Total Synthesis of the Antimicrobial Fatty Acid (5*Z*,9*Z*)-14-Methylpentadeca-5,9-dienoic Acid and its Longer-Chain Analog (5*Z*,9*Z*)-24-Methylpentacosa-5,9-dienoic Acid

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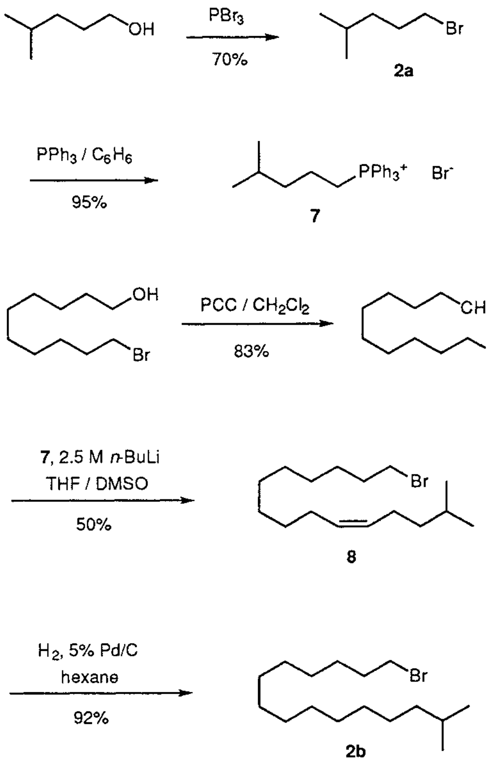
Dedicated to Professor Waldemar Adam (Würzburg) on the occasion of his 60th birthday

The antimicrobial marine fatty acid (5*Z*,9*Z*)-14-methylpentadeca-5,9-dienoic acid, recently identified in the phospholipids of the Caribbean gorgonian *Eunicea succinea*, and its longer-chain analog (5*Z*,9*Z*)-24-methylpentacosa-5,9-dienoic acid, initially identified in the phospholipids of the sponge *Petrosia ficiformis*, have been synthesized for the first time through a common synthetic route. A combination of alkyne–bromide coupling and Wittig reaction resulted in the best combination for assembling the $\Delta^{5,9}$ functionality in high yield and stereoselectivity.

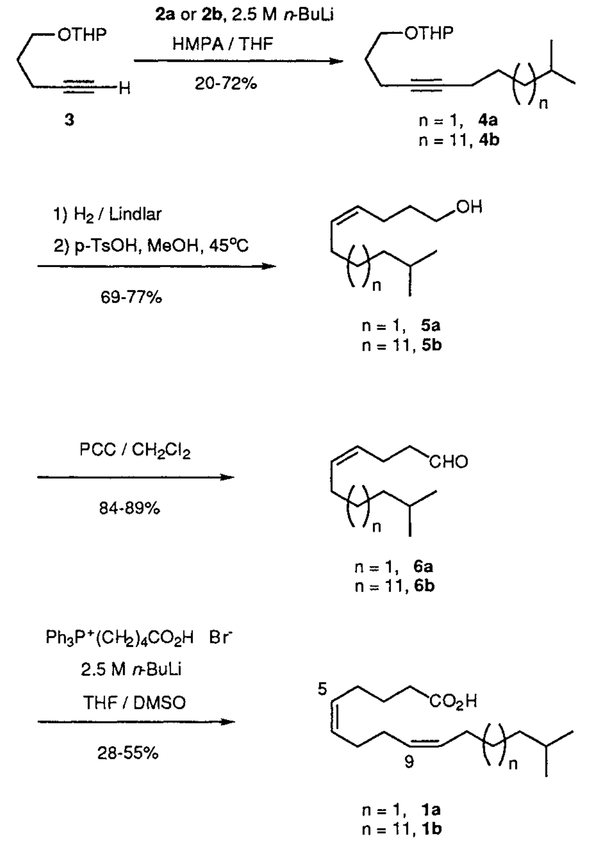
iso-Branched 5,9-dienoic fatty acids, with chain-lengths between 16 and 29 carbons, have been identified in the phospholipids of several marine organisms.[1,2] Just recently, the shortest member of the series, namely (5*Z*,9*Z*)-14-methylpentadeca-5,9-dienoic acid (**1a**), was isolated by us from the Caribbean gorgonian *Eunicea succinea*, and shown to be specifically active against pathogenic Gram-positive bacteria, such as *Staphylococcus aureus* and *Streptococcus faecalis*, but inactive against Gram-negative bacteria.[3] This bacterial specificity is of interest, and in order to facilitate the further biological scrutiny of these *iso*-branched 5,9-dienoic fatty acids, we required a fast and stereoselective synthesis of several analogs. A combination of lithium acetylide coupling and Wittig reaction provided the necessary versatility to assemble these fatty acids in high isomeric purity. We use this approach, herein, in the first total synthesis of two members of this series, namely the short-chain acid (5*Z*,9*Z*)-14-methylpentadeca-5,9-dienoic acid (**1a**), and the long-chain analog (5*Z*,9*Z*)-24-methylpentacosa-5,9-dienoic acid (**1b**).



Scheme 1

Our synthesis of (5*Z*,9*Z*)-14-methylpentadeca-5,9-dienoic acid (**1a**) started with commercially available 4-methylpentan-1-ol, which was converted with phosphorous tribromide to 1-bromo-4-methylpentane (**2a**) isolated in 70% yield (Scheme 1). Commercially available pent-4-yn-1-ol was also protected to the tetrahydropyranyl ether **3** in 85% yield (Scheme 2). Formation of the lithium acetylide of **3** with *n*-Buli (2.5 M), in THF, and subsequent addition of 1-bromo-4-methylpentane (**2a**), in hexamethylphosphoric acid triamide (HMPA), resulted in the isolation in 72% yield of the tetrahydropyranyl protected 9-methyldec-4-yn-1-ol (**4a**). It is important to mention that in the lithium acetylide coupling the bromoalkane has to be added in HMPA, otherwise the cross-coupling does not work so well.[4] Hydrogenation of the alkyne with Lindlar's catalyst and quinoline, in dry hexane, afforded 90% of the *cis* hydropyranyl protected 9-methyldec-4-en-1-ol and no traces of the *trans* isomer. Deprotection of the alcohol with *p*-toluenesulfonic acid (*p*-TsOH), in methanol, afforded (*Z*)-9-methyldec-4-en-1-ol (**5a**) isolated in 86% yield (Scheme 2). Pyridinium chlorochromate (PCC) oxidation of alcohol **5a** resulted in isolation in 84% yield of the labile (*Z*)-9-methyldec-4-enal (**6a**). Final Wittig reaction with (4-carboxybutyl)triphenylphosphonium bromide, in THF/DMSO, resulted in a 55% yield of isolated (5*Z*,9*Z*)-14-methylpentadeca-5,9-dienoic acid (**1a**). Around 5% of the isomer (5*E*,9*Z*)-14-methylpentadeca-5,9-dienoic acid was also detected by gas chromatography/mass spectrometry. The isomeric purity in **1a** was determined by ^{13}C NMR and IR. The synthetic acid **1a** co-injected nicely in GC, as the methyl ester, with an authentic sample from the gorgonian *Eunicea succinea*.[3] Acid **1a** was further submitted to cytotoxicity screening, and it displayed cytotoxicity against the human epidermoid carcinoma cells (A431) cell line (IC$_{50}$ = 48 μg/mL) and the human large cell lung carcinoma (NCI-H460) cell line (IC$_{50}$ = 51 μg/mL).[5]

We wanted to extend the synthetic approach used for **1a** to longer-chain lengths, which are more difficult to couple, and the synthesis of the longer-chain analog (5*Z*,9*Z*)-24-methylpentacosa-5,9-dienoic acid (**1b**) was undertaken by just changing the bromoalkane used in the acetylide cross-coupling reaction (Scheme 2). Acid **1b** was initially identified, mainly by gas chromatography/mass



Scheme 2

spectrometry, in the phospholipids of the sponge *Petrosia ficiformis*[1] and further detected in the phospholipids of other sponges such as *Cribrochalina vasculum* and *Geodia neptunis*.[6] Phospholipids with 5,9-dienoic acids, such as **1b**, are of interest for membrane studies, since these unusual phospholipids do not interact with sterols in cell membranes.[7] The synthesis of **1b** started with commercially available 10-bromodecan-1-ol which was oxidized with PCC to 10-bromodecanal, followed by Wittig coupling with 4-methyl-1-pentyltriphenylphosphonium bromide salt **(7)** to (*Z*)- and (*E*)-1-bromo-14-methylpentadec-10-ene **(8)**, as we previously described (Scheme 1).[8] Catalytic hydrogenation (5% Pd/C) of **8** afforded 1-bromo-14-methylpentadecane **(2b)** isolated in 92% yield. Lithium acetylide coupling of **2b** with **3**, in THF/HMPA, resulted in isolation of a 20% yield of the tetrahydropyranyl-protected 19-methyleicos-4-yn-1-ol. In this case the alcohol was deprotected first with *p*-toluenesulfonic acid, in methanol, affording an 80% yield of 19-methyleicos-4-yn-1-ol, which was further hydrogenated with Lindlar's catalyst and quinoline, in dry hexane, to (*Z*)-19-methyleicos-4-en-1-ol **(5b)** in 86% yield. Not even traces of the *trans*-isomer were observed in this case. Pyridinium chlorochromate (PCC) oxidation of alcohol **5b** resulted in an 89% yield of isolated (*Z*)-19-methyleicos-4-enal **(6b)**. Final Wittig reaction with (4-carboxybutyl)triphenylphosphonium bromide, in THF/DMSO, resulted in only a 28% yield of (5*Z*,9*Z*)-24-methylpentacosa-5,9-dienoic acid **(1b)**. No other isomers were detected by GC. Synthesized acid **1b**, as the methyl ester, co-injected nicely in GC with authentic samples from the sponges *Cribrochalina vasculum* and *Geodia neptuni*.[7] Acid **1b** was not antimicrobial (MIC > 100 μg/mL).

^{1}H NMR and ^{13}C NMR spectra were recorded either on a General Electric GN 300 spectrometer or on a Bruker Avance DPX 300 spectrometer. Chemical shifts are referenced to $CDCl_3$. Infrared spectra were run neat in a Magna-IR 750 Nicolet spectrometer. Mass spectra were measured at 70 eV either in a Hewlett-Packard 5972A MS ChemStation, equipped with a 30 m × 0.25 mm special performance capillary column (HP-5MS) crosslinked with 5% phenyl methylpolysiloxane, or in a VG AutoSpec high-resolution mass spectrometer.

1-[(Tetrahydropyran-2-yl)oxy]pent-4-yne (3):
4-Pentyn-1-ol (1.18 g, 14.1 mmol), in distilled $CHCl_3$ (85 mL), was stirred with dihydropyran (1.53 g, 17 mmol) and catalytic amounts of *p*-toluenesulfonic acid at r.t. for 5 h. The resulting mixture was washed with H_2O (1 × 100 mL), a saturated solution of $NaHCO_3$ (1 × 100 mL), and H_2O (1 × 100 mL) again. After drying over $MgSO_4$, the rotoevaporated crude product was purified by silica gel chromatography (hexane/Et_2O, 8 : 2); to furnish the previously reported **3**;[9] yield: 1.89 g (80%).

9-Methyl-1-[(tetrahydropyran-2-yl)oxy]dec-4-yne (4a):
To a stirred solution of **3** (0.96 g, 5.57 mmol), in dry THF (8 mL), was added *n*-BuLi (2.5 M, 8 mmol) in dry hexane (3.2 mL) while keeping the temperature below 10 °C. The alkyl halide **2a**, prepared from 4-methylpenten-1-ol as previously described,[8] was added dropwise (1.15 g, 7 mmol), in dry HMPA (12 mL), while maintaining the temperature below 25 °C. The reaction mixture was worked up within 1 h by pouring into a large volume of ice-water and extracting with hexane (2 × 25 mL). The organic layer was washed with H_2O (1 × 25 mL), and brine (1 × 25 mL) before drying (Na_2SO_4). Filtration and rotoevaporation of the solvent afforded the desired crude product **4a**; yield: 1.0 g (72%).

IR (neat): ν = 2953, 2919, 2869, 2849, 1463, 1454, 1441, 1383, 1366, 1353, 1200, 1137, 1120, 1077, 1062, 1034, 1021, 990, 869 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (d, 6 H, J = 6.56 Hz), 1.20–1.27 (m, 2 H), 1.42–1.59 (m, 6 H), 1.67–1.83 (m, 5 H), 2.08–2.13 (m, 2 H), 2.23–2.28 (m, 2 H), 3.46–3.51 (m, 2 H), 3.80–2.87 (m, 2 H), 4.59 (t, 1 H, J = 3.6 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.63, 18.99, 19.49, 22.56, 25.48, 27.01, 27.64, 29.28, 30.67, 38.20, 62.12, 66.07, 79.36, 80.61, 98.74.

MS: m/z (rel intensity, %) = 252 (M$^+$, 0.002), 251 (0.004), 237 (0.001), 209 (1), 195 (1), 179 (4), 167 (19), 135 (3), 123 (3), 109 (5), 101 (5), 97 (14), 85 (100), 79 (17), 67 (21), 55 (20).

HRMS: Calc. for $C_{16}H_{28}O_2$: 252.2089. Found: 252.2041.

(*Z*)-9-Methyl-1-[(tetrahydropyran-2-yl)oxy]dec-4-ene:
Into a 25-mL round-bottomed flask was placed Lindlar's catalyst (0.27 g), and the flask was flame-dried under N_2. After cooling to r.t., dry hexane (10 mL), alkyne **4a** (1.01 g, 4 mmol), and quinoline (0.1 mL) were added. The N_2 was exchanged for H_2, and the H_2 uptake of the stirred solution was measured at different time intervals with a graduated burette. After 4 h the reaction mixture was filtered, diluted with Et_2O (10 mL), and rotoevaporated under vacuum to afford (*Z*)-9-methyl-1-[(tetrahydropyran-2-yl)oxy]dec-4-ene; yield: 0.91 g (90%).

IR (neat): ν = 3005, 2952, 2939, 2869, 1467, 1454, 1441, 1384, 1366, 1353, 1322, 1260, 1200, 1183, 1136, 1120, 1077, 1063, 1034, 993, 905, 869, 815, 722 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, 6 H, J = 6.59 Hz), 1.13–1.21 (m, 2 H), 1.25–1.38 (m, 2 H), 1.48–1.86 (m, 9 H), 1.97–2.04 (m, 2 H), 2.07–2.16 (m, 2 H), 3.35–3.53 (m, 2 H), 3.70–3.91 (m, 2 H), 4.57 (t, 1 H, J = 4.07 Hz), 5.31–5.43 (m, 2 H, J_{cis} = 12.49 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.65, 22.61, 23.86, 25.50, 27.42, 27.50, 27.89, 29.77, 30.77, 38.64, 62.30, 67.01, 98.84, 128.97, 130.55.

MS: m/z (rel intensity, %) = 254 (M^+, 0.004), 181 (0.005), 169 (1), 152 (3), 137 (1), 124 (1), 109 (3), 101 (3), 96 (5), 85 (100), 84 (26), 81 (7), 67 (19), 55 (18).

HRMS: Calc. for $C_{16}H_{29}O_2$ ($M^+ - H$): 253.2167. Found: 253.2168.

(*Z*)-9-Methyldec-4-en-1-ol (5a):
(*Z*)-9-Methyl-1-[(tetrahydropyran-2-yl)oxy]dec-4-ene (0.74 g, 2.9 mmol), in MeOH (3.5 mL), with catalytic amounts of *p*-toluenesulfonic acid, was stirred at 45 °C until the starting material disappeared, as judged by TLC. The usual workup[10] and silica gel column chromatography (EtOAc) afforded the corresponding alcohol **5a**; yield: 0.42 g (86 %).

IR (neat): v = 3383, 3006, 2958, 2925, 2869, 2854, 1467, 1464, 1379, 1366, 1260, 1094, 1020, 867, 800, 671 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, 6 H, J = 6.58 Hz), 1.14–1.39 (m, 4 H), 1.45–1.67 (m, 3 H), 1.98–2.15 (m, 4 H), 3.65 (t, 2 H, J = 6.49 Hz), 5.32–5.41 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 130.81, 128.80, 62.64, 38.61, 32.63, 27.87, 27.50, 27.46, 27.41, 23.58, 22.59.

MS: m/z (rel intensity, %) = 170 (M^+, 2), 152 (1), 137 (5), 124 (3), 109 (26), 95 (47), 81 (87), 67 (100), 55 (87).

HRMS: Calc. for $C_{11}H_{20}$ ($M^+ - H_2O$): 152.1565. Found: 152.1555.

(*Z*)-9-Methyldec-4-enal (6a):
A mixture of **5a** (0.36 g, 2.1 mmol) and 0.57 g (2.6 mmol) of pyridinium chlorochromate (PCC) was stirred at r.t. in dry CH_2Cl_2 (15 mL). After 24 h, the mixture was poured into Et_2O and the residue was washed again with Et_2O (3 × 25 mL). The combined organic extracts were then passed through a Florisil column (Et_2O). Evaporation of the solvents afforded pure **6a**; yield: 0.30 g (84 %).

IR (neat): v = 3007, 2955, 2929, 2869, 2718, 1728, 1467, 1409, 1385, 1366, 1170, 1119, 1063, 720 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.85 (d, 6 H, J = 6.61 Hz), 1.28–1.38 (m, 2 H), 1.47–1.56 (m, 2 H), 1.97–2.05 (m, 3 H), 2.32–2.39 (m, 2 H), 2.47 (t, 2 H, J = 7.16 Hz), 5.27–5.46 (m, 2 H), 9.76 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.05, 22.56, 27.31, 27.40, 27.85, 38.57, 43.80, 126.98, 131.70, 202.17.

MS: m/z (rel intensity, %) = 168 (M^+, 1), 153 (1), 150 (5), 135 (8), 124 (8), 109 (12), 97 (31), 84 (100), 69 (78), 55 (99).

HRMS: Calc. for $C_{11}H_{20}O$: 168.1514. Found: 168.1509.

(5*Z*,9*Z*)-14-Methylpentadeca-5,9-dienoic Acid (1a):
Commercially available (4-carboxybutyl)triphenylphosphonium bromide (0.91 g, 2 mmol), previously dried under vacuum at 110 °C, was dissolved in dry DMSO (7 mL) and cooled to 0–10 °C. Then, *n*-BuLi (2.4 M, 5 mL) was added dropwise, followed by stirring for 0.5 h under N_2. Aldehyde **6a** (0.17 g, 1 mmol) in THF–DMSO (1 : 1, 5 mL), was added dropwise and the resulting mixture was stirred at r.t. for 3.5 h. The reaction mixture was then poured into a separatory funnel filled with ice and the aq phase was acidified with 1.5 N HCl. The acidic solution was extracted with Et_2O (2 × 15 mL), and the Et_2O layer was washed with H_2O (2 × 15 mL), dried over Na_2SO_4, and filtered. After rotoevaporation a yellow oil was obtained which was purified by silica gel column chromatography (hexane/Et_2O, 1 : 1) to furnish a 95 : 5 *cis-cis*/*trans-cis* mixture of **1a** as confirmed by gas chromatography,[3] yield: 0.14 g (55 %).

IR (neat): v = 3500–2500 (br), 3007, 2954, 2930, 2869, 1711, 1459, 1435, 1413, 1384, 1366, 1241, 938, 723 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, 6 H, J = 6.6 Hz), 1.16–1.23 (m, 4 H), 1.52–1.57 (m, 1 H), 1.72–1.75 (m, 2 H), 1.97–2.13 (m, 8 H), 2.35 (t, 2 H, J = 7.51 Hz), 5.30–5.44 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.61, 24.58, 26.47, 27.26, 27.38, 27.48, 27.88, 33.38, 38.63, 128.60, 128.91, 130.55, 179.60.

MS: m/z (rel intensity, %) = 252 (M^+, 3), 237 (0.01), 209 (0.01), 196 (1), 181 (1), 167 (3), 149 (4), 136 (6), 127 (17), 109 (31), 95 (23), 81 (61), 69 (100), 55 (65).

HRMS: Calc. for $C_{16}H_{28}O_2$: 252.2089. Found: 252.2073.

1-Bromo-14-methylpentadecane (2b):
1-Bromo-14-methylpentadec-10-ene (**8**) (1.38 g, 4.56 mmol) was hydrogenated in hexane (100 mL) using catalytic amounts of 5 % Pd/C. After 78 h the reaction was stopped, filtered, and the hexane was rotoevaporated to furnish the previously reported **2b**;[11] yield: 1.28 g (92 %).

HRMS: Calc. for $C_{16}H_{33}Br$: 304.1766. Found: 304.1662.

19-Methyl-1-[(tetrahydropyran-2-yl)oxy]eicos-4-yne (4b):
To a stirred solution of **3** (0.47 g, 2.8 mmol), in dry THF (4 mL), *n*-BuLi (2.5 M, 8.0 mmol) in dry hexane (1.2 mL) was added while keeping the temperature below 10 °C. The alkyl halide **2b** was then added dropwise (0.71 g, 2.3 mmol) in dry HMPA (9 mL) while maintaining the temperature below 25 °C. After 24 h the reaction mixture was worked up by pouring into a large volume of ice-water, and extracting with hexane (2 × 20 mL). The organic layer was washed with water (1 × 20 mL) and brine (1 × 20 mL) before drying (Na_2SO_4). Filtration and rotoevaporation of the solvent furnished **4b** which was used for the next step without further purification; yield: 0.16 g (55 %).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.84 (d, 6 H, J = 6.6 Hz), 1.14–1.40 (m, 24 H), 1.43–1.59 (m, 5 H), 1.69–1.85 (m, 2 H), 2.09–2.13 (2 H, m), 2.23–2.33 (m, 4 H), 3.42–3.51 (m, 2 H), 3.76–3.86 (m, 2 H), 4.57 (t, 1 H, J = 4.0 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.61, 18.71, 19.46, 22.61, 25.46, 27.38, 27.93, 28.85, 29.10, 29.15, 29.28, 29.53, 29.66, 29.68, 29.91, 30.62, 30.64, 39.03, 62.14, 66.03, 79.33, 80.56, 98.76.

MS: m/z (rel intensity, %) = 392 (M^+, 1), 349 (1), 335 (1), 319 (6), 308 (2), 265 (1), 195 (1), 181 (2), 167 (31), 153 (2), 139 (2), 121 (3), 107 (4), 101 (6), 97 (17), 85 (100), 67 (20), 55 (22).

19-Methyleicos-4-yn-1-ol:
Pyranyl ether **4b** (0.15 g, 0.38 mmol) in methanol (5 mL), and catalytic amounts of *p*-toluenesulfonic acid were stirred at 45 °C until the starting material disappeared, as judged by TLC. The solvent was rotoevaporated, hexane (2 mL) was added to crystallize excess *p*-toluenesulfonic acid, filtered, and rotoevaporated under high vacuum affording 0.085 g (80 %) of 19-methyleicos-4-yn-1-ol which was used for the next step without further purification; yield: 0.085 g (80 %).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, 6 H, J = 6.6 Hz), 1.16–1.40 (m, 24 H), 1.45–1.55 (m, 1 H), 1.72–1.78 (m, 2 H), 2.13 (m, 2 H), 2.28 (m, 2 H), 3.76 (t, 2 H, J = 6.0 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.44, 18.71, 22.64, 27.40, 27.95, 28.88, 29.06, 29.14, 29.53, 29.67, 29.70, 29.93, 31.53, 39.05, 62.14, 79.18, 81.21.

MS: m/z (rel intensity, %) = 308 (M^+, 0.1), 293 (0.1), 279 (0.1), 265 (1), 251 (0.1), 237 (0.1), 223 (0.1), 209 (1), 195 (1), 167 (1), 153 (6), 149 (1), 139 (6), 121 (10), 111 (19), 97 (100), 84 (49), 79 (44), 67 (44), 55 (65).

(*Z*)-19-Methyleicos-4-en-1-ol (5b):
Into a 10-mL round-bottomed flask was placed Lindlar's catalyst (0.018 g), and the flask was flame-dried under N_2. After cooling to r.t., dry hexane (2.5 mL), 19-methyleicos-4-yn-1-ol (0.085 g, 0.3 mmol), and quinoline (6.9 μL) were added. The N_2 was exchanged for H_2, and the H_2 uptake of the stirred solution was measured at different time intervals with a graduated burette. After 8 h the reaction mixture was filtered, diluted with Et_2O (10 mL), and rotoevaporated under vacuum to furnish pure **5b** as confirmed by gas chromatography; yield: 0.075 g (86 %).

IR (neat): v = 3355 (br), 3004, 2963, 2924, 2853, 1466, 1383, 1366, 1261, 1119, 1062, 1035, 801, 721 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, 6 H, J = 6.6 Hz), 1.13–1.41 (m, 24 H), 1.47–1.55 (m, 1 H), 1.58–1.74 (m, 2 H), 2.00–2.06 (m, 2 H), 2.09–2.13 (m, 2 H), 3.66 (t, 2 H, J = 6.5 Hz), 5.32–5.45 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.65, 23.59, 27.21, 27.41, 27.96, 28.89, 29.32, 29.56, 29.69, 29.94, 32.65, 39.05, 62.70, 128.78, 130.85.

MS: m/z (rel intensity, %) = 310 (M^+, 1), 292 (18), 264 (6), 250 (1), 236 (3), 222 (1), 208 (3), 194 (1), 180 (2), 166 (1), 151 (3), 137 (9), 123 (15), 109 (20), 96 (62), 82 (84), 67 (86), 55 (100).

HRMS: Calc. for $C_{21}H_{42}O$: 310.3236. Found: 310.3243.

(*Z*)-19-Methyleicos-4-enal (6b):

A mixture of **5b** (0.075 g 0.24 mmol) and 0.054 g (0.25 mmol) of PCC was stirred at r.t. in dry CH_2Cl_2 (10 mL). After 24 h, the mixture was poured into Et_2O and the residue was washed again with Et_2O (3 × 25 mL). The combined organic extracts were then passed through a Florisil column (Et_2O). Evaporation of the solvents afforded pure **6b** as determined by gas chromatography; yield: 0.066 g (89 %).

IR (neat): ν = 3007, 2924, 2853, 2714, 1730, 1466, 1383, 1366, 1260, 1119, 1035, 800, 720 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, 6 H, J = 6.6 Hz), 1.13–1.30 (m, 24 H), 1.44–1.55 (m, 1 H), 2.00–2.07 (m, 2 H), 2.33–2.40 (m, 2 H), 2.46–2.51 (m, 2 H), 5.28–5.47 (m, 2 H), 9.77 (t, 1 H, J = 1.58 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.08, 22.65, 27.23, 27.42, 27.97, 29.31, 29.54, 29.57, 29.63, 29.69, 29.72, 29.95, 39.06, 43.84, 126.99, 131.77, 202.26.

MS: m/z (rel intensity, %) = 308 (M^+, 1), 290 (2), 264 (7), 235 (0.1), 222 (1), 208 (1), 194 (0.1), 180 (0.1), 166 (1), 152 (1), 135 (2), 121 (3), 111 (7), 98 (28), 84 (100), 69 (18), 55 (28).

HRMS: Calc. for $C_{21}H_{40}O$: 308.3079. Found: 308.3073.

(5Z,9Z)-24-Methylpentacosa-5,9-dienoic Acid (1b):

Commercially available (4-carboxybutyl)triphenylphosphonium bromide (0.093 g, 0.02 mmol), previously dried under vacuum at 110 °C, was dissolved in dry DMSO (4 mL) and cooled to 0–10 °C. Then, *n*-BuLi (2.4 M, 0.2 mL) was added dropwise, followed by stirring for 0.5 h under N_2. Aldehyde **6b** (0.060 g, 0.20 mmol), in THF–DMSO (1 : 1, 4 mL), was then added dropwise and the resulting mixture was stirred at r.t. for 5 h. The reaction mixture was then poured into a separatory funnel filled with ice and the aq phase was acidified with 1.5 N HCl. The acidic solution was extracted with Et_2O (2 × 10 mL) and the Et_2O layer was washed with H_2O (2 × 15 mL), dried (Na_2SO_4), and filtered. After rotoevaporation a yellow oil was obtained which was initially purified by silica gel column chromatography (hexane/Et_2O, 1 : 1). Acid **1b** was immediately esterified with 1.5 N HCl in MeOH (5 mL), and finally purified by silica gel column chromatography (hexane/Et_2O, 9 : 1) to furnish **1b**; yield: 0.024 g (28 %).

IR (neat): ν = 3005, 2924, 2853, 1744, 1691, 1466, 1384, 1366, 1308, 1245, 1168, 1119, 720 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, 6 H, J = 6.6 Hz), 1.20 (s, 24 H), 1.43–1.53 (m, 1 H), 1.71 (m, 2 H), 2.02–2.11 (m, 8 H), 2.31 (t, 2 H, J = 7.53 Hz), 3.67 (s, 3 H), 5.30–5.45 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.61, 24.85, 26.19, 27.27, 27.41, 27.96, 29.32, 29.69, 29.94, 33.46, 39.06, 51.45, 128.78, 128.93, 130.43, 130.55, 174.16.

MS: m/z (rel intensity, %) = 406 (M^+, 2), 374 (1), 332 (1), 291 (1), 264 (3), 222 (1), 207 (3), 181 (1), 150 (19), 141 (36), 109 (59), 95 (23), 81 (100), 55 (73).

HRMS: Calc. for $C_{27}H_{50}O_2$: 406.3811. Found: 406.3825.

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