, 1.2 Hz, 1H, 10-H), 5.47 (dtt, *J* = 15.3, 6.7, 1.2 Hz, 1H, 9-H), 2.88 (d, *J* = 6.8 Hz, 2H, 11-H), 2.14 (t, *J* = 7.4 Hz, 2H, 13-H). – ^{13}C NMR (MeOH): δ = 212.2 (C=O), 177.4 (C-1), 135.8 (C-9), 123.3 (C-10), 47.3 (C-11), 42.6 (C-13). – MS (70 eV): *m/z* (%) = 296 (0.3) [M^+], 278 (0.2), 226 (0.1), 208 (0.4), 166 (4), 113 (100), 85 (42). – MS/CI (isobutane): *m/z* (%) = 297 (100) [MH^+], 279 (86).

(E)-12-Oxoheptacos-9-enoic Acid (**3ac**): Yield 0.78 g (37%), obtained by recrystallization of the (*E*)/(*Z*) mixture (3.1:1, GC) from hexane, m.p. 95.5–96°C. – ^1H NMR (C_6D_6): δ = 5.60 (dtt, *J* = 15.3, 6.9, 1.2 Hz, 1H, 10-H), 5.41 (dtt, *J* = 15.3, 6.7, 1.2 Hz, 1H, 9-H), 2.84 (d, *J* = 6.9 Hz, 2H, 11-H), 2.09 (t, *J* = 7.2 Hz, 2H, 13-H), 1.47 (m, 2H, 14-H). – ^{13}C NMR ($CDCl_3$): δ = 209.9 (C=O), 179.5 (C-1), 135.0 (C-9), 122.0 (C-10), 46.8 (C-11), 42.2 (C-13). – MS (70 eV): *m/z* (%) = 422 (8) [M^+], 405 (6), 239 (61), 226 (2), 208 (7), 166 (12), 58 (100). – MS/CI (isobutane): *m/z* (%) = 423 (100) [MH^+], 405 (40). – $C_{27}H_{50}O_3 \times H^+$: calcd. 423.3838, found 423.3826 (MS/CI).

12-Oxoheptacosanoic Acid (**4ac**): Catalytic hydrogenation of **3ac** (0.50 g) gave 0.48 g (94%) of **4ac**, m.p. 101.0–101.5°C. – $C_{27}H_{52}O_3$ (424.3) (**4ac**): calcd. C 76.42, H 12.26; found C 76.47, H 12.11.

rac-(E)-9-Acetyloctadec-10-enoic Acid (**6aa**) *and rac-(E)-10-Acetyloctadec-8-enoic Acid* (**7aa**) (1:1 mixture): Yield 0.75 g (55%), colorless liquid, $n_D^{21} = 1.4648$. – ^1H NMR ($CDCl_3$): δ = 5.57 and 5.55 (dt, *J* = 15.3, 6.8 Hz, 1H, 8-H and 11-H), 5.29 and 5.27 (ddt, *J* = 15.3, 8.3, 1.2 Hz, 1H, 9-H and 10-H), 3.0 [dt, *J* = 8.3, 7.4 Hz, 1H, 9(10)-H], 2.34 (2 t, *J* = 7.4 Hz, 2 × 2H, 2-H), 2.12 (s, 3H, $COCH_3$). – ^{13}C NMR ($CDCl_3$): δ = 210.7 (C=O), 179.8 (C-1), 134.8, 134.4, 128.0, 127.7 (C=C, **6aa** and **7aa**), 57.4 [C-9(10)]. – MS (70 eV): *m/z* (%) = 324 (4) [M^+], 306 (2), 281 (1), 263 (16), 181 (16), 44 (100). – MS/CI (isobutane): *m/z* (%) = 325 (100) [MH^+], 307 (78). – $C_{20}H_{36}O_3$ (324.2): calcd. C 74.07, H 11.11; found C 73.99, H 10.95.

rac-(E)-9-(1-Oxoheptyl)octadec-10-enoic Acid (**6ab**) *and rac-(E)-10-(1-Oxoheptyl)octadec-8-enoic Acid* (**7ab**) (1:1 mixture): Yield 0.66 g (40%), colorless liquid, $n_D^{22} = 1.4608$. – ^1H NMR ($CDCl_3$): δ = 5.54 and 5.52 (dt, *J* = 15.3, 6.7 Hz, 1H, 8-H and 11-H), 5.27 and 5.26 (dd, *J* = 15.3, 9.0 Hz, 1H, 9-H and 10-H), 3.0 [m, 1H, 9(10)-H], 2.45 (m, 4H, $COCH_2CH_2$). 2.35 and 2.34 (2 t, *J* = 7.4 Hz, 2 × 2H, 2-H, **6ab** and **7ab**). – ^{13}C NMR ($CDCl_3$): δ = 212.4 (C=O), 180.1, 180.0 (C-1, **6ab** and **7ab**), 134.3, 133.9, 128.4, 128.1 (C=C, **6ab** and **7ab**), 56.7 [C-9(10)], 41.3 ($CHCOCH_2$). – MS (70 eV): *m/z* (%) = 394 (0.8) [M^+], 309 (1.3), 291 (1), 263 (6), 113 (100), 85 (54). – $C_{25}H_{46}O_3$ (394.3): calcd. C 76.14, H 11.68; found C 76.05, H 11.79.

rac-9-(1-Oxoheptyl)octadecanoic Acid (**8ab**) *and rac-10-(1-Oxoheptyl)octadecanoic Acid* (**9ab**) (1:1 mixture): Catalytic hydrogenation of **6ab/7ab** (1:1 mixture, 0.5 g) gave 0.5 g (98%) of **8ab**, **9ab** colorless liquid, $n_D^{23} = 1.4580$. – ^1H NMR ($CDCl_3$): δ = 2.43 [m, 1H, 9(10)-H], 2.39 (t, *J* = 7.4 Hz, 2H, $COCH_2$), 1.60 (m, 2H, $COCH_2CH_2$). – ^{13}C NMR ($CDCl_3$): δ = 215.3 (C=O), 179.9 (C-1), 52.4 [C-9(10)], 42.2 ($CHCOCH_2$). – MS/CI (isobutane): *m/z* (%) = 397 (100) [MH^+], 379 (71).

(E)-4-Oxopentadec-6-enedioic Acid (**11aa**): Yield 0.71 g (50%), obtained by recrystallization of the (*E*)/(*Z*) mixture (2.9:1, GC) from ethyl acetate/petroleum ether (4:1), m.p. 92–94°C. – ^1H NMR (C_6D_6): δ = 5.46 (dt, *J* = 15.4, 6.6 Hz, 1H, 10-H), 5.36 (dt, *J* = 15.4, 6.7 Hz, 1H, 9-H), 2.78 (d, *J* = 6.6 Hz, 2H, 11-H), 2.37 (m, 2H, 13-H), 2.20 (m, 2H, 14-H). – ^{13}C NMR ($CDCl_3$): δ = 207.3 (C=O), 180.2 (C-1), 178.7 (C-15), 135.6 (C-9), 121.5 (C-10), 46.7 (C-11), 36.2 (C-13), 32.4 (C-14). – MS (70 eV): *m/z* (%) = 284 (1) [M^+], 266 (2), 248 (6), 166 (7), 101 (100), 73 (41). – MS/CI (isobutane): *m/z* (%) = 285 (30) [MH^+], 267 (100), 249 (74). – $C_{15}H_{24}O_5$ (284.2): calcd. C 63.38, H 8.45; found C 63.08, H 8.41.

(E)-5-Oxohexadec-7-enedioic Acid (**11ab**): Yield 1.0 g (67%), m.p. 120–120.5°C. – ^1H NMR (C_6D_6): δ = 5.48 (dt, *J* = 15.6, 6.5 Hz, 1H, 10-H), 5.37 (dt, *J* = 15.6, 6.4 Hz, 1H, 9-H), 2.75 (d, *J* = 6.5 Hz, 2H, 11-H), 2.11 (t, *J* = 7.0 Hz, 2H, 13-H), 2.07 (t, *J* = 6.9 Hz, 2H, 15-H), 1.75 (tt, *J* = 7.0, 6.9 Hz, 2H, 14-H). – ^{13}C NMR ($CDCl_3$): δ = 208.8 (C=O), 180.2 (C-1), 179.3 (C-16), 135.5 (C-9), 121.7 (C-10), 47.0 (C-11), 40.4 (C-13), 32.9 (C-15), 32.4 (C-14).

5-Oxohexadecanedioic Acid (**12ab**): Catalytic hydrogenation of **11ab** (0.5 g) gave 0.49 g (96%) of **12ab**, m.p. 106–108°C. – ^1H NMR (MeOH): δ = 2.52 (t, *J* = 7.2 Hz, 2H, 13-H), 2.43 (t, *J* = 7.4 Hz, 2H, 11-H), 2.29 (t, *J* = 7.2 Hz, 2H, 15-H), 1.81 (tt, *J* = 7.2, 7.2 Hz, 2H, 14-H), 1.56 (m, 2 × 2H, 3-H and 10-H). – ^{13}C NMR (MeOH): δ = 211.5 (C=O), 175.9 (C-1), 175.2 (C-16), 41.7 (C-11), 40.6 (C-13), 32.2 (C-15). – MS (70 eV): *m/z* (%) = 300 (1) [M^+], 264 (6), 213 (16), 130 (87), 115 (36), 112 (100), 87 (30). – MS/CI (isobutane): *m/z* (%) = 301 (100) [MH^+], 283 (31). – $C_{16}H_{28}O_5$ (300.2): calcd. C 64.0, H 9.33; found C 63.92, H 9.45.

(E)-9-(3-Carboxy-1-oxopropyl)octadec-10-enoic Acid (**13aa**) *and (E)-10-(3-Carboxy-1-oxopropyl)octadec-8-enoic Acid* (**14aa**) (1:1 mixture): Yield 0.64 g (40%), colorless liquid, $n_D^{21} = 1.417$. – ^1H NMR ($CDCl_3$): δ = 5.57 and 5.56 (dt, *J* = 15.3, 6.7 Hz, 1H, 8-H and 11-H), 5.27 [dd, *J* = 15.3, 8.4 Hz, 1H, 10(9)-H], 3.04 [dt, *J* = 8.4, 7.6 Hz, 1H, 9(10)-H], 2.73 (m, 2 × 2H, $COCH_2CH_2COOH$). – ^{13}C NMR ($CDCl_3$): δ = 209.9 (C=O), 180.2 (C-1), 178.9 (COOH),

134.8, 134.4, 127.9, 127.2 (C=C, **13aa** and **14aa**), 56.5 [C-9(10)], 35.5 ($CHCOCH_2$). – MS (70 eV): *m/z* (%) = 382 (6) [M^+], 364 (10), 346 (3), 309 (6), 282 (5), 264 (21), 221 (13), 101 (100). – MS/CI (isobutane): *m/z* (%) = 383 (46) [MH^+], 365 (100), 347 (46). – $C_{22}H_{38}O_5$ (382.2): calcd. C 68.75, H 10.42; found C 68.80, H 10.54.

rac-9-(3-Carboxy-1-oxopropyl)octadecanoic Acid (**15aa**) *and rac-10-(3-Carboxy-1-oxopropyl)octadecanoic Acid* (**16aa**) (1:1 mixture): Catalytic hydrogenation of **13aa/14aa** (1:1 mixture, 0.4 g) gave 0.41 g (100%), m.p. 52–54°C. – ^1H NMR ($CDCl_3$): δ = 2.73 (m, 2H, $COCH_2$), 2.61 (m, 2H, $COCH_2CH_2COOH$), 2.47 [m, 1H, 9(10)-H]. – ^{13}C NMR ($CDCl_3$): δ = 212.7 (C=O), 180.2 (C-1), 179.0 (COOH), 52.2 [C-9(10)], 36.4 ($CHCOCH_2$). – MS (70 eV): *m/z* (%) = 348 (1) [$M^+ - 2\ H_2O$], 283 (2), 265 (7), 222 (22), 101 (100), 73 (47).

rac-(E)-9-(4-Carboxy-1-oxobutyl)octadec-10-enoic Acid (**13ab**) *and rac-(E)-10-(4-Carboxy-1-oxobutyl)octadec-8-enoic Acid* (**14ab**) (1:1 mixture): Yield 0.82 g (49%), colorless liquid, $n_D^{23} = 1.4711$. – ^1H NMR ($CDCl_3$): δ = 5.55 and 5.54 (dt, *J* = 15.3, 6.7 Hz, 1H, 8-H and 11-H), 5.25 [dd, *J* = 15.3, 8.5 Hz, 1H, 10(9)-H], 3.0 [dt, *J* = 8.5, 7.6 Hz, 1H, 9(10)-H], 2.52 (m, 2H, $COCH_2[CH_2]_2COOH$), 2.36 (t, *J* = 7.0 Hz, 2H, $CO[CH_2]_2CH_2COOH$), 1.87 (tt, *J* = 7.2, 7.0 Hz, 2H, $COCH_2CH_2CH_2COOH$). – ^{13}C NMR ($CDCl_3$): δ = 211.2 (C=O), 180.2 (C-1), 179.5 (COOH), 134.6, 134.3, 128.0, 127.7 (C=C, **13ab** and **14ab**), 56.7 [C-9(10)], 39.8 ($COCH_2$). – MS (70 eV): *m/z* (%) = 396 (1) [M^+], 322 (2), 309 (1), 264 (12), 115 (100), 87 (54). – MS/CI (isobutane): *m/z* (%) = 397 (100) [MH^+], 379 (34), 361 (5). – $C_{23}H_{40}O_5$ (396.2): calcd. C 69.72, H 10.10; found C 69.63, H 9.96.

Acylation of Unsaturated Alcohols with Acyl Chlorides or Cyclic Anhydrides. – General Procedure: $EtAlCl_2$ (1 M in hexane, 10 ml, 10 mmol) was added to the appropriate unsaturated alcohols **1b** (5 mmol) or **3b** (4.2 mmol), dissolved in CH_2Cl_2 (30 ml). The solution was stirred magnetically under nitrogen (1 bar) for 5 min at −15°C. The acylating agent [acetyl chloride (**2a**), succinic anhydride (**10a**), or glutaric anhydride (**10b**), 5 mmol] was added in small portions. The sample was stirred for additional 2 h (with acetyl chloride) or 24 h (for anhydrides) at room temp. The reaction was stopped as described above for the acylation of unsaturated carboxylic acids. The acylation product was purified by column chromatography (**6ba/7ba** and **13bb/14bb**) or by recrystallization (**11bb**). – Catalytic hydrogenation of the acylation products **11bb** and **13bb/14bb** was carried out with Pd/C in CH_2Cl_2 at 2 bar. The reaction time was 24 h at room temp.

rac-(E)-9-Acetyloctadec-10-en-1-ol (**6ba**) *and rac-(E)-10-Acetyloctadec-8-en-1-ol* (**7ba**) (1:1 mixture): Yield 0.81 g (62%), colorless liquid, $n_D^{22} = 1.4662$. – ^1H NMR ($CDCl_3$): δ = 5.57 [dt, *J* = 15.3, 6.9 Hz, 1H, (11)8-H], 5.36 [dd, *J* = 15.3, 8.4 Hz, 1H, 10(9)-H], 3.62 (t, *J* = 6.2 Hz, 2H, 1-H), 3.0 [dt, *J* = 8.4, 7.3 Hz, 1H, 9(10)-H], 2.12 (s, 3H, $COCH_3$). – ^{13}C NMR ($CDCl_3$): δ = 210.3 (C=O), 134.5, 134.3, 127.6 (C=C, **6ba** and **7ba**), 62.6 (C-1), 57.2 [C-9(10)]. – MS (70 eV): *m/z* (%) = 310 (1) [M^+], 267 (1), 249 (1), 181 (8), 95 (100). – MS/CI (isobutane): *m/z* (%) = 311 (100) [MH^+]. – $C_{20}H_{38}O_2$ (310.2): calcd. C 77.48, H 12.26; found C 78.21, H 12.77.

rac-9-Acetyloctadecan-1-ol (**8ba**) *and rac-10-Acetyloctadecan-1-ol* (**9ba**) (1:1 mixture): Catalytic hydrogenation of **6ba/7ba** (1:1 mixture, 0.5 g) gave 0.48 g (94%) of **8ab/9ab**, colorless liquid, $n_D^{21} = 1.4609$. – $C_{20}H_{40}O_2$ (312.2): calcd. C 76.98, H 12.82; found C 76.90, H 12.98.

rac-(E)-9-(4-Carboxy-1-oxobutyl)octadec-10-en-1-ol (**13bb**) *and rac-(E)-10-(4-Carboxy-1-oxobutyl)octadec-8-en-1-ol* (**14bb**) (1:1 mixture): Yield 0.56 g (35%), colorless liquid, $n_D^{20} = 1.4556$. – ^1H NMR ($CDCl_3$): δ = 5.55 [dt, *J* = 15.3, 6.8 Hz, 1H, 11(8)-H], 5.25 [ddt, *J* = 15.3, 8.5, 1.4 Hz, 1H, 10(9)-H], 3.64 (t, *J* = 6.5 Hz, 2H, 1-H) and 3.63 (t, *J* = 6.6 Hz, 2H, 1-H), 3.0 [dt, *J* = 8.5, 7.2 Hz, 2H, 9(10)-H], 2.50 (m, 2H, $COCH_2[CH_2]_2COOH$], 2.34 (t, *J* = 7.2 Hz, 2H, CH_2COOH), 1.86 (tt, *J* = 7.2, 7.2 Hz, 2H, $COCH_2CH_2CH_2COOH$). – ^{13}C NMR ($CDCl_3$): δ = 211.4 (C=O), 177.9, 177.7 (COOH, **13bb** and **14bb**), 134.5 [C-10(8)], 127.9 (C-9, **14bb**), 127.8 (C-11, **13bb**), 62.8 (C-1), 56.7 [C-9(10)], 39.9 ($COCH_2$). – MS (70 eV): *m/z* (%) = 382 (2) [M^+], 364 (3), 308 (7), 295 (9), 253 (4), 235 (6), 115 (100), 87 (41).

rac-9-(4-Carboxy-1-oxobutyl)octadecan-1-ol (**15bb**) *and rac-10-(4-Carboxy-1-oxobutyl)octadecan-1-ol* (**16bb**) (1:1 mixture): Catalytic hydrogenation of **13bb/14bb** (1:1 mixture, 0.4 g) gave 0.39 g (95%) of **15bb**, **16bb**, m.p. 34–35°C. – ^1H NMR ($CDCl_3$): δ = 3.64 (t, *J* = 6.5 Hz, 2H, 1-H), 2.50 (t, *J* = 7.1 Hz, 2H, $COCH_2$), 2.42 [m, 1H, 9(10)-H], 2.40 (t, *J* = 7.1 Hz, 2H, CH_2COOH), 1.89 (tt, *J* = 7.1, 7.1 Hz, 2H, $COCH_2CH_2CH_2COOH$). – ^{13}C NMR ($CDCl_3$): δ = 214.2 (C=O), 177.9 (COOH), 63.0 (C-1), 52.4 [C-9(10)], 40.8 ($COCH_2$). – MS/CI (isobutane): *m/z* (%) = 385 (100) [MH^+], 367 (41). – $C_{23}H_{44}O_4$ (384.2) (**15bb/16bb**): calcd. C 71.93, H 11.46; found C 71.84, H 11.37.

(E)-15-Carboxy-12-oxopentadec-9-en-1-ol (**11bb**): Yield 0.55 g (39%), obtained by recrystallization of the (*E*)/(*Z*) mixture (3.2:1, GC) from ethyl acetate/petroleum ether (4:1), m.p. 72–74°C. – ^1H NMR (C_6D_6): δ = 5.49 (dt, *J* = 15.4, 6.7 Hz, 2H, 10-H), 5.37 (dt, *J* = 15.4, 6.7 Hz, 2H, 9-H), 2.73 (d, *J* = 6.7 Hz, 2H, 11-H), 2.09 (t, *J* = 7.0 Hz, 2H, 13-H), 2.03 (t, *J* = 7.1 Hz, 2H, 15-H), 1.75 (tt, *J* = 7.0, 7.1 Hz, 2H, 14-H). – ^{13}C NMR ($CDCl_3$): δ = 208.8 (C=O), 177.7 (C-16), 135.5 (C-9), 121.6 (C-10), 63.0 (C-1), 46.9 (C-11), 40.6 (C-13), 32.8 (C-15), 32.6 (C-14). – MS (70 eV): *m/z* (%) = 284 (1) [M^+], 266 (1), 210 (0.4), 197 (0.4), 115 (100), 87 (50). – $C_{16}H_{28}O_4$ (284.2): calcd. C 67.66, H 9.86; found C 67.71, H 9.86.

15-Carboxy-12-oxopentadecan-1-ol (**12bb**): Catalytic hydrogenation of **11bb** (0.4 g) gave 0.4 g (98%) of **12bb**, m.p. 86–88°C. – ^1H NMR ($CDCl_3$): δ = 3.65 (t, *J* = 6.6 Hz, 2H, 1-H), 2.50 (t, *J* = 7.2 Hz, 2H, 13-H), 2.39 (t, *J* = 7.2 Hz, 2 × 2H, 11-H and 15-H), 1.88 (tt, *J* = 7.2, 7.2 Hz, 2H, 14-H). – ^{13}C NMR (MeOH): δ = 210.6 (C=O), 178.0 (C-16), 63.0 (C-1), 42.9 (C-11), 41.3 (C-13), 32.9 (C-15), 32.7 (C-14). – MS/CI (isobutane): *m/z* (%) = 287 (100) [MH^+], 269 (74), 251 (14). – $C_{16}H_{30}O_4$ (286.2): calcd. C 67.19, H 10.49; found C 67.19, H 10.33.

Intramolecular Acylation of Petroselinyl Chloride (**17**): A mixture of **17** (4.1 mmol) and $EtAlCl_2$ (1 M in hexane, 3 ml, 3 mmol) was stirred magnetically under nitrogen (1 bar) for 2 h at room temp. The reaction was stopped as described above. The product was purified by flash chromatography with petroleum ether/diethyl ether (8:2). Catalytic hydrogenation of the cyclization product **18** was carried out with Pd/C in CH_2Cl_2 at 2 bar. The reaction time was 24 h at room temp.

(E)-2-Dodecylidenecyclohexanone (**18**): Yield 0.62 g (58%), colorless liquid, $n_D^{18} = 1.4821$. – ^1H NMR ($CDCl_3$): δ = 6.63 (tt, *J* = 7.4, 2.0 Hz, 1H, C=C*H*), 2.48 (t, *J* = 6.2 Hz, 2H, 3-H), 2.42 (t, *J* = 6.6 Hz, 2H, 6-H), 2.09 (dt, *J* = 7.4 Hz, 2H, $C{=}CHCH_2$), 1.85 (tt, *J* = 6.6, 6.0 Hz, 2H, 5-H), 1.74 (tt, *J* = 6.2, 6.0 Hz, 2H, 4-H). – ^{13}C NMR ($CDCl_3$): δ = 201.2 (C=O), 139.8 (C=*C*H), 136.0 (C-2), 40.1 (C-6). – MS (70 eV): *m/z* (%) = 264 (54) [M^+], 246 (8), 137 (98), 111 (100), 98 (94). – MS/CI (isobutane): *m/z* (%) = 265 (100) [MH^+]. – $C_{18}H_{32}O \times H^+$: calcd. 265.2531, found 265.2543 (MS/CI).

rac-2-Dodecylcyclohexanone (**19**): Catalytic hydrogenation of **18** (0.45 g) gave 0.44 g (97%) of **19**, colorless liquid, $n_D^{18} = 1.4665$. –

^{1}H NMR ($CDCl_3$): δ=2.19 (m, 3H, 2- and 6-H), 1.95 (m, 2H, 5-H), 1.76–1.45 (m, 4H, 3- and 4-H). – ^{13}C NMR ($CDCl_3$): δ=212.5 (C=O), 50.5 (C-2), 41.7 (C-6), 33.7 (C-3). – MS (70 eV). *m/z* (%) = 266 (5) [M^+], 111 (10), 98 (100). – MS/CI (isobutane): *m/z* (%)=267 (100) [MH^+]. – $C_{18}H_{34}O \times H^+$: calcd. 267.2688, found 267.2690 (MS/CI).

[1] J. K. Groves, *Chem. Soc. Rev.* **1972**, *1*, 73–97.
[2] S. C. Eyley in *Comprehensive Organic Synthesis* (Ed.: B. M. Trost, J. Fleming), Pergamon Press, Exeter, **1991**, vol. 2, p. 707.
[3] P. Beak, K. R. Berger, *J. Am. Chem. Soc.* **1980**, *102*, 3848–3856.
[4] M. Santelli, A. Tubul, C. Nord-Fourrier in *Selectivities in Lewis Acid Promoted Reactions* (Ed.: D. Schinzer), Kluwer Academic Publishers, Dordrecht, **1989**, p. 147.
[5] B. B. Snider, A. C. Jackson, *J. Org. Chem.* **1982**, *47*, 5393–5395.
[6] J. O. Metzger, U. Biermann, *Synthesis* **1992**, *5*, 463–465.
[7] H. Baumann, M. Bühler, H. Fochem, T. Hirsinger, H. Zoebelein, J. Falbe, *Angew. Chem.* **1988**, *100*, 41–63; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 41.
[8] N. Weber, *Fat Sci. Technol.* **1992**, *94*, 546–554.
[9] G. Solladié, C. Gerber, *Synlett* **1992**, *5*, 449–450.
[10] B. B. Snider, G. B. Phillips, *J. Org. Chem.* **1983**, *48*, 464–469.
[11] C. Santelli-Rouvier, M. Santelli, *Synthesis* **1983**, 429–442.
[12] S. H. Nahm, H. N. Cheng, *J. Org. Chem.* **1986**, *51*, 5093–5100.
[13] J. O. Metzger, R. Mahler, *Liebigs Ann. Chem.* **1993**, 203–205.
[14] J. K. Crandall, J. P. Arrington, J. Hen, *J. Am. Chem. Soc.* **1967**, *89*, 6208–6213.
[15] S. Moon, T. F. Kolesar, *J. Org. Chem.* **1974**, *39*, 995–998.
[16] M. J. Astle, M. L. Pinns, *J. Org. Chem.* **1959**, *24*, 56–60; T. Nakano, S. Irifune, S. Umano, A. Inada, Y. Ishii, M. Ogawa, *J. Org. Chem.* **1987**, *52*, 2239–2244.
[17] U. S. Rubber Co., U.S.P. **1947**, 2577133 (Beilstein, 4. Ergänzungswerk Bd. 3/3, p. 1672).
[18] J. Nichols, E. Schipper, *J. Am. Chem. Soc.* **1958**, *80*, 5705–5717.

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