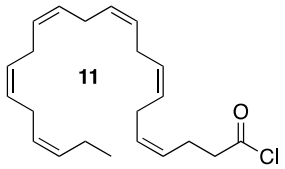
Experimental

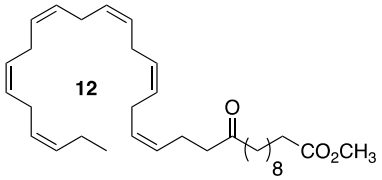
General. Unless specified otherwise, glassware was flame dried under a N_2 atmosphere prior to use. Reactions were performed using common dry, inert atmosphere techniques. Solvents were purified according to the guidelines in Purification of Common Laboratory Chemicals (Perrin, Armarego, and Perrin: Oxford, 1966). Zinc dust (>98%, <10 μm) was freshly activated prior to use. Reactions were monitored by TLC and visualized by a dual short wave/long wave UV lamp and stained with an ethanolic solution of potassium permanganate or p-anisaldehyde. Flash column chromatography was performed using F60 grade silica gel, 230—400 mesh. NMR spectra were recorded on Varian VXR-500, Varian Inova-500, or Varian Inova-400 spectrometers. Chemical shifts for ^{1}H NMR were reported as δ, parts per million (ppm), relative to the signal of tetramethylsilane at 0 ppm or the $CHCl_3$ signal at 7.26 ppm. Chemical shifts for ^{13}C NMR were reported as δ, parts per million, relative to the center line signal of the $CDCl_3$ triplet at 77.2 ppm. The abbreviations s, d, t, q, dd, p, and m stand for the resonance multiplicity singlet, doublet, triplet, quartet, doublet of doublet, pentet, and multiplet, respectively. IR spectra were recorded on a Nicolet iS10 FTIR Spectrometer. Mass spectra were recorded at the Mass Spectrometry Facility in the Department of Chemistry at the University of Utah using a Finnigan MAT 95 double focusing high resolution mass spectrometer. Concentration refers to removal of solvent under reduced pressure (house vacuum at ca. 20 mmHg).

Activation of Zinc

A 1 L beaker was charged with zinc dust (80 g, 1.22 mol). To this was slowly added a solution of 2% HCl (aq., 250 mL). The resulting mixture was stirred for 10 minutes until small bubbles appeared on the surface of the zinc. The solution above the zinc was carefully removed, leaving behind a slurry that was washed with water (2 x 400 mL) and ethanol (1 x 400 mL). The solid was distributed equally among three 50 mL centrifuge tubes and the zinc was further washed with acetone (2 x 25 mL per tube), and diethyl ether (25 mL per tube). The resulting activated zinc was dried under vacuum at 120 °C overnight.

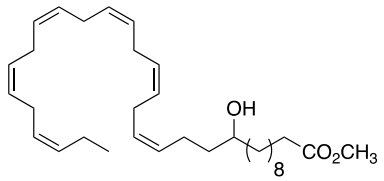


Synthesis of (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoyl chloride (11). To a solution of docosahexaenoic acid (3.07 g, 9.35 mmol) and 60 mL of $CHCl_3$ was added thionyl chloride (0.88 mL, 12 mmol). The resulting mixture was heated to reflux and stirred for 10 h. The reaction mixture was then cooled to rt and concentrated to give a purple slurry that was used in the subsequent coupling reaction without additional purification.



Synthesis of methyl(14Z,17Z,20Z,23Z,26Z,29Z)-11-oxodotriaconta-14,17,20,23,26,29-hexaenoate (12). A dry three-necked flask was charged with freshly activated zinc powder (19.6 g, 300. mmol) and anhydrous lithium chloride (LiCl) (16.7 g, 393 mmol). The mixture was then

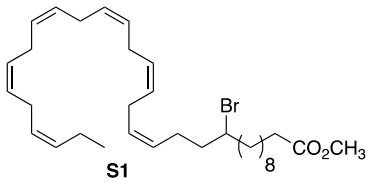
subjected to flame-drying under an inert atmosphere. Once the flask had cooled to room temperature (rt), tetrahydrofuran (THF) (250 mL) that had been purged with argon for 15 minutes was added to the flask via cannula. To this was slowly added 1,2-dibromoethane (2.6 mL, 30. mmol) and trimethylsilyl chloride (TMSCl) (1.8 mL, 15 mmol). The resulting mixture was heated to reflux for 30 minutes, during which time gas evolution was observed, and then cooled to rt. To this was added methyl 10-bromodecanoate **9** (9.9 g, 37 mmol); the reaction mixture was heated to reflux and stirred at that temperature for 24 h. The formation of the zincate intermediate was monitored by ^{1}H NMR analysis by quenching small aliquots of the reaction mixture with 1 M hydrochloric acid (HCl) (aq.). Once the zincate had formed, it was cooled to rt and a solution of tetrakis(triphenylphosphine)palladium(0) (0.87 g, 0.56 mmol) in hot toluene (20 mL) was added to it followed by triphenyl phosphine (0.582 g, 2.20 mmol) and dimethyl acetamide (3.0 mL, 32 mmol). The resulting mixture was heated to reflux. After 20 min. a solution of **11** (9.35 mmol) in tetrahydrofuran (THF) (50 mL) was slowly added to the mixture over 2 h. The reaction mixture was stirred at reflux for 18 hours and then cooled to rt. The reaction was quenched by adding 1 M HCl (aq., 250 mL) and stirring for 1 h. he mixture was filtered and the phases were separated. The aqueous phase was extracted with ethyl acetate (EtOAc) (3 x 200 mL). The combined organic extracts were washed with brine (300 mL), dried over sodium sulfate (Na_2SO_4), and concentrated. The resulting residue was purified using flash chromatography using a gradient of toluene:hexanes (1:1 to 100% toluene), yielding 3.40 g (73% yield) of ketone **12** as a slightly impure pale-yellow oil (contaminated with Pd waste).^{1}H NMR (500 MHz, CDCl3) δ 5.69 – 5.15 (m, 12H), 3.65 (s, 3H), 2.76-2.91(m, 10H), 2.45 (t, J = 7.4 Hz, 2H), 2.37 (t, J = 7.5 Hz, 2H), 2.36 – 2.26 (m, 4H), 2.01-2.12 (m, 2H), 1.69 – 1.49 (m, 2H), 1.16-1.35 (m, 12H), 0.96 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.74, 174.49, 174.44, 135.26, 132.14, 128.96, 128.66, 128.56, 128.36, 128.32, 128.28, 128.25, 128.20, 127.98, 127.12, 51.58, 43.06, 42.53, 34.23, 34.20, 29.80, 29.77, 29.72, 29.58, 29.46, 29.38, 29.37, 29.33, 29.31, 29.27, 29.22, 25.75, 25.73, 25.69, 25.65, 25.08, 25.04, 23.90, 21.75, 20.68, 14.41. IR (neat) 3011, 2926, 2854, 1738, 1715, 1435, 1362, 1252, 1195, 1170, 1115, 719 cm^{-1}.



13

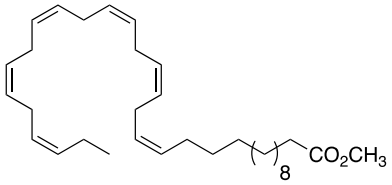
Synthesis of methyl (14*Z*,17*Z*,20*Z*,23*Z*,26*Z*,29*Z*)-11-hydroxydotriaconta-14,17,20,23,26,29-hexaenoate(13). To a solution of ketone **12** (6.82 mmol) and MeOH (300 mL) at 0 °C was slowly added $NaBH_4$ (3.81g, 100. mmol). The resulting mixture was warmed to rt and stirred overnight. After re-cooling the reaction mixture to 0 °C, the reaction was quenched with 1 M HCl (aq., 100 mL). Following concentration, water (150 ml) was added to the resulting slurry and the aqueous phase was extracted with EtOAc (4 x 150 mL) The organic extracts were combined, washed with water (500 mL), and brine (500 mL), and dried (Na_2SO_4). Concentration and flash column chromatography (1:15 EtOAc:hexanes) have 3.00 g of alcohol **13** as a colorless oil. (64 % yield over 3 steps) ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.52 – 5.18 (m, 12H), 3.66 (s, 3H), 3.60 (broad, 1H), 2.84 (m, 10H), 2.30 (t, J = 7.6 Hz, 2H), 2.26 – 2.14 (m, 2H), 2.07 (m, 2H), 1.60 (m, 2H), 1.50 (m, 6H), 1.28 (m, 10H), 0.97 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.49, 132.19, 129.97, 128.72, 128.49, 128.41, 128.39, 128.34, 128.32, 128.24, 128.22, 128.02, 127.15, 71.71, 51.60, 37.71, 37.31, 34.25, 29.85, 29.80, 29.68, 29.51, 29.37, 29.27, 25.79, 25.77, 25.68, 25.08, 23.75, 20.70, 14.43. IR (neat) 3441, 3012, 2853, 1740, 1653, 1436, 1391, 1363, 1262, 1196, 1170, 1110,

1067, 925, 711, 599, 581cm^{-1}; (ESI) calcd for $C_{33}H_{54}NaO_3$ [M+Na]+ (m/z) 521.3971, found 521.3966.



S1

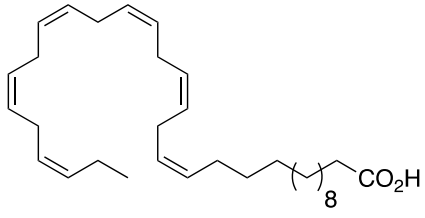
Synthesis of methyl (14Z,17Z,20Z,23Z,26Z,29Z)-11-bromodotriaconta-14,17,20,23,26,29-hexaenoate(S1). To a solution of CBr_4 (2.89 g, 8.71 mmol) in CH_2Cl_2 (200 mL) at rt was added PPh_3 (2.86 g, 10.9 mmol). After the resulting yellow reaction mixture had stirred for 20 minutes, a solution of C32-alcohol **13** (1.09 g, 2.19 mmol) in CH_2Cl_2 (20 mL) was gradually introduced, causing the color of the reaction mixture to gradually fade. After stirring for 3.5 hours, the mixture was poured into cold hexanes (200 mL, 0 °C), and then cooled at –20 °C for 30 minutes. The mixture was then filtered, and the obtained filtrate was concentrated. The resulting residue was dissolved in a minimum volume of CH_2Cl_2 and cold hexanes (100 mL) was added to the solution. The mixture was then cooled to -20 °C for an additional 1 h, filtered, and concentrated. The resulting residue was purified using flash chromatography (toluene:hexanes = 1:2) and concentrated to give 1.06 g (86% yield) of **S1** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.49 – 5.26 (m, 12H), 4.02 (tt, J = 8.6, 4.2 Hz, 1H), 3.67 (s, 3H), 2.92 – 2.79 (m, 10H), 2.30 (m, 4H), 2.13 – 2.06 (m, 2H), 1.90 – 1.78 (m, 4H), 1.62 (m, 2H), 1.56 – 1.51 (m, 2H), 1.44 – 1.39 (m, 2H), 1.29 (s, 8H), 0.98 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.29, 132.02, 129.13, 128.56, 128.41, 128.26, 128.23, 128.19, 128.17, 128.15, 128.10, 127.88, 127.02, 77.25, 76.99, 76.74, 58.09, 51.42, 39.27, 38.90, 34.09, 29.39, 29.33, 29.19, 29.11, 29.02, 27.56, 25.74, 25.67, 25.65, 25.63, 25.54, 25.42, 24.93, 20.55, 14.26. IR (neat) 3012, 2927, 2854,1740, 1435, 1392, 1363, 1195, 1170, 970, 915, 709, 615cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{53}BrNaO_2$ $[M+Na]^+$ (*m/z*) 583.3127, found 583.3130.



14

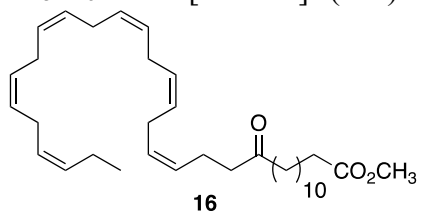
Synthesis of methyl (14Z,17Z,20Z,23Z,26Z,29Z)-dotriaconta-14,17,20,23,26,29-hexaenoate (14). To a 1 L three-necked flask containing freshly activated zinc powder (21.6 g, 332 mmol) was added a mixture of THF (156 mL) and of MeOH (125 mL). The resulting slurry was cooled to 0 °C and purged with argon gas for 15 minutes. To this was added a solution of bromide **S1** (1.87 g, 3.33 mmol) in THF (10 mL) followed by the slow addition of 6 M HCl (42 mL) over 0.5 h. The resulting reaction mixture was allowed to warm to rt over 8 h. The remaining zinc was removed by filtration and the filtrate was diluted with water (100 mL). If a white solid appeared during this process, 1 M HCl was added until the white precipitate disappeared. Once it was homogeneous, the reaction mixture was concentrated to approximately 200 mL and the aqueous phase was extracted with EtOAc (3 x 250 mL). The extracts were dried (Na_2SO_4) and concentrated. Flash chromatography using toluene and hexanes (2:3) gave 1.29 g (80% yield) of ester **14** as a colorless oil.^{1}H NMR (500 MHz, $CDCl_3$) δ 5.46 – 5.27 (m, 12H), 3.66 (s, 3H), 2.89 – 2.74 (m, 10H), 2.30 (t, J = 7.6 Hz, 2H), 2.12 – 1.99 (m, 4H), 1.61 (p, J = 7.3 Hz, 2H), 1.43 – 1.16 (m, 24H), 0.97 (t, J = 7.5 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 174.39, 132.04, 130.50, 128.58, 128.56, 128.25, 128.24, 128.11, 127.88, 127.86, 127.53, 127.01, 51.47, 34.13, 29.68, 29.66, 29.62, 29.59, 29.48,

29.35, 29.29, 29.17, 27.28, 25.64, 25.63, 25.54, 24.97, 20.57, 14.31, 1.04. IR (neat) 3013, 2923, 2853, 1741, 1462, 1435, 1261, 1195, 1169, 713cm-1; HRMS (ESI) calcd for $C_{33}H_{54}NaO_2$ [M+ Na]+ (m/z) 505.4022, found 505.4024.



1

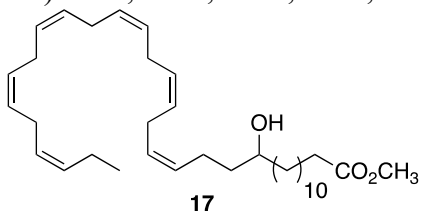
Synthesis of (14Z,17Z,20Z,23Z,26Z,29Z)-dotriaconta-14,17,20,23,26,29-hexaenoic acid 1. A solution of ester **14** (1.29 g, 2.67 mmol) in a mixture of THF (248 mL) and MeOH (186 mL) was cooled to 0 °C and purged with Argon for 10 minutes. To this was slowly added a solution of 10 M NaOH (aq., 62 mL) over 0.5 h. The reaction mixture was warmed to rt over 2.5 hours. Once **14** had been consumed (by TLC), the reaction mixture was cooled to 0 °C, and the reaction was quenched by the slow addition of 6 M HCl (aq., 100 mL) to a final pH of 2-3. The resulting mixture was concentrated, and the resulting slurry was extracted with EtOAc (3 x 200 mL). The organic extracts were combined, dried (Na_2SO_4), and concentrated. Purification using flash column chromatography (EtOAc:hexanes = 1:10 with 0.5% acetic acid) gave 1.12 g of VLC-PUFA **1** as a colorless oil (90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.38 (d, J = 5.5 Hz, 12H), 2.91 – 2.72 (m, 10H), 2.35 (t, J = 7.5 Hz, 2H), 2.13 – 2.00 (m, 4H), 1.58-1.68 (m, 2H), 1.26 (d, J = 2.6 Hz, 18H), 0.97 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.47, 132.19, 130.65, 128.73, 128.71, 128.40, 128.39, 128.26, 128.03, 128.01, 127.67, 127.16, 34.05, 29.82, 29.79, 29.75, 29.73, 29.60, 29.49, 29.41, 29.22, 27.42, 25.79, 25.77, 25.69, 24.83, 20.71, 14.44. IR (neat) 3416, 2923, 2852, 1711, 1463, 1173, 1074 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{52}O^-$ $[M]^-$ (m/z) 467.3884 found 467.3895. HRMS (ESI) calcd for $C_{32}H_{52}O_2Na$ $[M + Na]^+$ (m/z) 491.3865; found 491.3857.



16

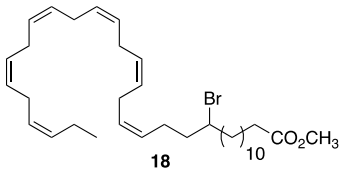
Methyl (16Z,19Z,22Z,25Z,28Z,31Z)-13-oxotetratriaconta-16,19,22,25,28,31-hexaenoate [34:6n-3 ketone](16). A dry three-necked flask was charged with freshly activated zinc powder (20.9 g, 320. mmol) and anhydrous lithium chloride (LiCl) (21.5 g, 507 mmol). The mixture was then flame-dried under an inert atmosphere. Once the flask had cooled to room temperature (rt), tetrahydrofuran (THF) (250 mL) that had been purged with argon for 15 minutes was added to the flask via cannula. To the slurry was slowly added 1,2-dibromoethane (2.6 mL, 30. mmol) and trimethylsilyl chloride (TMSCl) (2.0 mL, 16 mmol). The mixture was heated to reflux for 0.5 h during which time a significant amount of gas was released. Upon cooling, methyl 12-bromodecanoate (10.2 g, 36.5 mmol) was added. The reaction mixture was heated to reflux and stirred at that temperature for 24 hours. The formation of the zincate intermediate was monitored by ^{1}H NMR analysis as described for the generation of **12**. To this was added a solution of triphenyl phosphine (0.582 g, 2.2 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.871 g, 0.750 mmol) in toluene (10 mL) and dimethyl acetamide (3 mL) followed by a solution of **11** (prepared from 3.06 g of DHA (9.32 mmol)) in THF (50 mL) over a 2 h time frame. The reaction mixture

was heated to reflux and stirred at that temperature for 18 h. The reaction mixture was cooled to rt and the reaction was quenched by adding 1 M HCl (aq., 250 mL) and allowing the resulting mixture to stir at rt for 1 h The mixture was filtered, the phases were separated, and the aqueous phase was extracted with ethyl acetate (EtOAc) (3 x 200 mL). The combined organic extracts were washed with brine (300 mL), dried (Na_2SO_4), and concentrated. The resulting residue was purified using flash chromatography (toluene:hexanes gradient, 2:1 to 100% toluene) to give 3.58 g of ketone **16** (73%) as a pale-yellow oil that was contaminated with a small amount of Pd by-products. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.41 – 5.25 (m, 12H), 3.65 (s, 3H), 2.87 – 2.77 (m, 10H), 2.44 (d, J = 7.4 Hz, 2H), 2.37 (t, J = 7.5 Hz, 2H), 2.28 (m, 4H), 2.10 – 2.01 (m, 2H), 1.65 – 1.52 (m, 4H), 1.23 (m, 14H), 0.96 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.71, 174.37, 132.02, 128.84, 128.54, 128.44, 128.24, 128.20, 128.16, 128.13, 128.08, 127.87, 127.00, 51.46, 42.96, 42.41, 34.10, 29.70, 29.51, 29.44, 29.41, 29.26, 29.24, 29.13, 25.63, 25.61, 25.57, 25.53, 24.94, 23.82, 21.63, 20.56, 14.29. IR (neat) 2917, 2849, 1739, 1711, 1437, 1176, 1120 cm^{-1}.



17

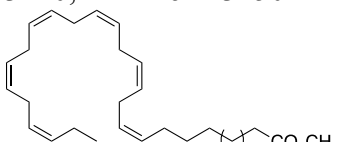
Methyl (16Z,19Z,22Z,25Z,28Z,31Z)-13-hydroxytetratriaconta-16,19,22,25,28,31-hexaenoate[34:6n-3 alcohol](17). To a solution of the impure ketone **16** from above (6.82 mmol) and MeOH (300 mL) at 0 °C was added $NaBH_4$ (3.81g 100. mmol) slowly. The resulting mixture was warmed to rt and stirred overnight. After cooling the reaction mixture back to 0 °C, the reaction was quenched with 1 M HCl (aq., 100 mL). Following concentration, H_2O (150 ml) was added to the resulting slurry and the aqueous phase was extracted with EtOAc (4 x 150 mL). The organic extracts were combined, washed with water (500 mL) and brine (500 mL), dried (Na_2SO_4), and concentrated. Flash chromatography (1:15 EtOAc:hexanes) gave 2.70 g of alcohol **17** (55 % yield from DHA) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.46 – 5.31 (m, 12H), 3.66 (s, 3H), 3.60 (broad, 1H), 2.84 (m, 10H), 2.30 (t, J = 7.6 Hz, 2H), 2.23 – 2.14 (m, 2H), 2.07 (m, 2H), 1.61 (m, 2H), 1.55 – 1.37 (m, 6H), 1.36 – 1.18 (m, 14H), 0.97 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.40, 132.06, 129.85, 128.58, 128.36, 128.27, 128.25, 128.20, 128.18, 128.10, 128.08, 127.88, 127.01, 71.59, 51.49, 37.58, 37.16, 34.13, 29.71, 29.63, 29.58, 29.44, 29.26, 29.15, 25.68, 25.65, 25.63, 25.54, 24.96, 23.62, 20.57, 14.31. IR (neat) 3442, 3012, 2923, 2853, 1740, 1435, 1393, 1364, 1260, 1170, 1111, 1069, 969, 917, 719, 601cm^{-1}; (ESI) calcd for $C_{35}H_{58}NaO_3$ $[M+Na]^+$ (m/z) 549.4284, found 549.4221.



18

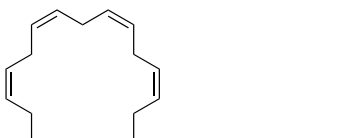
Methyl (16Z,19Z,22Z,25Z,28Z,31Z)-13-bromotetratriaconta-16,19,22,25,28,31-hexaenoate[34:6n-3 bromide](18). To a solution of CBr_4 (3.13 g, 9.44 mmol) in CH_2Cl_2 (280 mL) at rt was added PPh_3 (3.10 g, 11.8 mmol). After the resulting yellow reaction mixture had stirred for 20 min, a solution of alcohol **17** (1.24 g, 2.36 mmol) in CH_2Cl_2 (20 mL) was gradually introduced, causing the reaction mixture's color to temporarily fade. The resulting mixture was left to stir at rt for 3.5 h and the mixture was poured into cold hexanes (200 mL, 0 °C). The resulting mixture was further cooled to –20 °C for 0.5 h, filtered, and the filtrate was concentrated. This

sequence was repeated. That is, the residue was dissolved in a minimum volume of CH_2Cl_2 and cold hexanes (100 mL, 0 °C) was added to the solution. The mixture was refrigerated at -20 °C for an additional 1 h and filtered. The filtrate was concentrated and the resulting residue was purified using flash chromatography (toluene:hexanes = 1:2). Concentration provided 1.14 g of bromide **18** (82%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47 – 5.25 (m, 12H), 4.01 (tt, J = 8.7, 4.5 Hz, 1H), 3.66 (s, 3H), 2.84 (m, 10H), 2.31 (m, 4H), 2.13 – 2.00 (m, 2H), 1.90 – 1.74 (m, 4H), 1.61 (t, J = 7.3 Hz, 2H), 1.52 (m, 2H), 1.42 – 1.38 (m, 2H), 1.26 (m, 12H), 0.97 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.50, 132.17, 129.26, 128.69, 128.56, 128.39, 128.37, 128.32, 128.31, 128.27, 128.23, 128.01, 127.15, 58.33, 51.61, 39.43, 39.02, 34.25, 29.68, 29.67, 29.62, 29.57, 29.40, 29.28, 29.20, 27.73, 25.88, 25.81, 25.79, 25.77, 25.68, 25.56, 25.09, 20.70, 14.44. IR (neat) 2924, 2853,1735, 1436, 1170, 1064, 971, 910, 731, 648cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{57}BrNaO_2$ $[M+Na]^+$ (m/z) 611.3440, found 611.3450.



19

Methyl (16Z,19Z,22Z,25Z,28Z,31Z)-tetratriaconta-16,19,22,25,28,31-hexaenoate[34:6n-3 ester](19). A flame-dried three-necked flask was charged with of activated zinc powder (1.25 g, 19.1 mmol) and anhydrous LiCl (1.08 g, 25.5 mmol). The mixture was flame-dried under a flow of and cooled to rt. After adding freshly distilled THF (75 mL), the resulting slurry was purged with N_2. To this was sequentially added 1,2-dibromoethane (0.46 mL, 5.3 mmol) and TMSCl (0.34 mL, 2.7 mmol) slowly resulting in gas evolution. The resulting mixture was heated at reflux for 30 min. After cooling to rt, **18** (303 mg, 0.514 mmol) was added. The reaction mixture was heated to reflux and stirred at that temperature overnight. The reaction flask was cooled to 0 °C. To this was carefully added a solution of 1 M HCl (aq., 25 mL) and MeOH (50 mL). The mixture was allowed to stir for another 3 h, filtered, and concentrated to remove the organics. The resulting aqueous phase was extracted with EtOAc (4 x 120 ml), and the combined organic layers were washed with H_2O (1 x 250 ml) and brine (1 x 250 ml). The extracts were dried (Na_2SO_4) and concentrated. The resulting residue was purified by flash chromatography (toluene:hexanes 2:3) yielding 130 mg of **19** (50 % yield) as a colorless oil.^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47 – 5.26 (m, 12H), 3.66 (s, 3H), 2.84 (dd, J = 17.6, 5.8 Hz, 10H), 2.30 (t, J = 7.6 Hz, 2H), 2.14 – 2.02 (m, 4H), 1.61 (m, 2H), 1.29 – 1.13 (m, 22H), 0.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.51, 132.18, 130.65, 128.73, 128.71, 128.40, 128.38, 128.26, 128.02, 128.00, 127.67, 127.16, 77.41, 77.16, 76.91, 51.59, 34.27, 29.83, 29.80, 29.76, 29.73, 29.62, 29.49, 29.42, 29.31, 27.42, 25.79, 25.77, 25.69, 25.11, 20.71, 14.43. IR (neat) 3011, 2922, 2851, 1740, 1650, 1435, 1251, 1195, 1169, 1069, 968, 916, 718 cm^{-1}. HRMS (ESI) calcd for C35H58NaO2 $[M+Na]^+$ (m/z) 533.4335, found 533.4330.



20 VLC-PUFA 34:6 n-3

(16Z,19Z,22Z,25Z,28Z,31Z)-tetratriaconta-16,19,22,25,28,31-hexaenoic acid [VLC-PUFA 34:6 n-3] (20). To a solution of **19** (28 mg, 0.0548 mmol) in mixture of THF (4 mL) and MeOH (2 mL) at 0 °C was slowly added of 10 M NaOH (aq., 1 mL). After 10 minutes tthe ice bath was

removed and the reaction mixture was allowed to warm to rt over 1.5 hours (monitored by TLC). After the **19** had disappeared by TLC, the reaction mixture was cooled to 0 °C and the reaction was quenched with 1 M HCl (aq., ca. 1 mL, to a final pH of 2-3). The mixture was concentrated, the resulting residue was partitioned in a mixture of EtOAc (15 mL) and H_2O (15 mL). The phases were separated and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organics were dried (Na_2SO_4) concentrated. Flash chromatography (EtOAc:hexanes = 1:10 with 0.5% acetic acid added to the eluent) gave 21 mg of VLC-PUFA **20** (77% yield) as a colorless oil. ^{1}H NMR (500 MHz, DMSO) δ 11.85 (s, 1H), 5.34 (m , 12H), 2.90 – 2.69 (m, 10H), 2.17 (t, J = 7.4 Hz, 2H), 2.08 – 1.88 (m, 4H), 1.54 – 1.44 (m, 2H), 1.23 (m, 22H), 0.92 (t, J = 7.6 Hz, 3H). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.50 – 5.37 (m, 12H), 2.97 – 2.80 (m, 10H), 2.35 (t, 2H), 2.16 – 2.01 (m, 4H), 1.63 (m, 2H), 1.26 (m, 22H), 0.97 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 174.50, 131.55, 129.93, 128.12, 127.90, 127.87, 127.84, 127.80, 127.67, 127.61, 127.52, 126.92, 33.66, 29.04, 29.01, 28.94, 28.86, 28.77, 28.62, 28.57, 26.64, 25.28, 25.25, 25.22, 25.14, 25.13, 24.51, 20.06, 14.13. IR (neat) 3011, 2922, 2852, 1708, 1462, 1260, 1020, 865, 794, 705, 609 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{55}O_2$ $[M]^+$ (m/z) 495.4197, found 495.4206.