Total Synthesis of the Lipoxygenase Substrates (5*Z*,8*Z*,11*Z*,14*Z*)-Nonadeca-5,8,11,14-tetraene-1,19-dioic Acid and (5*Z*,8*Z*,11*Z*,14*Z*)-20,20-Dimethylheneicosa-5,8,11,14-tetraenoic Acid

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Abstract: For mechanistic studies on the lipoxygenase reaction, the special substrate fatty acids (5*Z*,8*Z*,11*Z*,14*Z*)-nonadeca-5,8,11,14-tetraene-1,19-dioic and (5*Z*,8*Z*,11*Z*,14*Z*)-20,20-dimethylheneicosa-5,8,11,14-tetraenoic acids were synthesized. The synthetic scheme involves a joint route for the formation of (5*Z*,8*Z*,11*Z*,14*Z*)-nonadeca-5,8,11,14-tetraene-1,19-dioic acid, which is based on the polyacetylenic approach. Regioselective reduction of the ω-carboxylic group to the primary alcohol, exchange of an OH-group to corresponding iodine and subsequent coupling with low-order organocuprates (*t*-Bu_2CuLi) resulted in the formation of (5*Z*,8*Z*,11*Z*,14*Z*)-20,20-dimethylheneicosa-5,8,11,14-tetraenoic acid with an overall yield of 11%.

Key words: polyunsaturated fatty acids, cross-coupling reaction, copper(I) catalysis, Gilman cuprates, lipoxygenase

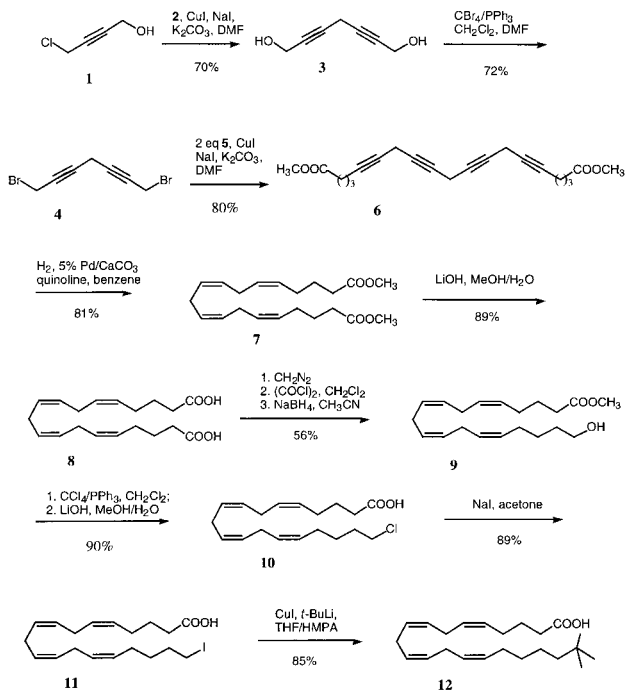
The products of oxidative metabolism of polyenoic fatty acids via lipoxygenase and/or cyclooxygenase pathway[1,2] are of biological importance. Lipoxygenase products such as leukotrienes and lipoxins constitute important mediators of anaphylactic disorders[3] and have also been implicated in inflammation,[3] cell differentiation[2] and atherogenesis.[2] Polyenoic fatty acids, which are modified at the ω-terminus are useful tools for mechanistic studies on the LOX reaction.[4] Such studies may lead to the development of powerful LOX inhibitors, which constitute potential anti-asthmatic and anti-inflammatory drugs.[5]

Here we report the total synthesis of novel ω-modified polyenoic fatty acids which can be used to investigate the mechanism of oxidative fatty acid metabolism of mammalian cells. The aim of our study was to develop a divergent synthetic approach, which allows the preparation of different arachidonic acid analogs bearing either hydrophilic (carboxy-, hydroxy-) or bulky hydrophobic substituents at the ω-terminus in the frame of a single synthetic scheme. This approach should be flexible enough to allow variations in the type of the ω-substituent.

Wittig olefination traditionally used for the preparation of linear, *cis*-skipped polyenes usually leads to formation of coupling products containing 10−20% of *Z*,*E*-isomers. In contrast, preparation of olefins from acetylenic precursors via stereoselective hydrogenation on Lindlar's catalyst gives *Z*,*Z*-products in high yield and with high geometric purity.[6] Based on the polyacetylenic approach our synthetic scheme started with cross-coupling of the easily available 4-chlorobut-2-yn-1-ol (**1**)[7] and 2-propyne-1-ol (**2**) under copper(I) catalysis.[8] This reaction afforded the diacetylenic diol **3** in 70% yield (Scheme). Subsequent displacement of both hydroxy groups with bromine using PPh_3/CBr_4 as a reagent gave the bispropargilicbromide **4** in 72% yield. Cross-coupling of **4** with 2 equivalents of commercially available methyl 5-hexynoate (**5**) in the presence CuI, NaI and K_2CO_3 afforded the dimethyl ester of nonadeca-5,8,11,14-tetrayne-1,19-dioic acid **6** in ~80% yield. Hydrogenation of the tetraynoate **6** in dry benzene with Lindlar's catalyst in the presence of quinoline gave the dimethylester of (5*Z*,8*Z*,11*Z*,14*Z*)-nonadeca-5,8,11,14-tetraene-1,19-dioic acid **7** in 83% yield. The crude dimethylester **7** contained about 7% of UV-absorbing impurities as indicated by analytical RP-HPLC ($MeOH/H_2O$, 85:15, by vol.). These impurities were removed by preparative RP-HPLC and the dimethylester **7** was hydrolyzed in the presence of LiOH to form the free dicarboxylic acid **8**. This acid was monomethylated by treatment with stoichiometric amounts of diazomethane and the resulting monomethylester was purified by column chromatography on silica gel. In principle, methyl esters can be reduced to primary alcohols with a large molar excess of $NaBH_4$.[9] However, all attempts failed to reduce preparative amounts of our tetraenedioic acid monomethyl ester. Therefore the non-methylated carboxylic group was derivatized with oxalyl chloride and the resulting chloroanhydride was reduced to the primary alcohol **9** in 56% yield. The ω-hydroxy fatty acid methylester was then converted to the corresponding ω-chloride **10** and subsequently to the iodide **11**.

Although unactivated tosylates are more suitable for substitution reactions with Gilman cuprates (R_2CuLi)[10,11] than halides (I, Br) our attempts to prepare fatty acid **12** from the corresponding tosylate were not successful. This was probably due to the limited stability of the polyenoic tosylates and/or their low reactivity. Thus, sequential preparation of the halides (Scheme) was used as a method of choice. The complete substitution of chlorine by iodine, which was carried out with NaI in anhydrous acetone, took about 20 hours as indicated by repeated RP-HPLC analysis.

The final step of the synthetic procedure, the incorporation of *t*-Bu group at the ω-terminus of the fatty acid, was carried out by coupling the iodide **11** with *t*-Bu_2CuLi, pre



Scheme

pared from one equivalent of CuI and two equivalents of *t*-BuLi in THF/HMPA (hexamethylphosphoramide). After HPLC purification of the final product, an 85% yield of the last synthetic step was calculated.

^{1}H and ^{13}C NMR spectra were recorded either on a Bruker MSL 200 MHz or on a Bruker MSL 300 MHz spectrometer in $CDCl_3$. Chemical shifts are relative to TMS as an internal standard for ^{1}H NMR or to the deuterium lock signal of $CDCl_3$ (δ ^{13}C = 77.24 ppm) and that of CD_3OD (δ ^{13}C = 49.50 ppm). IR spectra were recorded on Shimadzu IR-435. RP-HPLC analysis was carried out on a Shimadzu LC-10Avp liquid chromatograph connected to SPD-10Advp UV detector. Fatty acid analysis was performed on a Nucleosil C18-column; 150 × 4 mm, 5 µm particle size (Machery−Nagel, Düren, Germany). A solvent system of MeOH/H_2O/AcOH (85:15:0.1) and a flow rate of 1mL/min were used for all compounds except for the final synthesised product **12**. For this product, a solvent system of MeOH/CH_3CN/H_2O (47.5:47.5:5) and a flow rate of 1.2 mL/min were employed. Preparative purification was carried out on a Lichrospher 100 RP18 column, 250 × 22.5 mm, 10 µm particle size (Knauer, Berlin, Germany). For EIMS analysis a Shimadzu GC-MS QP-2000 system was used with an ion source temperature of 180 °C and an electron energy of 70 eV. For thin-layer chromatography we employed precoated silica gel 60 F_{254} sheets (Merck, Darmstadt, Germany). Column chromatography was carried out on silica gel 60.; 70−230 mesh (Merck, Darmstadt, Germany). THF was freshly distilled from sodium/benzophenone ketyl, and HMPA was dried over CaH_2. All other solvents used were of extra pure grade and purchased from Merck or Aldrich (Germany). *t*-Butyllithium was titrated as described by Watson.[12] Prior to use, all glassware and syringes were dried at 140 °C overnight and all reactions were carried out under Ar atm.

Hepta-2,5-diyne-1,7-diol (3)

The chloride **1** (2.18 g, 20.95 mmol) (bp 50 °C/0.5 mbar, n_D^{20} 1.4980) and 2-propyn-1-ol (**2**) (1.64 g, 29.28 mmol) were added to a suspension of the previously dried salts; CuI (7.98 g, 41.90 mmol), NaI (6.28 g, 41.90 mmol) and K_2CO_3 (4.33 g, 31.42 mmol) in DMF (25 mL) under a stream of Ar. The mixture was stirred overnight at 30 °C, the reaction was then quenched with sat. NH_4Cl (400 mL) and the lipophilic products were extracted with Et_2O (5 × 60 mL). The combined organic extracts were washed with sat. NaCl (2 × 100 mL), dried (Na_2SO_4) and the solvent was evaporated under vacuum. The residue was purified on silica gel (hexane/EtOAc, 1:7) to give **3,** yield: 1.83 g (70%), mp 58−59 °C.

IR (neat): ν = 3040 (OH), 2240 (C≡C) cm^{-1}.

^{1}H NMR (200 MHz, CD_3OD): δ = 3.32 (m, 2H, 4-CH_2), 4.20 (t, 4H, *J* = 2.5 Hz, 1-CH_2, 7-CH_2).

^{13}C NMR (75 MHz, CD_3OD): δ = 10.76, 64.73 (2C), 79.44 (2C), 80.78 (2C).

Anal. Calcd for $C_7H_8O_2$: C, 67.73; H, 6.49. Found: C, 67.56; H, 6.71.

1,7-Dibromohepta-2,5-diyne (4)

A solution of PPh_3 (8.31 g, 7.21 mmol) in dry CH_2Cl_2 (50 mL) was added dropwise over 30 min to a stirred solution of the diol **3** (1.79 g, 14.42 mmol) and CBr_4 (10.53g, 31.71 mmol) in CH_2Cl_2 (20 mL) and DMF (6 mL) at 0 °C. This mixture was then stirred for 1 h at 0−10 °C and the reaction was quenched with MeOH (5 mL). The solvents were evaporated under reduced pressure and the residue was purified by chromatography on silica gel using a linear solvent gradient (hexane−hexane/Et_2O, 1:1) to give **4**, yield: 2.59 g (72%).

IR (neat): ν = 2240, 2170 (C≡C), 600 (CH_2Br) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.27 (m, 2H, 4-CH_2), 3.87 (t, 4H, *J* = 3.0 Hz, 1-CH_2, 7-CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.56, 14.45 (2C), 76.27 (2C), 80.47 (2C).

Anal. Calcd for $C_7H_6Br_2$: C, 33.64; H, 2.42. Found: C, 33.89; H, 2.65.

Nonadeca-5,8,11,14-tetrayne-1,19-dioic Acid Dimethyl Ester (6)

In a dry Ar filled round-bottomed flask equipped with a magnetic stirrer, anhyd K_2CO_3 (3.44 g, 24.9 mmol), NaI (4.99 g, 33.2 mmol) and CuI (6.34 g, 33.2 mmol) were suspended in DMF (25 mL). Methyl 5-hexynoate (**5**) (2.20 g, 17.47 mmol) and the dibromide **4** (2.08 g, 8.32 mmol) were added, and the mixture was vigorously stirred overnight at r.t. The reaction was quenched with sat. NH_4Cl (200 mL). The lipophilic products were extracted with Et_2O (4 × 100 mL) and the combined organic layers were washed with sat. NaCl (2 × 150 mL). After drying (Na_2SO_4), the ethereal solution was concentrated under vacuum. The residue was purified by chromatography on silica gel (hexane/Et_2O, 1:2) under Ar to give pure **6,** yield: 2.27g (80%).

TLC: R_f = 0.51 (hexane/Et_2O, 1:4, with 1% AcOH).

IR (neat): ν = 2170 (C≡C), 1740 (C = O) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.79 (m, 4H, 3-CH_2, 17-CH_2), 2.22 (tt, 4H, *J* = 6.8, 2.2 Hz, 4-CH_2, 16-CH_2), 2.42 (t, 4H, *J* = 7.0 Hz, 2-CH_2, 18-CH_2), 3.12 (m, 6H, 7-CH_2, 10-CH_2, 13-CH_2), 3.66 (s, 6H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.72 (3C), 18.21 (2C), 23.94(2C), 32.88 (2C), 51.44 (2C), 74.26 (2C), 74.85 (2C), 75.03 (2C), 79.52 (2C), 174.91(2C).

Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 73.95; H, 7.33.

(5*Z*,8*Z*,11*Z*,14*Z*)-Nonadeca-5,8,11,14-tetraene-1,19-dioic Acid Dimethyl Ester (7)

To a 250 mL Erlenmeyer flask containing Lindlar's catalyst (1.60 g), dry benzene (40 mL) was added. The mixture was saturated with

H_2 at r.t. and cooled to 10 °C, and a solution of **6** (1.01 g, 2.94 mmol) in benzene (40 mL) and quinoline (1.5 mL) were added under a stream of Ar. After the Ar was exchanged with H_2, the reaction mixture was stirred for 1 h at 10 °C. H_2 uptake was measured with a gas burette. The reaction mixture was filtered, washed with HCl (2 M, 2 × 50 mL) and the solvent was evaporated. The crude residue was purified by preparative RP-HPLC (MeOH/H_2O, 9:1) to yield 0.83 g (81%) of pure **7**.

Analytical RP-HPLC: t_R = 4.57 min.

TLC: R_f = 0.64 (hexane/Et_2O, 1:4, with 1% AcOH).

IR (neat): ν = 3030, 1670 (CH=CH), 1740 (C=O) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.70 (m, 4H, 3-CH_2, 17-CH_2), 2.09 (m, 4H, 4-CH_2, 16-CH_2), 2.32 (t, 4H, *J* = 7.0 Hz, 2-CH_2, 18-CH_2), 2.80 (m, 6H, 7-CH_2, 10-CH_2, 13-CH_2), 3.67 (s, 6H, OCH_3), 5.35−5.45 (m, 8H, CH=CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.60 (2C), 25.80 (3C), 26.55 (2C), 33.56 (2C), 51.42 (2C), 128.28 (2C), 128.39 (2C), 128.95 (2C), 129.13 (2C), 174.04 (2C).

MS (EI): *m/z* = 348 (M^+).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.25. Found: C, 72.18; H, 9.47.

(5*Z*,8*Z*,11*Z*,14*Z*)-Nonadeca-5,8,11,14-tetraene-1,19-dioic Acid (8)

An aq solution of LiOH (1.8 M, 20 mL) was added to a solution of the diester **7** (820 mg, 2.35 mmol) in MeOH (80 mL) under Ar and the mixture was stirred at r.t. for 8 h. After the reaction was complete, MeOH was removed by evaporation, the pH was adjusted carefully to 5.0 using HCl (1 M) and the lipophilic compounds were extracted with Et_2O (3 × 40 mL). The combined organic extracts were dried (Na_2SO_4), concentrated under reduced pressure, and the product was purified by chromatography on silica gel (hexane/Et_2O, 1:3), yield: 670 mg (89%).

TLC: R_f = 0.23 (hexane/Et_2O, 1:4, with 1% AcOH).

IR (neat): ν = 3030, 1670 (CH=CH), 1705 (C=O) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.70 (m, 4H, 3-CH_2, 17-CH_2), 2.10 (m, 4H, 4-CH_2, 16-CH_2), 2.35 (t, 4H, *J* = 7.0 Hz, 2-CH_2, 18-CH_2), 2.80 (m, 6H, 7-CH_2, 10-CH_2, 13-CH_2), 5.35−5.45 (m, 8H, CH=CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.60 (2C), 25.81 (3C), 26.55 (2C), 33.46 (2C), 128.28 (2C), 128.39 (2C), 128.94 (2C), 129.31 (2C), 180.21 (2C).

MS (EI): *m/z* (%) = 320 (M^+, 30), 302 (M^+-H_2O, 12.6), 284 (M^+-2H_2O, 9.8).

Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.48; H, 8.51.

(5*Z*,8*Z*,11*Z*,14*Z*)-19-Hydroxynonadeca-5,8,11,14-tetraenoic Acid Methyl Ester (9)

The dicarboxylic acid **8** (500 mg, 1.56 mmol) dissolved in Et_2O (4 mL) was methylated with a small molar excess of diazomethane (1.60 mmol). Et_2O was removed by evaporation in a stream of Ar and the residue was purified by column chromatography on silica gel (hexane/Et_2O, 1:2). Fractions containing the product, R_f = 0.40 (hexane/Et_2O, 1:4 with 1% AcOH), were pooled, the solvent was removed under vacuum and the residue was redissolved in CH_2Cl_2 (4 mL). To this solution cooled to 0−10 °C, a 10-fold molar excess of oxalyl chloride (0.54 mL, 6.24 mmol) was added in one portion and the mixture was stirred for 0.5 h at 10 °C. After the volatile components had been removed under vacuum, a suspension of $NaBH_4$ (100 mg, 2.65 mmol) in CH_3CN (6 mL) was added and the mixture was stirred for 3 h at r.t. The reaction was quenched with ice-water (10 mL), the solution was acidified with HCl (1 M) to pH 5.0 and the lipophilic products were extracted with Et_2O (3 × 30 mL). The combined organic extracts were washed with H_2O (40 mL) and dried (Na_2SO_4). After evaporation of the solvents, the resulting yellow oil was subjected to column chromatography on silica gel (hexane/Et_2O, 1:3). Purified compound **9** was obtained in a yield of 282 mg (56.5%).

Analytical RP-HPLC: t_R = 3.65 min.

TLC: Rf = 0.34 (hexane/Et_2O, 1:4, with 1% AcOH).

IR (neat): ν = 3600−3200 (OH), 3030, 1670 (CH=CH), 1740 (C=O) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.45−1.75 (m, 6H, 3-CH_2, 17-CH_2, 18-CH_2), 2.09 (m, 4H, 4-CH_2, 16-CH_2), 2.32 (t, 2H, *J* = 7.0 Hz, 2-CH_2), 2.79 (m, 6H, 7-CH_2, 10-CH_2, 13-CH_2), 3.62 (t, 2H, *J* = 6.4 Hz, 19-CH_2), 3.64 (s, 3H, OCH_3), 5.30−5.40 (m, 8H, CH=CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.89, 25.74 (3C), 25.92, 26.69, 27.06, 32.47, 33.53, 51.43, 62.79, 128.10 (2C), 128.32 (2C), 128.54, 128.98 (2C), 130.05, 174.04.

MS (EI): *m/z* (%) = 320 (M^+, 7.2), 261 ($M^+-COOCH_3$, 5.7).

Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 75.12; H, 9.87.

(5*Z*,8*Z*,11*Z*,14*Z*)-19-Chlorononadeca-5,8,11,14-tetraenoic Acid (10)

To a solution of ester **9** (200 mg, 0.62 mmol) in CCl_4 (3 mL), a solution of PPh_3 (245 mg, 0.93 mmol) in CH_2Cl_2 (4 mL) was added at r.t. After the reaction mixture was stirred for 24 h, the solvent was removed under reduced pressure. Column chromatography on silica gel (hexane/Et_2O, 1:1) gave 199 mg of a product with Rf = 0.57 (hexane/Et_2O, 1:2). This compound was >99% pure as indicated by RP-HPLC. Subsequent saponification was carried out by a procedure analogous to that used for the preparation of acid **8**. Final column chromatography on silica gel (hexane/Et_2O, 1:2) afforded pure **10** in a yield of 181 mg (90%).

Analytical RP-HPLC: t_R = 2.47 min.

TLC: R_f = 0.38 (hexane/Et_2O, 1:2, with 1% AcOH).

IR (neat): ν = 3030, 1670 (CH=CH), 1705 (C=O), 720, 640 (C-Cl) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.45−1.70 (m, 6H, 3-CH_2, 17-CH_2, 18-CH_2), 2.10 (m, 4H, 4-CH_2, 16-CH_2), 2.35 (t, 2H, *J* = 7.0 Hz, 2-CH_2), 2.80 (m, 6H, 7-CH_2, 10-CH_2, 13-CH_2), 3.51 (t, 2H, *J* = 6.5 Hz, 19-CH_2), 5.30−5.40 (m, 8H, CH=CH).

^{13}C NMR (75 MHz, CDCl3): δ = 24.78, 25.89 (3C), 26.70 (2C), 27.07, 32.42, 33.62, 45.02, 128.44 (2C), 128.54 (2C), 128.69, 129.03, 129.29, 129.69, 179.86.

MS (EI): *m/z* = 324 (M^+).

Anal. Calcd for $C_{19}H_{29}O_2Cl$: C, 70.24; H, 8.99. Found: C, 70.47; H, 9.01.

(5*Z*,8*Z*,11*Z*,14*Z*)-19-Iodononadeca-5,8,11,14-tetraenoic Acid (11)

A mixture of acid **10** (150 mg, 0.46 mmol) and NaI (207 mg, 1.38 mmol) in dry acetone (4 mL) was stirred at 65 °C for 20 h. After acetone was evaporated, the residue was redissolved in Et_2O (60 mL), the resulting mixture was washed with H_2O (2 × 40 mL) and the organic layer was dried (Na_2SO_4). After evaporation of the solvent, under reduced pressure, the crude residue was purified on silica gel (hexane/Et_2O, 1:1) to yield **11** as a colorless oil, which was analyzed to be >98% pure by RP-HPLC, yield: 170 mg (89%).

Analytical RP-HPLC: t_R = 2.95 min.

IR (neat): ν = 3030, 1670 (CH=CH), 1705 (C=O), 570 (C-I) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.47 (m, 2H, 18-CH_2), 1.75 (m, 4H, 3-CH_2, 17-CH_2), 2.10 (m, 4H, 4-CH_2, 16-CH_2), 2.35 (t, 2H, *J* = 7.0 Hz, 2-CH_2), 2.79 (m, 6H, 7-CH_2, 10-CH_2, 13-CH_2), 3.17 (t, 2H, *J* = 6.5 Hz, 19-CH_2), 5.30−5.40 (m, 8H, CH=CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 6.60, 24.79, 25.89 (3C), 26.34, 26.74, 30.64, 33.32, 33.61, 128.32, 128.40(2C), 128.51(2C), 128.69, 129.02, 129.28, 179.59.

MS (EI): *m/z* (%) = 416 (M^+, 4.9), 289 (M^+−I, 38).

Anal. Calcd for $C_{19}H_{29}O_2I$: C, 54.81; H, 7.02. Found: C, 55.01; H, 7.27.

(5*Z*,8*Z*,11*Z*,14*Z*)-20,20-Dimethylheneicosa-5,8,11,14-tetraenoic Acid (12)

To a cooled (−78 °C) suspension of CuI (175 mg, 0.92 mmol) in THF/HMPA (8 mL and 3 mL, respectively) *t*-BuLi (1.26 mL, 1.84 mmol) was added with a syringe. The mixture was stirred for 45 min at −75 °C until a dark, nearly homogenous solution was formed. After addition of a solution of acid **11** (154 mg, 0.37 mmol) in THF (2 mL), the resulting mixture was warmed to −45 °C and stirred for 1 h. Afterwards the sample was poured into a separatory funnel containing sat. NH_4Cl, acidified with HCl (1 M) to pH 5.0, and the organic products were extracted with Et_2O (2 × 50 mL). The combined organic extracts were washed with sat. NaCl, dried (Na_2SO_4), and concentrated under vacuum. The crude residue was purified by preparative RP-HPLC (MeOH/CH_3CN/H_2O, 47.5:47.5:5) to give pure **12,** yield: 109 mg (85%).

Analytical RP-HPLC: t_R = 2.49 min.

TLC: R_f = 0.36 (hexane/Et_2O, 1:1, with 1% AcOH).

IR (neat): ν = 3030, 1670 (CH=CH), 1705 (C=O), 1390 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.84 (s, 9H, $C(CH_3)_3$), 1.25−1.35 (m, 6H, 17-CH_2, 18-CH_2, 19-CH_2), 1.70 (m, 2H, 3-CH_2), 2.08 (m, 4H, 4-CH_2, 16-CH_2), 2.35 (t, 2H, *J* = 7.0 Hz, 2-CH_2), 2.79 (m, 6H, 7-CH_2, 10-CH_2, 13-CH_2), 5.30−5.40 (m, 8H, CH=CH)

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.49, 24.75, 24.85(3C), 26.69, 27.50, 29.53(3C), 30.48, 30.81, 33.60, 44.37, 127.80, 128.09, 128.32, 128.50, 128.83, 128.94, 129.31, 130.67, 179.70.

MS (EI): *m/z* (%) = 346 (M^+, 19), 331 (M^+−CH_3, 5.8).

Anal. Calcd for $C_{23}H_{38}O_2$: C, 79.71; H, 11.05. Found: C, 79.54; H, 10.89.

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