Supporting Information

17(*R*),18(*S*)-Epoxyeicosatetraenoic Acid, A Potent Eicosapentaenoic Acid (EPA)-Derived Regulator of Cardiomyocyte Contraction: Structure-Activity Relationships and Stable Analogs

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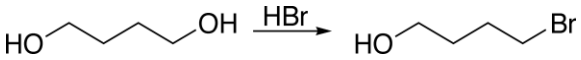
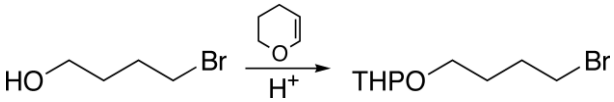
General Information

EPA and 17,18-EETeTr (**1**) were purchased from Cayman Chemical. Melting points are uncorrected. Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with TMS as internal standard. Enantiomers **2** and **3** were isolated via chiral phase HPLC of **1** on a Chiralcel OB column (250 × 4.6 mm; Daicel) using hexane containing 0.3% isopropyl alcohol and 0.05% acetic acid as solvent.[1] Diol **4** was prepared by acetic acid-mediated hydrolysis of **1**, purified by reversed-phase HPLC and identified by gas chromatography-mass spectrometry as described previously.[2] Final compounds were judged ≥95% pure by HPLC using a Zorbax Eclipse C18 (250 × 4.6 mm; Agilent) connected to an Agilent 1200 API/LC-MS with acetonitrile/water combinations as solvent; enantiomers were also analyzed by chiral phase HPLC using a Chiralcel OJ-H column (250 × 4.6 mm; Daicel) with hexane/isopropyl alcohol combinations as solvent and judged to be ≥95% e.e.

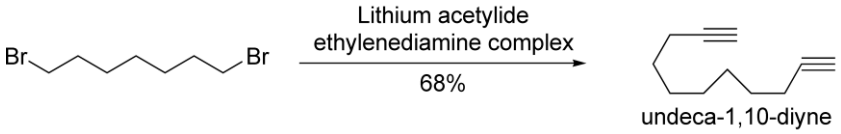
Synthetic Procedures



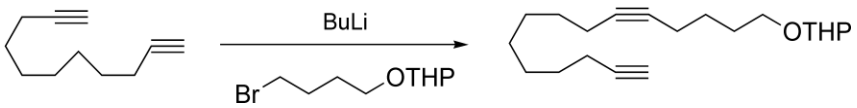
4-Bromobutan-1-ol.[3] 1,4-Butanediol (32 g, 35.55 mmol; Alfa Aesar) and aq. 48% HBr (45 mL) were heated under reflux in benzene (380 mL) with water removal using a Dean-Stark apparatus. After 12 h, all volatiles were removed *in vacuo* and the residue was purified by SiO_2 column chromatography using a gradient of 10-30% EtOAc/hexanes as eluent to give 4-bromobutan-1-ol[3] (29.20 g, 68%). TLC: 30% EtOAc/hexanes, $R_f \approx 0.30$; ^{1}H NMR (300 MHz) δ 3.70 (t, J = 6.1 Hz, 2H), 3.45 (t, J = 6.1 Hz, 2H), 1.92-2.04 (m, 2H), 1.68-1.78 (m, 2H).



2-(4-Bromobutoxy)tetrahydro-2*H*-pyran.[4] 3,4-Dihydro-2*H*-pyran (8.0 g, 95.36 mmol) was added to a 0 °C solution of 4-bromobutan-1-ol (12.0 g, 79.47 mmol) in dichloromethane (150 mL) followed by *p*-toulenesulphonic acid (20 mg). After 1 h, the reaction was carefully quenched with sat. aq. $NaHCO_3$ solution (5 mL), washed with water (100 mL), brine (70 mL), and concentrated in vacuo. The residue was purified by SiO_2 column chromatography using 2% EtOAc/hexanes as eluent to give 2-(4-bromobutoxy)tetrahydro-2*H*-pyran[4] (16.57 g, 88%) as a colorless oil. TLC: 10% EtOAc/hexanes, $R_f \approx 0.50$; ^{1}H NMR (300 MHz) δ 4.58 (t, J = 2.5 Hz, 1H), 3.90-3.72 (m, 2H), 3.38-3.50 (m, 4H), 1.92-2.04 (m, 2H), 1.65-1.80 (m, 4H), 1.60-1.50 (m, 4H).

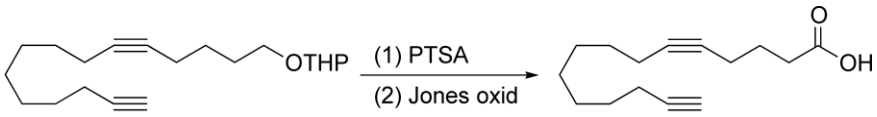


Undec-1,10-diyne.[5] A solution of 1,7-dibromoheptane (13.5 g, 52.32 mmol) in anhydrous dimethylsulfoxide (25 mL) was added dropwise to a stirring, 0 °C solution of lithium acetylide ethylenediamine complex (12.04 g, 130.8 mmol) in anhydrous dimethylsulfoxide (125 mL) under an argon atmosphere. After stirring at 5-8 °C for 2 h, the reaction mixture was diluted with ether (100 mL) and washed with water (2 × 40 mL). The aqueous washes were extracted with ether (2 × 50 mL). The combined ethereal fractions were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography using hexanes as eluent to give undec-1,10-diyne[5] as a colorless oil (5.3 g, 68%). TLC: SiO_2, hexane (100%), $R_f \approx 0.8$; ^{1}H NMR (300 MHz) δ 2.14-2.18 (m, 4H), 1.92 (t, *J* = 2.55 Hz, 2H), 1.50-1.53 (m, 4H), 1.40-1.42 (m, 4H), 1.23-1.25 (m, 2H).



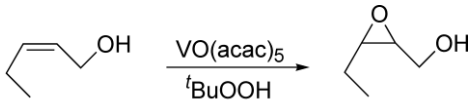
2-(Pentadeca-5,14-diynyloxy)tetrahydro-2*H*-pyran.[6] *n*BuLi (4.86 mL of 2.5 M soln in hexanes, 12.16 mmol) was added dropwise to a –78 °C solution of undec-1,10-diyne (2.0 g, 13.51 mmol) in dry tetrahydrofuran/HMPA (105 mL, 6:1) under an argon atmosphere. After 30 min, the reaction mixture was warmed to –10 °C over 2 h and maintained at this temperature for 20 min, then re-cooled to –78 °C. To this was added a solution of 2-(4-bromobutoxy)-tetrahydro-2*H*-pyran (2.4 g, 10.14 mmol) in dry THF (15 mL). The resulting mixture was warmed to room temperature over 3 h, maintained at this temperature for 12 h, then quenched with sat. aq. NH_4Cl (25 mL). After 20 min, the mixture was extracted with ether (2 × 125 mL). The combined ethereal extracts were washed with water (2 × 100 mL), brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography using 5% EtOAc/hexanes as eluent to give 2-(pentadeca-5,14-diynyloxy)tetrahydro-2*H*-pyran[6] (1.97 g, 64%) as a colorless oil. TLC: 10% EtOAc/hexanes, $R_f \approx 0.6$; ^{1}H NMR (400 MHz) δ 4.58 (t, *J* = 2.5 Hz, 1H), 3.82-3.89 (m, 1H), 3.71-3.78 (m, 1H), 3.43-3.53 (m, 1H), 3.36-3.47 (m, 1H), 2.01-2.20 (m, 6H), 1.93 (t, *J* = 2.5 Hz, 1H), 1.27-1.81 (m, 20H).

The reaction also produced approximately 10% of the dialkylated adduct. TLC: 10% EtOAc/hexanes, $R_f \approx 0.3$; ^{1}H NMR (300 MHz) δ 4.58 (t, *J* = 2.5 Hz, 2H), 3.82-3.89 (m, 2H), 3.71-3.78 (m, 2H), 3.43-3.53 (m, 2H), 3.36-3.47 (m, 2H), 2.01-2.20 (m, 8H), 1.27-1.81 (m, 30H).



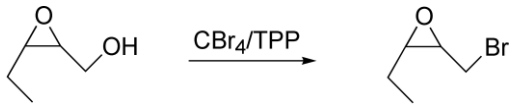
Pentadeca-5,14-diynoic acid. A solution of 2-(pentadeca-5,14-diynyloxy)tetrahydro-2*H*-pyran (4.05 g, 13.27 mmol) and *p*-toluenesulphonic acid (42 mg) in MeOH (100 mL) was stirred at room temperature for 4 h. All volatiles were then removed in vacuo and the residue was purified by SiO_2 column chromatography using 15% EtOAc/hexanes as eluent to give pentadeca-5,14-diyn-1-ol (2.77 g, 95%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 3.85 (t, 2H, *J* = 7.0 Hz), 2.03-2.30 (m, 6H), 1.93 (t, 1H, *J* = 2.6 Hz), 1.26-1.83 (m, 14H); ^{13}C NMR (100 MHz) δ.83.61, 79.82, 69.42, 61.91, 31.02, 29.32, 28.72, 28.53, 28.42, 27.64, 25.03, 19.21, 19.10, 18.75. HRMS calcd for $C_{15}H_{25}O$ $[M+1]^+$ 221.1905, found 221.1910.

Jones reagent (10 mL of a 10 N solution in water) in acetone (25 mL) was added to a stirring, –40 °C solution of above alcohol (1.9 g, 4.55 mmol) in acetone (75 mL). After 1 h, the reaction mixture was warmed to –10 °C and maintained for another 2 h, then quenched with excess (5 equiv) of isopropanol. The green chromium salts were removed by filtration and the filter cake was washed with acetone. The combined filtrates were concentrated *in vacuo* and the obtained residue was dissolved in EtOAc (100 mL), washed with water (50 mL) and again concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography using 15% EtOAc/hexanes as eluent to give pentadeca-5,14-diynoic acid (2.42 g, 82%). TLC: 40% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (400 MHz) δ 2.48 (t, 2H, *J* = 7.3 Hz), 2.10-2.17 (m, 6H), 1.93 (t, 1H, *J* = 2.6 Hz), 1.75-1.86 (m, 2H), 1.25-1.55 (m, 10H); ^{13}C NMR (100 MHz) δ203.31, 83.82, 82.41, 81.11, 68.84, 33.42, 29.13, 28.52, 28.31, 28.24, 27.81, 25.26, 19.12, 18.52, 18.46. HRMS calcd for $C_{15}H_{23}O_2$ $[M+1]^+$ 235.3419, found 235.3415.

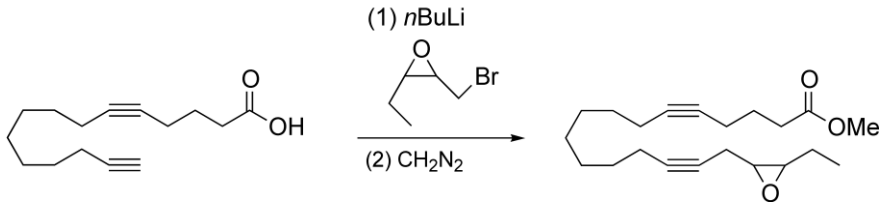


(*Z*)-(3-Ethyloxiranyl)methanol.[7] *tert*-Butyl hydroperoxide (15.72 g, 33 mL of a 5.2 M solution in decane) was added to a stirring solution of pent-2(*Z*)-en-1-ol (5.00 g, 58.14 mmol) and vanadium(III) acetylacetonate (150 mg) in dry benzene (200 mL) under an argon atmosphere. The initial pale green solution turned pink. After 3 h, the reaction was quenched with dimethylsulfide (52 g, 87.33 mmol, 5 equiv). After an additional 1 h, the reaction was diluted with an equal volume of Et_2O (250 mL), washed with water (2 × 250 mL), brine (200 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography using 30% EtOAc/hexanes as eluent to give (*Z*)-(3-ethyloxiranyl)methanol[7] (4.86 g, 82%) as a pale yellow oil.

TLC: 40% EtOAc/hexanes, $R_f \approx 0.3$; ^{1}H NMR (400 MHz) δ 3.86 (dd, 1H, *J* = 12.1, 4.0 Hz), 3.67 (dd, 1H, *J* = 6.8, 4.0 Hz), 3.17 (ddd, 1H, *J* = 4.1, 4.3, 6.8 Hz), 3.01 (ddd, 1H, *J* = 4.3, 6.4, 6.4 Hz) 1.46-1.71 (m, 2H), 1.04 (t, 3H, *J* = 7.6 Hz).

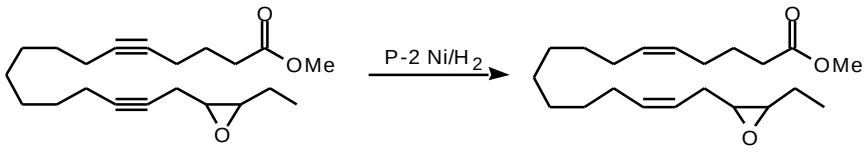


(*Z*)-2-Bromomethyl-3-ethyloxirane.[8] A solution of carbon tetrabromide (10.8 g, 32.64 mmol) in CH_2Cl_2 (25 mL) was stirred into a –10 °C solution of triphenylphosphine (8.6 g, 32.94 mmol) and the above epoxy alcohol (2.8 g, 27.45 mmol) in dry CH_2Cl_2 (100 mL) under an argon atmosphere. After 30 min, the reaction mixture was washed with water (75 mL), brine (50 mL), dried over anhydrous Na_2SO_4, and all volatiles were removed under reduced pressure. The residue was purified by SiO_2 column chromatography using 5% EtOAc/hexanes as eluent to give (*Z*)-2-bromomethyl-3-ethyloxirane[8] (2.92 g, 65%) as a colorless oil. TLC: 20% EtOAc/hexanes, $R_f \approx 0.6$; ^{1}H NMR (400 MHz) δ 3.49-3.53 (dd, 1H, *J* = 4.9, 9.3 Hz), 3.22-3.31 (m, 2H), 3.01-3.06 (m, 1H), 1.54-1.62 (m, 2H), 1.08 (t, 3H, *J* = 7.6 Hz).

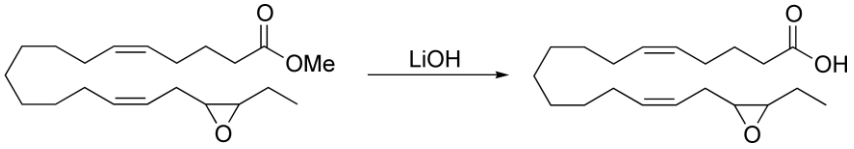


Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-5,14-diynoate. *n*-BuLi (1.8 mL of a 2.5 M hexanes solution, 4.48 mmol) was added slowly to a –70 °C solution of pentadeca-5,14-diynoic acid (0.5 g, 2.14 mmol) in dry tetrahydrofuran (30 mL) and HMPA (8 mL) under an argon atmosphere. The resulting mixture was stirred at –75 °C for 30 min, then allowed to warm to 0 °C over 2 h. After 1 h at 0 °C, the reaction mixture was re-cooled –72 °C and a solution of (*Z*)-2-bromomethyl-3-ethyloxirane (0.46 g, 2.56 mmol) in dry THF (10 mL) was introduced. The resulting mixture was warmed to room temperature over 3 h. After stirring at room temperature for 12 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL), stirred for 20 min, and then extracted with ether (3 × 75 mL). The combined ethereal extracts were washed with water (2 × 100 mL), brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in 5% MeOH/ether, cooled to 0 °C, and treated with an excess of ethereal diazomethane until the yellow color persisted for 10 min. After 1 h, all volatiles were removed under reduced pressure and the residue was purified by SiO_2 column chromatography using 5% EtOAc/hexanes as eluent to give methyl 16-[(*Z*)-3-

ethyloxiranyl]hexadeca-5,14-diynoate (0.39 g, 56%) as a colorless oil. TLC: 10% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (400 MHz) δ 3.65 (s, 3H), 3.07-3.12 (m, 1H), 2.88-2.92 (m, 1H), 2.51-2.58 (m, 1H), 2.41 (t, 2H, *J* = 7.3), 2.08-2.26 (m, 7H), 1.74-1.81 (m, 2H), 1.22-1.64 (m, 12H), 1.05 (t, 3H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz) δ 173.4, 80.8, 82.3, 79.6, 77.4, 60.7, 56.4, 51.2, 32.2, 28.2, 28.3, 27.8, 24.2, 24.1, 19.2, 19.0, 11.8. HRMS calcd for $C_{21}H_{33}O_3$ $[M+1]^+$ 333.2430, found 333.2428.

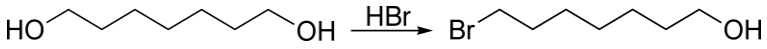


Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-5(*Z*),14(*Z*)-dienoate. $NaBH_4$ (33 mg, 0.88 mmol) was added portionwise to a stirring solution of nickel(II) acetate tetrahydrate (190 mg, 0.76 mmol) in absolute ethanol (5 mL) under a hydrogen blanket (1 atm). After 15 min, freshly distilled ethylenediamine (200 mg, 3.24 mmol) was added followed by a solution of methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-5,14-diynoate (360 mg, 1.08 mmol) in absolute ethanol (5 mL). The heterogeneous mixture was stirred at room temperature for 90 min, then diluted with ether (15 mL) and filtered through a short pad of silica gel. The filter cake was washed with ether (3 × 5 mL). The combined ethereal filtrates were dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-5(*Z*),14(*Z*)-dienoate (0.35 g, 97%) as a colorless oil sufficiently pure to be used in the next step without purification. TLC: 20% EtOAc/hexanes, $R_f \approx 0.6$; ^{1}H NMR (400 MHz) δ 5.24-5.54 (m, 4H), 3.62 (s, 3H), 2.82-2.92 (m, 2H), 2.26-2.38 (m, 1H), 2.29 (t, 2 H, *J* = 7.3 Hz), 2.10-2.18 (m, 1H), 1.93-2.06 (m, 6H), 1.60-1.69 (m, 2H), 1.46-1.59 (m, 2H), 1.20-1.34 (m, 10H), 1.01 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (100 MHz) δ 174.24, 133.12, 130.16, 128.62, 124.12, 58.6, 56.8, 51.96, 33.72, 29.91, 29.84, 29.58, 29.46, 27.54, 27.48, 26.84, 26.43, 25.06, 21.21, 10.08.

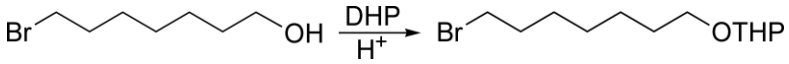


16-[(*Z*)-3-Ethyloxiranyl]hexadeca-5(*Z*),14(*Z*)-dienoic acid (5). LiOH (1 mL, 2 M aqueous solution) was added to a 0 °C solution of methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-5(*Z*),14(*Z*)-dienoate (90 mg, 0.266 mmol) in THF (8 mL) and deionized H_2O (2 mL). After stirring at room temperature overnight, the reaction mixture was cooled to 0 °C, the pH was adjusted to 4 with 1 M aq. oxalic acid, and extracted with ethyl acetate (2 × 20 mL). The combined extracts were washed with water (30 mL), brine (25 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The

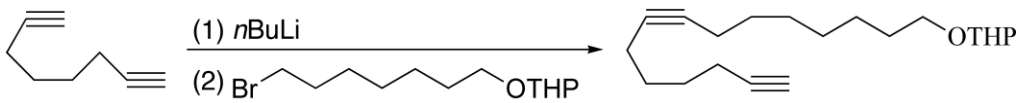
residue was purified by SiO_2 column chromatography using 25% EtOAc/hexanes as eluent to give **5** (82 mg, 92%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.3$; ^{1}H NMR (400 MHz) δ 5.26-5.51 (m, 4H), 2.88-2.98 (m, 2H), 2.31-2.44 (m, 1H), 2.35 (t, 2H, *J* = 7.7 Hz), 2.13-2.20 (m, 1H), 1.96-2.11 (m, 6H), 1.64-1.70 (m, 2H), 1.48-1.61 (m, 2H), 1.22-1.37 (m, 10H), 1.05 (t, 3H, *J* = 7.5); ^{13}C NMR (100 MHz) δ 179.96, 133.02, 131.87, 128.40, 123.97, 58.85, 57.73, 33.86, 30.04, 29.96, 29.94, 29.88, 29.81, 27.64, 27.42, 26.81, 26.24, 24.86, 21.28, 10.81. HRMS calcd for $C_{20}H_{35}O_3$ $[M+1]^+$ 323.2586, found 323.2587.



7-Bromoheptan-1-ol. Heptane-1,7-diol (36.0 g, 272 mmol; Alfa Aesar) and aq. 48% HBr (38 mL) was heated under reflux in benzene (400 mL) with water removal using a Dean-Stark apparatus. After 12 h, all volatiles were removed *in vacuo* and the residue was purified by SiO_2 column chromatography using a gradient of 10-30% EtOAc/hexanes as eluent to give 7-bromoheptan-1-ol (26.22 g, 62%) as a colorless oil identical with a commercial sample (Aldrich Chem. Co.). TLC: 50% EtOAc/hexanes, $R_f \approx 0.4$; ^{1}H NMR (400 MHz) δ 3.61 (t, 2H, *J* = 7.1 Hz), 3.39 (t, 2H, *J* = 6.8 Hz), 1.80-1.88 (m, 2H), 1.52-1.58 (m, 2H), 1.30-1.46 (m, 6H).

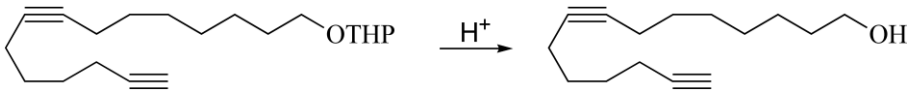


2-(7-Bromoheptyloxy)tetrahydro-2*H*-pyran. 7-Bromoheptane-1-ol (11.0 g, 56.7 mmol) from above was protected as its THP ether as described above to give 2-(7-bromoheptyloxy)tetrahydro-2*H*-pyran (14.50 g, 92%) as a colorless oil. TLC: 10% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (400 MHz) δ 4.58 (t, *J* = 2.5 Hz, 1H), 3.84-3.88 (m, 1H), 3.68-3.77 (m, 1H), 3.46-3.3.51 (m, 1H), 3.33-3.43 (m, 3H), 1.80-1.81 (m, 2H), 1.30-1.62 (m, 14H); ^{13}C NMR (100 MHz) δ 24.4, 28.0, 28.4, 28.8, 30.7, 32.1, 35.4, 37.4, 62.6, 66.6, 117.4. HRMS calcd for $C_{11}H_{22}BrO_2$ $[M+1]^+$ 265.0803, found 265.0806.

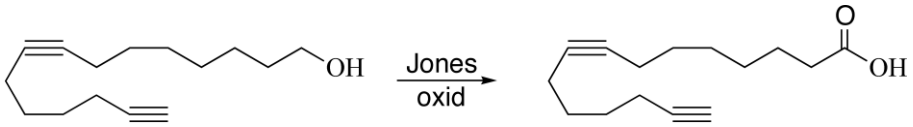


2-(Pentadeca-8,14-diynyloxy)tetrahydro-2*H*-pyran. Oct-1,7-diyne (6.3 g, 59.3 mmol) was alkylated with 2-(7-bromoheptyloxy)tetrahydro-2*H*-pyran (11 g, 39.56 mmol) as described above to give 2-(pentadeca-8,14-diynyloxy)tetrahydro-2*H*-pyran (7.82 g, 64%) as a colorless oil. TLC: 10% EtOAc/hexanes, $R_f \approx 0.6$; ^{1}H NMR (400 MHz) δ 4.57 (t, *J* = 2.5 Hz, 1H), 3.82-3.87 (m, 1H), 3.70-3.77 (m, 1H), 3.46-3.51 (m, 1H), 3.36-3.42 (m, 1H), 2.14-2.20 (m, 6H), 1.93 (t, *J* = 2.6 Hz, 1H),

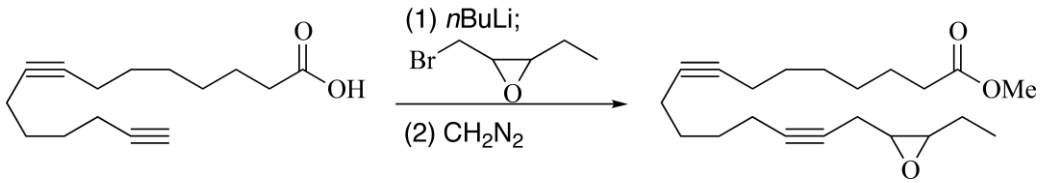
1.46-1.72 (m, 20 H); ^{13}C NMR (100 MHz) δ 17.4, 18.1, 19.3, 23.8, 27.7, 27.8, 28.6, 28.7, 29.2, 29.6, 30.1, 34.4, 64.0, 67.4, 68.5, 80.0, 80.1, 84.0, 116.6. HRMS calcd for $C_{19}H_{31}O_2$ $[M+1]^+$ 291.2324, found 291.2322.



Pentadeca-8,14-diyn-1-ol. 2-(Pentadeca-8,14-diynyloxy)tetrahydro-2*H*-pyran (5 g, 16.45 mmol) was cleaved using *p*-toluenesulphonic acid (60 mg) in MeOH (100 mL) as described above and the product was purified by SiO_2 column chromatography using 15% EtOAc/hexanes as eluent to give pentadeca-8,14-diyn-1-ol (3.26 g, 90%) as a colorless oil that was used in the next step without purification. TLC: 30% EtOAc/hexanes, $R_f \approx 0.35$; ^{1}H NMR (400 MHz) δ 3.63 (t, 2H, *J* = 5.5 Hz), 2.10-2.18 (m, 6H), 1.93 (t, 1H, *J* = 2.6 Hz), 1.24-1.62 (m, 14H).

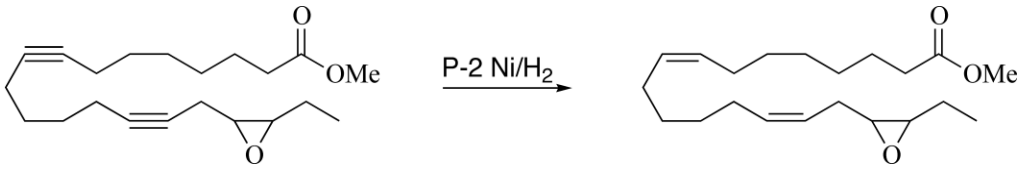


Pentadeca-8,14-diynoic acid. Oxidation of pentadeca-8,14-diyn-1-ol (3.0 g, 13.69 mmol) using Jones reagent as described above and purified by SiO_2 column chromatography using 15% EtOAc/hexanes as eluent gave pentadeca-8,14-diynoic acid (2.80 g, 87%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.33$; ^{1}H NMR (400 MHz) δ 2.34 (t, *J* = 7.0 Hz, 2H), 2.10-2.18 (m, 6H), 1.93 (t, *J* = 2.6 Hz, 1H,), 1.55-1.67 (m, 6H), 1.33-1.49 (m, 6H); ^{13}C NMR (100 MHz) δ 16.8, 18.8, 25.6, 27.7, 27.8, 28.2, 28.4, 28.6, 29.0, 34.5, 68.2, 79.6, 84.4, 181.0. HRMS calcd for $C_{15}H_{23}O_2$ $[M+1]^+$ 235.1698, found 235.1699.

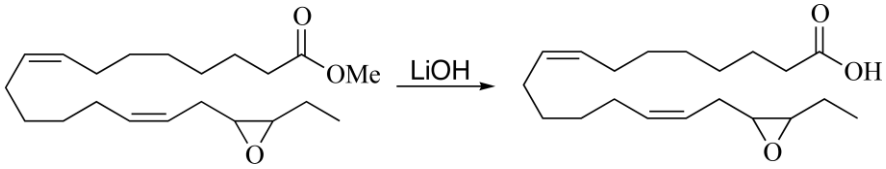


Methyl 16-[(*Z*)-3-ethyloxiran-2-yl]hexadeca-8,14-diynoate. Pentadeca-8,14-diynoic acid (0.80 g, 3.42 mmol) was alkylated with (*Z*)-2-(bromomethyl)-3-ethyloxirane (0.74 g, 4.10 mmol) as described above and esterified using diazomethane to give methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-5,14-diynoate (658 mg, 58%) as a colorless oil. TLC: 10% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (400 MHz) δ 3.65 (s, 3H), 3.07-3.12 (m, 1H), 2.88-2.92 (m, 1H), 2.51-2.61 (m, 1H), 2.32-2.50 (m, 1H),

2.30 (t, *J* = 7.5 Hz, 3H), 2.08-2.25 (m, 6H), 1.25-1.65 (m, 14H), 1.06 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz) δ 12.5, 19.1, 19.2, 19.3, 24.3, 24.4, 25.3, 28.0, 28.1, 28.2, 28.3, 28.9, 34.6, 53.2, 58.6, 61.4, 76.5, 77.8, 79.0, 79.2, 174.5. HRMS calcd for $C_{21}H_{33}O_3$ $[M+1]^+$ 333.2430, found 333.2429.



Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-8(*Z*),14(*Z*)-dienoate. Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-8,14-diynoate was subjected to the semi-hydrogenation procedure above to give methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-8(*Z*),14(*Z*)-dienoate (97%) as a colorless oil. TLC: 20% EtOAc/hexanes, $R_f \approx 0.55$; ^{1}H NMR (400 MHz) δ 5.31-5.56 (m, 4H), 3.66 (s, 3H), 2.86-2.96 (m, 2H), 2.25-2.42 (m, 1H), 2.28 (t, 2H, *J* = 7.33 Hz), 2.12-2.20 (m, 1H), 1.96-2.08 (m, 6H), 1.52-1.64 (m, 4H), 1.26-1.39 (m, 10H), 1.03 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (100 MHz) δ 174.30, 132.60, 129.99, 129.84, 124.13, 58.40, 56.73, 51.51, 34.17, 29.66, 29.47, 29.30, 29.18, 29.03, 27.46, 27.27, 27.20, 26.28, 25.05, 21.21, 10.76. HRMS calcd for $C_{21}H_{37}O_3$ $[M+1]^+$ 337.2743, found 337.2742.



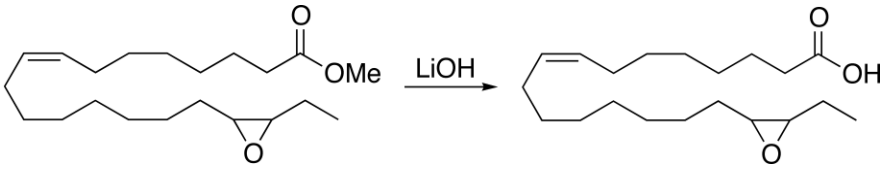
16-[(*Z*)-3-Ethyloxiranyl]hexadeca-8(*Z*),14(*Z*)-dienoic acid (6). Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-8(*Z*),14(*Z*)-dienoate was hydrolyzed as described above to give 16-[(*Z*)-3-ethyloxiranyl]hexadeca-8(*Z*),14(*Z*)-dienoic acid (**6**) (93%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.3$; ^{1}H NMR (300 MHz) δ 5.31-5.53 (m, 4H), 2.87-2.98 (m, 2H), 2.33-2.43 (m, 1H), 2.33 (t, *J* = 7.3 Hz, 2H), 2.13-2.22 (m, 1H), 1.94-2.08 (m, 6H), 1.52-1.64 (m, 4H), 1.30-1.38 (m, 10H), 1.04 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz) δ 180.06, 132.54, 130.03, 130.01, 125.03, 58.87, 57.73, 34.16, 29.86, 29.74, 29.71, 29.52, 29.45, 27.84, 27.67, 27.42, 26.33, 24.75, 21.48, 10.82. HRMS calcd for $C_{20}H_{35}O_3$ $[M+1]^+$ 323.2586, found 323.2584.

Synthesis of Methyl (*Z*)-16-(3-Ethyloxiranyl)hexadec-14(*Z*)-enoate and Methyl 16-[(*Z*)-3-Ethyloxiranyl]hexadec-8(*Z*)-enoate. Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-8(*Z*),14(*Z*)-dienoate was partially reduced using diimide as described above. $AgNO_3$-impregnated PTLC using 2% CH_2Cl_2/benzene: $R_f \approx 0.2$, 0.5, 0.6, and 0.85 for unreacted methyl 16-[(*Z*)-3-ethyloxiranyl]hexadeca-8(*Z*),14(*Z*)-dienoate, methyl (*Z*)-16-(3-ethyloxiranyl)hexadec-14(*Z*)-

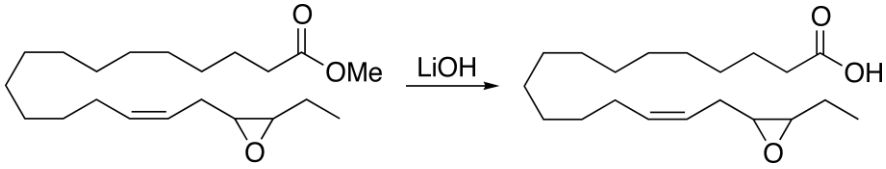
enoate, methyl 16-[(*Z*)-3-ethyloxiranyl]hexadec-8(*Z*)-enoate, and methyl 16-[(*Z*)-3-ethyloxiranyl]hexadecanoate, respectively, isolated in a ratio of 2:3:3:2, respectively.

Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadec-8(*Z*)-enoate: ^{1}H NMR (300 MHz) δ 5.31-5.35 (m, 2H), 3.66 (s, 3H), 2.84-2.91 (m, 2H), 2.27 (t, *J* = 7.3 Hz, 2H,), 1.97-2.08 (m, 4H), 1.47-1.64 (m, 4H), 1.22-1.39 (m, 18H), 1.03 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz) δ 179.96, 132.64, 131.13, 130.05, 129.45, 58.67, 57.93, 34.36, 29.66, 29.74, 29.73, 29.54, 29.65, 27.86, 27.54, 27.43, 26.35, 24.78, 21.51, 11.02.

Methyl 16-[(*Z*)-ethyloxiranyl]hexadec-14(*Z*)-enoate: ^{1}H NMR (300 MHz) δ 5.35-5.53 (m, 2H), 3.63 (s, 3H), 2.84-2.95 (m, 2H), 2.32-2.39 (m, 1H), 2.27 (t, *J* = 7.3 Hz, 2 H), 2.12-2.95 (m, 1H), 1.98-2.04 (m, 2H), 1.48-1.64 (m, 4H), 1.20-1.34 (m, 18H), 1.04 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz) 174.62, 132.86, 123.86, 58.84, 56.92, 51.76, 34.48, 29.96, 29.89, 29.84, 29.79, 29.74, 29.68, 29.66, 29.59, 29.57, 27.76, 26.36, 25.17, 21.33, 10.07.

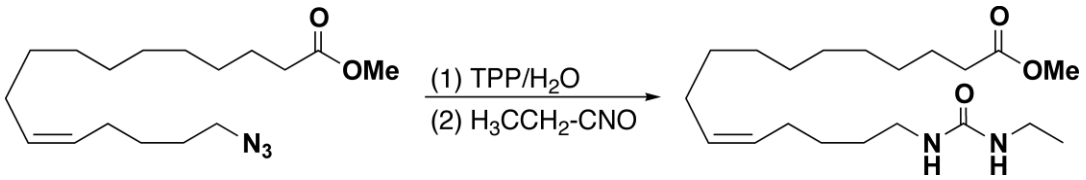


16-[(*Z*)-3-Ethyloxiranyl]hexadec-8(*Z*)-enoic acid (9). Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadec-8(*Z*)-enoate was hydrolyzed as described above to afford 16-[(*Z*)-3-ethyloxiranyl]hexadec-8(*Z*)-enoic acid (**9**) (91%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.33$; ^{1}H NMR (400 MHz) δ 5.34-5.40 (m, 2H), 2.90-2.96 (m, 2H), 2.36 (t, 2 H, *J* = 7.7 Hz), 2.01-2.05 (m, 4H), 1.22-1.65 (m, 22H), 1.07 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (75 MHz) δ 180.08, 130.52, 129.66, 58.54, 57.47, 34.23, 29.81, 29.61, 29.56, 29.36, 29.16, 29.13, 29.07, 28.86, 27.53, 26.78, 26.61, 24.49, 21.46, 10.78. HRMS calcd for $C_{20}H_{37}O_3$ $[M+1]^+$ 325.2743, found 325.2743.



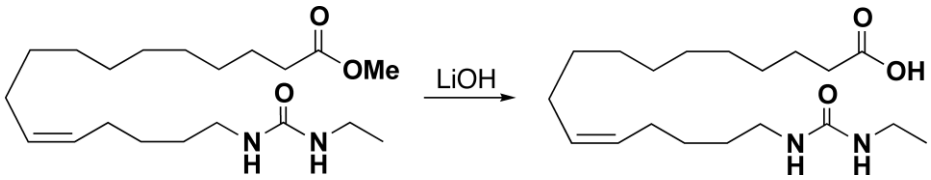
16-[(*Z*)-3-Ethyloxiranyl]hexadec-14(*Z*)-enoic acid (11). Methyl 16-[(*Z*)-3-ethyloxiranyl]hexadec-14(*Z*)-enoate was hydrolyzed as described above to afford 16-[(*Z*)-3-ethyloxiranyl]hexadec-14(*Z*)-enoic acid (**11**) (90%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.32$; ^{1}H NMR (300 MHz) δ 5.36-5.59 (m, 2H), 2.87-2.98 (m, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 2.31-2.43 (m, 1H), 2.12-2.22 (m, 1H), 1.99-2.06 (m, 2H), 1.50-1.64 (m, 4H), 1.20-1.35 (m, 18H), 1.04 (t,

J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz) δ 180.04, 133.06, 123.96, 58.46, 57.42, 34.12, 30.06, 30.04, 30.01, 29.98, 29.84, 28.76, 28.69, 28.65, 28.45, 27.88, 26.38, 25.01, 21.27, 10.92. HRMS calcd for $C_{20}H_{37}O_3$ $[M+1]^+$ 325.2743, found 325.2744.

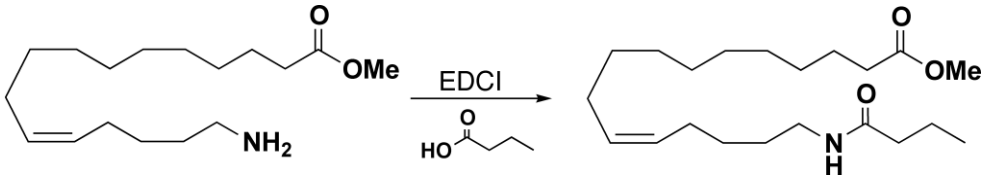


Methyl 16-(3-ethylureido)hexadec-11(*Z*)-enoate.[9] Triphenylphosphine (1.15 g., 4.41 mmol) was added to a room temperature solution of methyl 16-azidohexadec-11(*Z*)-enoate (**42**) (1.05 g., 3.4 mmol) in THF (25 mL). After 2 h, water (200 mL) was added and the stirring was continued for another 8 h. The reaction mixture was then diluted with EtOAc (20 mL), washed with water (20 mL) and brine (25 mL). Aqueous layers were back-extracted with EtOAc (2 × 30 mL). The combined organic extracts were dried over Na_2SO_4, concentrated under reduced pressure and further dried under high vacuum for 4 h. The crude methyl 16-aminohexadec-11(*Z*)-enoate was used in the next step without additional purification.

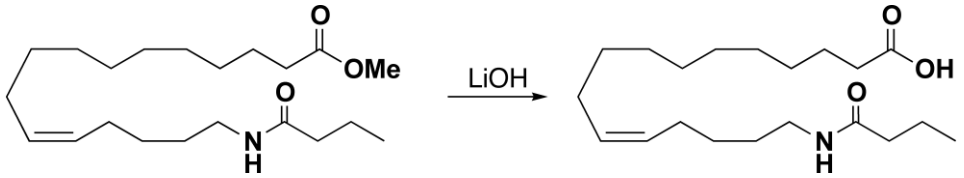
Ethyl isocyanate (60 mg, 0.85 mmol) was added to a room temperature solution of the above crude methyl 16-aminohexadec-11(*Z*)-enoate (200 mg. 0.71 mmol) in dry THF (20 mL). After 6 h, the reaction mixture was concentrated under reduced pressure and the residue was purified by SiO_2 column chromatography using 30% EtOAc/hexanes as eluent to give methyl 16-(3-ethylureido)hexadec-11(*Z*)-enoate (223 mg, 86%) as a colorless, thick oil identical with an authentic sample.[9] TLC: 50% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 5.23-5.38 (m, 2H), 5.08 (br s, 2H), 3.63 (s, 3H), 3.09-3.20 (m, 4H), 2.27 (t, *J* = 7.1 Hz, 2H), 1.93-2.04 (m, 4H), 1.20-1.62 (m, 18H), 1.08 (t, *J* = 7.3 Hz, 3H).



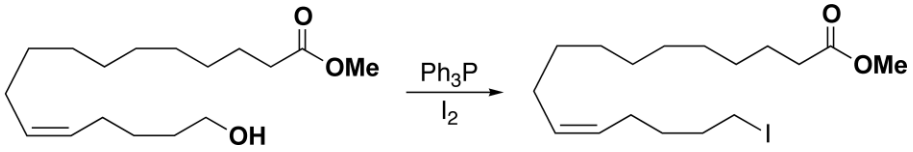
16-(3-Ethylureido)hexadec-11(*Z*)-enoic acid (19).[9] Methyl 16-(3-ethylureido)hexadec-11(*Z*)-enoate was hydrolyzed as described above to give 16-(3-ethylureido)hexadec-11(*Z*)-enoic acid (**19**) (82%) as a white powder, mp 83.1-83.3 °C, identical with an authentic sample.[9] TLC: SiO_2, 75% EtOAc/hexanes, $R_f \approx 0.3$; ^{1}H NMR (300 MHz) δ 5.26-5.42 (m, 2H), 4.89 (br s, 1H), 3.06-3.24 (m, 4H), 2.32 (t, *J* = 7.1 Hz, 2H), 1.97-2.08 (m, 4H), 1.22-1.64 (m, 18H), 1.14 (t, *J* = 7.3 Hz, 3H).



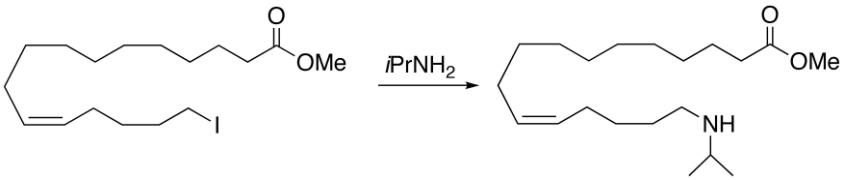
Methyl 16-(butyrylamino)hexadec-11(*Z*)-enoate. Butyric acid (100 mg, 1.10 mmol), 1-hydroxybenzotriazole (145 mg, 1.10 mmol; HOBt) and diisopropylethylamine (150 mg, 1.10 mmol; DIPEA) were added to a stirring solution of the previously described crude methyl 16-aminohexadec-11(*Z*)-enoate (240 mg, 0.85 mmol) in anhydrous DMF (20 mL) under an argon atmosphere. After 5 min, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (210 mg, 1.10 mmol; EDCI) was added as a solid. After stirring for 12 h at room temperature, the reaction mixture was diluted with EtOAc (30 mL), washed with water (30 mL), and brine (20 mL). The combined aqueous layers were back-extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried over Na_2SO_4, concentrated under reduced pressure, and the residue was purified by SiO_2 column chromatography using 30% EtOAc/hexanes as eluent to give methyl 16-(butyrylamino)hexadec-11(*Z*)-enoate (246 mg, 82%) as a viscous oil. TLC: 50% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (300 MHz) δ 5.58 (br s, 1H), 5.26-5.40 (m, 2H), 3.65 (s, 3H), 3.19-3.26 (m, 2H), 2.25-2.31 (m, 2H), 2.12 (t, *J* = 7.1 Hz, 2H), 1.95-2.08 (m, 4H), 1.22-1.66 (m, 18H), 0.92 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz) δ 174.61, 173.26, 130.71, 129.31, 51.67, 39.60, 38.99, 34.32, 29.90, 29.66, 29.60, 29.50, 29.45, 29.34, 27.43, 27.21, 27.01, 25.15, 19.46, 13.98.



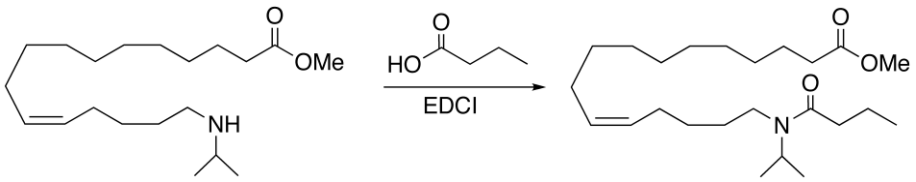
16-(Butyrylamino)hexadec-11(*Z*)-enoic acid (25). Methyl 16-(butyrylamino)hexadec-11(*Z*)-enoate was hydrolyzed as described above to give 16-(butyrylamino)hexadec-11(*Z*)-enoic acid **(25)** (88%) as a white solid, mp 99.2-99.6 °C. TLC: 75% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (CD_3OD, 300 MHz) δ 5.28-5.41 (m, 2H), 3.15 (t, 2H, *J* = 7.3 Hz), 2.01-2.21 (m, 8H), 1.22-1.64 (m, 20H), 0.93 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (75 MHz) δ 174.89, 130.10, 129.17, 39.07, 37.88, 29.67, 29.55, 29.49, 29.20, 28.89, 27.00, 26.95, 26.66, 26.52, 22.96, 19.31, 12.85. HRMS calcd for $C_{20}H_{38}NO_3$ $[M+1]^+$ 340.2852, found 340.2849.



Methyl 16-Iodohexadec-11(*Z*)-enoate. Triphenylphosphine (730 mg, 2.78 mmol) and imidazole (190 mg, 2.78 mmol) were added to a 0 °C solution of methyl 16-hydroxyhexadec-11(*Z*)-enoate (660 mg, 2.32 mmol) in dry THF (50 mL) under an argon atmosphere. After 10 min, solid iodine (700 mg, 1.2 equiv) was added portionwise. After stirring at room temperature for 3 h, the reaction mixture was quenched with sat. aq. sodium bisulfite solution (10 mL). After an additional 1 h, the solution was washed with water (2 × 30 mL), concentrated under reduced pressure, and the residue was purified by flash column chromatography using 10% EtOAc/hexanes as eluent to give methyl 16-iodohexadec-11(*Z*)-enoate (505 mg, 76%) that was used immediately in the next step. TLC: 10% EtOAc/hexanes, $R_f \approx 0.55$; ^{1}H NMR (300 MHz) δ 5.28-5.42 (m, 2H), 3.66 (s, 3H), 3.18 (t, *J* = 7.0 Hz, 2H), 2.30 (t, *J* = 7.6 Hz, 2H), 1.98-2.08 (m, 4H), 1.24-1.85 (m, 18H).

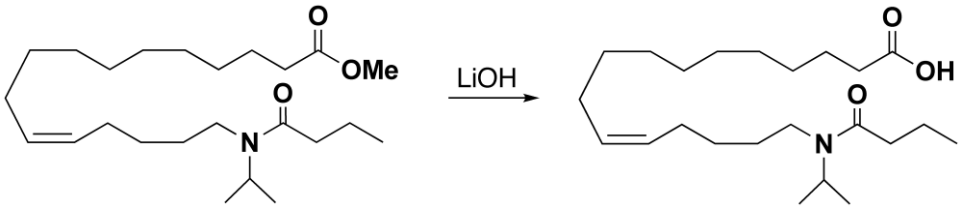


Methyl 16-(N-isopropylamino)hexadec-11(*Z*)-enoate. Isopropylamine (220 mg, 3.8 mmol) was added to a solution of methyl 16-iodohexadec-11(*Z*)-enoate (300 mg, 0.76 mmol) from above and potassium carbonate (320 mg) in THF (20 mL) under an argon atmosphere in a sealed tube. After heating at 90 °C for 10 h, the reaction mixture was cooled to room temperature, diluted with EtOAc (50 mL), washed with water (20 mL), dried, and concentrated under high vacuum for 5 h. The crude methyl 16-(N-isopropylamino)hexadec-11(*Z*)-enoate was used in the next reaction without further purification. TLC: 20% MeOH/CH_2Cl_2, $R_f \approx 0.20$; ^{1}H NMR (300 MHz) δ 5.28-5.40 (m, 2H), 3.66 (s, 3H), 2.72-2.84 (m, 1H), 2.58 (t, *J* = 7.2 Hz, 2H), 2.29 (t, *J* = 7.6 Hz, 2H), 1.98-2.08 (m, 4H), 1.22-1.62 (m, 18H), 1.05 (d, 6H, *J* = 6.4 Hz); ^{13}C NMR (100 MHz) δ 22.9, 25.2, 27,4, 27.5, 29.0, 29.1, 29.3, 29.6, 29.7, 29.8, 29.9, 32.0, 33.3, 47.7, 52.4, 54.5, 131.0, 131.5, 171.9. HRMS calcd for $C_{20}H_{40}NO_2$ $[M+1]^+$ 326.3059, found 326.3054.

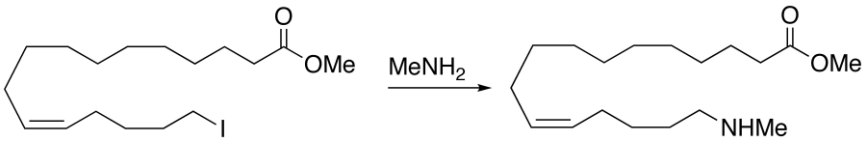


Methyl 16-(N-isopropylbutyramido)hexadec-11(*Z*)-enoate. Methyl 16-(N-isopropylamino)hexadec-11(*Z*)-enoate (400 mg, 1.2 mmol) was acylated with *n*-butyric acid (130 mg, 1.47 mmol) as described above to give methyl 16-(N-isopropylbutyramido)hexadec-11(*Z*)-

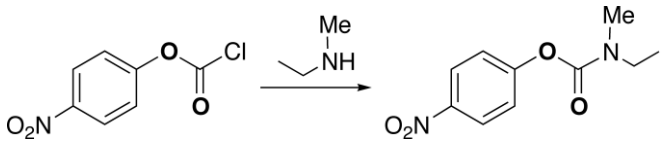
enoate (348 mg, 74%). TLC: 50% EtOAc/hexanes, $R_f \approx 0.30$; ^{1}H NMR (300 MHz, 60/40 ratio of amide rotamers) δ 5.28-5.42 (m, 2H), 4.61-4.67 and 3.99-4.10 (m, 1H for two rotamers), 3.66 (s, 3H), 3.06-3.16 (m, 2H), 2.21-2.36 (m, 4H), 1.95-2.10 (m, 4H), 1.20-1.72 (m, 20H), 1.17 and 1.12 (d, *J* = 6.6 Hz, 3H for two rotamers), 0.96 and 0.95 (t, 3H, *J* = 7.3 Hz for two rotamers).



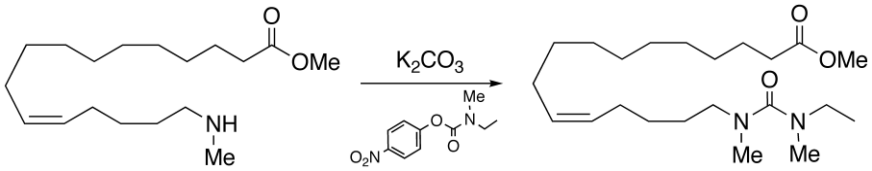
16-(N-isopropylbutyramido)hexadec-11(*Z*)-enoic acid (24). Methyl 16-(N-isopropylbutyramido)hexadec-11(*Z*)-enoate (320 mg, 0.81 mmol) was hydrolyzed as described above to give 16-(N-isopropylbutyramido)hexadec-11(*Z*)-enoic acid (**24**) (254 mg, 83%) as a thick, colorless oil. TLC: 75% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz, 60/40 ratio of amide rotamers) δ 5.26-5.41 (m, 2H), 4.63-4.69 and 4.00-4.10 (m, 1H for two rotamers), 3.06-3.17 (m, 2H), 2.22-2.37 (m, 4H), 1.98-2.12 (m, 4H), 1.50-1.72 (m, 4H), 1.22-1.40 (m, 16H), 1.18 and 1.12 (d, *J* = 7.0 Hz, 6H for two rotamers), 0.96 and 0.95 (t, *J* = 7.3 Hz, 3H for two rotamers); ^{13}C NMR (75 MHz, 60/40 ratio of rotamers) δ 179.07, 178.95, 173.42, 172.89, 131.03, 130.35, 129.70, 128.99, 48.51, 45.70, 43.58, 41.22, 35.98, 35.83, 34.37, 31.20, 29.90, 29.86, 29.67, 29.61, 29.53, 29.48, 29.39, 28.37, 29.28, 27.84, 27.50, 27.46, 27.35, 27.19, 26.90, 25.00, 21.54, 20.75, 19.35, 19.22, 14.23; HRMS calcd for $C_{23}H_{43}NO_3$ $[M]^+$ 381.3243, found 381.3245.



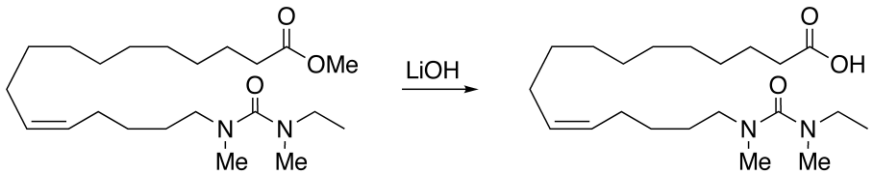
Methyl 16-(methylamino)hexadec-11(*Z*)-enoate. Methylamine (1 mL of a 1.0 M THF soln, 33 mg) was added to a solution of methyl 16-iodohexadec-11(*Z*)-enoate (300 mg, 0.76 mmol) from above and potassium carbonate (320 mg, 2.28 mmol, 3 equiv) in THF (20 mL) under an argon atmosphere in a sealed tube. After heating at 90 °C for 12 h, the reaction mixture was cooled to room temperature, diluted with EtOAc (50 mL), washed with water (20 mL), dried, and concentrated under high vacuum for 5 h. The crude methyl 16-(methylamino)hexadec-11(*Z*)-enoate was used in the next reaction without further purification. TLC: 10% MeOH/CH_2Cl_2, $R_f \approx 0.2$; ^{1}H NMR (300 MHz) δ 5.28-5.40 (m, 2H), 3.66 (s, 3H), 2.56 (t, *J* = 6.8 Hz, 2H), 2.42 (s, 3H), 2.29 (t, *J* = 7.6 Hz, 2H), 1.96-2.06 (m, 4H), 1.24-1.64 (m, 18H).



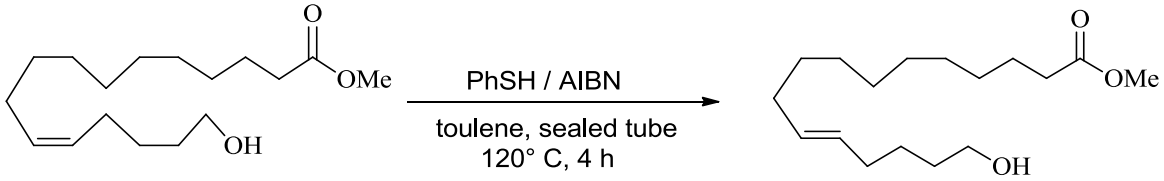
4-Nitrophenyl ethyl(methyl)carbamate.[10] Triethylamine (12.84 g, 127.11 mmol) and *p*-nitrophenyl chloroformate (63.56 mmol, 12.8 g) were added to a room temperature solution of N-ethylmethylamine (2.50 g, 42.37 mmol) in dry DMF (70 mL) under an argon atmosphere. After 2 h, the reaction mixture was quenched with water, diluted with EtOAc (200 mL), washed with water (2 × 100 mL), and brine (75 mL). All volatiles were removed under reduced pressure and the residue was purified by SiO_2 column chromatography using 10% EtOAc/hexanes to afford 4-nitrophenyl ethyl(methyl)carbamate[10] (5.8 g, 76%) as a pale yellow oil. TLC: 20% EtOAc/hexanes, $R_f \approx 0.50$; ^{1}H NMR (300 MHz) δ 8.18-8.21 (m, 2H), 7.25-7.29 (m, 2H), 3.37-3.46 (m, 2H), 3.05 and 2.97 (s, 3H for two rotamers in 60/40 ratio), 1.17-1.22 (m, 3H).



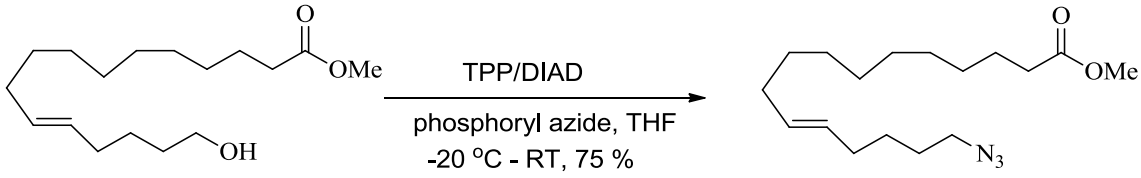
Methyl 16-(3-ethyl-1,3-dimethylureido)hexadec-11(*Z*)-enoate. A solution of crude methyl 16-(methylamino)hexadec-11(*Z*)-enoate from above (150 mg, 0.51 mmol) in anhydrous acetonitrile (20 mL) was added to a mixture of 4-nitrophenyl ethyl(methyl)carbamate (161 mg, 0.72 mmol) and K_2CO_3 (230 mg, 1.5 mmol.) in dry acetonitrile (20 mL) at room temperature. After heating under reflux for 36 h, the solvent was removed under reduced pressure, the residue was diluted with water (30 mL), and then extracted into EtOAc (2 × 30 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography using 15% EtOAc/hexanes as eluent to afford methyl 16-(3-ethyl-1,3-dimethylureido)hexadec-11(*Z*)-enoate (65 mg, 34%) as a colorless oil. TLC: 40% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 5.27-5.40 (m, 2H), 3.66 (s, 3H), 3.10-3.18 (m, 4H), 2.77 (s, 3H), 2.75 (s, 3H), 2.29 (t, *J* = 7.2 Hz, 2H), 1.97-2.05 (m, 4H), 1.50-1.68 (m, 4H), 1.20-1.42 (m, 14H), 1.12 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz) δ 177.61, 165.73, 130.51, 129.56, 51.47, 49.18, 48.35 45.28, 37.83, 36.43, 34.15, 29.64, 29.63, 28.69, 28.38, 27.33, 26.58, 24.89, 22.34, 12.24



16-(3-Ethyl-1,3-dimethylureido)hexadec-11(*Z*)-enoic acid (20). Methyl 16-(3-ethyl-1,3-dimethylureido)hexadec-11(*Z*)-enoate (30 mg, 0.08 mmol) was hydrolyzed as described above to give 16-(3-ethyl-1,3-dimethylureido)hexadec-11(*Z*)-enoic acid (**20**) (15 mg, 75%) as a colorless oil. TLC: 50% EtOAc/hexanes, $R_f \approx 0.30$; ^{1}H NMR (400 MHz) δ 5.33-5.41 (m, 2H), 3.12-3.19 (m, 4H), 2.79 (s, 3H), 2.76 (s, 3H), 2.31-2.38 (m, 2H), 1.98-2.06 (m, 4H), 1.20-1.68 (m, 18H), 1.13 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz) δ 177.52, 166.83, 130.61, 129.56, 51.58, 45.38, 37.91, 36.93, 34.12, 29.74, 29.67, 28.72, 28.42, 27.43, 26.68, 24.99, 22.64, 15.34. HRMS calcd for $C_{21}H_{41}N_2O_3$ $[M+1]^+$ 369.3117, found 369.3119.

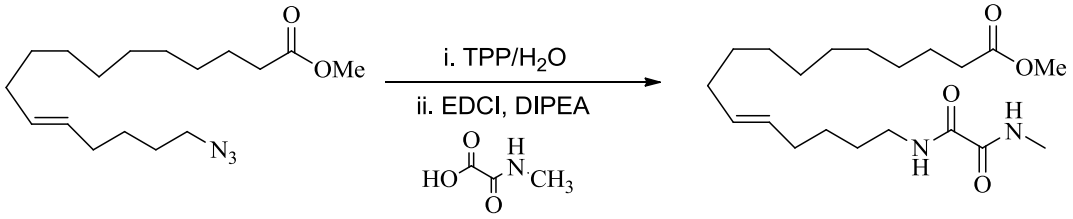


Methyl 16-hydroxyhexadec-11(*E*)-enoate. AIBN (60 mg, 0.35 mmol) was added to a warm (40 °C) solution of methyl 16-hydroxyhexadec-11(*Z*)-enoate (250 mg, 0.8 mmol) and thiophenol (50 mg, 0.44 mmol) in dry benzene (10 mL) and then heated to 90 °C. After 4 h, the reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography using 10% EtOAc/hexanes as eluent to afford methyl 16-hydroxyhexadec-11(*E*)-enoate (88%) as a thick oil. TLC: 40% EtOAc/hexane, $R_f \approx 0.4$ (SiO_2); ^{1}H NMR (300 MHz) δ 5.21-5.32 (m, 2H), 3.55 (s, 3H), 3.49 (t, *J* = 7.3 Hz, 2H), 2.77 (br s, 1H), 2.19 (t, *J* = 7.05 Hz, 2H), 1.82-1.96 (m, 4H), 1.18-1.57 (m, 18H); ^{13}C NMR (75 MHz) δ 174.45, 130.80, 130.04, 62.59, 51.56, 34.19, 32.70, 32.46, 32.30, 29.84, 29.71, 29.55, 29.54, 29.37, 29.25, 27.33, 27.09, 26.06, 25.90, 25.06. HRMS calcd for $C_{17}H_{32}O_3$ $[M+1]^+$ 285.2430, found 285.2434.



Methyl 16-azidohexadec-11(*E*)-enoate. Methyl 16-hydroxyhexadec-11(*E*)-enoate (350 mg, 1.23 mmol) was converted into its azide as described above to give methyl 16-azidohexadec-11(*E*)-enoate (298 mg, 78%) obtained as a thick, colorless oil. TLC: 6% EtOAc/hexanes, $R_f \approx 0.6$; ^{1}H

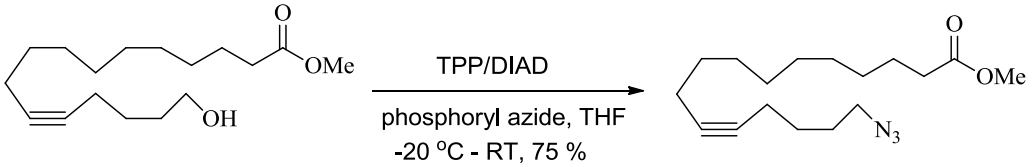
NMR (300 MHz) δ 5.27-5.44 (m, 2H), 3.64 (s, 3H), 3.24 (t, *J* = 7.0 Hz 2H), 2.28 (t, *J* = 7.15 Hz, 2H), 1.91-2.08 (m, 4H), 1.54-1.63 (m, 4H), 1.21-1.42 (m, 14H); ^{13}C NMR (75 MHz) δ 174.58, 131.28, 129.71, 51.70, 51.56, 34.32, 32.68, 32.22, 29.54, 29.21, 29.08, 28.95, 28.47, 27.42, 26.81, 25.13. HRMS calcd for $C_{17}H_{32}N_3O_2$ $[M+1]^+$ 310.2495, found 310.2494.



Methyl 16-(2-(methylamino)-2-oxoacetamido)hexadec-11(*E*)-enoate. Methyl 16-azidohexadec-11(*E*)-enoate (180 mg, 0.64 mmol) was converted into its free amine as described above and, without purification, condensed with 2-(methylamino)-2-oxoacetic acid as previously described to give methyl 16-(2-(methylamino)-2-oxoacetamido)hexadec-11(*E*)-enoate (68% over two steps) as a white powder, mp 86.2-2-88.4 °C. TLC: 50% EtOAc/hexane, $R_f \approx 0.3$ (SiO_2); ^{1}H NMR (300 MHz) δ 7.48 (br s, 1H), 5.27-5.44 (m, 2H), 3.66 (s, 3H), 3.27-3.34 (m, 2H), 2.90 (d, 3H, *J* = 5.2 Hz), 2.29 (t, 2H, *J* = 7.3 Hz), 1.92-2.04 (m, 4H), 1.22-1.64 (m, 18H); ^{13}C NMR (75 MHz) δ 174.60, 160.81, 159.94, 130.87, 129.08, 51.68, 39.79, 34.33, 29.91, 29.68, 29.63, 29.50, 29.46, 29.36, 29.02, 27.46, 27.08, 26.91, 26.40, 25.17.

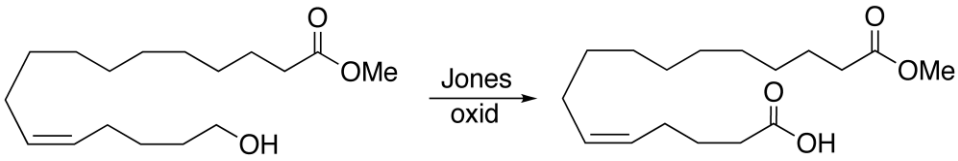
16-(2-(Methylamino)-2-oxoacetamido)hexadec-11(*E*)-enoic acid (22). Hydrolysis of methyl 16-(2-(methylamino)-2-oxoacetamido)hexadec-11(*E*)-enoate using LiOH as described above afforded 16-(2-(methylamino)-2-oxoacetamido)hexadec-11(*E*)-enoic acid (**22**) (92%) as a colorless oil. ^{1}H NMR (300 MHz) δ 7.40 (br s, 1H), 5.25-5.50 (m, 2H), 3.26-3.38 (m, 2H), 2.95 (d, 3H, *J* = 5.2 Hz), 2.29 (t, 2H, *J* = 7.3 Hz), 1.92-2.04 (m, 4H), 1.22-1.64 (m, 18H); ^{13}C NMR (75 MHz) δ 174.58, 160.71, 159.98, 130.76, 129.12, 39.80, 34.39, 29.93, 29.73, 29.56, 29.50, 29.47, 29.36, 29.07, 27.55, 27.12, 26.90, 26.41, 25.20. HRMS calcd for $C_{19}H_{34}N_2O_4$ $[M+1]^+$ 354.2519, found 354.2519.

Synthesis of Methyl 16-(2-(methylamino)-2-oxoacetamido)hexadec-11-ynoate (23)

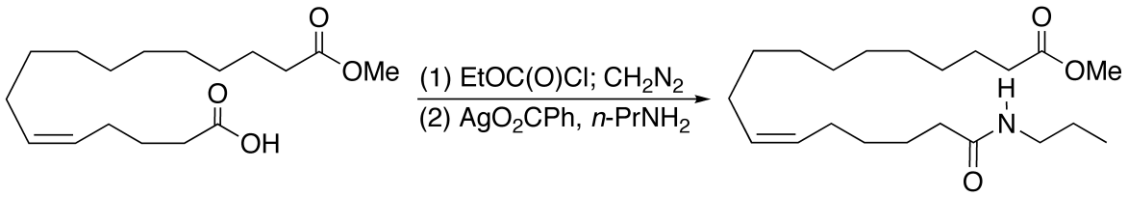


16-(2-(Methylamino)-2-oxoacetamido)hexadec-11-ynoic acid. Methyl 16-hydroxyhexadec-11-ynoate was converted into its azide as described above to give methyl 16-azidohexadec-11-ynoate

(75%) as a colorless oil. TLC: 10% EtOAc/hexane, $R_f \approx 0.45$ (SiO_2); ^{1}H NMR (300 MHz) δ 3.66 (s, 3H), 3.29 (t, *J* = 7.0 Hz, 2H), 2.30 (t, *J* = 7.15 Hz, 2H), 1.97-2.23 (m, 4H), 1.22-1.76 (m, 18H); ^{13}C NMR (75 MHz) δ 174.44, 80.98, 79.99, 51.64, 51.22, 34.20, 29.78, 29.00, 28.83, 28.63, 28.13, 27.46, 26.29, 25.02, 18.83, 18.51. HRMS calcd for $C_{17}H_{30}N_3O_2$ $[M+1]^+$ 308.2338, found 308.2342. XXX



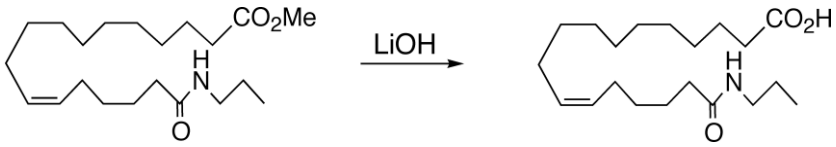
16-Methoxy-16-oxohexadec-5(*Z*)-enoic acid. Jones oxidation of methyl 16-hydroxyhexadec-11(*Z*)-enoate (2.0 g, 7.04 mmol) as described above gave 16-methoxy-16-oxohexadec-5(*Z*)-enoic acid (1.72 g, 83%) as a colorless oil. TLC: 40% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 5.27-5.45 (m, 2H), 3.66 (s, 3H), 2.36 (t, 2H, *J* = 7.7 Hz), 2.30 (t, 2H, *J* = 7.4 Hz), 1.98-2.12 (m, 4H), 1.57-1.72 (m, 4H), 1.20-1.41 (m, 12H); ^{13}C NMR (75 MHz) δ 24.68, 25.45, 26.88, 27.75, 29.13, 29.72, 29.80, 29.90, 30.21, 33.48, 34.01, 51.76, 128.90, 130.22, 178.93, 178.98. HRMS calcd for $C_{17}H_{31}O_4$ $[M+1]^+$ 299.2222, found 200.2223.



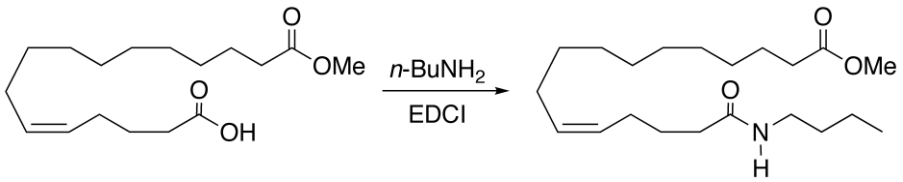
16-Methoxy-16-oxohexadec-5(*Z*)-enoic acid. Triethylamine (122 mg, 1.18 mmol) and ethyl chloroformate (130 mg, 1.13 mmol) were added to a –15 °C solution of 16-methoxy-16-oxohexadec-5(*Z*)-enoic acid (300 mg, 1.06 mmol) in dry THF (50 mL) under an argon atmosphere. After 15 min, the reaction mixture was warmed to –5 °C and an ethereal solution of diazomethane was added slowly until the yellow color of diazomethane persisted for 15 min. Afterwards, the reaction mixture was stirred at room temperature for an additional 3 h, then the excess diazomethane was evaporated under a stream of argon. The reaction solution was washed with sat. aq. $NaHCO_3$ (50 mL), sat. aq. NH_4Cl (50 mL), brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was rapidly purified by SiO_2 column chromatography using 20% EtOAc/hexanes as eluent to

give methyl 17-diazo-16-oxoheptadec-11(*Z*)-enoate (180 mg, 55%) as a light yellow oil that was used immediately in the next step.[11] TLC: 40% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (C_6D_6, 300 MHz) δ 5.25-5.48 (m, 2H), 4.13 (s, 1H), 3.32 (s, 3H), 2.07 (t, 2H, *J* = 7.4 Hz), 1.85-2.04 (m, 6H), 1.44-1.61 (m, 4H), 1.15-1.38 (m, 12H).

A solution of silver benzoate (5 mg, 10 mol %) in triethylamine (68 mg, 100 μL, 0.66 mmol) was added to a –25 °C solution of methyl 17-diazo-16-oxoheptadec-11(*Z*)-enoate (70 mg, 0.22 mmol) and *n*-propylamine (40 mg, 10 equiv) in dry THF (20 mL) under an argon atmosphere with exclusion of light.[11] The reaction mixture was warmed to room temperature over 3 h, diluted with ether (10 mL), quenched with 0.2 N HCl (5 mL), washed with brine (30 mL), sat. aq. $NaHCO_3$ (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography using 20% EtOAc/hexanes as eluent to give methyl 17-oxo-17-(*n*-propylamino)heptadec-11(*Z*)-enoate (49 mg, 64%). TLC: 30% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 5.47 (br s, 1H), 5.27-5.40 (m, 2H), 3.66 (s, 3H), 3.17-3.24 (m, 2H), 2.29 (t, 2H, *J* = 7.1 Hz), 2.16 (t, 2H, *J* = 7.1 Hz), 1.96-2.07 (m, 4H), 1.24-1.67 (m, 20H), 0.91 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (75 MHz) δ 174.62, 173.22, 130.59, 129.41, 51.68, 41.40, 37.05, 34.33, 29.93, 29.67, 29.63, 29.48, 29.36, 27.44, 27.16, 25.73, 25.17, 23.14, 11.60.

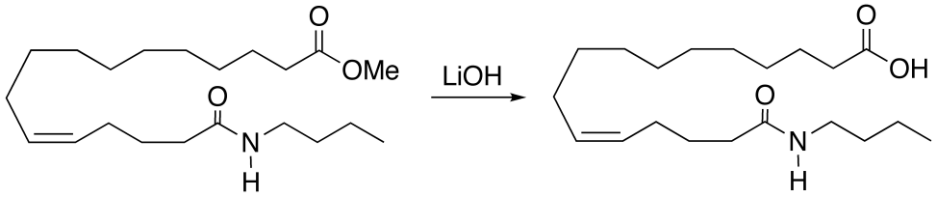


17-Oxo-17-(*n*-propylamino)heptadec-11(*Z*)-enoate (26). Methyl 17-oxo-17-(*n*-propylamino)heptadec-11(*Z*)-enoate (48 mg, 0.14 mmol) was hydrolyzed as described above to give 17-oxo-17-(*n*-propylamino)heptadec-11(*Z*)-enoate (**26**) as a white solid, mp 84.8-85.2 °C. TLC: 75% EtOAc/hexanes, $R_f \approx 0.30$; ^{1}H NMR of sodium salt (CD_3OD, 300 MHz) δ 5.30-5.42 (m, 2H), 3.16 (t, 2H, *J* = 7.0 Hz), 2.00-2.22 (m, 8H), 1.22-1.68 (m, 20H), 0.93 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR of sodium salt (CD_3OD, 75 MHz) δ 180.33, 174.88, 130.08, 129.22, 39.07, 37.88, 36.80, 29.70, 29.53, 29.49, 29.45, 29.21, 28.90, 27.02, 26.96, 26.68, 26.12, 19.32, 12.88. HRMS calcd for $C_{20}H_{38}NO_3$ $[M+1]^+$ 340.2852, found 340.2851.



Methyl 16-(*n*-butylamino)-16-oxohexadec-11(Z)-enoate. 16-Methoxy-16-oxohexadec-5(*Z*)-enoic acid (230 mg, 0.77 mmol) was condensed with *n*-butylamine (70 mg, 1.08 mmol) using EDCI

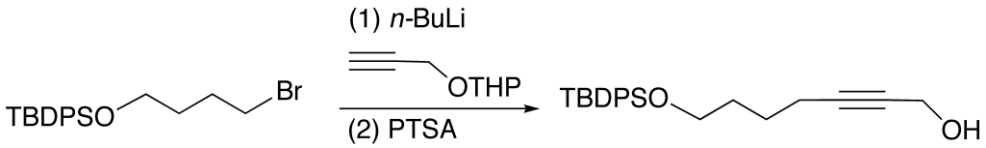
as described to give methyl 16-(*n*-butylamino)-16-oxohexadec-11(*Z*)-enoate (185 mg, 68%) as a colorless oil. TLC: 50% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 5.26-5.42 (m, 2H), 3.66 (s, 3H), 3.21-3.29 (m, 2H), 2.30 (t, 2H, *J* = 7.2 Hz), 2.16 (t, 2H, *J* = 7.1 Hz), 1.97-2.08 (m, 4H), 1.55-1.74 (m, 4H), 1.24-1.54 (m, 14H), 0.92 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (75 MHz) δ 174.60, 173.1, 131.18, 128.83, 51.67, 39.42, 36.44, 34.32, 31.98, 29.91, 29.66, 29.60, 29.49, 29.45, 29.34, 27.47, 26.87, 25.95, 25.15, 20.30, 13.98.



16-(*n*-Butylamino)-16-oxohexadec-11(*Z*)-enoic acid (27). Methyl 16-(*n*-butylamino)-16-oxohexadec-11(*Z*)-enoate (150 mg, 0.44 mmol) was hydrolyzed to give 16-(*n*-butylamino)-16-oxohexadec-11(*Z*)-enoic acid (**27**) (114 mg, 82%) as a white solid, mp 78.2-78.8 °C. TLC: 75% EtOAc/hexanes, $R_f \approx 0.3$; ^{1}H NMR (300 MHz) δ 5.81 (br s, 1H), 5.24-5.40 (m, 2H), 3.18-3.24 (m, 2H), 2.30 (t, 2H, *J* = 7.3 Hz), 2.16 (t, 2H, *J* = 7.2 Hz), 1.93-2.06 (m, 4H), 1.19-1.70 (m, 20H), 0.88 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (75 MHz) δ 178.98, 173.78, 131.19, 128.74, 39.54, 36.36, 34.37, 31.84, 29.84, 29.56, 29.53, 29.40, 29.38, 29.22, 27.42, 26.85, 25.99, 24.98, 20.26, 13.96. HRMS calcd for $C_{20}H_{38}NO_3$ $[M+1]^+$ 340.2852, found 340.2850.

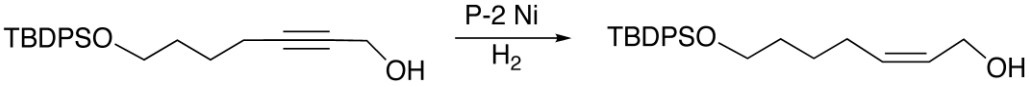
Chiral HPLC of Methyl 16-[(*Z*)-3-Ethyloxiranyl]hexadec-11(*Z*)-enoate (37). Chromatography of methyl 16-[(*Z*)-3-ethyloxiranyl]hexadec-11(*Z*)-enoate (**37**) using a Chiralcel® OJ-H column (250 × 4.6 mm) with hexane/*i*PrOH (99.7:0.3) at a flow rate of 1 mL/min, uv detection at 195 nm, furnished the *R*,*S*-enantiomer (R_t = 15.17 min) and *S*,*R*-enantiomer (R_t = 17.68 min). Preparative separation: Chiralcel® OJ-H column (250 × 20 mm) using hexane/*i*PrOH (99.5:0.5) at a flow rate of 8 mL/min, uv detection at 195 nm, injecting 7 mg/100 µL in mobile phase. The stereochemistry of the enantiomers was confirmed by spectral and chromatographic comparisons with an authentic sample of the *S*,*R*-enantiomer whose preparation is described below. Saponification of the methyl esters as described above afforded **13** and **14**, respectively.

Synthesis of 16-[(1*S*,2*R*)-3-ethyloxiranyl]hexadec-11(*Z*)-enoate (14)

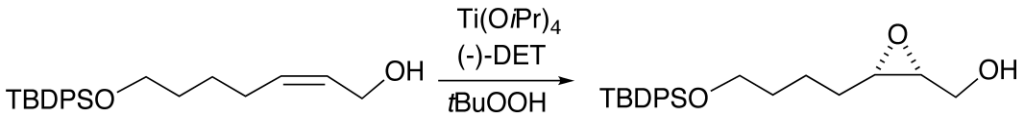


***tert*-Butyldiphenyl(7-(tetrahydro-2*H*-pyran-2-yloxy)hept-5-ynyloxy)silane.** 2-(Prop-2-ynyloxy)tetrahydro-2*H*-pyran (5.6 g, 36.36 mmol) was alkylated with (4-bromobutoxy)(*tert*-butyl)diphenylsilane (18.5 g, 47.2 mmol) as described above to give *tert*-butyldiphenyl(7-(tetrahydro-2*H*-pyran-2-yloxy)hept-5-ynyloxy)silane[12] (10.64 g, 65%) that was used after extractive isolation without further purification. TLC: 10% EtOAc/hexanes, $R_f \approx 0.5$.

7-(*tert*-Butyldiphenylsilyloxy)hept-2-yn-1-ol.[12] Removal of the THP ether from *tert*-butyldiphenyl(7-(tetrahydro-2*H*-pyran-2-yloxy)hept-5-ynyloxy)silane (10 g, 22.22 mmol) as described above furnished 7-(*tert*-butyldiphenylsilyloxy)hept-2-yn-1-ol[12] (7.15 g, 88%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 7.65-7.67 (m, 4H), 7.33-7.42 (m, 6H), 4.22-4.26 (m, 2H), 3.64 (t, 2H, *J* = 6.4 Hz), 2.12-2.16 (m, 2H), 1.40-1.46 (m, 4H), 1.03 (s, 9H).

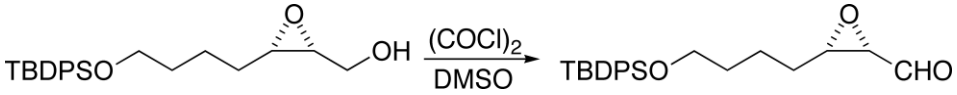


7-(*tert*-Butyldiphenylsilyloxy)hept-2(*Z*)-en-1-ol.[13] Semi-hydrogenation of 7-(*tert*-butyldiphenylsilyloxy)hept-2-yn-1-ol (7.4 g, 20.22 mmol) as described above furnished 7-(*tert*-butyldiphenylsilyloxy)hept-2(*Z*)-en-1-ol[13] (7.3 g, 98%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (400 MHz) δ 7.65-7.69 (m, 4H), 7.40-7.44 (m, 6H), 5.44-5.64 (m, 2H), 4.16 (d, 2H, *J* = 6.1 Hz), 3.65 (t, 2H, *J* = 6.1 Hz), 2.03-2.10 (m, 2H), 1.42-1.60 (m, 4H), 1.04 (s, 9H).

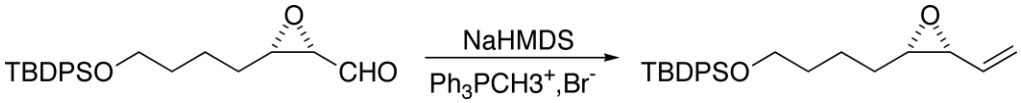


((2*R*,3*S*)-3-(4-(*tert*-Butyldiphenylsilyloxy)butyl)oxiran-2-yl)methanol.[14] (-)-Diethyl tartrate (570 mg, DET) and titanium tetra(isopropoxide) (775 mg) were added sequentially to a stirring, -20 °C suspension of activated, powdered type 4Å molecular sieves (2 g) in dry CH_2Cl_2 (50 mL) under an argon atmosphere. After 30 min, a solution of 7-(*tert*-butyldiphenylsilyloxy)hept-2(*Z*)-en-1-ol (5 g, 13.58 mmol) in dry CH_2Cl_2 (20 mL) was added slowly and the resulting mixture was stirred for 2 h at the same temperature. A solution of *tert*-butyl hydroperoxide (2.5 g, 5.1 mL of a 5.5 M solution in decane; TBHP) was added very slowly. After stirring at – 20 °C for 2 d, water (2 mL) was added

and the mixture was allowed to stir at 0°C for 1 h. A solution of 1 M aq. NaOH (5 mL) was added and stirred for 30 min. The reaction mixture was then washed with water (100 mL) and concentrated under reduced pressure. Purification of the residue by SiO_2 column chromotography using 10% EtOAc/hexanes as eluent gave ((2*R*,3*S*)-3-(4-(*tert*-butyldiphenylsilyloxy)butyl)oxiran-2-yl)methanol[14] (3.23 g, 62%) as a colorless oil. Chiral HPLC analysis as described above revealed the sample was 60% ee. TLC: 30% EtOAc/hexanes, $R_f \approx 0.4$; ^{1}H NMR (400 MHz) δ 7.64-7.68 (m, 4H), 7.35-7.44 (m, 6H), 3.79-3.88 (m, 1H), 3.61-3.69 (m, 3H), 3.12-3.17 (m, 1H), 2.98-3.04 (m, 1H), 1.53-1.65 (m, 4H), 1.03 (s, 9H).

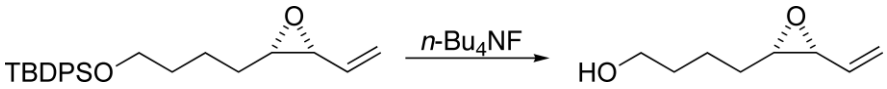


(2*S*,3*S*)-3-[4-(*tert*-Butyldiphenylsilanyloxy)-butyl]-oxirane-2-carbaldehyde. Dry DMSO (114 mg, 0.4 mmol) was added dropwise to a stirring, –80 °C solution of oxalyl chloride (110 mg, 0.3 mmol) in dry CH_2Cl_2 (10 mL) under an argon atmosphere. After 20 min, a solution of ((2*R*,3*S*)-3-(4-(*tert*-butyldiphenylsilyloxy)butyl)oxiran-2-yl)methanol (200 mg, 0.1 mmol) in dry CH_2Cl_2 (50 mL) was added slowly. After 45 min, triethylamine (200 mg, 0.5 mmol) was added and the reaction mixture was warmed to 0 °C. After 0.5 h, the reaction mixture was quenched with water (50 mL). The aqueous layer was separated and back-extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water, brine, and dried over anhydrous Na_2SO_4, and evaporated *in vacuo*. The residue was purified via SiO_2 column chromatography using 5% EtOAc/hexanes to give (2*S*,3*S*)-3-[4-(*tert*-butyldiphenylsilanyloxy)-butyl]-oxirane-2-carbaldehyde. The crude aldehyde was used for the next reaction without further purification.

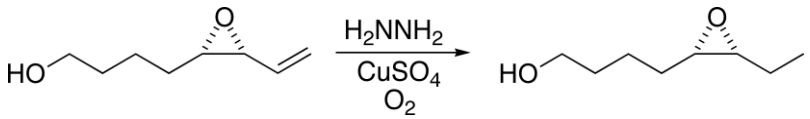


(3*R*,4*S*)-*tert*-Butyldiphenyl-[4-(3-vinyl-oxiranyl)-butoxy]-silane. Sodium bis(trimethylsilyl)amide (2.4 g, 13.08 mmol, 13.1 mL of a 1.0 M soln in THF) was added to a stirring, 0 °C solution of methyl triphenylphosphonium bromide (4.68 g, 13.08 mmol) in dry THF (10 mL). After 30 min, the reaction mixture was cooled to –50 °C and a solution of (2*S*,3*S*)-3-[4-(*tert*-butyldiphenylsilanyloxy)-butyl]-oxirane-2-carbaldehyde (2.5 g, 6.55 mmol) in THF (10 mL) was added over 5 min. The solution was warmed to room temperature over 1 h. After an additional 2

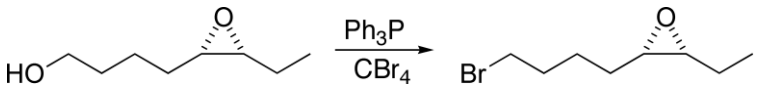
h at room temperature, the reaction mixture was quenched with water (30 mL) and extracted with ether (3 × 60 mL). The combined ethereal extracts were washed with water (2 × 100 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography using 5% EtOAc/hexanes to give (3*R*,4*S*)-*tert*-butyldiphenyl-[4-(3-vinyl-oxiranyl)-butoxy]-silane (1.84 g, 76%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.4$; ^{1}H NMR (400 MHz) δ 7.65-7.69 (m, 4H), 7.35-7.44 (m, 6H), 5.64-5.76 (m, 1H), 5.32-5.50 (m, 2H), 3.67 (t, 2H, *J* = 7.1 Hz), 3.38-3.42 (m, 1H), 3.02-3.11 (m, 1H), 1.44-1.68 (m, 4H), 1.05 (s, 9H); ^{13}C NMR (100 MHz) δ 24.63, 27.69, 32.01, 32.28, 32.38, 61.11, 62.34, 64.42, 120.23, 129.78, 130.25, 130.76, 132.71, 135.20. HRMS calcd for $C_{24}H_{33}O_2Si$ $[M+1]^+$ 381.2250, found 381.2250.



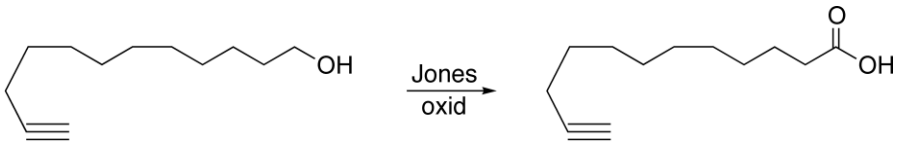
(3*R*,4*S*)-4-(3-Vinyl-oxiranyl)-butan-1-ol.[15] Desilylation of (3*R*,4*S*)-*tert*-butyldiphenyl-[4-(3-vinyl-oxiranyl)-butoxy]silane as described above gave (3*R*,4*S*)-4-(3-vinyl-oxiranyl)-butan-1-ol[15] (92%) as a colorless oil. TLC: 40% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (400 MHz) δ 5.65-5.77 (m, 1H), 5.33-5.50 (m, 2H), 3.65 (t, 2H, *J* = 6.1 Hz), 3.38-3.43 (m, 1H), 3.06-3.11 (m, 1H), 1.44-1.66 (m, 6H).



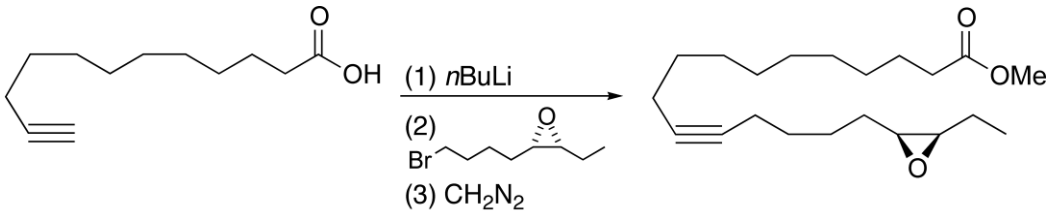
4(*S*)-[3(*R*)-Ethyloxiranyl]butan-1-ol.[15] 4(*S*)-(3(*R*)-Vinyloxiranyl)-butan-1-ol was reduced using diimide generated in situ as described above to give 4(*S*)-[3(*R*)-ethyloxiranyl]butan-1-ol[15] (92%) as a colorless oil. TLC: 40% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (400 MHz) δ 3.66 (t, 2H, *J* = 6.1 Hz), 2.85-2.94 (m, 2H), 1.49-1.65 (m, 8H), 1.03 (t, *J* = 7.2 Hz, 3H).



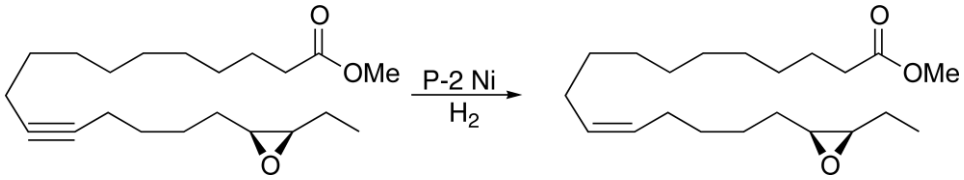
2(*S*)-(4-Bromobutyl)-3(*R*)-ethyloxirane. Treatment of 4(*S*)-[3(*R*)-ethyloxiranyl]butan-1-ol with Ph_3P/CBr_4 as described above gave 2(*S*)-(4-bromobutyl)-3(*R*)-ethyloxirane (64%) as a colorless oil. TLC: 10% EtOAc/hexanes, $R_f \approx 0.7$; ^{1}H NMR (400 MHz) δ 3.52-3.46 (t, 2H, *J* = 6.8 Hz), 2.55-2.48 (m, 2H), 1.82-1.75 (m, 2H), 1.52-1.36 (m, 4H), 1.29-1.20 (m, 2H), 0.89 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (75 MHz) δ 60.6, 60.4, 36.0, 33.4, 28.4, 25.1, 24.1, 13.0. HRMS calcd for $C_8H_{15}BrO$ $[M]^+$ 206.0306, found 206.0306.



Dodec-11-ynoic acid.[9] Jones oxidation of dodec-10-yn-1-ol[9] (2.5 g, 13.73 mmol) as described above afforded dodec-11-ynoic acid[9] (2.3 g, 86%). ^{1}H NMR (400 MHz) δ 2.34 (t, 2H, *J* = 7.0 Hz), 2.14-2.21 (m, 2H), 1.93 (t, 1H, *J* = 2.75 Hz), 1.21-1.64 (m, 22H).

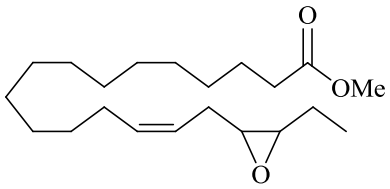


Methyl 16(*S*)-[3(*R*)-ethyloxiranyl]-hexadec-11-ynoate. Alkylation of dodec-11-ynoic acid (580 mg) with 2(*S*)-(4-bromobutyl)-3(*R*)-ethyloxirane (500 mg) as described above furnished 16(*S*)-[3(*R*)-ethyloxiranyl]-hexadec-11-ynoic acid (64%) which was esterified with diazomethane to give methyl 16(*S*)-[3(*R*)-ethyloxiranyl]-hexadec-11-ynoate as a colorless oil. TLC: 10% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (400 MHz) δ 3.66 (s, 3H), 2.82-2.88 (m, 2H), 2.29 (t, 2H, *J* = 7.3 Hz), 2.10-2.17 (m, 4H), 1.28-1.63 (m, 22H), 1.03 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (100 MHz) δ 12.24, 18.90, 19.05, 24.38, 24.75, 24.85, 28.34, 29.02, 29.33, 29.73, 29.85, 29.87, 29.90, 29.98, 33.64, 52.90, 61.42, 61.56, 78.70, 174.51. HRMS calcd for $C_{21}H_{37}O_3$ $[M+1]^+$ 337.2743, found 337.2743.



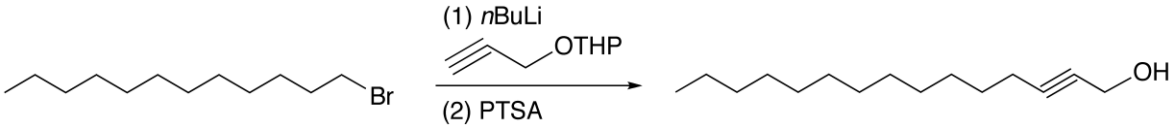
Methyl 16(*S*)-[3(*R*)-ethyloxiranyl]-hexadec-11(*Z*)-enoate. Semi-hydrogenation of methyl 16(*S*)-[3(*R*)-ethyloxiranyl]-hexadec-11-ynoate as described above gave methyl 16(*S*)-[3(*R*)-ethyloxiranyl]-hexadec-11(*Z*)-enoate (96%) as a colorless oil that was identical by NMR and TLC with an authentic racemic sample (methyl ester of **10**) prepared above. This sample was only used to identify the enantiomers obtained via chiral HPLC. Biological testing was conducted with the enantiomerically pure isomers obtained chromatographically as described above. TLC: 10% EtOAc/hexanes, $R_f \approx$

0.55; ^{1}H NMR (400 MHz) δ 5.31-5.36 (m, 2H), 3.64 (s, 3H), 2.84-2.91 (m, 2H), 2.28 (t, 2 H, *J* = 7.3 Hz), 1.96-2.06 (m, 4 H), 1.36-1.61 (m, 6 H), 1.21-1.35 (m, 16H), 1.03 (t, 3H, *J* = 7.3 Hz).



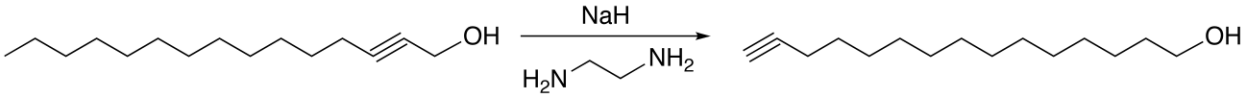
Chiral HPLC of Methyl 16-[(*Z*)-3-Ethyloxiranyl]hexadec-14(*Z*)-enoate (11). Chromatography of methyl 16-[(*Z*)-3-ethyloxiranyl]hexadec-14(*Z*)-enoate (**11**) using a Chiralcel® OJ-H column (250 × 4.6 mm) with hexane/*i*PrOH (99.98:0.02) at a flow rate of 1 mL/min, uv detection at 195 nm, furnished the *S*,*R*-enantiomer (R_t = 22.17 min) and *R*,*S*-enantiomer (R_t = 24.84 min). Preparative separation: Chiralcel® OJ-H column (250 × 20 mm) using hexane/*i*PrOH (99.97:0.03) at a flow rate of 8 mL/min, uv detection at 195 nm, injecting 7 mg/100 µL in mobile phase. The stereochemistry of the enantiomers was confirmed by spectral and chromatographic comparisons with an authentic sample of the *S*,*R*-enantiomer whose preparation is described below.

Synthesis of 16-(3-Ethylureido)hexadec-14(*Z*)-enoic Acid (30)



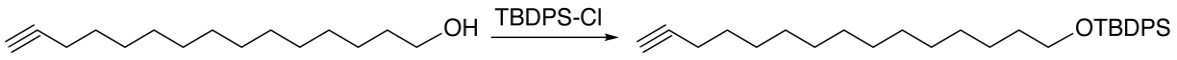
Pentadec-2-yn-1-ol.[16] Alkylation of 2-(prop-2-ynyloxy)tetrahydro-2*H*-pyran (15.5 g, 110.71 mmol) with commercial 1-bromododecane (34.0 g, 132.04 mmol) as described above gave 2-(pentadec-2-ynyloxy)tetrahydro-2*H*-pyran (27.2 g, 80%) which was used without further purification. TLC: 10% EtOAc/hexanes, $R_f \approx 0.5$.

Cleavage of the THP ether from crude 2-(pentadec-2-ynyloxy)tetrahydro-2*H*-pyran (30 g) using PTSA as described above gave pentadec-2-yn-1-ol[16] (18.6 g, 85%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 4.25 (s, 2H), 2.17-2.23 (m, 2H), 1.70 (br s, 1H), 1.40-1.53 (m, 2H), 1.20-1.48 (m, 18H), 0.87 (t, 3H, *J* = 7.3 Hz).

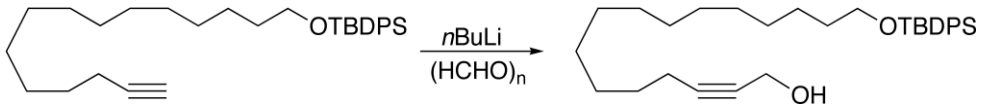


Pentadec-14-yn-1-ol.[17] Isomerization of pentadec-2-yn-1-ol (12.5 g, 54.95 mmol) using NaH/ethylenediamine as described above furnished pentadec-14-yn-1-ol[17] (9.4 g, 76%) as a

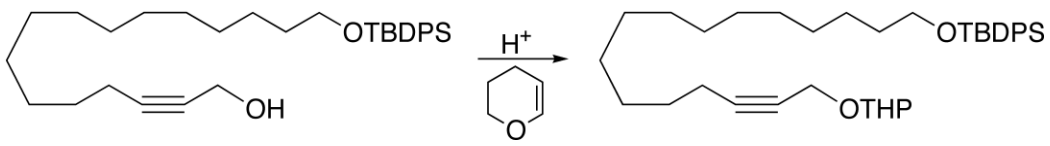
white solid, 54.2-54.8 °C. TLC: 30% EtOAc/hexanes, $R_f \approx 0.45$; ^{1}H NMR (400 MHz) δ 3.60-3.65 (m, 2H), 2.16 (dt, 2H, *J* = 7.1 Hz, 2.4 Hz), 1.92 (t, 1H, *J* = 2.4 Hz), 1.47-1.60 (m, 4H), 1.22-1.35 (m, 18H).



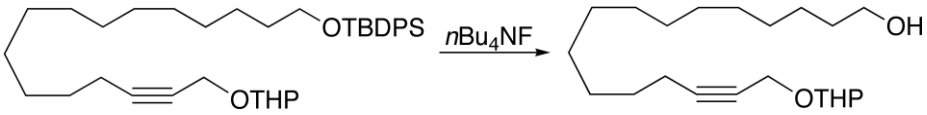
***tert*-Butyl(pentadec-14-ynyloxy)diphenylsilane**. Silylation of pentadec-14-yn-1-ol (8.80 g, 39.28 mmol) using TBDPSCl (12.92 g, 47.14 mmol) as described above gave *tert*-butyl(pentadec-14-ynyloxy)diphenylsilane (16.7 g, 87%) as a colorless oil. TLC: 6% EtOAc/hexanes, $R_f \approx 0.6$; ^{1}H NMR (300 MHz) δ 7.65-7.68 (m, 4H), 7.34-7.42 (m, 6H), 3.65 (t, *J* = 7.3 Hz, 2H), 2.15-2.21 (m, 2H), 1.94 (t, *J* = 1.9 Hz, 1H), 1.20-1.60 (m, 22H), 1.04 (s, 9H); ^{13}C NMR (100 MHz) δ18.86, 24.79, 27,71, 28.26, 28.60, 28.68, 28.91, 29.08, 29.37, 29.39, 29.41, 29.42, 29.44, 30.17, 31.25, 62.63, 66.62, 80.48, 128.84, 129.52, 129.86, 133.61. HRMS calcd for $C_{31}H_{47}OSi$ $[M+1]^+$ 463.3396, found 463.3398.



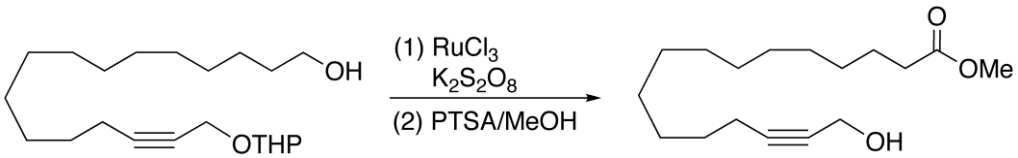
16-(*tert*-Butyldiphenylsilyloxy)hexadec-2-yn-1-ol. *n*-BuLi (2.5 M solution in hexanes, 1.29 g, 8 mL, 20.24 mmol) was added to a stirring, –40 °C solution of *tert*-butyl(pentadec-14-ynyloxy)diphenylsilane (8.5 g, 18.40 mmol) in THF (175 mL) under an argon atmosphere. After 30 min, the reaction mixture was gradually warmed over 3 h to –10 °C, held at this temperature for 20 min, then re-cooled to –50 °C. Then, a solution of paraformaldehyde (3.05 g, 92.2 mmol) in THF (30 mL) was cannulated into the stirring reaction mixture. After 30 min, the temperature was gradually warmed over 3 h to room temperature. Following 1 h at room temperature, the reaction mixture was quenched with sat. aq. NH_4Cl (10 mL), diluted with ether (100 mL), and washed with water (2 × 75 mL). The combined aqueous washes were back-extracted with ether (2 × 50 mL). The combined organic extracts were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography using 5% EtOAc/hexanes as eluent to give 16-(*tert*-butyldiphenylsilyloxy)hexadec-2-yn-1-ol (6.12 g, 68%). TLC: 30% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (300 MHz) δ 7.70-7.74 (m, 4H), 7.34-7.44 (m, 6H), 4.3 (t, 2H, *J* = 2.1 Hz), 3.65 (t, 2H, *J* = 7.3 Hz), 2.12-2.17 (m, 2H), 1.20-1.61 (m, 22H), 1.04 (s, 9H); ^{13}C NMR (100 MHz) δ 18.74, 25.69, 27.60, 27.92, 28.12, 28.23, 28.36, 28.55, 28.59, 28. 61, 28.86, 29.48, 30.97, 34.63, 47.99, 63.85, 77.02, 84.52, 128.30, 129.58, 129.74, 131.31. HRMS calcd for $C_{32}H_{49}O_2Si$ $[M+1]^+$ 493.3502, found 493.3501.



***tert*-Butyldiphenyl(16-(tetrahydro-2*H*-pyran-2-yloxy)hexadec-14-ynyloxy)silane**. 16-(*tert*-Butyldiphenylsilyloxy)hexadec-2-yn-1-ol (6.0 g, 12.5 mmol) was converted to the corresponding THP ether as described above to give *tert*-butyldiphenyl(16-(tetrahydro-2*H*-pyran-2-yloxy)hexadec-14-ynyloxy)silane (6.12 g, 87%). TLC: 10% EtOAc/hexanes, $R_f \approx 0.5$; ^{1}H NMR (300 MHz) δ 7.70-7.73 (m, 4H), 7.35-7.43 (m, 6H), 4.82 (t, 1H, *J* = 3.1 Hz), 4.16-4.32 (m, 2H), 3.80-3.88 (m, 1H), 3.64 (t, 2H, *J* = 6.6 Hz), 3.50-3.56 (m, 1H), 2.17-2.23 (m, 2H), 1.22-1.81 (m, 28H), 1.05 (s, 9H); ^{13}C NMR (100 MHz) δ 18.88, 19.54, 23.47, 24.53, 25.39, 27.41, 28.02, 28.72, 28.74, 28.79, 28.48, 28.75, 29.06, 29.79, 30.03, 31.78, 32.53, 52.91, 62.85, 64.40, 82.34, 84.82, 103,26, 128.92, 129.20, 131.11, 135.68. HRMS calcd for $C_{37}H_{57}O_3Si$ $[M+1]^+$ 577.4077, found 577.4080.



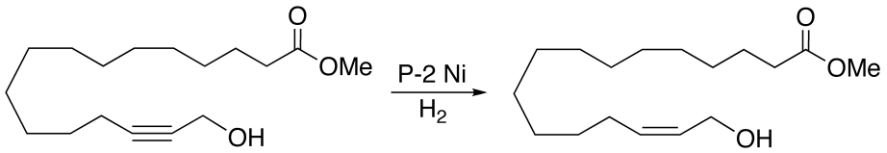
16-(Tetrahydro-2*H*-pyran-2-yloxy)hexadec-14-yn-1-ol. Desilylation of *tert*-butyldiphenyl (16-(tetrahydro-2*H*-pyran-2-yloxy)hexadec-14-ynyloxy)silane (6.1 g, 10.6 mmol) as described above furnished 16-(tetrahydro-2*H*-pyran-2-yloxy)hexadec-14-yn-1-ol (3.26 g, 91%) as a colorless oil. TLC: 40% EtOAc/hexanes, $R_f \approx 0.4$; ^{1}H NMR (300 MHz) δ 4.83 (t, 1H, *J* = 3.0 Hz), 4.17-4.31 (m, 2H), 3.82-3.87 (m, 1H), 3.66 (t, 2H, *J* = 7.2 Hz), 3.51-3.57 (m, 1H), 2.18-2.24 (m, 2H), 1.20-1.82 (m, 28H); ^{13}C NMR (100 MHz) δ 18.26, 19.46, 23.68, 25.78, 28.63, 28.97, 30.41, 30.38, 31.00, 31.06, 31.27, 31.28, 31.38, 32.48, 53.98, 63.21, 63.84, 82.30, 85.51, 106.78. HRMS calcd for $C_{21}H_{39}O_3$ $[M+1]^+$ 339.2899, found 339.2896.



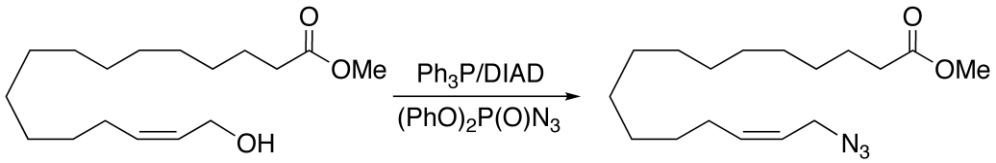
Methyl 16-hydroxyhexadec-14-ynoate. $RuCl_3$ (10 mg) and potassium persulphate (2.8 g, 10.2 mmol) were added to a solution of 16-(tetrahydro-2*H*-pyran-2-yloxy)hexadec-14-yn-1-ol (1.2 g, 3.55 mmol) in acetonitrile (20 mL). After 10 min, KOH (30 mL of a 2 M soln) was added. After an additional 3 h, the reaction mixture was neutralized to pH 7, diluted with EtOAc

(100 mL) and washed with water (3 × 75 mL). The combined aqueous extracts were back-extracted with EtOAc (3 × 75 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography using 20% EtOAc/hexanes as eluent to give 16-(tetrahydro-2*H*-pyran-2-yloxy)hexadec-14-ynoic acid (1.05 g, 91%) as a colorless oil that was used without further purification. TLC: 50% EtOAc/hexanes, $R_f \approx 0.35$.

Concomitant esterification of the carboxylic acid and cleavage of the THP ether in 16-(tetrahydro-2*H*-pyran-2-yloxy)hexadec-14-ynoic acid (1.0 g, 2.84 mmol) as described above furnished methyl 16-hydroxyhexadec-14-ynoate (665 mg, 83%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 4.22-4.26 (m, 2H), 3.66 (s, 3H), 2.29 (t, 2H, *J* = 7.3 Hz), 2.20 (tt, 2H, J = 2.1, 6.8 Hz), 1.21-1.66 (m, 20H); ^{13}C NMR (100 MHz) δ 19.8, 23.5, 27.8, 27.9, 28.4, 28.6, 28.7, 29.0, 29.4, 29.5, 32.3, 51.0, 53.7, 84.6, 85.5, 179.6. HRMS calcd for $C_{17}H_{31}O_3$ $[M+1]^+$ 283.2274, found 283.2274.

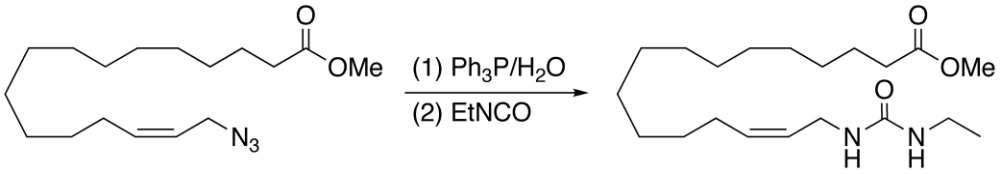


Methyl 16-hydroxyhexadec-14(*Z*)-enoate. Semi-hydrogenation of methyl 16-hydroxyhexadec-14-ynoate (650 mg, 2.30 mmol) as described above furnished methyl 16-hydroxyhexadec-14(*Z*)-enoate (640 mg, 98%) as a colorless oil. TLC: 30% EtOAc/hexanes, $R_f \approx 0.45$; ^{1}H NMR (300 MHz) δ 5.49-5.62 (m, 2H), 4.17-4.21 (m, 2H), 3.66 (s, 3H), 2.30 (t, 2H, *J* = 7.6 Hz), 2.02-2.09 (m, 2H), 1.42-1.68 (m, 4H), 1.20-1.41 (m, 16H); ^{13}C NMR (100 MHz) δ 22.5, 23.7, 24.2, 28.1, 28.2, 28.4, 28.6, 28.7, 29.0, 29.4, 29.5, 32.3, 33.5, 53.7, 132.3, 132.6, 180.6. HRMS calcd for $C_{17}H_{33}O_3$ $[M+1]^+$ 285.2430, found 369.2426.

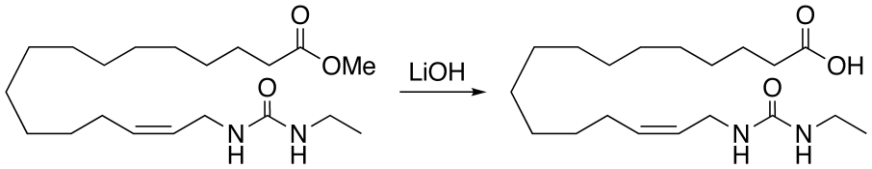


Methyl 16-azidohexadec-14(*Z*)-enoate. Conversion of methyl 16-hydroxyhexadec-14(*Z*)-enoate (0.6 g, 2.11 mmol) to the corresponding azide as described above gave methyl 16-azidohexadec-14(*Z*)-enoate (510 mg, 78%) as white solid, mp 42.5-42.8 °C. TLC: 10% EtOAc/hexanes, $R_f \approx 0.50$; ^{1}H NMR (300 MHz) δ 5.66-5.82 (m, 1H), 5.46-5.55 (m, 1H), 3.80 (d, 2H, *J* = 7.4 Hz), 3.66 (s, 3H), 2.30 (t, 2H, *J* = 7.3 Hz), 2.02-2.14 (m, 2H), 1.21-1.40 (m, 20H); ^{13}C NMR (75 MHz) δ 176.78,

131.68, 130.19, 51.64, 49.54, 36.26, 34.47, 31.64, 29.74, 29.62, 29.53, 29.40, 29.32, 29.21, 27.32, 26.75, 25.89, 21.00. HRMS calcd for $C_{17}H_{32}N_3O_2$ $[M+1]^+$ 310.2495, found 310.2494.

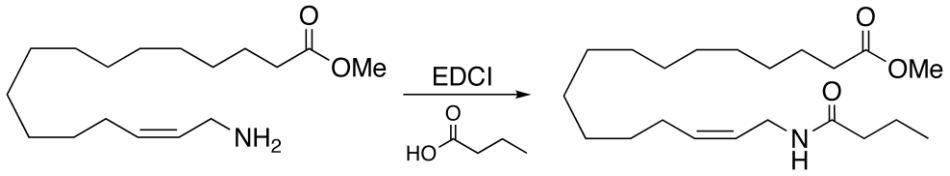


Methyl 16-(3-ethylureido)hexadec-14(*Z*)-enoate. Methyl 16-azidohexadec-14(*Z*)-enoate (150 mg, 0.48 mmol) was reduced using Ph_3P and the resultant crude amine, methyl 16-aminohexadec-14(*Z*)-enoate, was reacted with ethyl isocyanate as described above to give methyl 16-(3-ethylureido)hexadec-14(*Z*)-enoate (118 mg, 70% over two steps) as a white solid, mp 63.4-63.6 °C. TLC: 50% EtOAc/hexanes, $R_f \approx 0.30$; ^{1}H NMR (300 MHz) δ 5.31-5.52 (m, 2H), 5.08-5.22 (br s, 2H), 3.76 (t, 2H, *J* = 5.2 Hz), 3.63 (s, 3H), 3.15 (q, 2H, *J* = 6.7 Hz), 2.27 (t, 2H, *J* = 7.3 Hz), 1.95-2.04 (m, 2H), 1.54-1.64 (m, 2H), 1.18-1.38 (m, 18H), 1.07 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz) δ 174.69, 159.03, 132.91, 126.75, 51.67, 37.67, 35.27, 34.32, 29.81, 29.74, 29.64, 29.50, 29.46, 29.34, 27.57, 25.15, 15.76. HRMS calcd for $C_{20}H_{39}N_2O_3$ $[M+1]^+$ 355.2961, found 355.2961.

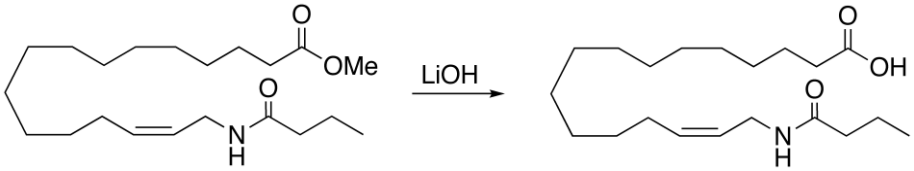


16-(3-Ethylureido)hexadec-14(*Z*)-enoic acid (30). Hydrolysis of methyl 16-(3-ethylureido)hexadec-14(*Z*)-enoate as described above furnished 16-(3-ethylureido)hexadec-14(*Z*)-enoic acid (**30**) (92%) as a white solid, mp 59-60 °C. TLC: 75% EtOAc/hexanes, $R_f \approx 0.30$; ^{1}H NMR (CD_3OD, 300 MHz) δ 5.33-5.56 (m, 2H), 3.74 (d, 2H, *J* = 6.3 Hz), 3.13 (q, 2H, *J* = 7.0 Hz), 2.26 (t, 2H, *J* = 7.2 Hz), 1.98-2.12 (m, 2H), 1.52-1.64 (m, 2H), 1.18-1.38 (m, 18H), 1.06 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (CD_3OD, 75 MHz) δ 176.69, 159.94, 132.31, 126.57, 36.98, 34.70, 33.96, 29.63, 29.61, 29.54, 29.50, 29.34, 29.26, 29.15, 27.20, 24.98, 14.52. HRMS calcd for $C_{19}H_{37}N_2O_3$ $[M+1]^+$ 341.2804, found 341.2805.

Synthesis of 16-butyramidohexadec-14(*Z*)-enoic acid (28)

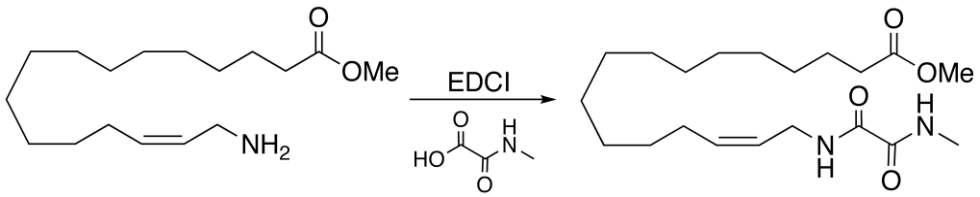


Methyl 16-butyramidohexadec-14(*Z*)-enoate. Crude methyl 16-aminohexadec-14(*Z*)-enoate (crude 150 mg) was condensed with *n*-butyric acid (48 mg, 0.55 mmol) as described above to give methyl 16-butyramidohexadec-14(*Z*)-enoate (100 mg, 71%) as a colorless oil. TLC: 50% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 5.28-5.64 (m, 2H), 3.78-3.90 (m, 2H), 3.65 (s, 3H), 2.30 (t, 2H, *J* = 7.2 Hz), 2.14 (t, 2H, *J* = 7.6 Hz), 1.97-2.08 (m, 2H), 1.54-1.65 (m, 4H), 1.20-1.38 (m, 18H), 0.93 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (75 MHz) δ 174.62, 173.18, 134.12, 125.84, 51.67, 41.65, 38.94, 38.88, 36.82, 34.32, 32.45, 29.79, 29.72, 29.65, 29.46, 29.36, 27.58, 25.16, 19.40, 13.99. HRMS calcd for $C_{21}H_{40}NO_3$ $[M+1]^+$ 354.3008, found 354.3005.



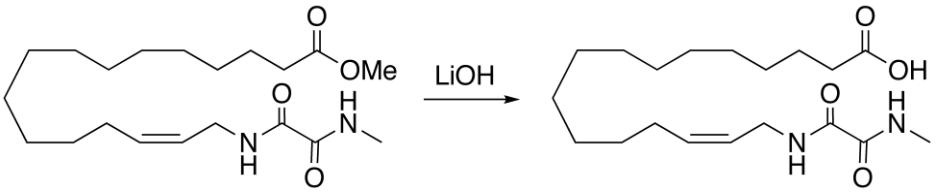
16-Butyramidohexadec-14(*Z*)-enoic acid (28). Hydrolysis of methyl 16-butyramidohexadec-14(*Z*)-enoate (96 mg, 0.27 mmol) as described above gave 16-butyramidohexadec-14(*Z*)-enoic acid (**28**) (82 mg, 91%) as a white solid, mp 72.7-73.1 °C. TLC: 75% EtOAc/hexanes, $R_f \approx 0.40$; ^{1}H NMR (300 MHz) δ 5.28-5.70 (m, 4H), 3.76-3.90 (m, 2H), 2.31 (t, 2H, *J* = 7.4 Hz), 2.15 (t, 2H, *J* = 6.9 Hz), 1.97-2.18 (m, 2H), 1.56-1.68 (m, 4H), 1.20-1.40 (m, 18H), 0.92 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (75 MHz) δ 179.27, 173.58, 134.23, 125.66, 41.75, 38.86, 38.80, 36.91, 34.37, 32.44, 29.76, 29.70, 29.66, 29.62, 29.44, 29.37, 29.29, 24.98, 19.42, 13.98. HRMS calcd for $C_{20}H_{38}NO_3$ $[M+1]^+$ 340.2852, found 340.2852.

Synthesis of 16-(2-(Methylamino)-2-oxoacetamido)hexadec-14(*Z*)-enoic acid (29)



Methyl 16-(2-(methylamino)-2-oxoacetamido)hexadec-14(*Z*)-enoate. Condensation of methyl 16-aminohexadec-14(*Z*)-enoate (crude 140 mg) with 2-(methylamino)-2-oxoacetic acid (54 mg, 0.52 mmol) as described above gave methyl 16-(2-(methylamino)-2-

oxoacetamido)hexadec-14(*Z*)-enoate (92 mg, 72%) as a white solid, mp 104.5-104.8 °C. TLC: 75% EtOAc/hexanes, $R_f \approx 0.40$. ^{1}H NMR (300 MHz) δ 7.80 (br s, 2H), 5.32-5.71 (m, 2H), 3.82-3.96 (m, 2H), 3.62 (s, 3H), 2.82 (s, 3H), 2.28 (t, 3H, *J* = 7.1 Hz), 1.93-2.08 (m, 2H), 1.56-1.64 (m, 2H), 1.22-1.36 (m, 18H); ^{13}C NMR (100 MHz) δ 182.00, 163.75, 160.10, 134.21, 124.53, 52.3, 41.33, 36.33, 34.14, 32.20, 29.62, 29.48, 29.32, 29.17, 29.15, 27.30, 27.36, 25.12. HRMS calcd for $C_{20}H_{37}N_2O_4$ $[M+1]^+$ 369.2753, found 369.2754.



16-(2-(Methylamino)-2-oxoacetamido)hexadec-14(*Z*)-enoic acid (29). Hydrolysis of methyl 16-(2-(methylamino)-2-oxoacetamido)hexadec-14(*Z*)-enoate (75 mg, 0.20 mmol) as described above gave 16-(2-(methylamino)-2-oxoacetamido)hexadec-14(*Z*)-enoic acid (**29**) (63 mg, 88%) as a white solid, mp 118.9-119.3 °C. TLC: 100% EtOAc, $R_f \approx 0.30$; ^{1}H NMR (300 MHz) δ 5.12-5.47 (m, 2H), 3.58-3.72 (m, 2H), 2.66 (s, 3H), 2.05 (t, 3H, *J* = 7.2 Hz), 1.76-1.86 (m, 2H), 0.99-1.41 (m, 20H); ^{13}C NMR (75 MHz) δ 182.04, 163.77, 160.03, 134.06, 124.53, 41.28, 36.54, 34.11, 32.22, 29.62, 29.50, 29.35, 29.17, 29.08, 27.33, 27.56, 25.03. HRMS calcd for $C_{19}H_{35}N_2O_4$ $[M+1]^+$ 355.2597, found 355.2599.

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