

Supporting Information

Synthesis of haloacetate derivatives of methyl vernolate (IVa and IVb) and of vernonia oil (Va and Vb). Since, as mentioned above, vernolic acid constitutes about 70% of the fatty acids of vernonia oil, thus conferring an average of 2.1 epoxy functionalities per molecule, all calculations for the reactions of vernonia oil were performed on the basis of this content.

9-Octadecenoic, 13 [(chloroacetyl) oxy]-12-hydroxy-, methyl ester (IVa, X=Cl):

A mixture containing 3.1 g, (0.01 mol) of methyl vernolate **III** and 1.23 g, (0.013 mol) of chloroacetic acid was dissolved in 15 ml of toluene. The mixture was heated for 14 hours at 90°C. The course of the reaction was monitored by TLC. At the end of the reaction, the reaction mixture was dissolved in diethyl ether and washed 3-4 times with water. The organic layer was separated, dried and the solvent was evaporated off under reduced pressure to yield 3.6 (90%) of a crude product containing 0.25% epoxy groups. The crude product was purified by silica gel column chromatography, using n-hexane and diethyl ether (1:1 v/v) as the eluent to give 2.83g (70%) of **IVa**.

IR (neat, cm^{-1}): 3450 (OH), 1280, and 1300 (chloroacetate), 780 (C-Cl).

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ ppm: 0.88 (CH_3), 1.3 ($(\text{CH}_2)_7$),

1.63 ($\text{CH}_3\text{-O-CO-CH}_2\text{-CH}_2\text{-}$), 1.99 ($\text{-CH}_3\text{-CH}_2\text{-}$), 2.27 ($\text{CH}_3\text{-O-CO-CH}_2\text{-}$), 3.48 (CH-OH), 3.67 ($\text{CH}_3\text{-O-CO-}$), 4.04-4.09 ($\text{CH}_2\text{-Cl}$), 4.8-4.95 ($\text{-CH-O-CO-CH}_2\text{-Cl}$), 5.33-5.53 (CH=CH)

$^{13}\text{C NMR}$ (500 MHz, CDCl_3) δ ppm: 14.03 (CH_3), 29.1 (CH_2)_n, 33.66 and 34.12 ($\text{CH}_3\text{O-CO-CH}_2\text{-}$), 41.04 ($\text{CH}_2\text{-Cl}$), 51.53 (CH_3OCO), 71.87 and 71.98

(-CH-OH), 78.29($\text{-CH-O-CO-CH}_2\text{Cl}$), 123.33-124.01 and 133.71-133.96

(-CH=CH-), 167.09 and 167.24 ($\text{-CHO-CO-CH}_2\text{Cl}$), 174.41 ($\text{CH}_3\text{O-CO-CH}_2$)

Elemental analysis: Calcd. for $\text{C}_{21}\text{H}_{37}\text{O}_5\text{Cl}$ (M.W.=404.5): Cl 8.78. Found: 8.34

9-Octadecenoic, 13 [(bromoacetyl) oxy]-12-hydroxy-, methyl ester (IVb, X=Br)

Compound **IVb** was prepared in the same way as compound **IVa** with 3.1 g, (0.01 mol) of methyl vernolate **III** and 1.80 g, (0.013 mol) of bromoacetic acid. The crude product 3.8 g (85%) contained 0.2% epoxy group and was purified by silica gel column chromatography, using n-hexane and diethyl ether (1:1 v/v) as eluent, to give 3.1 g (70%) of **IVb**

IR (neat, cm⁻¹): 3450 (OH), 1280 (bromo acetate),

¹H-NMR (500 MHz, CDCl₃), δ ppm: 0.87 (CH₃), 1.3 (CH₂)₇, 1.63 (CH₃-O-CO-CH₂-CH₂-), 2.02 (CH₃-CH₂-), 2.28 (CH₃-O-CO-CH₂-), 3.65 (CH₃-O-CO-), 3.67 (CH-OH), 3.82--3.87 (CH₂-Br), 4.85-4.91 (CH-O-CO-CH₂-Br), 5.29 - 5.57 (CH=CH)

¹³C-NMR (500 MHz, CDCl₃) δ ppm: 13.99 (CH₃), 25.26 (CH₂-Br), 29.07 (CH₂)_n, 34.07 (CH₃O-CO-CH₂-), 51.48 (CH₃OCO), 71.88 and 72.03 (CH-OH), 78.12 (-CH-O-CO-CH₂Br), 122.29-124.05 and 133.62-133.86 (CH=CH), 166.94 and 167.13 (CHO-CO-CH₂Br) 174.36 (CH₃O-CO-CH₂)

Elemental analysis. Calcd. for C₂₁H₃₇O₅Br (M.W. = 449): Br 17.81. Found: Br 17.70.

9-Octadecenoic, 13 [(chloroacetyl) oxy]-12-hydroxy-, 1,2,3-propanetriyl ester (Va, X=Cl)

A mixture of 13.23 g of vernonia oil **I** (70% of vernolic acid by GC, 0.01mol) and 3.69 g chloroacetic acid (0.039 mol) was dissolved in 50 ml toluene and the solution was heated at 90°C for 22 hours. The course of the reaction was monitored by TLC. After cooling to room temperature, diethyl ether was added and the reaction mixture was washed twice with a 5% sodium bicarbonate solution, and with water (4 times).

The organic layer was separated off, dried over sodium sulfate. and the solvent was removed under reduced pressure to yield 14.20 g (85% yield) of the derivative **Va**

IR (neat, cm⁻¹): 3450 (OH), 1280 and 1300 (chloroacetate group), and 780 (C-Cl);

¹H-NMR (500 MHz, CDCl₃) δ ppm: 0.78 (CH₃), 3.59 (-CH-OH), 3.94-4.03 (CH₂-Cl), 4.07 and 4.20 (-CH₂-OCO), 4.80-4.86 (-CH-O-CO-CH₂Cl), 5.17 (-OCO-CH₂-CH-OCO-), 5.24-5.47 (-CH=CH-)

¹³C-NMR (500 MHz, CDCl₃) δ ppm 13.90 (CH₃) 40.90(CH₂-Cl), 62.02 (CH-CH₂-OCO), 68.82 (-OCO-CH₂-CH-O-CO-), 71.86 and 72.19 (-CH-OH), 78.16 (-CH-OCOCH₂-Cl), 123.27-133.65 (-CH=CH-), 166.94 and 167.09 (-CH-O-CO-CH₂Cl), 172.76 and 173.18 (-CO-O-CH₂-CH) and (-OCO-CH₂-CH-O-CO).

Elemental Analysis: Calcd. for the crude product, which contains about 70% of the derivative C₆₃H₁₀₇O₁₅Cl₃ (M.W. = 1209.5): Cl 6.16. Found: 5.63.

9-Octadecenoic, 13 [(bromoacetyl) oxy]-12-hydroxy-, 1,2,3-propanetriyl ester (Vb, X=Br)

Vb was prepared by the same method as described above for the trichloroderivative **Va**. A solution of 13.23 g of vernonia oil **I** (70% of vernolic acid by GC, 0.01mol) and 5.42 g (0.039 mol) of bromoacetic acid in 40 ml toluene was heated at 90°C for 24 hours. After cooling to room temperature, diethyl ether was added and the reaction mixture was washed twice with a 5% solution of sodium bicarbonate, and then several times with water. After phase separation, the organic layer was dried over sodium sulfate and the solvent was removed under reduced pressure to yield 15.3 g (85% yield) of **Vb**. The product contained 0.2 % of epoxy groups.

IR (neat, cm⁻¹): 3450 (OH), 1280 (bromoacetate).

$^1\text{H-NMR}$ (500 MHz, CDCl_3), δ ppm: 0.86 (CH_3), 3.60 (CH-OH) 3.81-3.90 ($\text{CH}_2\text{-Br}$), 4.07 and 4.21 ($\text{CH}_2\text{-O-CO}$), 4.84-4.91 ($\text{CH-O-CO-CH}_2\text{Br}$), 5.17 ($\text{OCOCH}_2\text{-CH-OCO}$), 5.24 -5.51 (CH=CH).

$^{13}\text{C-NMR}$ (500 MHz, CDCl_3), δ ppm: 13.94 (CH_3), 25.86 ($\text{CH}_2\text{-Br}$), 62.02 ($\text{CH-CH}_2\text{-O-CO}$), 68.81 ($\text{O-CO-CH}_2\text{-CH-O-CO}$), 71.76 and 71.94 (CH-OH), 78.03 ($\text{CH-O-CO-CH}_2\text{Br}$), 123.28-133.62 (CH=CH), 167.01 and 167.06 ($\text{CH-O-CO-CH}_2\text{Br}$), 172.78 and 173.20 ($\text{CO-O-CH}_2\text{CH}$) and ($\text{OCOCH}_2\text{CH-O-CO}$)

Elemental analysis: Calcd. for the crude product, which contains about 70% of the derivative $\text{C}_{63}\text{H}_{107}\text{O}_{15}\text{Br}_3$ (MW=1343): Br 12.50 Found: 12.70.

Synthesis of the quaternary ammonium salts (VI and VII) based on the haloacetate derivatives of methyl vernolate and of vernonia oil.

1-Dodecanaminium, N-[2-[(2-hydroxy-13-methoxy-13-oxo-1-pentyl-4-tridecenyloxy]-2oxoethyl]-N,N-dimethyl, chloride (VIa X=Cl)

A mixture of **IVa** (90% purity 0.81 g, 0.002 mol) and *N,N*-dimethyldodecylamine (0.43 g, 0.002 mol) in 5 ml of acetone was refluxed for 3 hours. The solvent was removed under reduced pressure to give 1.20 g (95%) of the quaternary ammonium salt as a viscous product. Purification by silica gel column chromatography of the crude product with chloroform:methanol 9:1 (v/v) as the eluent yielded 0.5g (50 %) yield of compound **VIa**. The amount of the chloride anion was determined by argentometric titration.

IR (neat, cm^{-1}): 3350 (OH), 1740 (carboxylic ester group), 1240, and 1200 (C-O-C);

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ ppm: 0.85 (CH_3), 3.48-3.50 ($\text{N}^+(\text{CH}_3)_2$); 3.57 (CH-OH), 3.60 ($\text{CH}_3\text{-O}$), 3.63-3.73 ($-\text{N}^+(\text{CH}_3)_2\text{-CH}_2\text{-CH}_2-$), 4.55-4.71 ($\text{CO-CH}_2\text{-N}^+(\text{CH}_3)_2$), 4.88-4.96 ($-\text{CH-O-CO}$); 5.44-5.52 ($\text{CO-CH}_2\text{-N}^+(\text{CH}_3)_2$ and CH=CH)

^{13}C -NMR (500 MHz, CDCl_3) δ ppm: 14.03 (CH_3), 51.39 and 51.55 ($\text{N}^+(\text{CH}_3)_2$), 51.99 (CH_3O) 61.52 ($\text{O}-\text{CO}-\text{CH}_2-\text{N}^+(\text{CH}_3)_2$), 64.66 ($\text{N}^+(\text{CH}_3)_2\text{CH}_2-\text{CH}_2$), 71.34 and 71.68 ($\text{CH}-\text{OH}$); 79.76 and 79.84 ($\text{CH}-\text{O}-\text{CO}$), 123.46, 124.67 and 132.06, 133.19 ($\text{CH}=\text{CH}$ -), 164.71 and 164.89 ($\text{O}-\text{CO}-\text{CH}_2-\text{N}^+(\text{CH}_3)_2$); 174.26 ($\text{CH}_3-\text{O}-\text{CO}$).

Elemental analysis: Calcd. for $\text{C}_{35}\text{H}_{68}\text{NO}_5\text{Cl}$ (MW=618): N 2.27, Cl 5.74.

Found: N 2.2% and Cl 5.72) ESI-MS m/z [617-Cl]=582

The quaternization reaction for the preparation of **VIa** was performed in a similar way using *iso*-propyl alcohol as the solvent at the reflux temperature for about 3h.

1-Dodecanaminium, N-[2-[(2-hydroxy-13-methoxy-13-oxo-1-pentyl-4-tridecenyl)oxy]-2oxoethyl]-N,N-dimethyl, bromide (VIb X = Br)

Compound **IVb** (90%purity 0.9g, 0.002 mol) and *N,N*-dimethyldodecylamine (0.43g, 0.002 mol) in 5 ml acetone were refluxed for 2 h. The solvent was removed under reduced pressure to give 1.20 g (90%) of the crude quaternary compound. Purification by silica gel column chromatography of this crude product with chloroform=methanol 9:1 (v/v) as the eluent allowed to obtain 0.79 g (60%) of product **VIb**.

IR (neat, cm^{-1}): 3380, 1740 (ester group), 1235 and 1200.

^1H -NMR (500 MHz, CDCl_3), δ ppm: 0.88 (CH_3), 3.52-3.54 [$\text{N}^+(\text{CH}_3)_2$]; 3.62 ($\text{CH}-\text{OH}$), 3.65 (CH_3-O), 3.72-3.74 [$\text{N}^+(\text{CH}_3)_2-\text{CH}_2-\text{CH}_2$], 4.56-4.71 ($\text{CO}-\text{CH}_2-\text{N}^+(\text{CH}_3)_2$) 4.92-4.96 ($-\text{CH}-\text{O}-\text{CO}$), 5.45-5.54($\text{CO}-\text{CH}_2-\text{N}(\text{CH}_3)_2$) and ($\text{CH}=\text{CH}$).

^{13}C -NMR (500 MHz, CDCl_3), δ ppm: 14.07 (CH_3), 51.42 and 51.93 [$\text{N}^+(\text{CH}_3)_2$]; 51.24 (CH_3-O), 61.74 ($-\text{CO}-\text{CH}_2-\text{N}^+(\text{CH}_3)_2-$); 65.11 ($\text{N}^+(\text{CH}_3)_2-\text{CH}_2-\text{CH}_2$), 71.51 and 72.74 ($\text{CH}-\text{OH}$), 79.75 and 79.87 ($-\text{CH}-\text{O}-\text{CO}-\text{CH}_2$), 123.19, 124.3 and 132.06, 133.17 ($\text{CH}=\text{CH}$), 164.78 and 164.88 ($\text{O}-\text{CO}-\text{CH}_2-\text{N}^+(\text{CH}_3)_2$), 174.21 ($\text{CH}_3\text{O}-\text{CO}$).

Elemental analysis. Calcd. for $C_{35}H_{68}NO_5Br$ (M.W = 662): N 2.11%, Br 12.07%. Found: N 2.09%, Br 12.03% ESI-MS m/z [662-Br]=582

Propane-1,2,3-tri[octadec-9-en-12(13)-hydroxy-13(12)-(oxycarbonyl-N-methylene-N,N-dimethyl-N-dodecylammonium chloride)oate] (VIIa X=Cl)

The crude trichloroacetoxy **Va** (17.3 g, 0.01 mol) and *N, N*-dimethyldodecylamine (6.4 g, 0.03 mol) were refluxed in 35 ml of acetone for 5 hours. The solvent was removed under reduced pressure. The residue was triturated several times with diethyl ether to remove the unreacted DMD and then dried under vacuum at room temperature to give 21.3 g of the product as a viscous oil (90 % yield by argentometric titration).

IR (neat, cm^{-1}): 3300, 1740, 1235, and 1200;

1H -NMR (500 MHz, $CDCl_3$) δ ppm: 0.84 (\underline{CH}_3), 3.43 and 3.45 ($N^+(\underline{CH}_3)_2$), 3.52 ($-\underline{CH}-OH$), 3.66 ($-(N^+(CH_3)_2)-\underline{CH}_2-\underline{CH}_2-$), 4.07 and 4.22 ($\underline{CH}_2-O-CO-$), 4.25 ($OCO-\underline{CH}_2-N^+(CH_3)_2$), 4.83-4.86 ($-\underline{CH}-O-CO-\underline{CH}_2-N^+(CH_3)_2$), 5.20-5.42 ($-(OCO-\underline{CH}_2-\underline{CH}-O-CO, \underline{CH}=\underline{CH}$ and $(OCO-\underline{CH}_2-N^+(CH_3)_2)$

^{13}C -NMR (500 MHz, $CDCl_3$) δ ppm: 13.91 (\underline{CH}_3), 51.29 and 51.64 ($N^+(\underline{CH}_3)_2$), 61.42 ($O-CO-\underline{CH}_2$), 61.86 ($\underline{CH}-\underline{CH}_2-O-CO$), 64.54 ($N^+(CH_3)_2-\underline{CH}_2-\underline{CH}_2$), 68.65 ($O-CO-\underline{CH}_2-\underline{CH}-O-CO-$), 71.20 and 71.67 ($-\underline{CH}-OH$), 79.56 ($\underline{CH}-O-CO-\underline{CH}_2-N^+(CH_3)_2$), 123.01 and 133.14 ($-\underline{CH}=\underline{CH}-$), 164.59 and 164.77 ($\underline{CH}-O-\underline{CO}-\underline{CH}_2-N^+(CH_3)_2$), 172.61 and 173.01 ($-\underline{CO}-O-\underline{CH}_2-\underline{CH}$ and $-\underline{OCO}-\underline{CH}_2-\underline{CH}-O-\underline{CO}-$)

Elemental Analysis: Calcd. for the crude product, which contains about 70% of the derivative $C_{105}H_{200}O_{15}N_3Cl_3$ (M.W.=1849.7): Cl 4.03; N 1.59. Found: Cl 3.9; N 1.53.

Propane-1,2,3-tri[octadec-9-en-12(13)-hydroxy-13(12)-(oxycarbonyl-N-methylene-N,N-dimethyl-N-dodecylammonium bromide)ate] (VIIb X=Br)

The crude tribromoacetate **Vb** (19.18 g, 0.01 mol) and *N,N*-dimethyldodecylamine (6.4 g, 0.03 mol) were refluxed in 40 ml of acetone for 3 hours. After removal of the solvent under reduced pressure the residue was triturated with diethyl ether and dried under vacuum at room temperature to give 23.0 g (90%) of the product **VIIb** that was obtained as a viscous liquid.

IR (neat, cm^{-1}) 3350, 1740 (ester groups), 1235 and 1200 (C-O-C)

$^1\text{H-NMR}$ (500 MHz, CDCl_3 δ ppm: 0.88 (CH_3), 3.43 and 3.46 ($\text{N}^+(\text{CH}_3)_2$), 3.53 (CH-OH), 3.66 ($\text{N}^+(\text{CH}_3)_2\text{-CH}_2\text{-CH}_2$), 4.06 and 4.21 ($\text{CH}_2\text{-O-CO}$), 4.25 ($\text{OC-CH}_2\text{-N}^+(\text{CH}_3)_2$), 4.84-4.86 ($\text{CH-O-CO-CH}_2\text{-N}^+(\text{CH}_3)_2$), 5.20-5.41 [$\text{(OCO-CH}_2\text{-CH-O-CO)}$, (CH=CH) and ($\text{OCO-CH}_2\text{-N(CH}_3)_2$)]

$^{13}\text{C-NMR}$ (500 MHz CDCl_3), δ ppm: 14.04 (CH_3), 51.56 and 51.91 ($\text{N}^+(\text{CH}_3)_2$), 61.40 ($\text{OCO-CH}_2\text{-N(CH}_3)_2$); 62.03 ($\text{CH-CH}_2\text{-O-CO}$), 65.80 ($\text{N}^+(\text{CH}_3)_2\text{-CH}_2\text{-CH}_2$), 68.60 ($\text{O-CO-CH}_2\text{-CH-O-CO}$), 71.46 and 71.78 (CH-OH), 79.6 ($\text{CH-O-CO-CH}_2\text{-N}^+(\text{CH}_3)_2$), 123.34 - 133.31 (CH=CH), 164.6 and 164.5 ($\text{CH-O-CO-CH}_2\text{-N}^+(\text{CH}_3)_2$), 172.75 and 173.12 ($\text{CO-O-CH}_2\text{-CH}$ and ($\text{-O-CO-CH}_2\text{-CH-O-CO}$))

Elemental analysis: Calcd. for the crude product, which contains about 70% of the derivative $\text{C}_{105}\text{H}_{200}\text{O}_{15}\text{N}_3\text{Br}_3$ (M.W. = 1982): Br. 8.47. Found: Br 8.43.