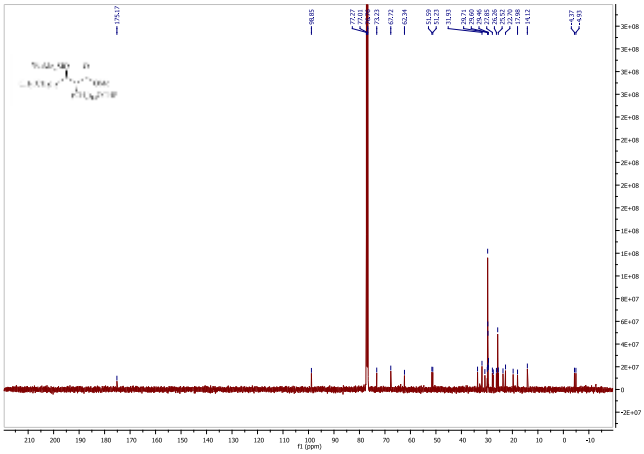
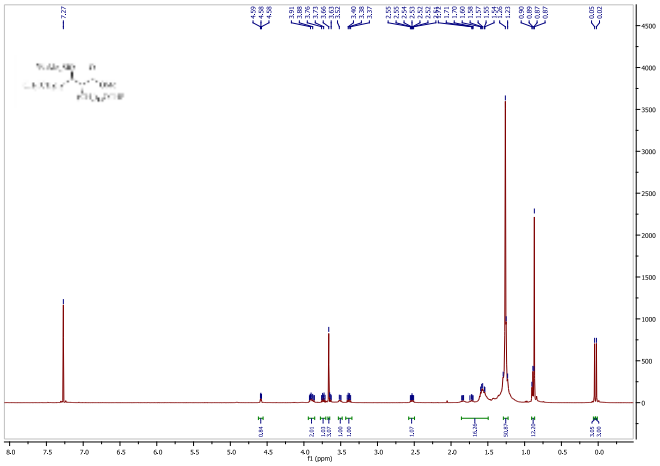
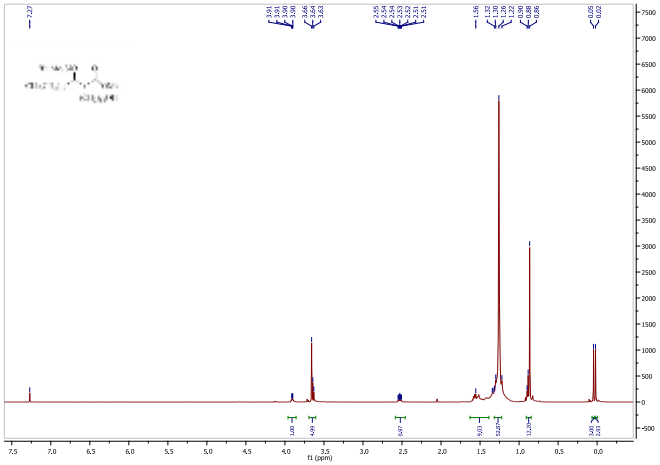
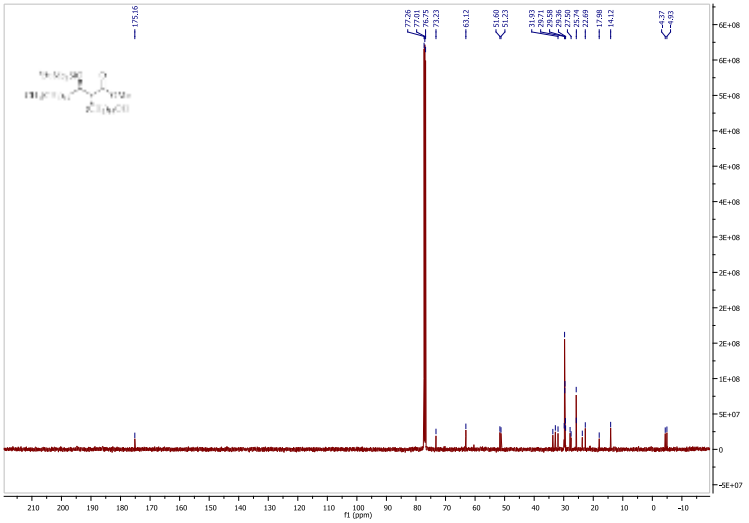
Supplementary information

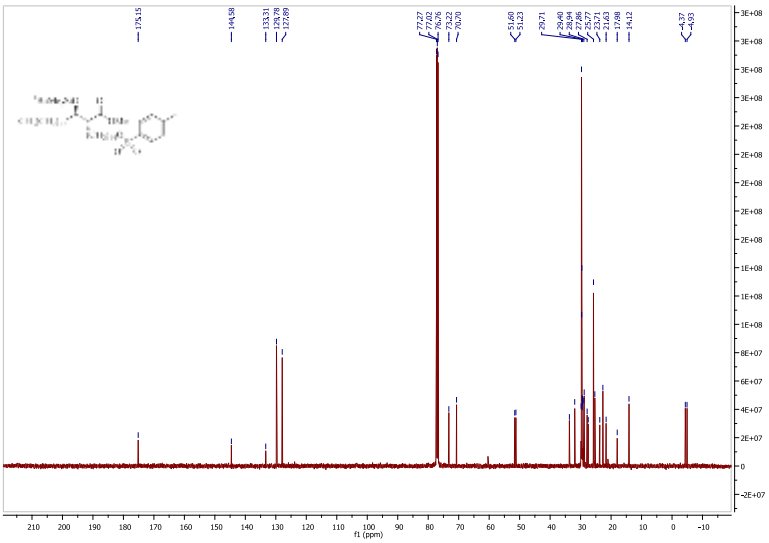
Proton and carbon NMR

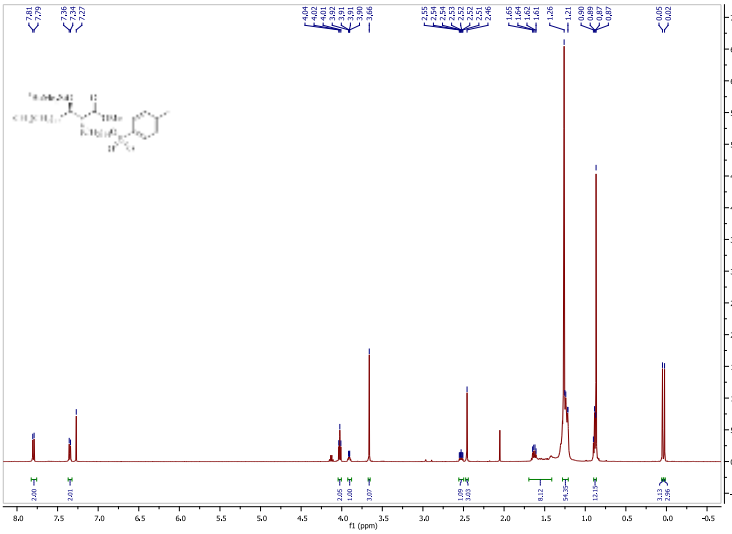


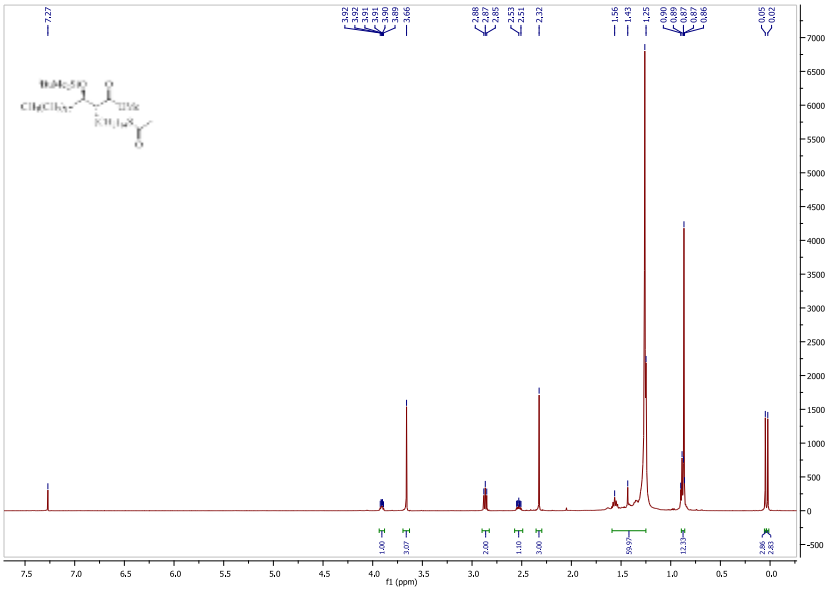


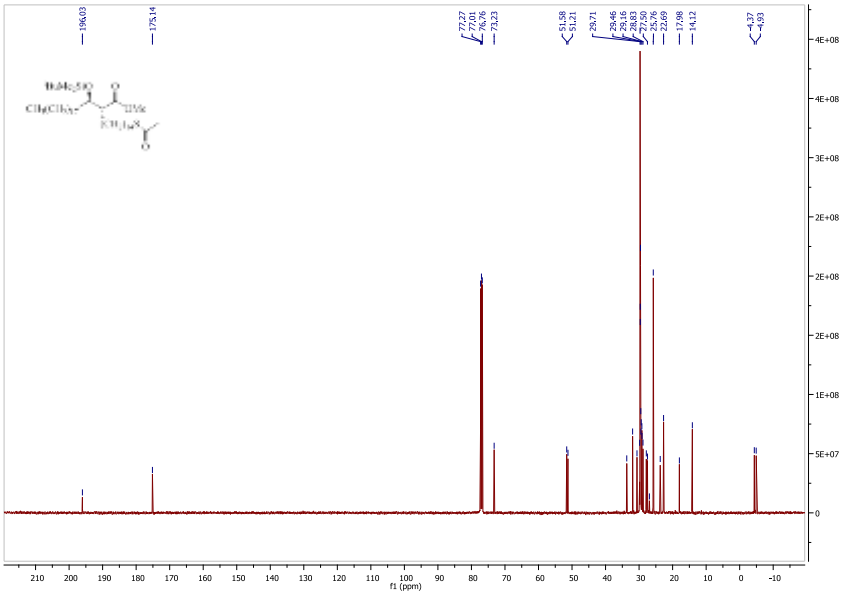


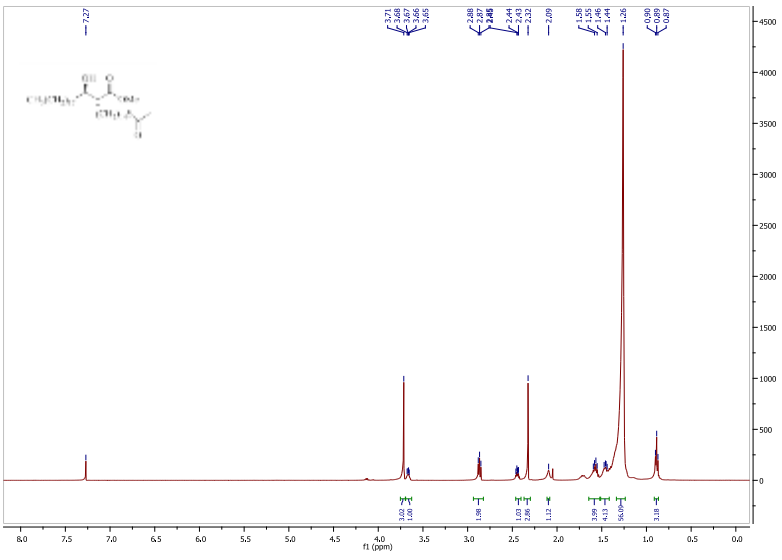


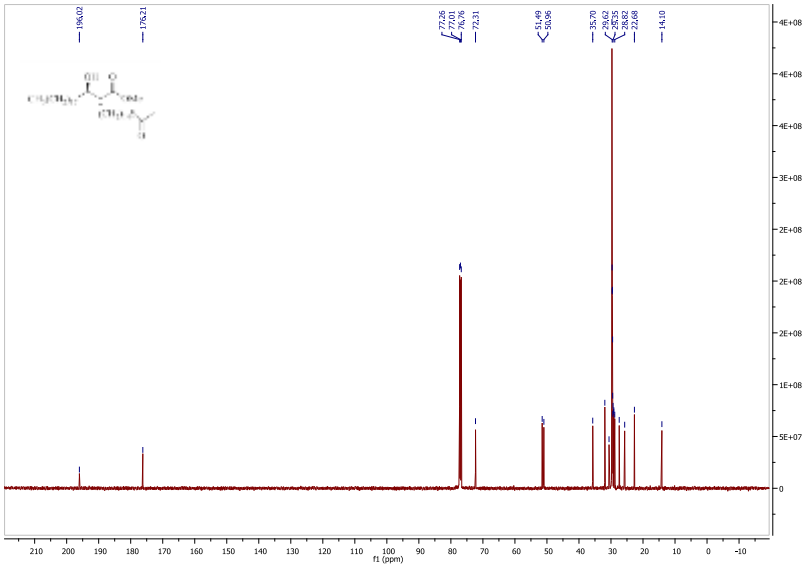








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77.01
76.76
72.31
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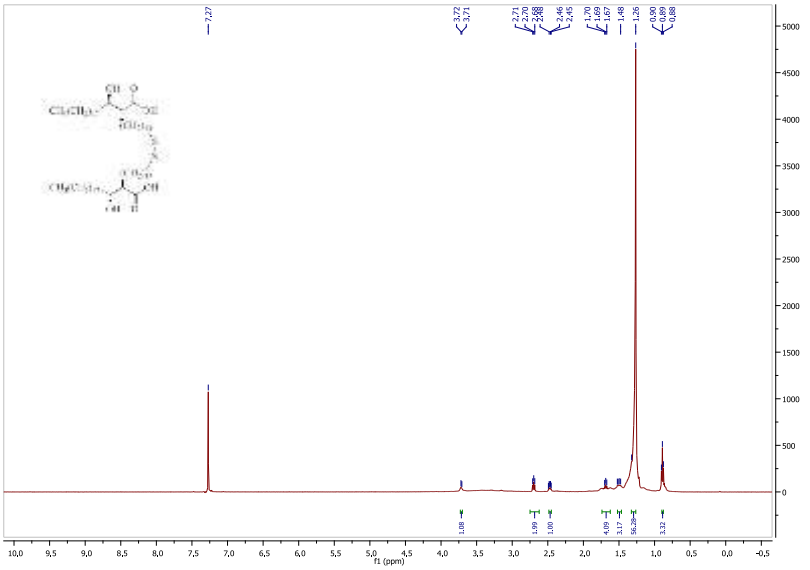
29.02
28.25
28.02
22.68
14.10
f1 (ppm)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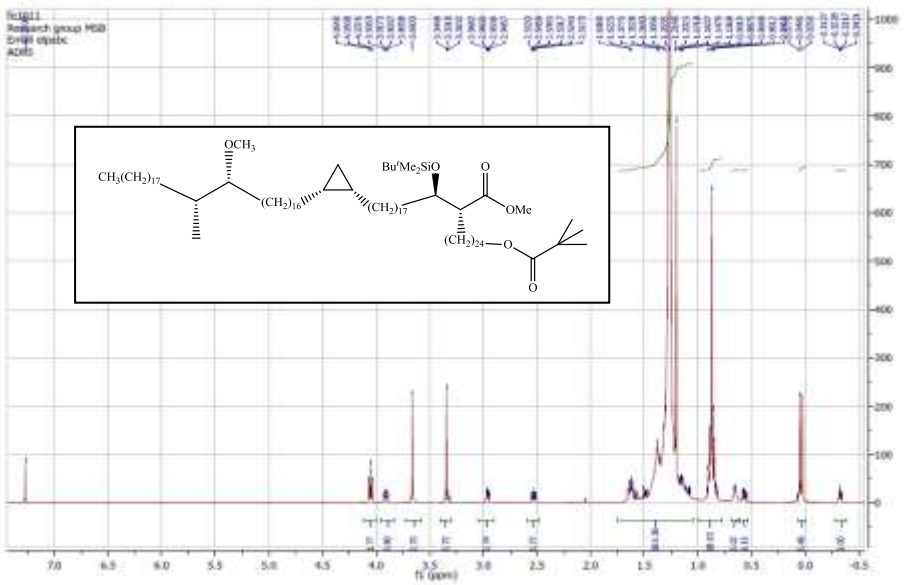
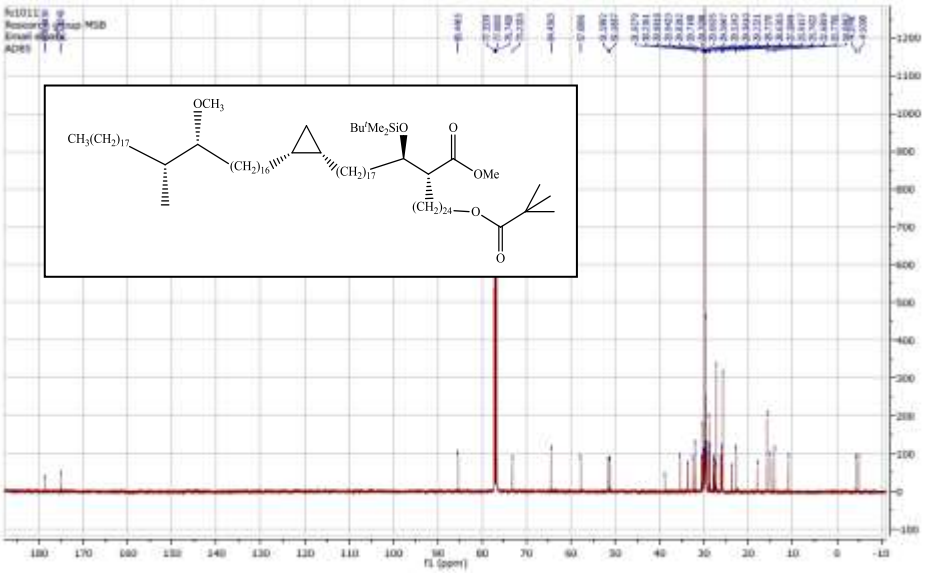
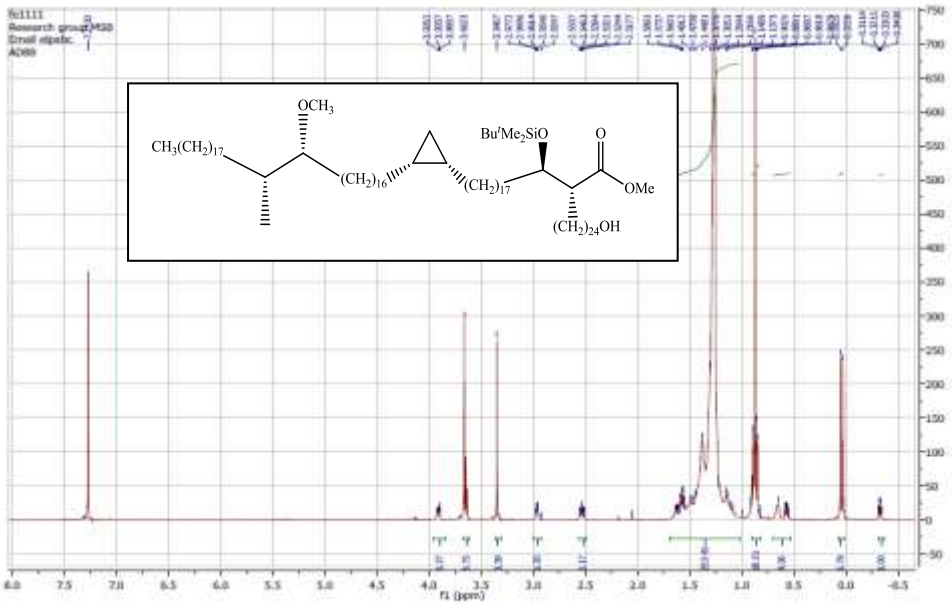
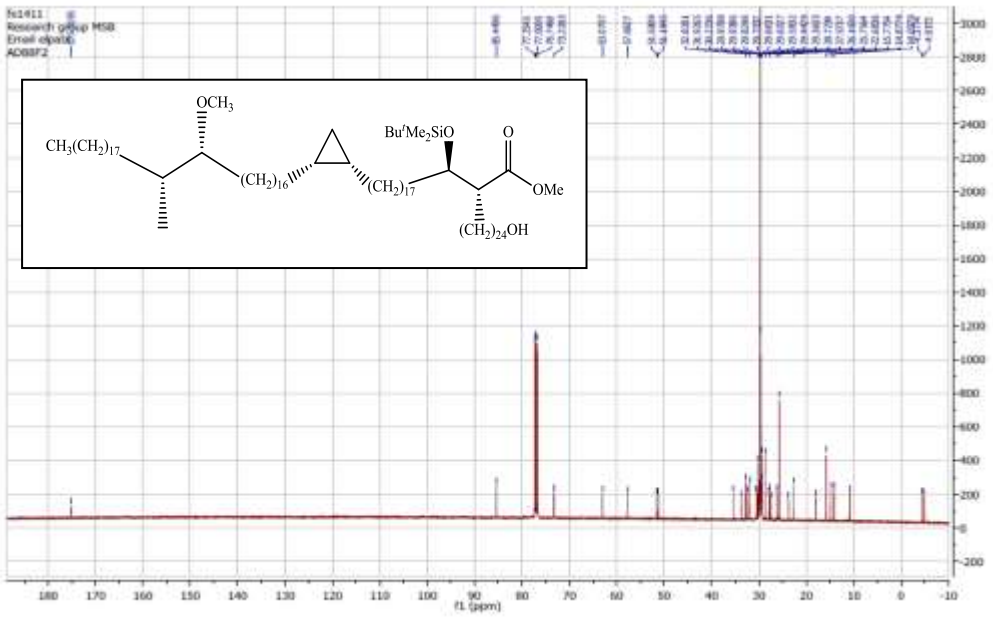
3.72
3.71
2.71
2.70
2.68
2.66
2.46
2.45
1.70
1.69
1.65
1.48
1.26
0.90
0.89
0.88
1.08
1.99
1.00
4.09
3.17
36.28
3.32
f1 (ppm)


OCH3
CH3(CH2)17
(CH2)16
(CH2)17
Bu^tMe2SiO
O
OMe
(CH2)24
O
O
f1 (ppm)

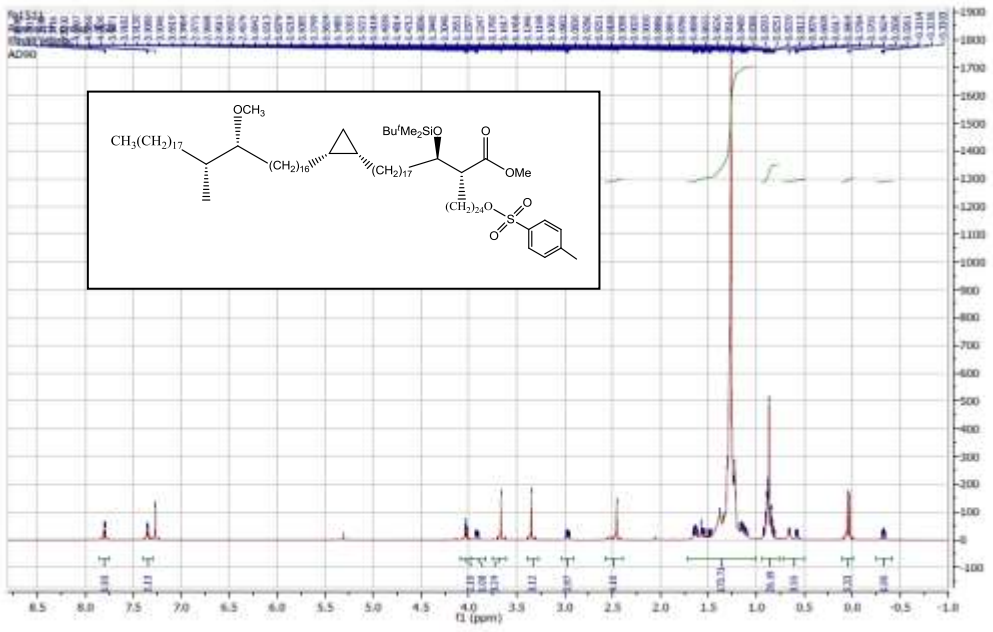


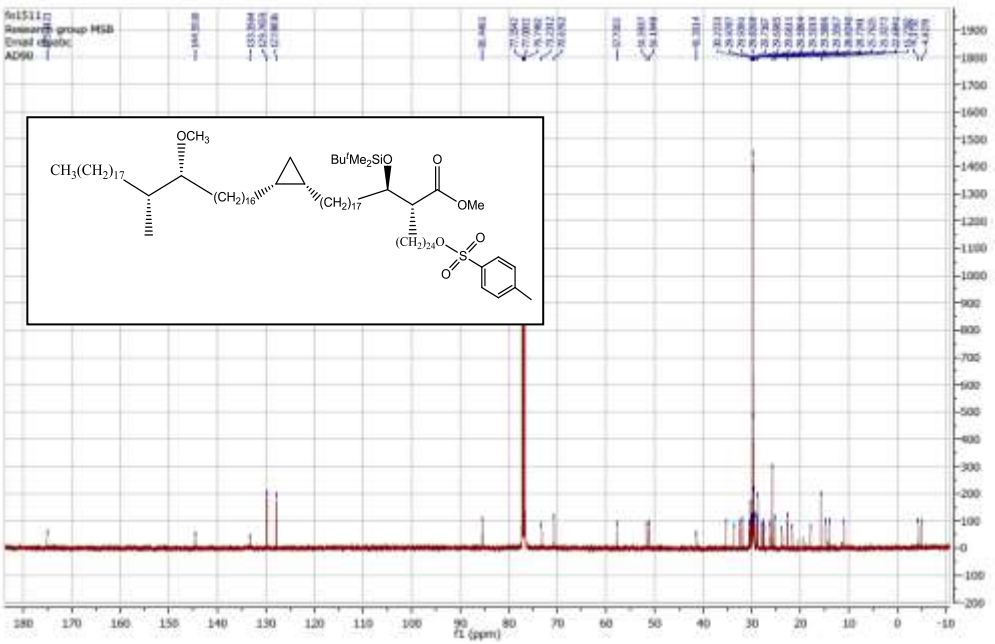
(R)-methyl2-((R)-1-(tert-butyldimetheylsiloxy)-18-(1S,2R)-2-(17R,18R)-17-methoxy-18-methylhexatriacontyl) cyclopropyl)octadecyl)-26-(pivaloyloxy) hexacosanoate



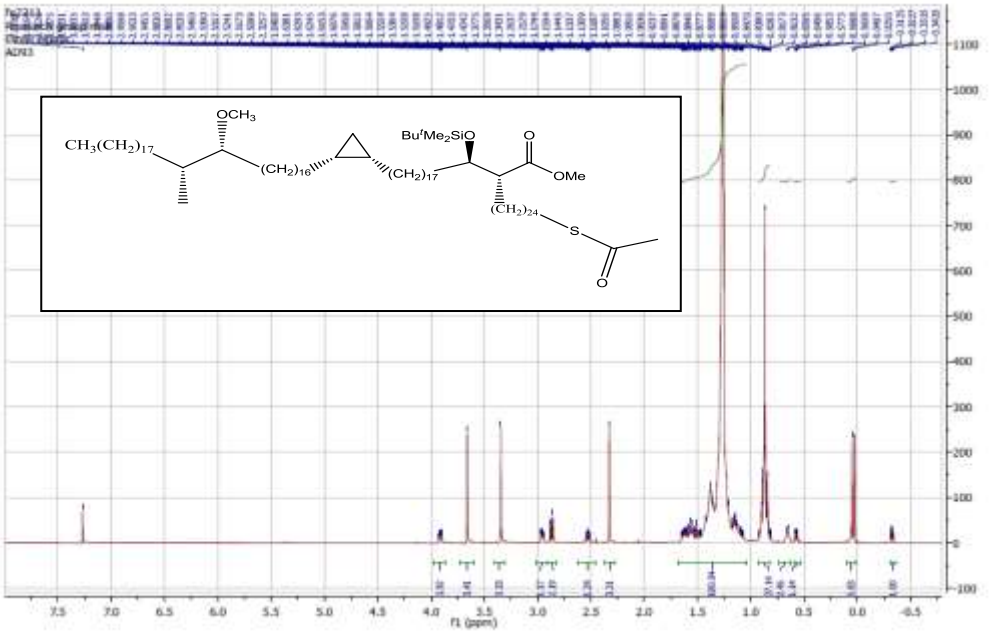


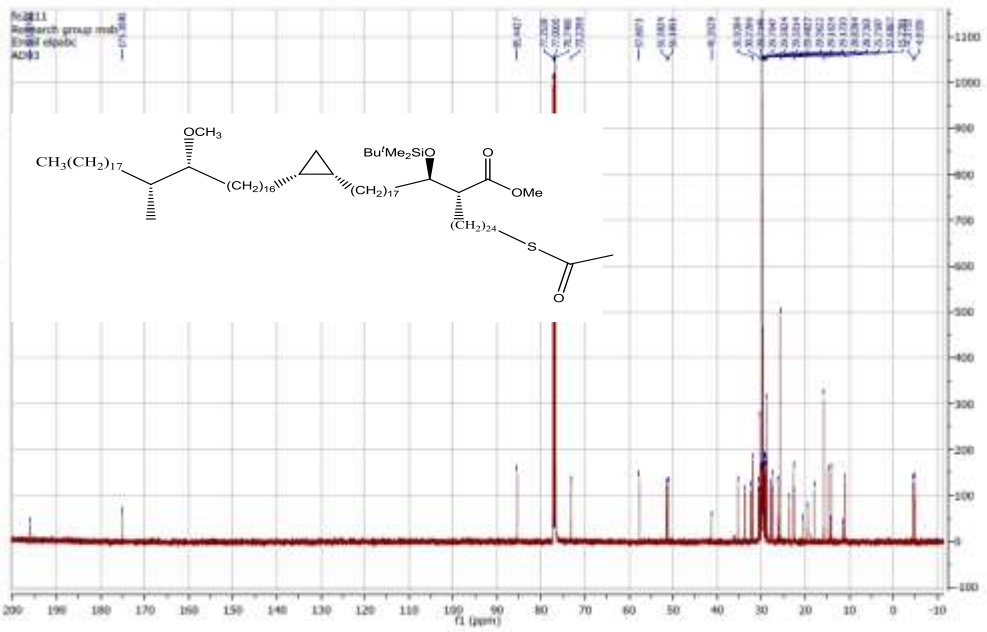
(R)-methyl-2-((R)-1-(tert-butyldimetheylsiloxy)-18-(1S,2R)-2-(17R,18R)-17-methoxy-18-methyl hexatriacontyl)cyclopropyl) octadecyl)-26-hydroxyhexacosanoate



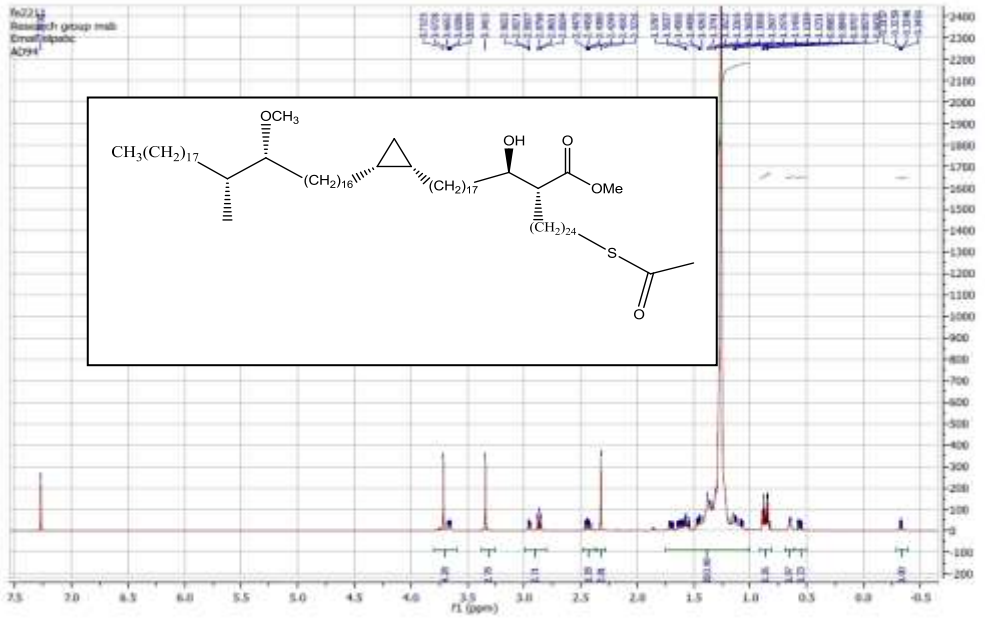


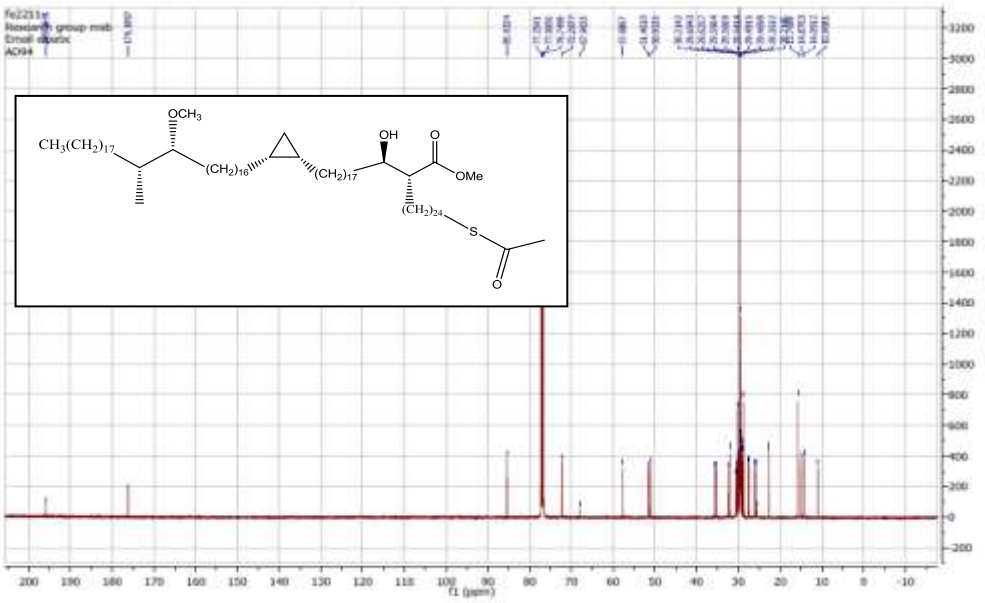
(R)-methyl-2-((R)-1-(tert-butyldimetheylsiloxy)-18-(1S,2R)-2-(17R,18R)-17-methoxy-18-methylhexatriacontyl)cyclopropyl) octadecyl)-26-(tosyloxy)hexacosanoate



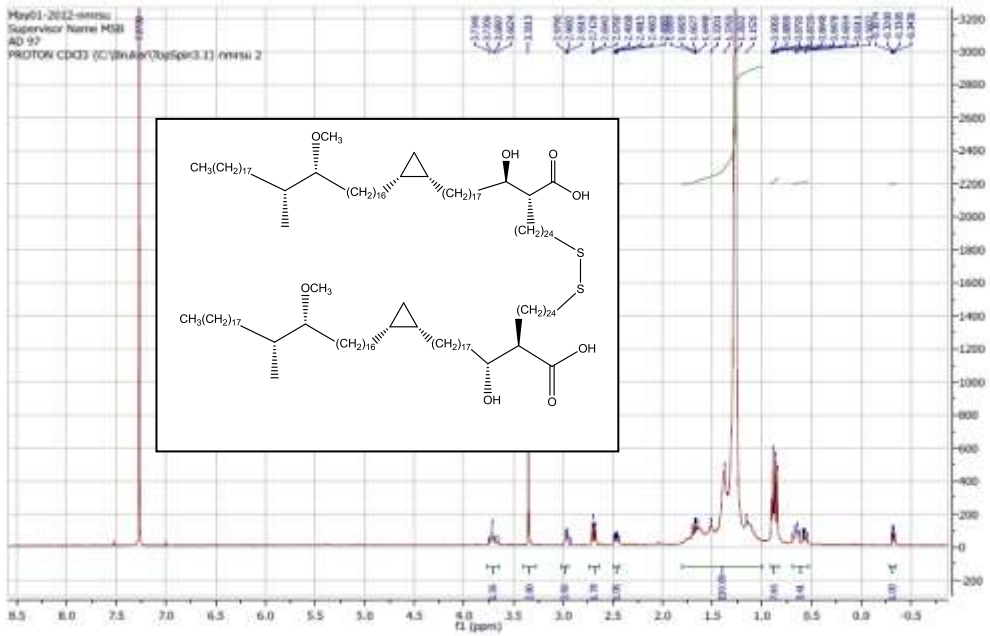


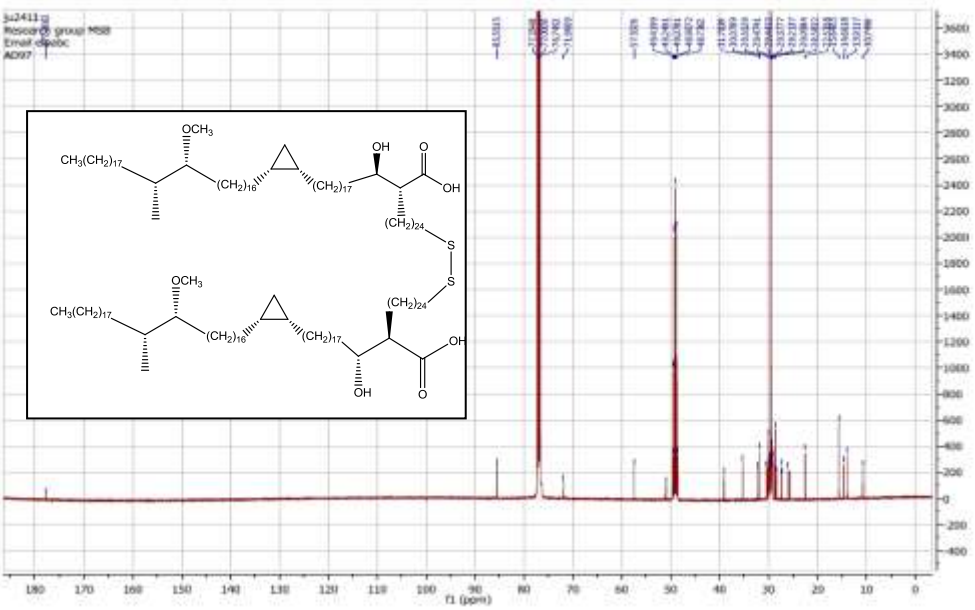
(R)-methyl-26-(acetylthio)-2-((R)-1-(tert-butyldimetheylsiloxy)-18-(1S,2R)-2-(17R, 18R)-17-methoxy-18-methylhexatriacontyl) cyclopropyl)octadecyl)hexacosanoate



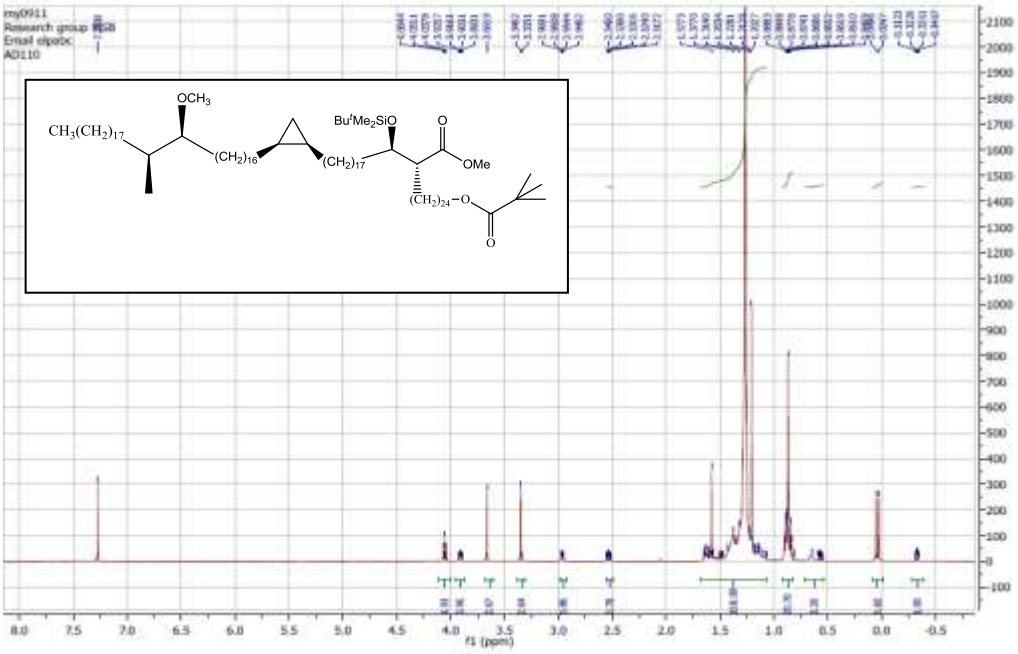


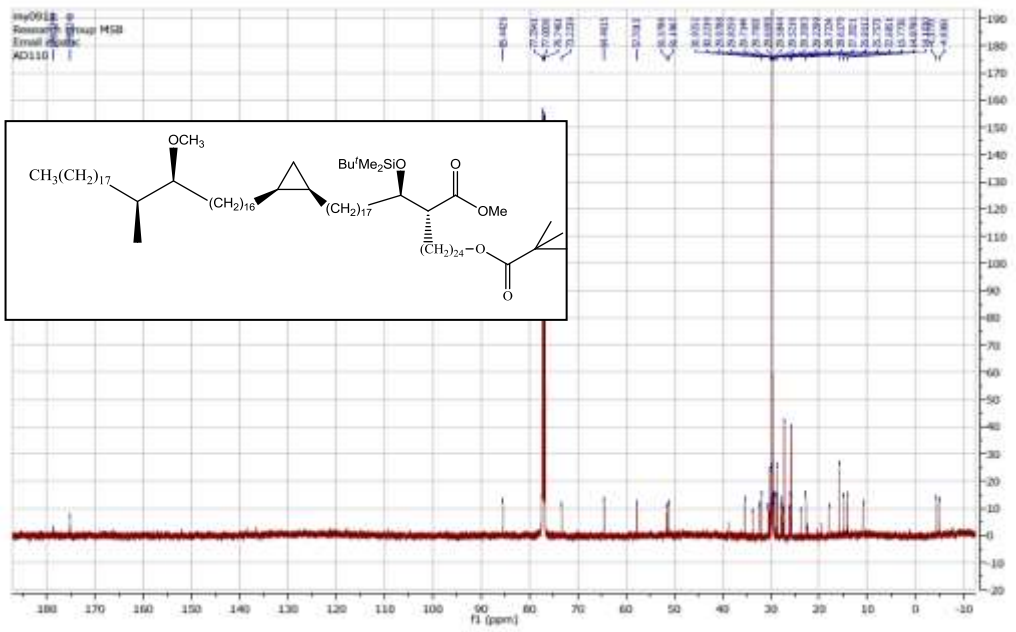
(R)-methyl-26-(acetylthio)-2-((R)-1-hydroxy-18-(1S,2R)-2-(17R,18R)-17-methoxy-18-methyl hexatriacontyl)cyclopropyl) octadecyl)hexacosanoate



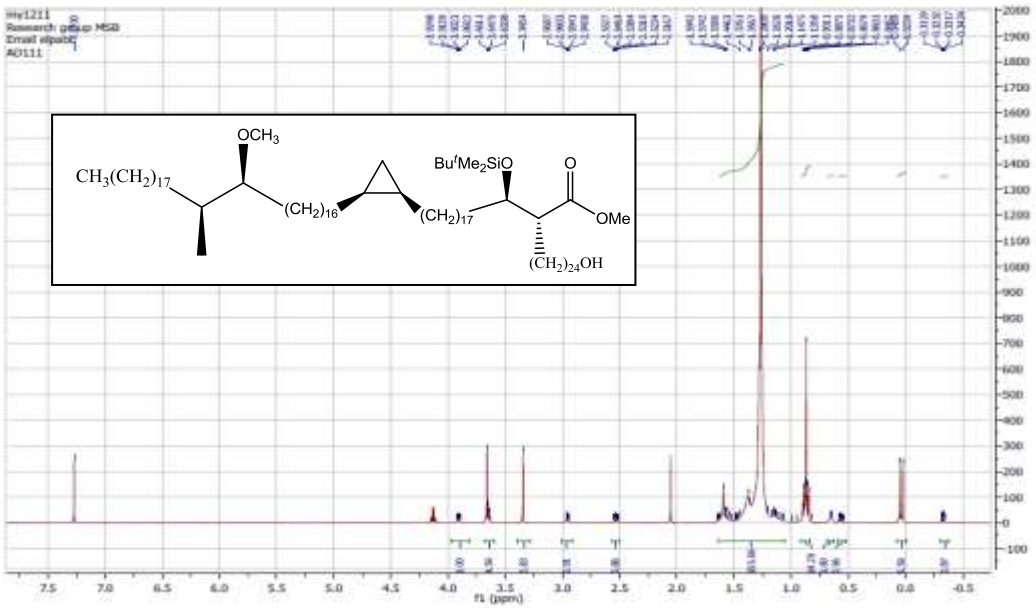


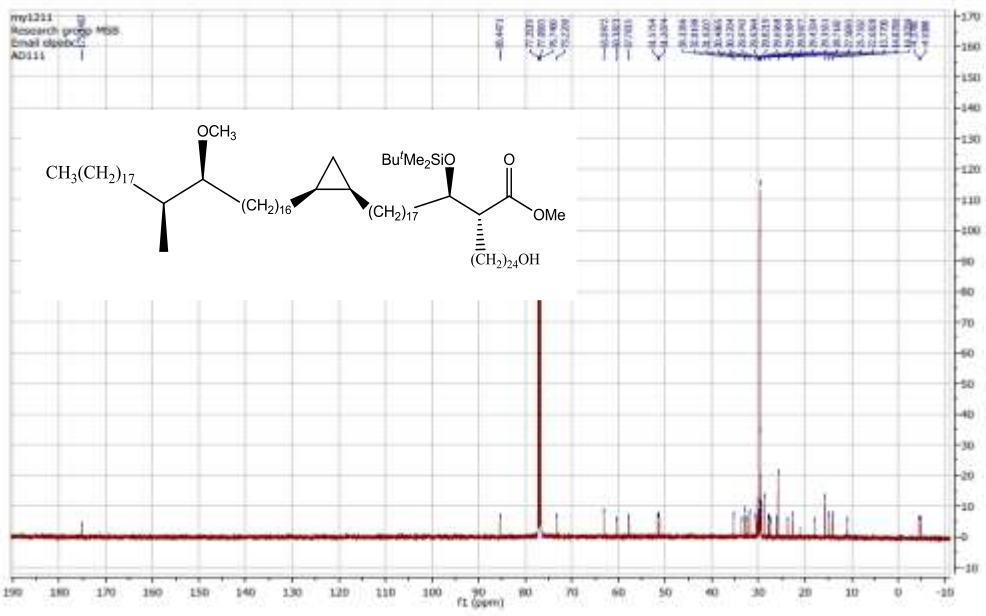
(*R*,*R*,*R*,*S*,*R*,2*R*,2'*R*)-26,26'-disulfanediylbis(2-((*R*)-1-hydroxy-18-((1*S*,2*R*)-2-((17*R*, 18*R*)-17-methoxy-18-methylhexatriacontylcyclopropyl)octadecyl)hexacosanoic acid)



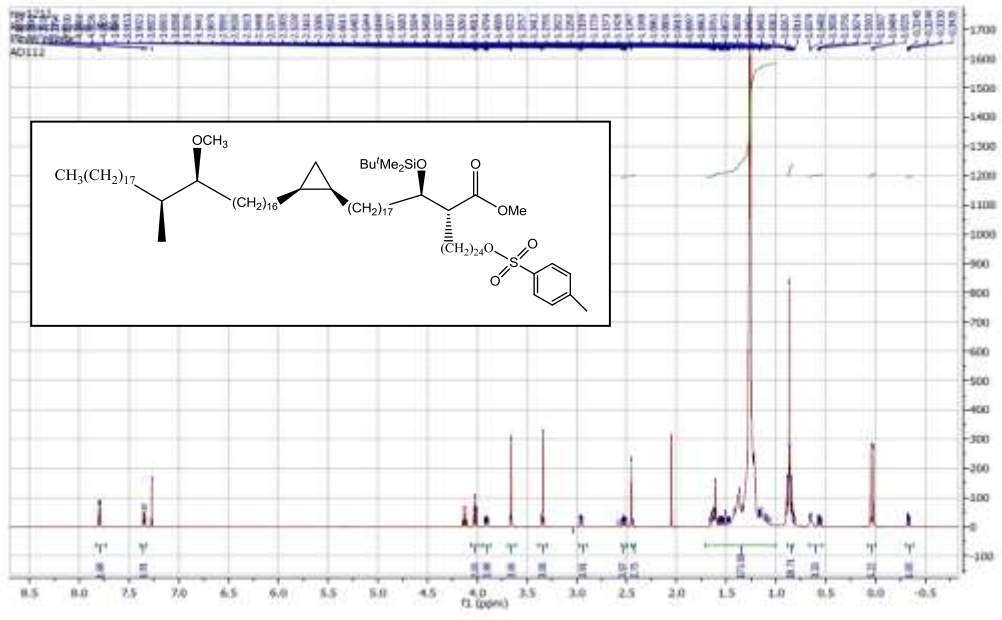


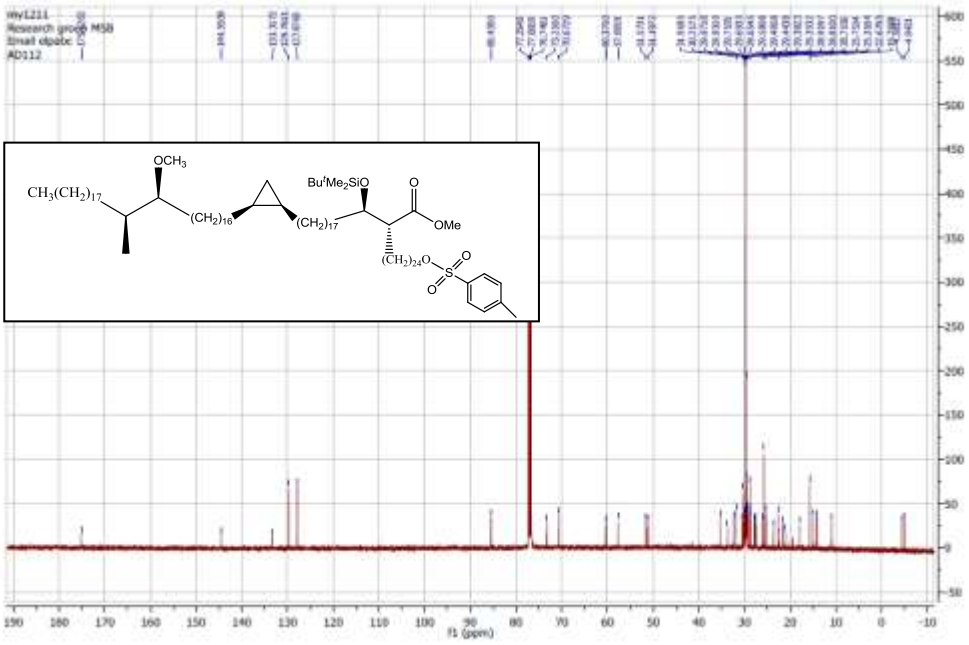
(R)-methyl-2-((R)-1-(tert-butyldimetheylsiloxy)-18-(1R,2S)-2-(17S,18S)-17-methoxy-18-methylhexatriacontyl)cyclopropyl) octadecyl)-26-(pivaloyloxy)hexacosanoate



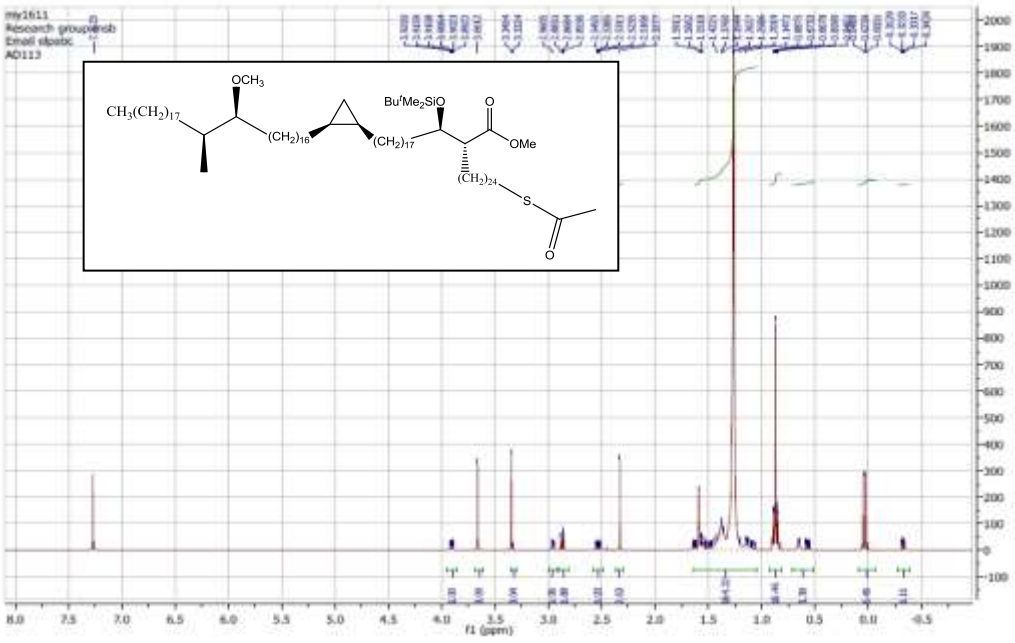


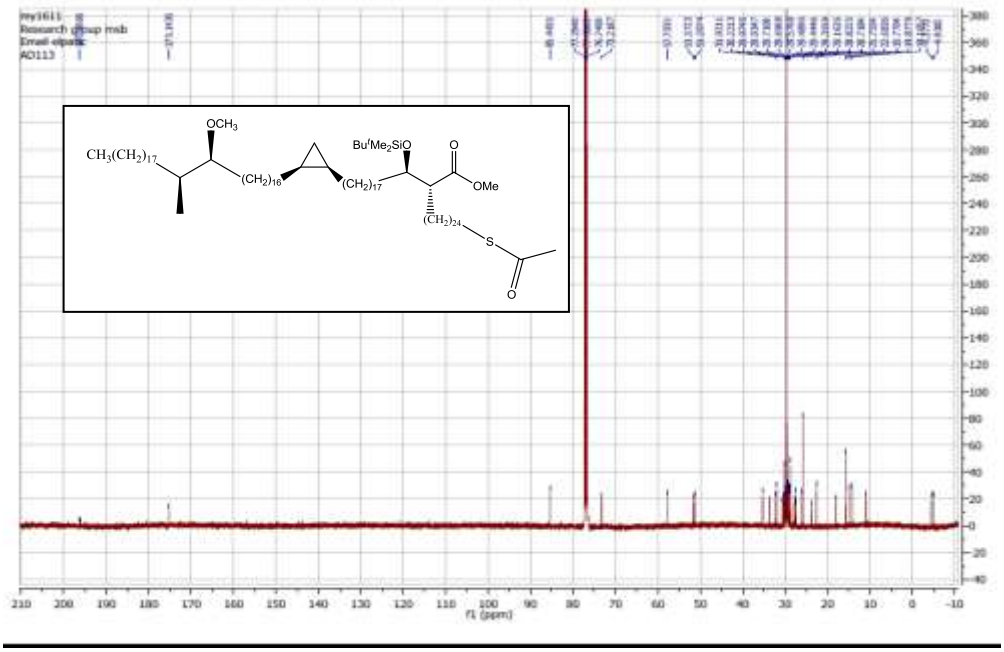
(R)-methyl-2-((R)-1-(tert-butyldimetheylsiloxy)-18-(1S,2R)-2-(17R,18R)-17-methoxy-18-methyl hexatriacontyl) cyclopropyl)octadecyl)-26-hydroxyhexacosanoate



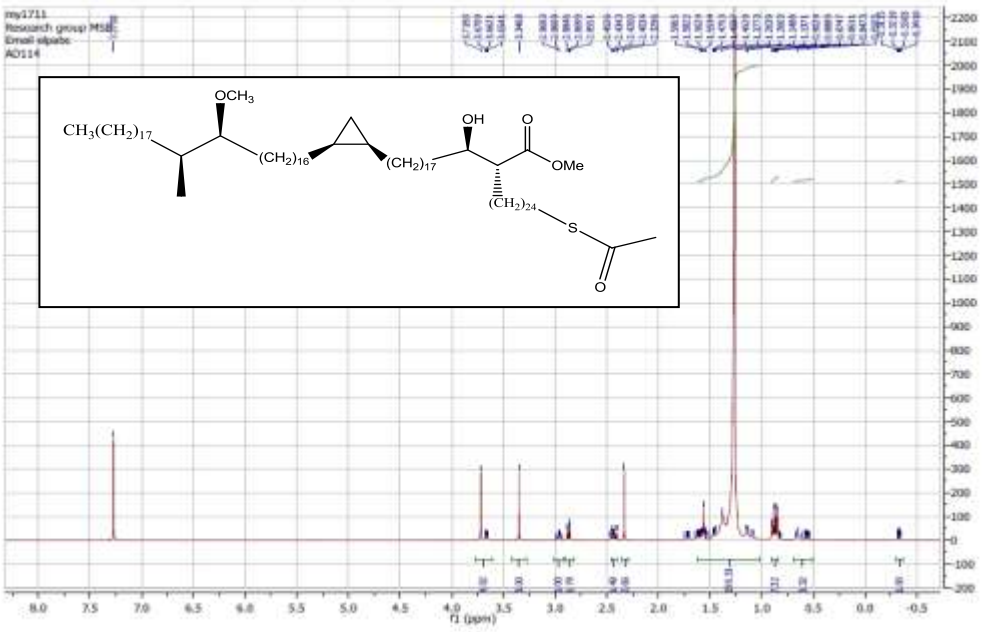


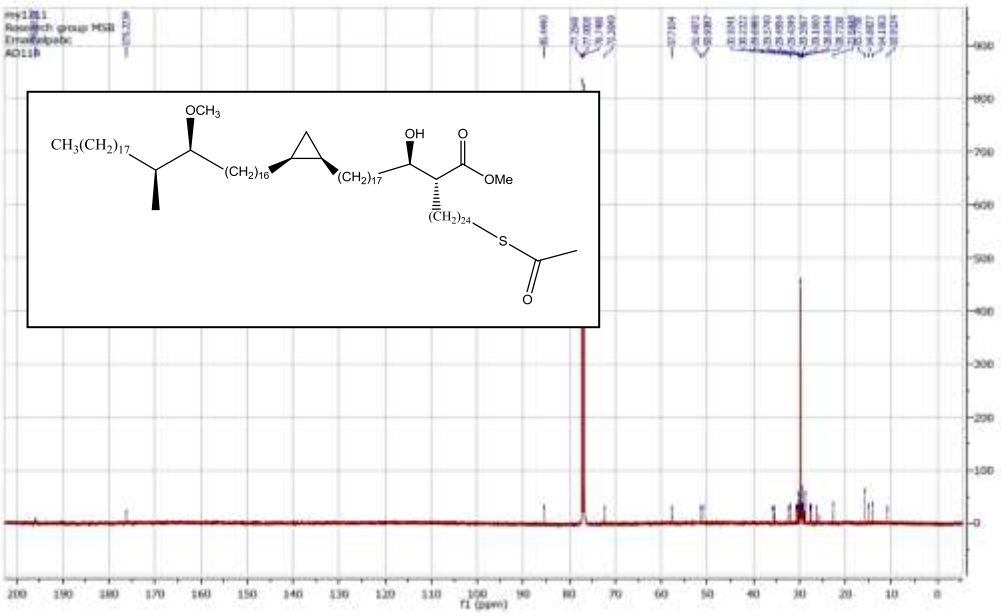
(R)-methyl-2-((R)-1-(tert-butyldimetheylsiloxy)-18-(1S,2R)-2-(17R,18R)-17-methoxy-18-methylhexatriacontyl)cyclopropyl) octadecyl)-26-(tosyloxy)hexacosanoate



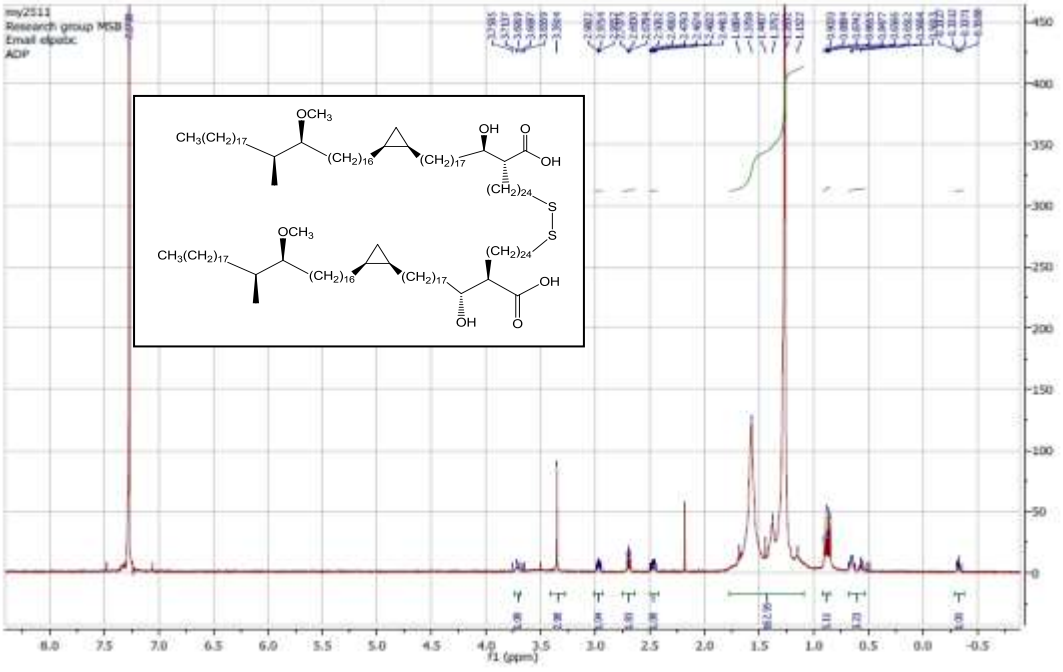


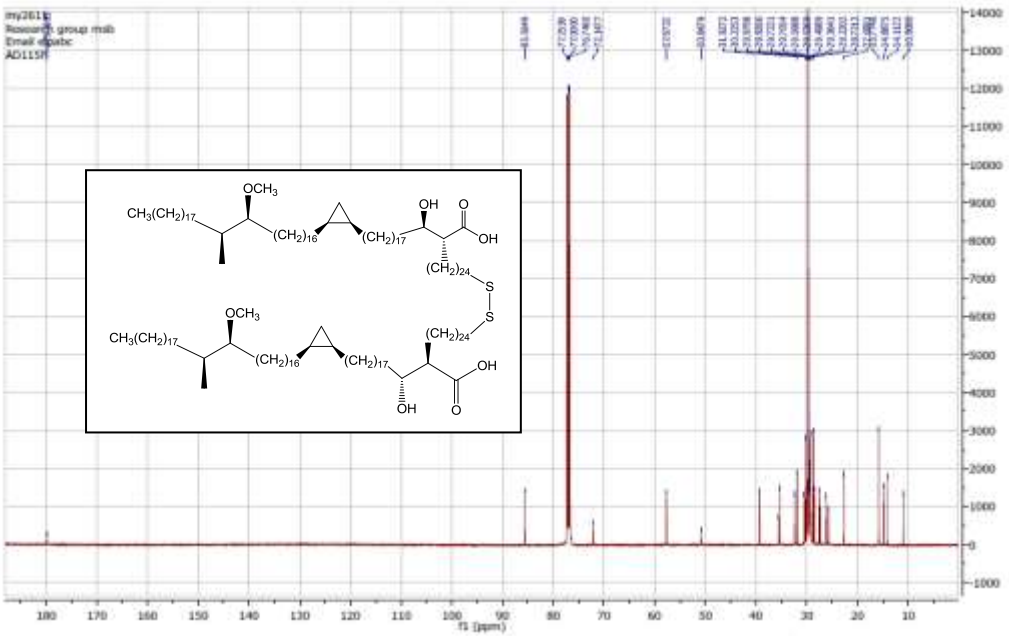
(R)-methyl-26-(acetylthio)-2-((R)-1-(tert-butyldimetheylsiloxy)-18-(1S,2R)-2-(17R, 18R)-17-methoxy-18-methylhexatriacontyl) cyclopropyl)octadecyl)hexacosanoate



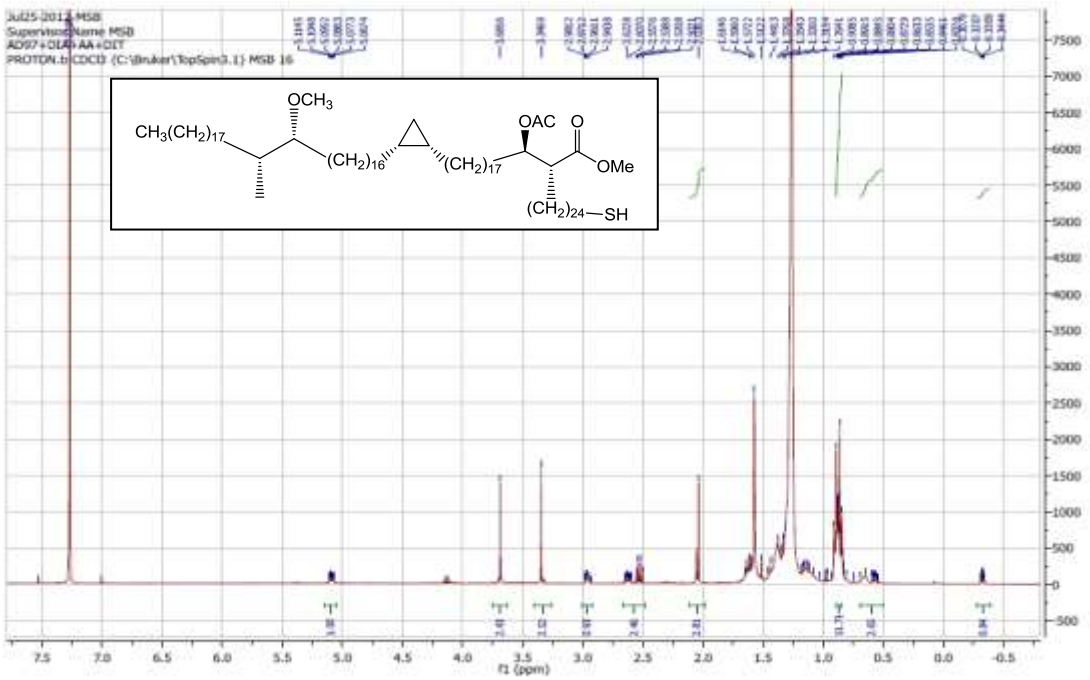


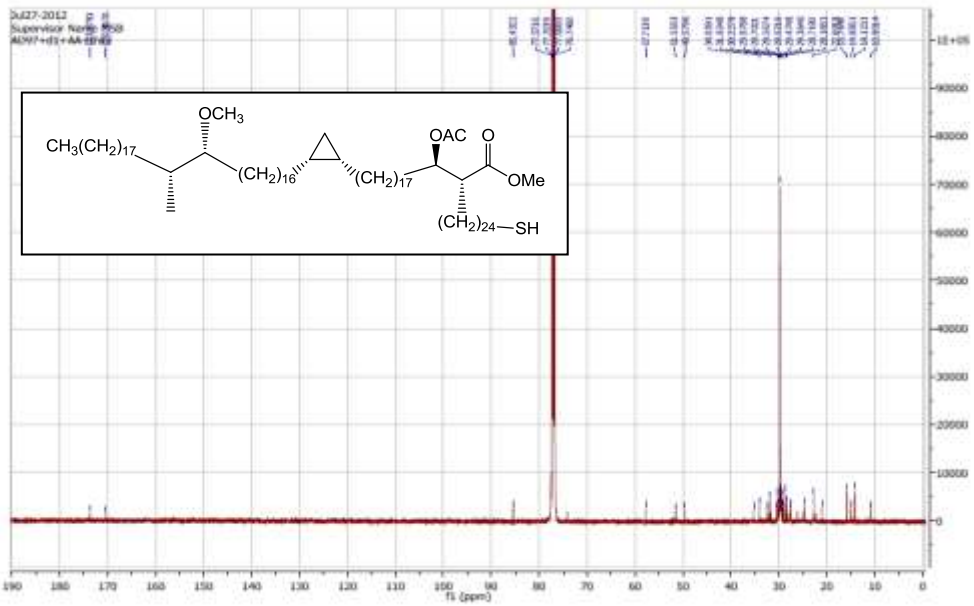
(R)-methyl-26-(acetylthio)-2-((R)-1-hydroxy-18-(1S,2R)-2-(17R,18R)-17-methoxy-18-methyl hexatriacontyl)cyclopropyl) octadecyl)hexacosanoate



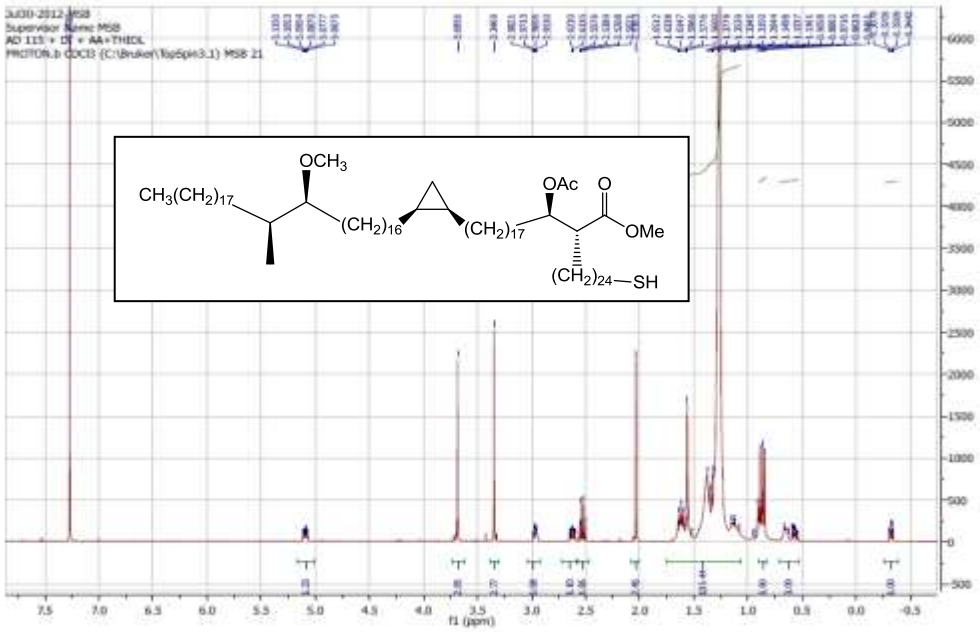


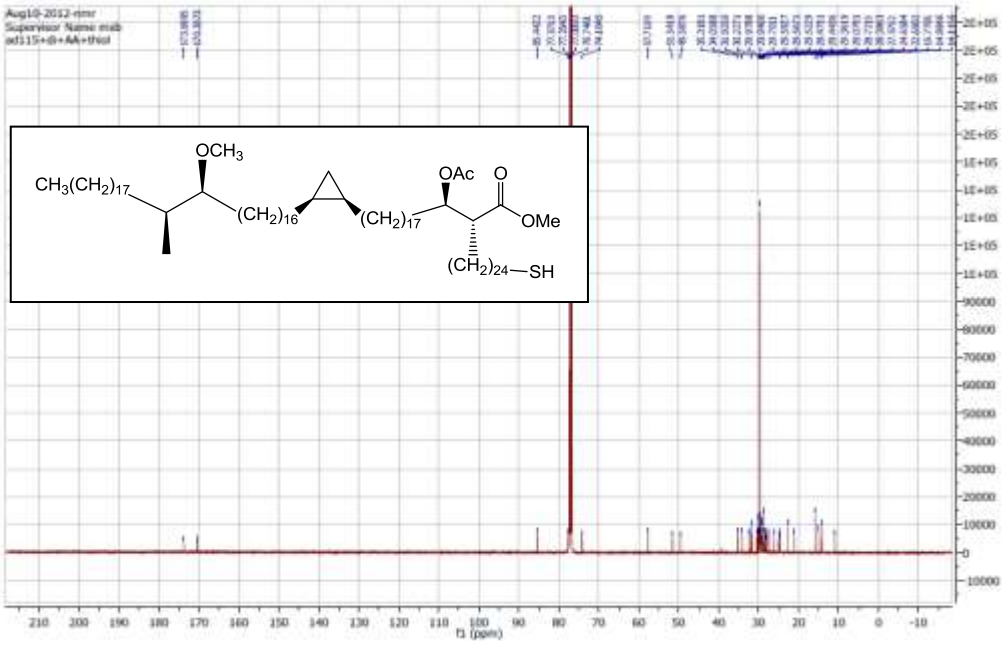
(*R*,*R*,*R*,*S*,*R*,2*R*,2'*R*)-26,26'-disulfanediylbis(2-((*R*)-1-hydroxy-18-((1*R*,2*S*)-2-((17*S*,18*S*)-17-methoxy-18-methylhexatriacontyl) cyclopropyl)octadecyl)hexacosanoic acid)



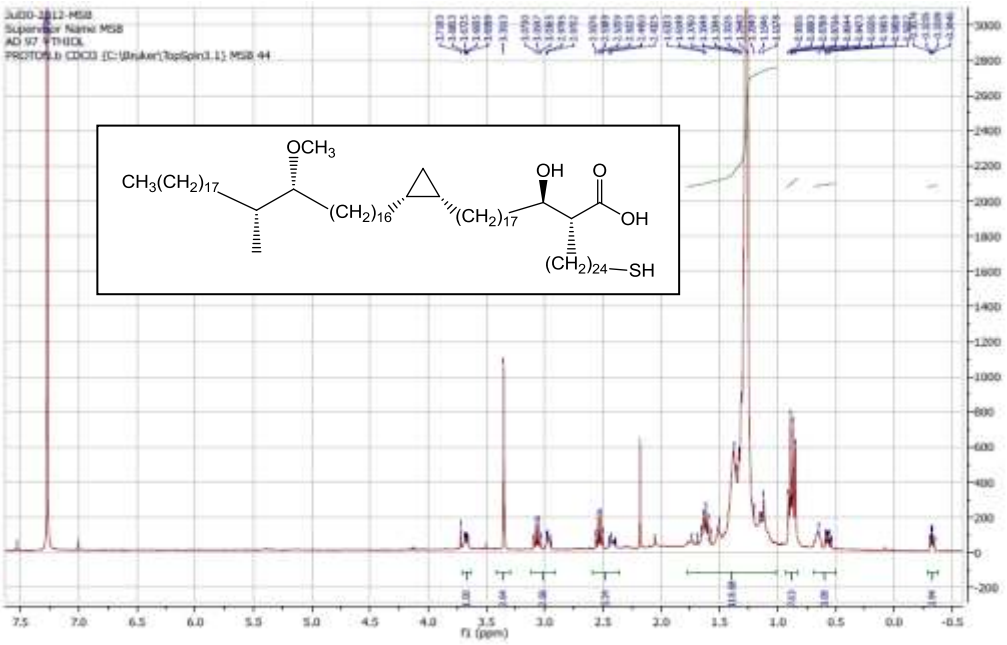


(*R*)-methyl-2-((*R*)-1-acetoxy-18-((1*S*,2*R*)-2-((17*R*,18*R*)-17-methoxy-18-methylhexatriacontyl)cyclopropyl) octadecyl)-26-mercaptohexacosanoate

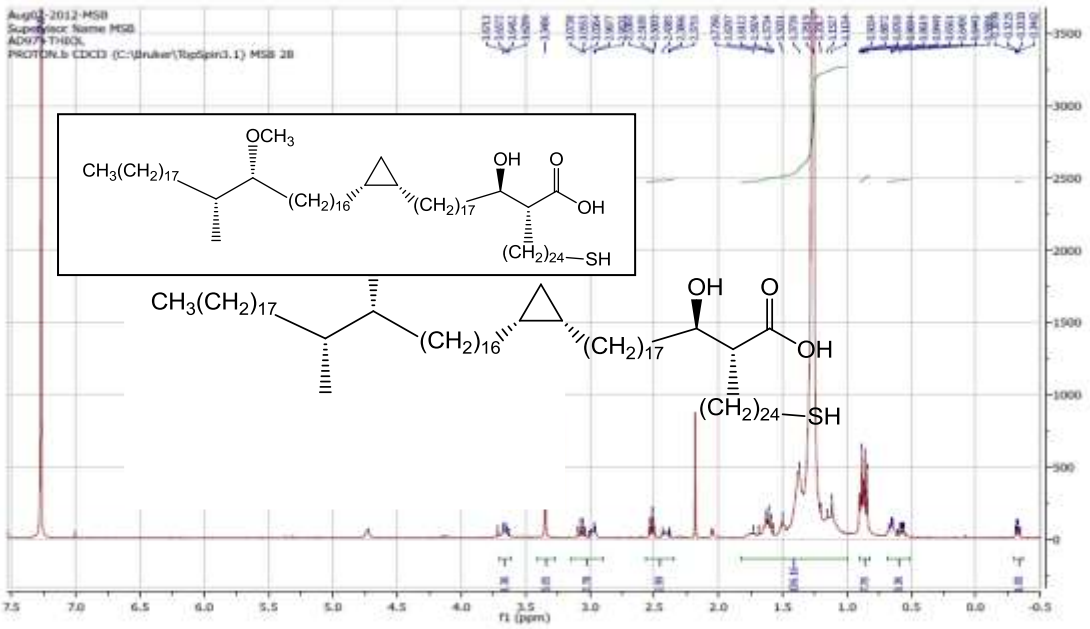




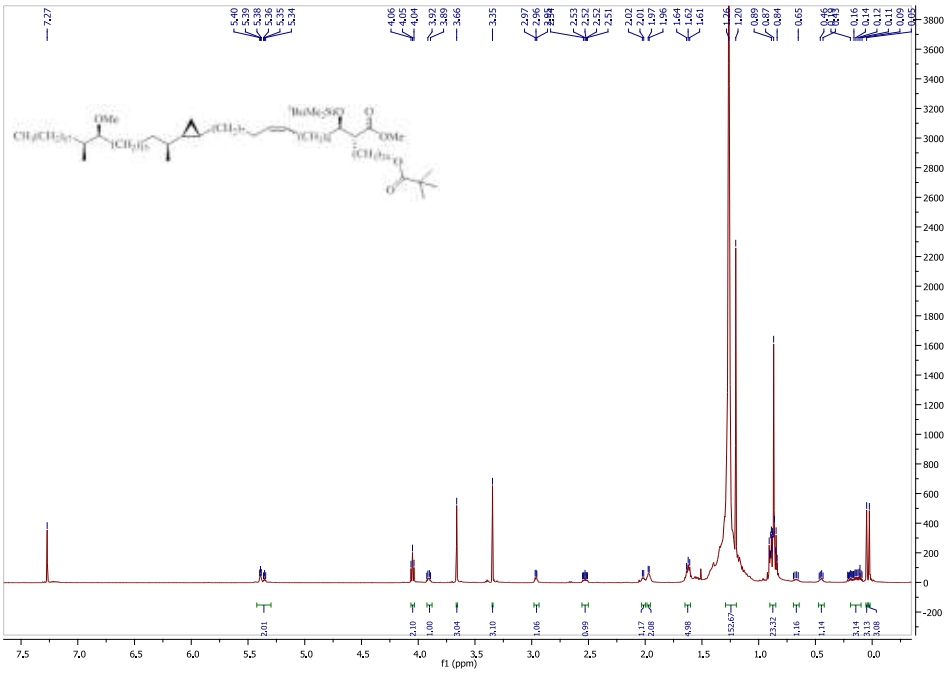
(*R*)-methyl-2-((*R*)-1-acetoxy-18-((1*R*,2*S*)-2-((17*S*,18*S*)-17-methoxy-18-methylhexatriacontyl)cyclopropyl)octadecyl)-26-mercaptohexacosanoate

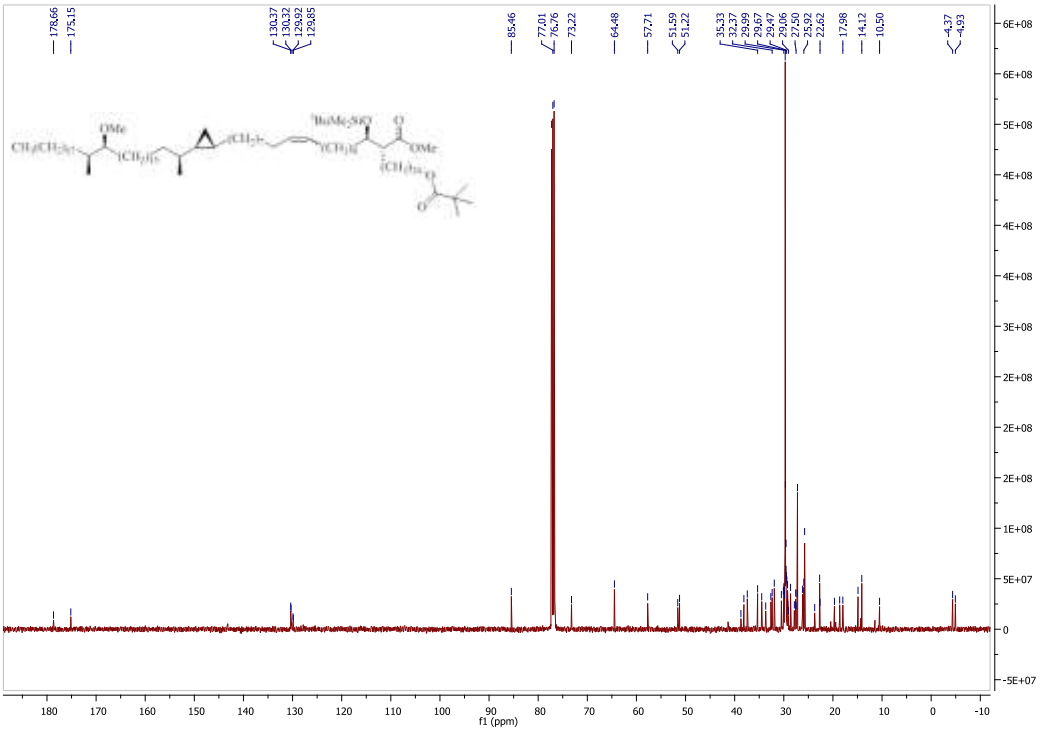


(*R*)-2-((*R*)-1-hydroxy-18-((1*S*,2*R*)-2-((17*R*,18*R*)-17-methoxy-18-methylhexatria-contyl)cyclopropyl)octadecyl)-26-mercaptohexacosanoic acid



(*R*)-2-((*R*)-1-hydroxy-18-((1*S*,2*R*)-2-((17*R*,18*R*)-17-methoxy-18-methylhexatria -contyl)cyclopropyl)octadecyl)-26-mercaptohexacosanoic acid [D_2O]

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51.22
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32.37
29.99
29.67
29.47
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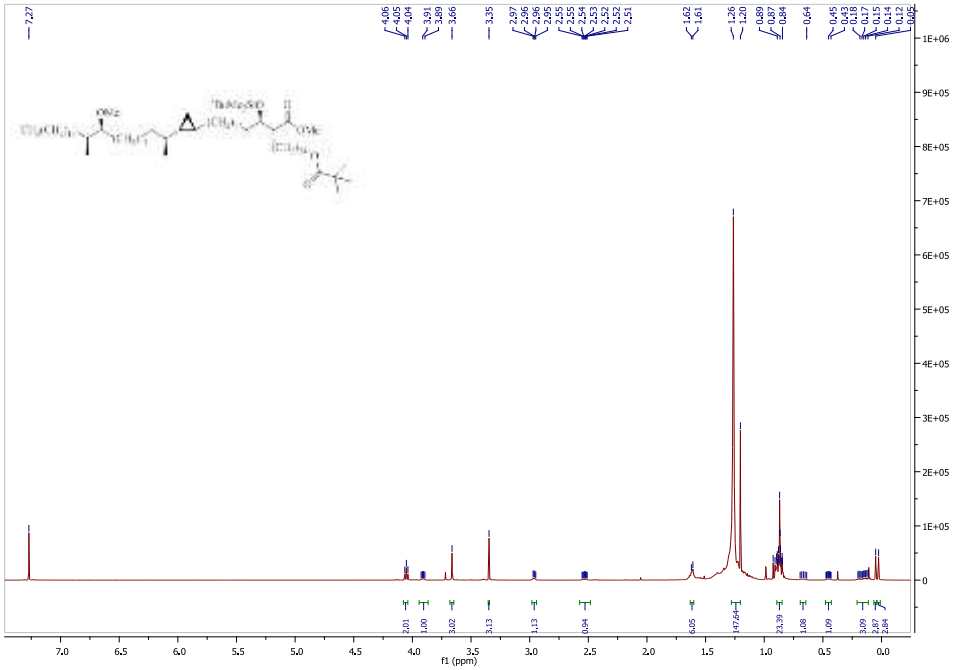
27.50
25.92
22.62
17.98
14.12
10.50
-4.37
-4.93
f1 (ppm)


7.27
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2.96
2.96
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2.54
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2.52
2.52
2.51
1.62
1.61
1.26
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0.84
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0.18
0.17
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0.14
0.12
0.05
2.01
1.00
3.02
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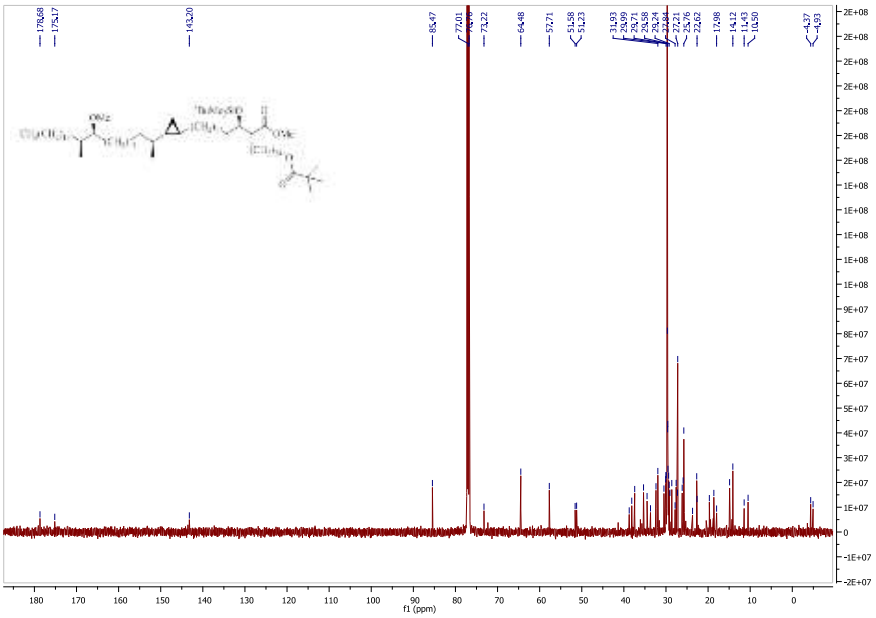
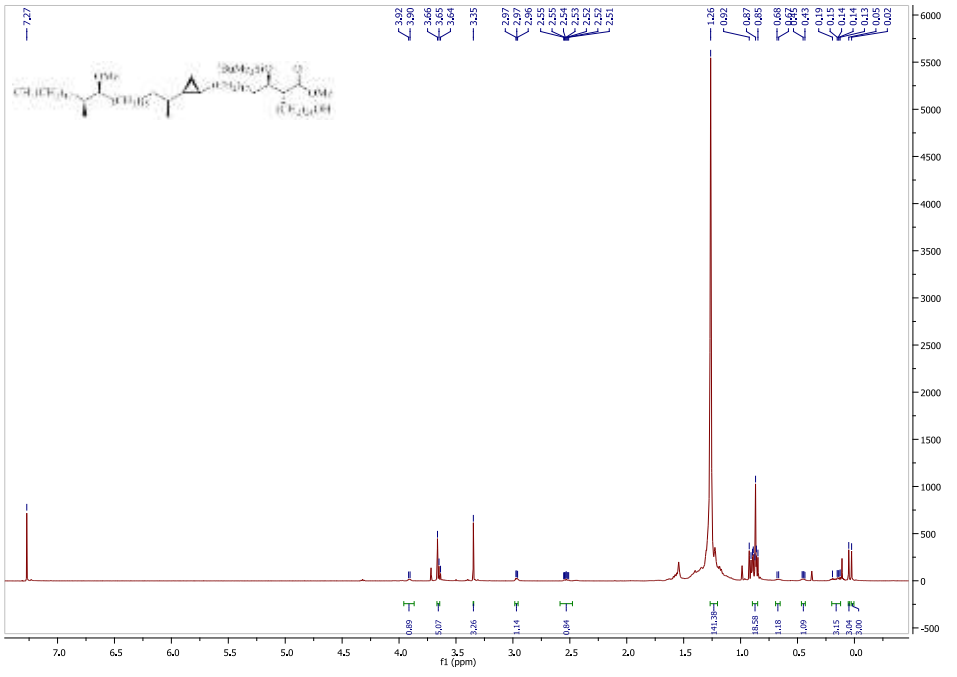
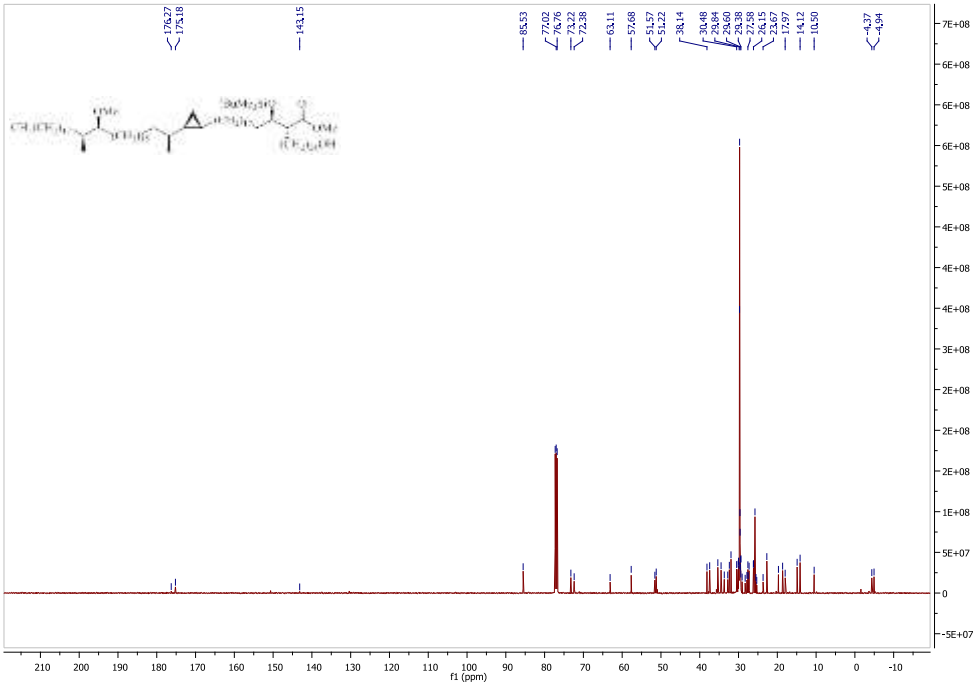
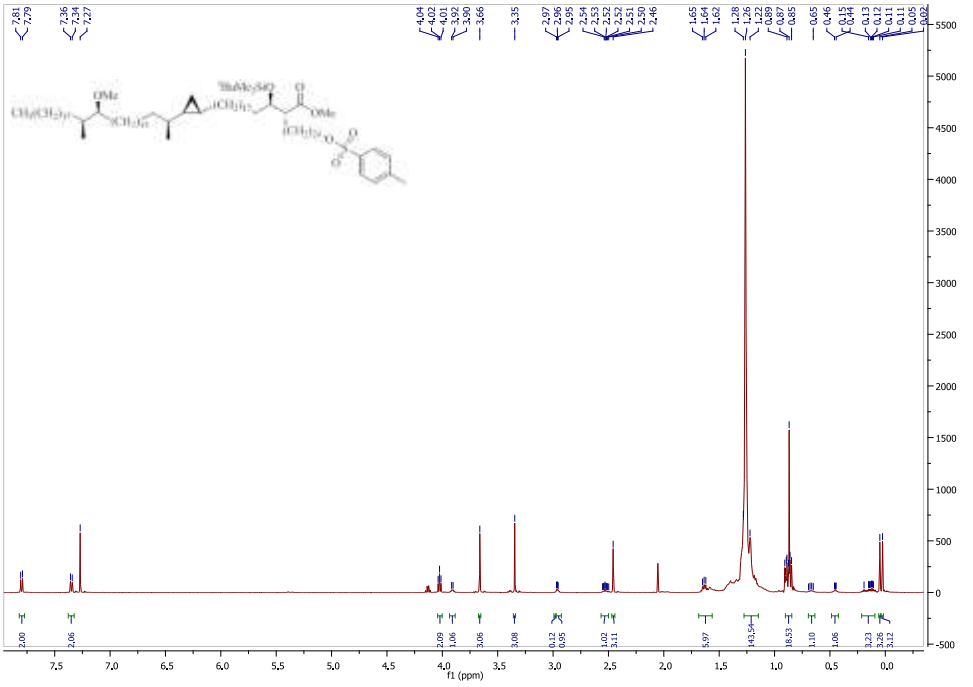
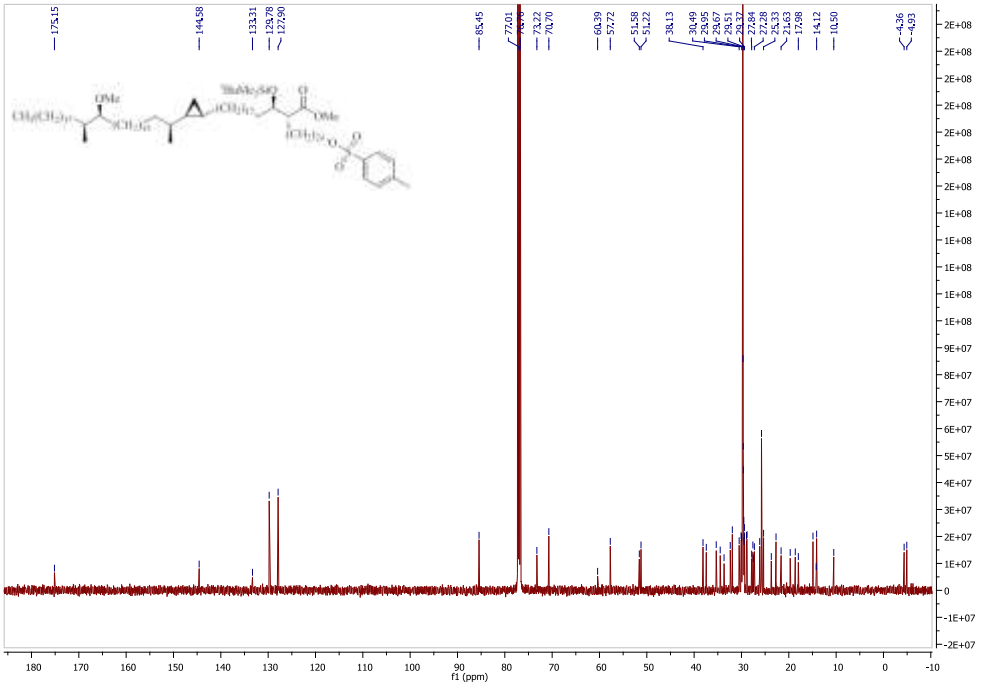
2.84
f1 (ppm)







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133.31
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77.01
73.22
70.70
60.39
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51.58
51.22
36.13
30.49
29.95
29.67
29.51
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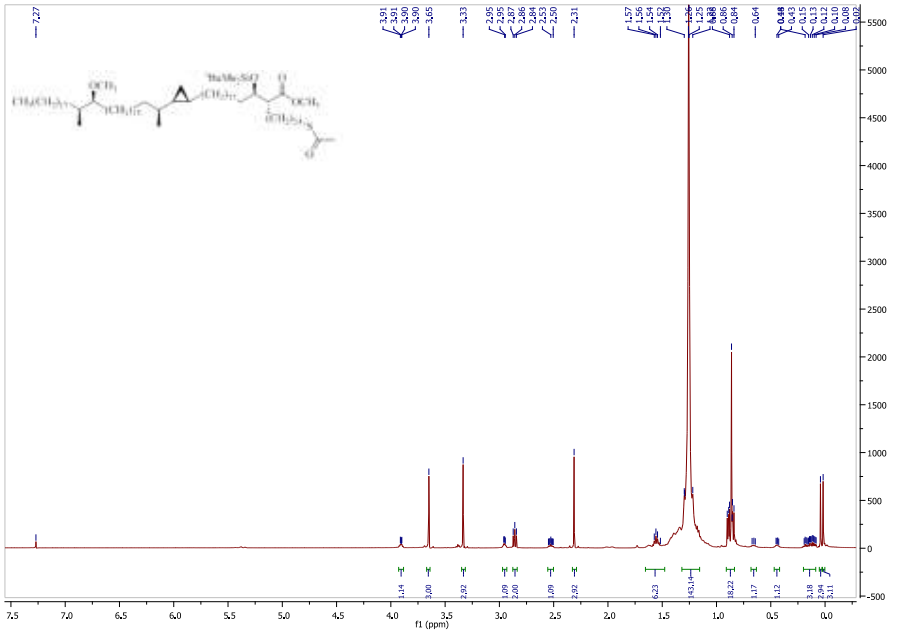
27.28
25.33
21.63
17.98
14.12
10.50
-4.36
-4.93
f1 (ppm)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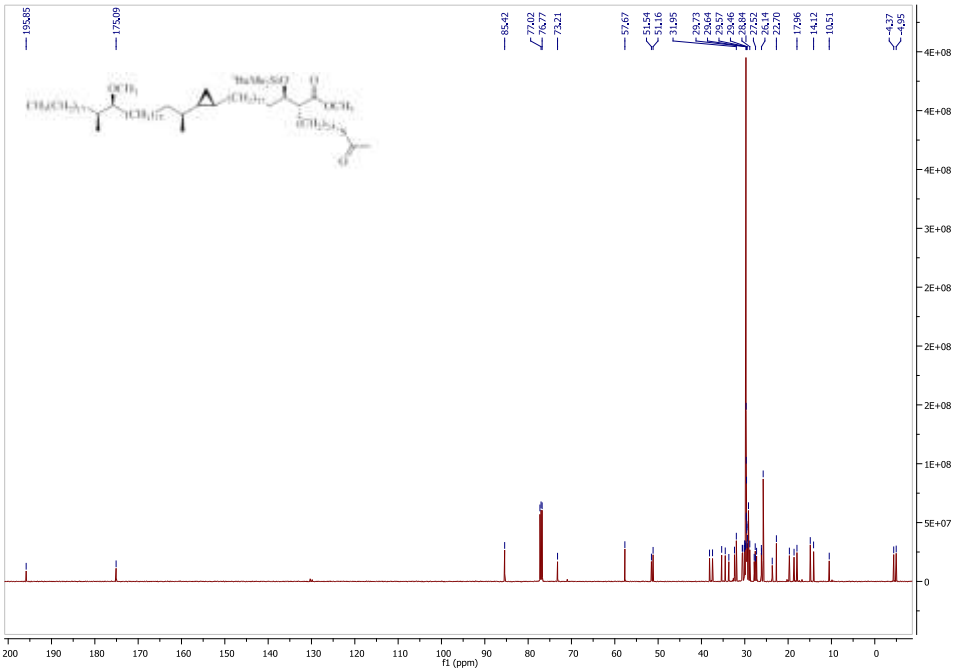
2.53
2.50
2.31
1.57
1.56
1.54
1.53
0.86
0.84
0.64
0.15
0.13
0.12
0.10
0.08
1.14
3.00
2.02
1.09
2.00
1.09
2.02
6.23
45.14
18.22
1.17
1.12
3.18
2.04
3.11
f1 (ppm)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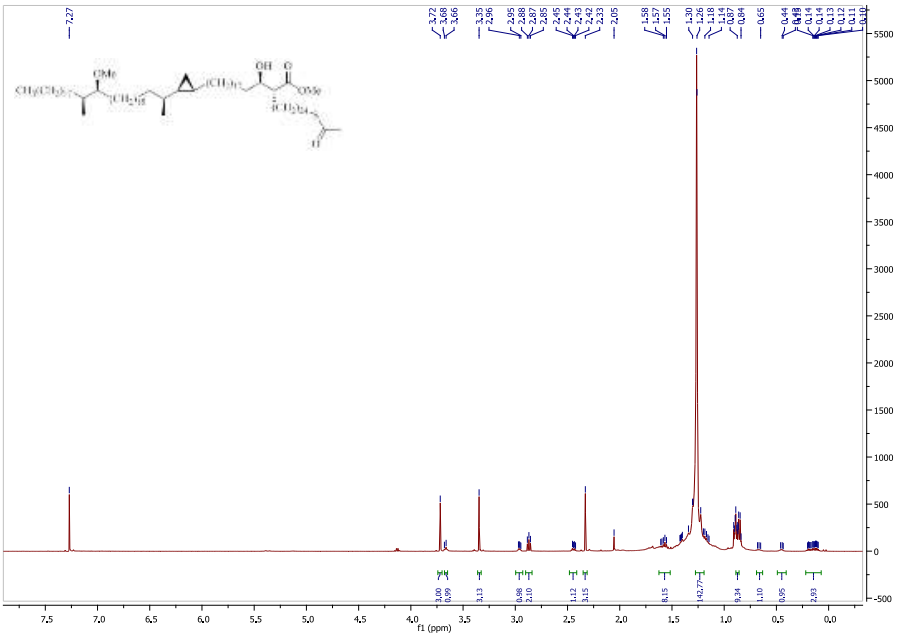
-4.95
f1 (ppm)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2.42
2.33
2.05
1.58
1.57
1.55
1.30
1.26
1.18
1.14
1.07
0.84
0.65
0.44
0.14
0.13
0.12
0.11
0.10
1.00
0.99
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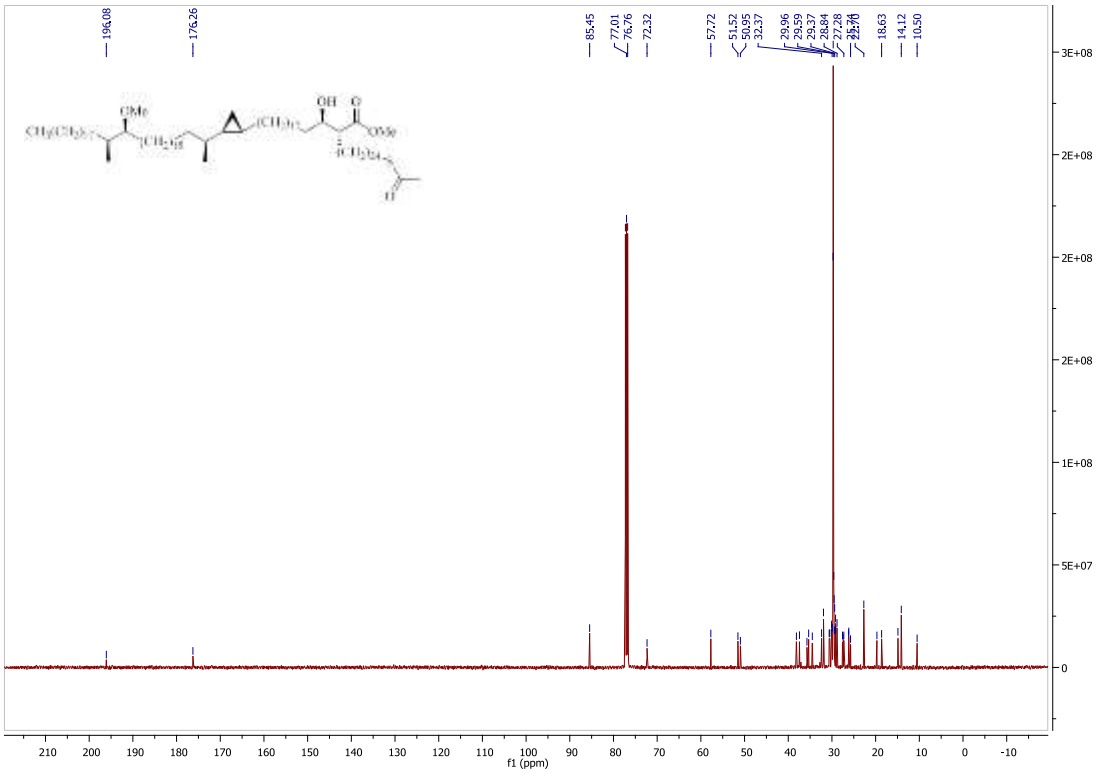
f1 (ppm)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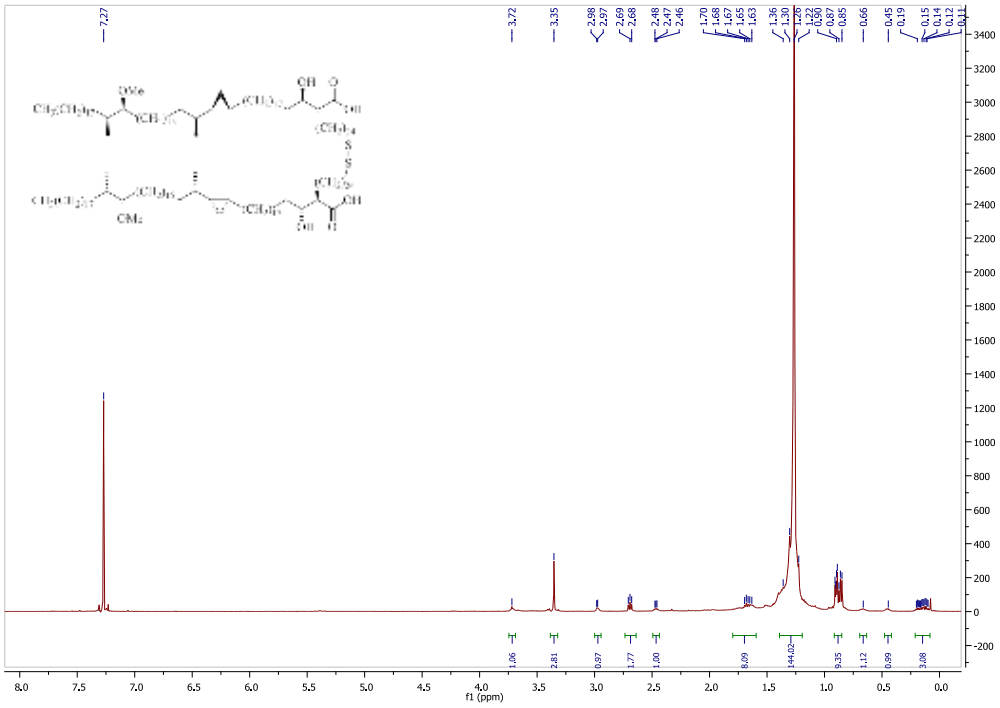
18.63
14.12
10.50
f1 (ppm)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1.63
1.36
1.30
1.26
1.22
0.90
0.87
0.85
0.66
0.45
0.19
0.15
0.14
0.12
0.11
1.06
2.81
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1.77
1.00
8.09
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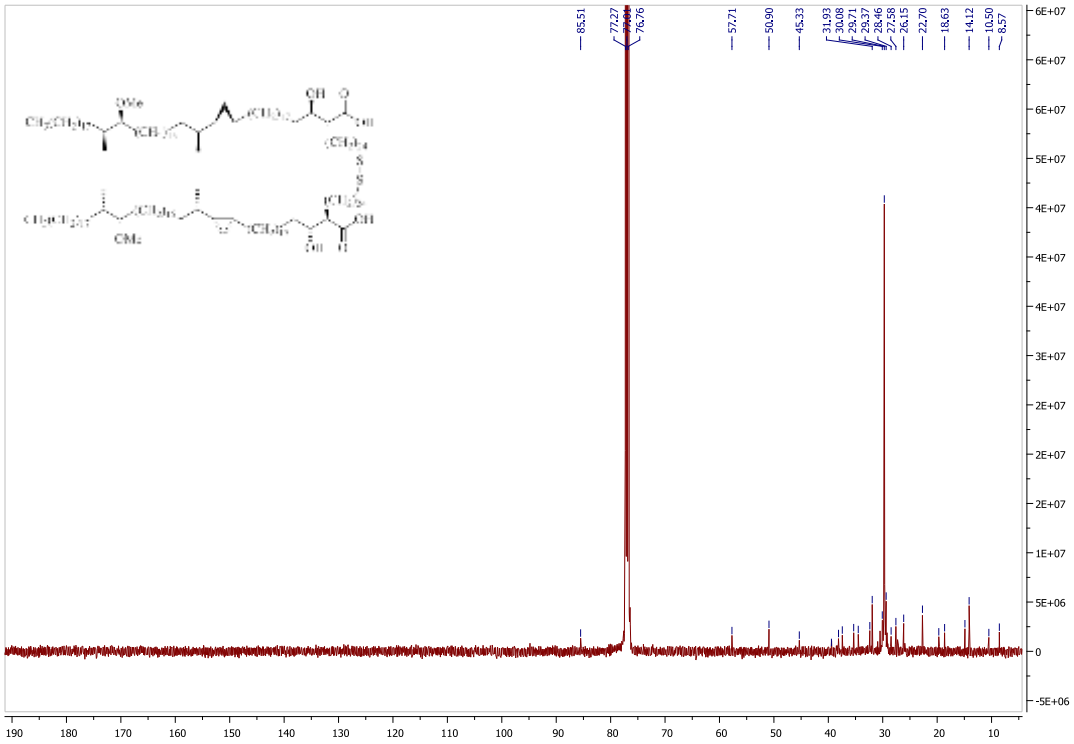
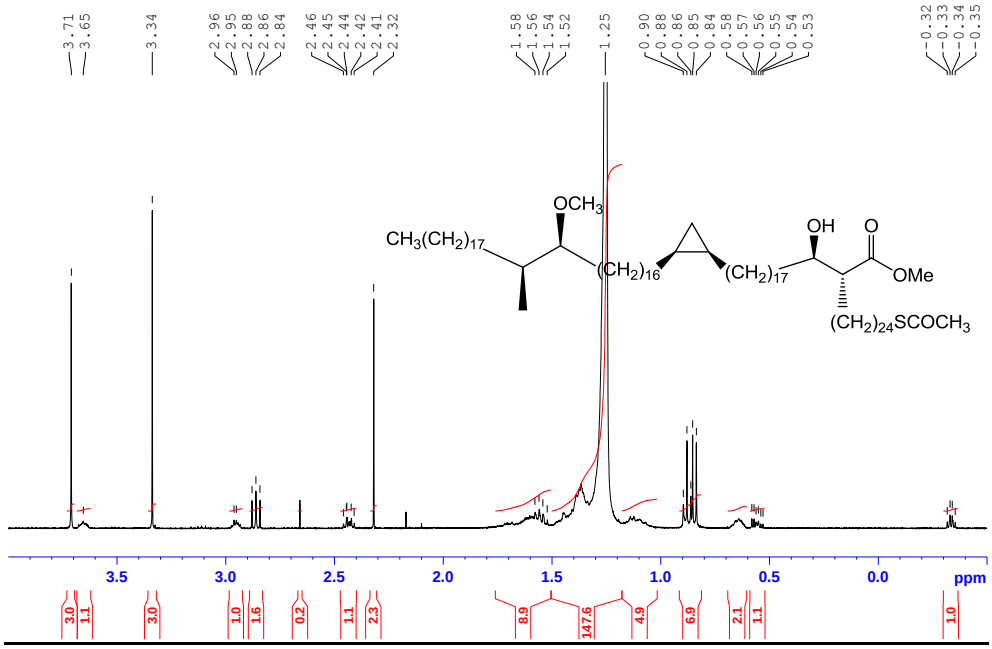
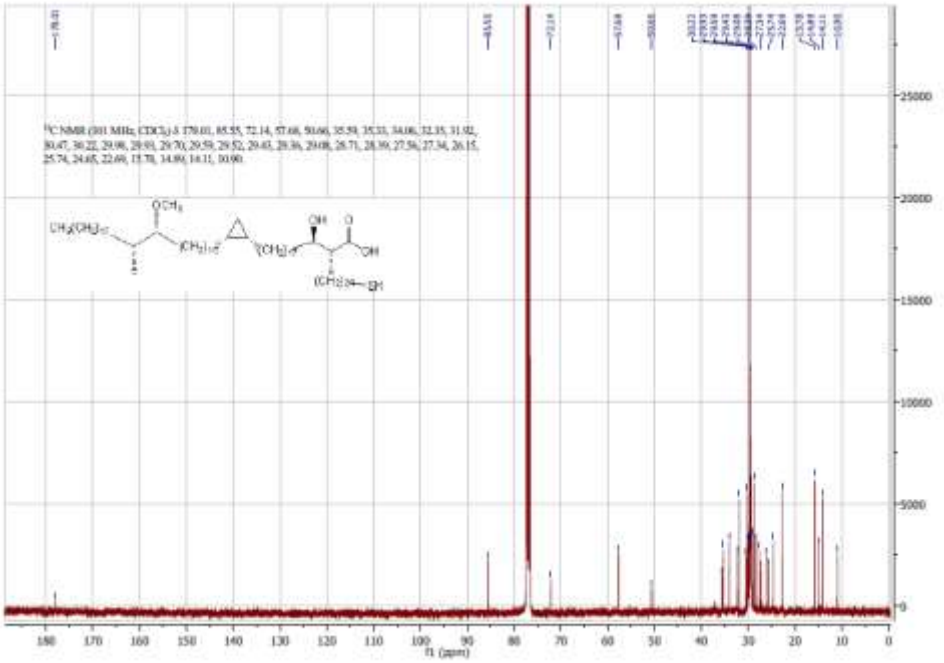
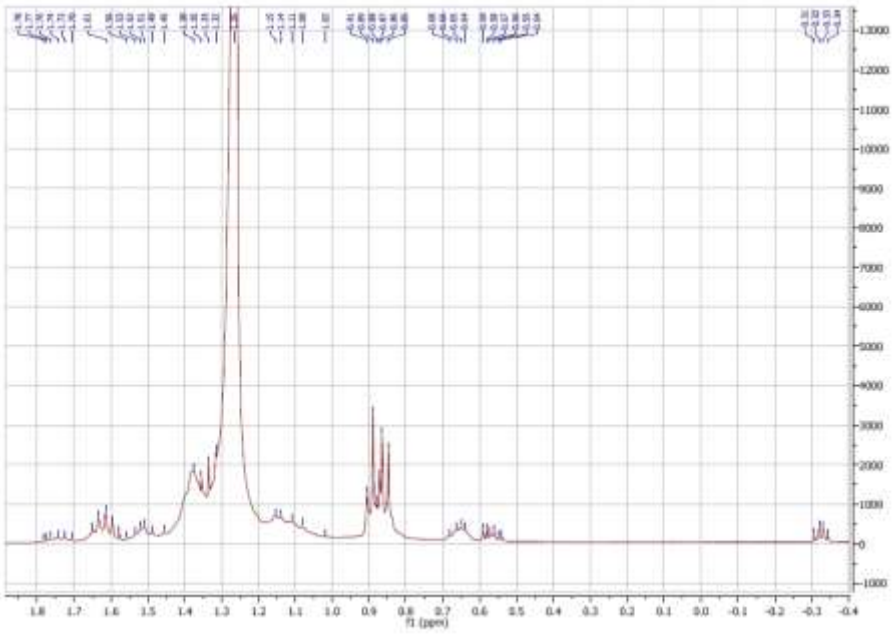
9.35
1.12
0.99
3.08
f1 (ppm)

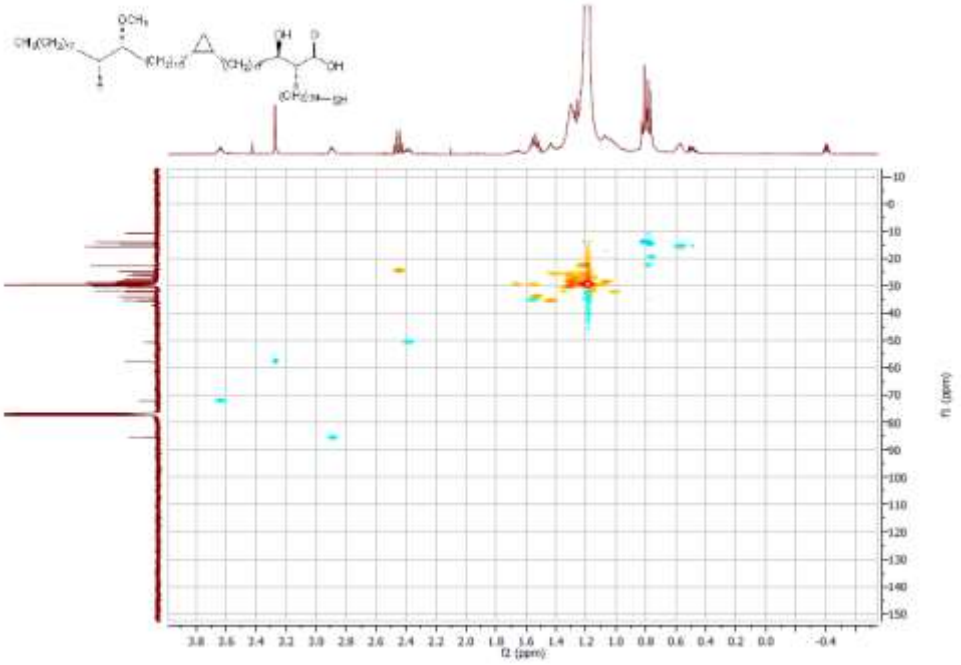


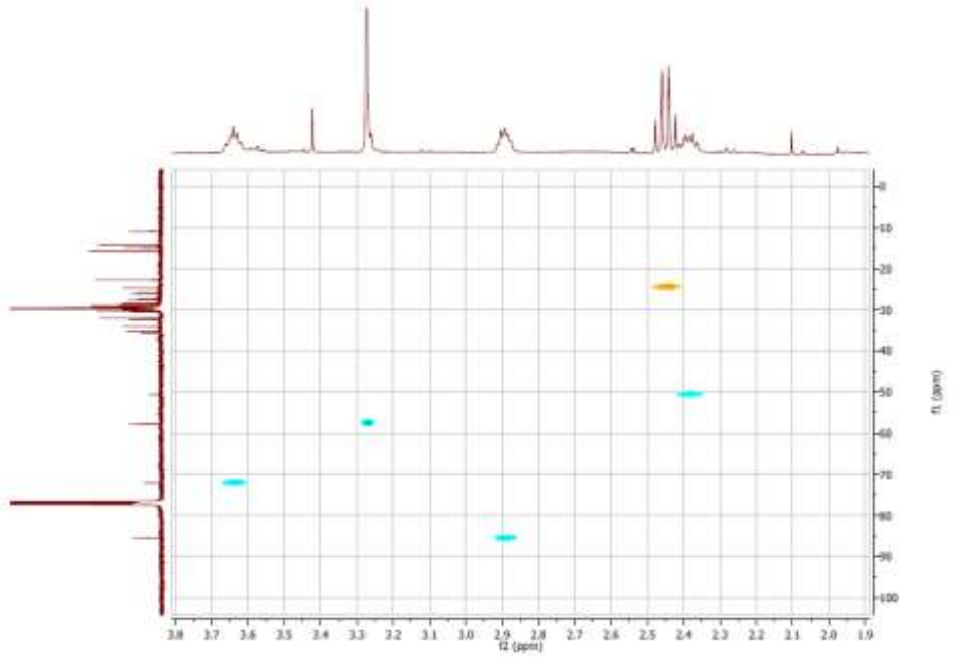
^{1}H NMR Spectrum of compound (**23**) (400 MHz, $CDCl_3$)

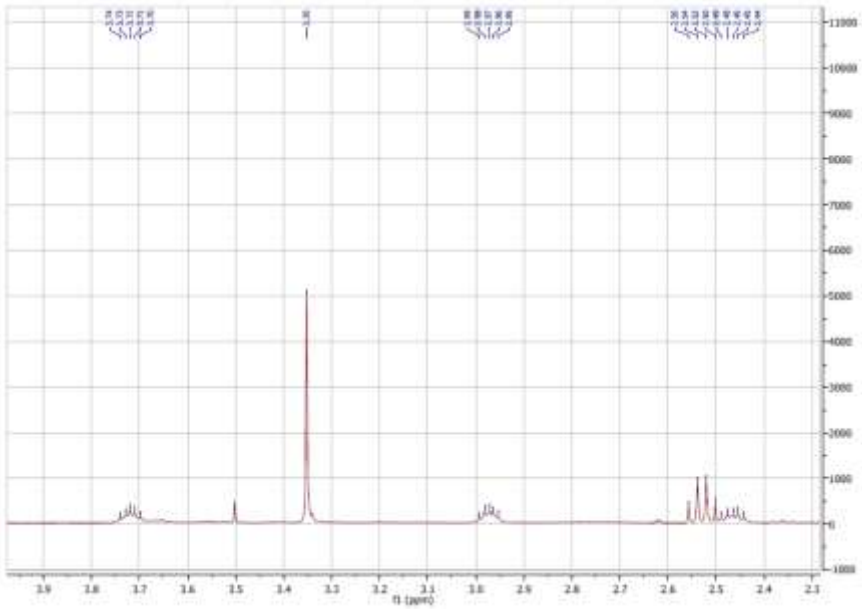


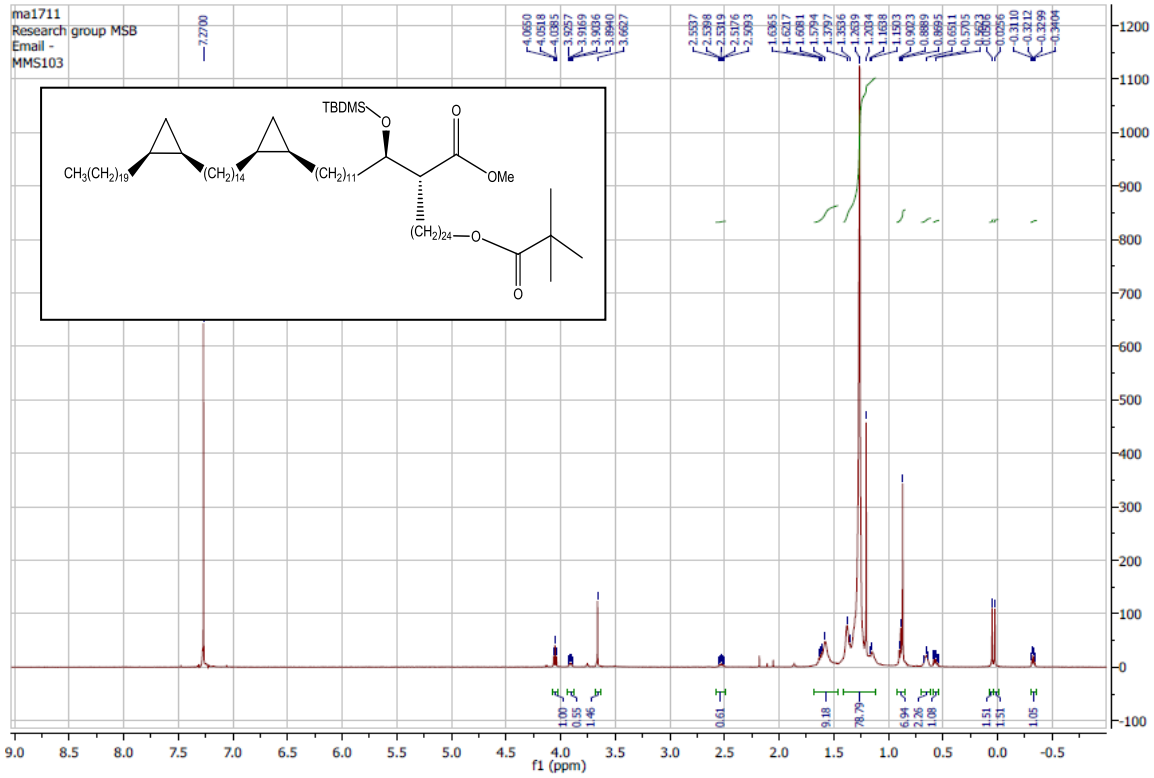


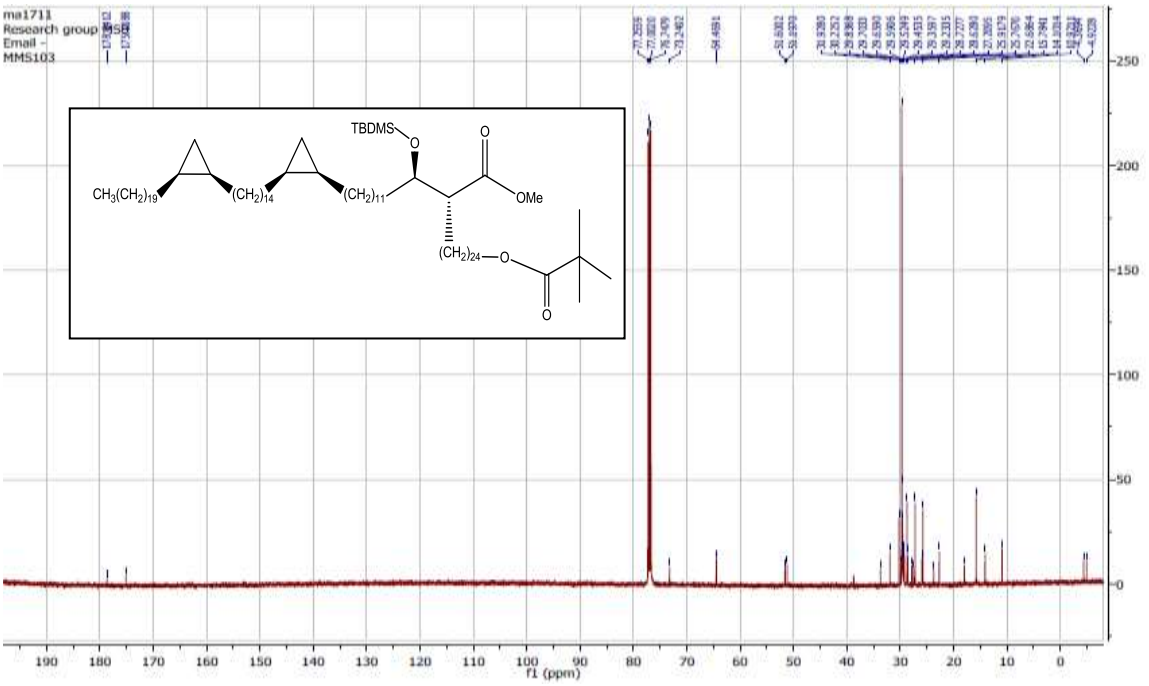




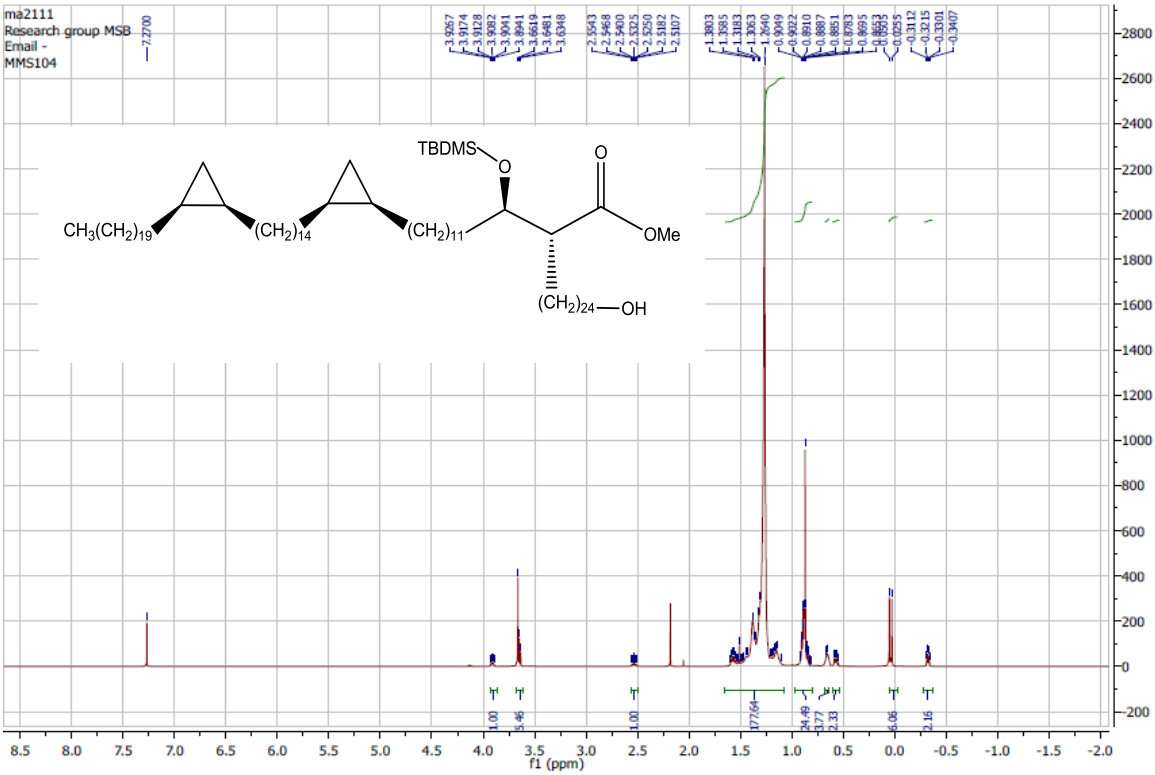


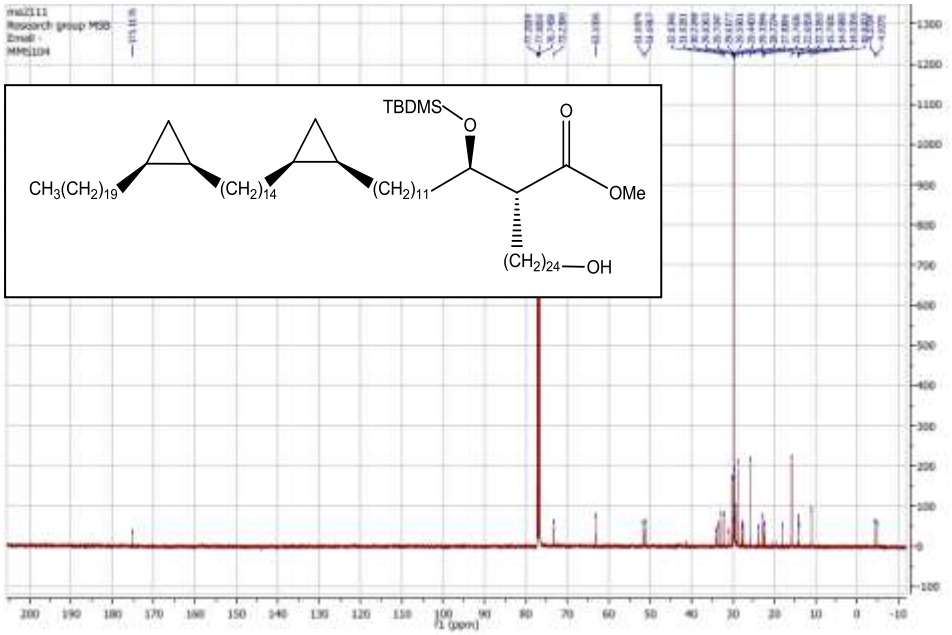



ma1711
Research group MSB
Email -
MMS103
TBDMS
OMe
f1 (ppm)

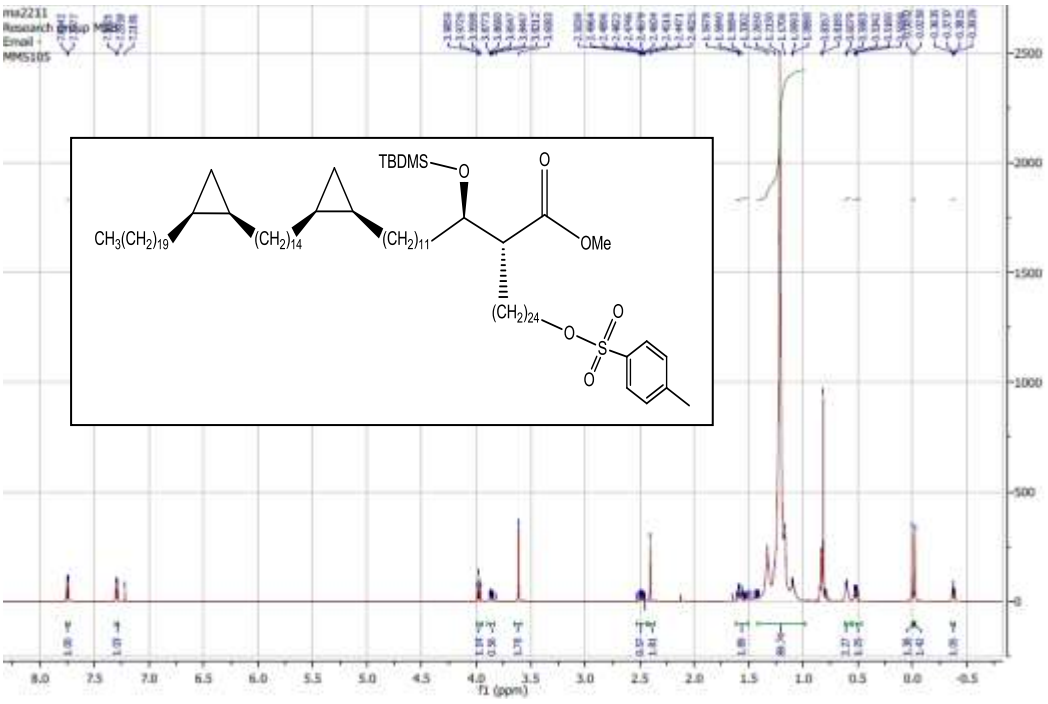


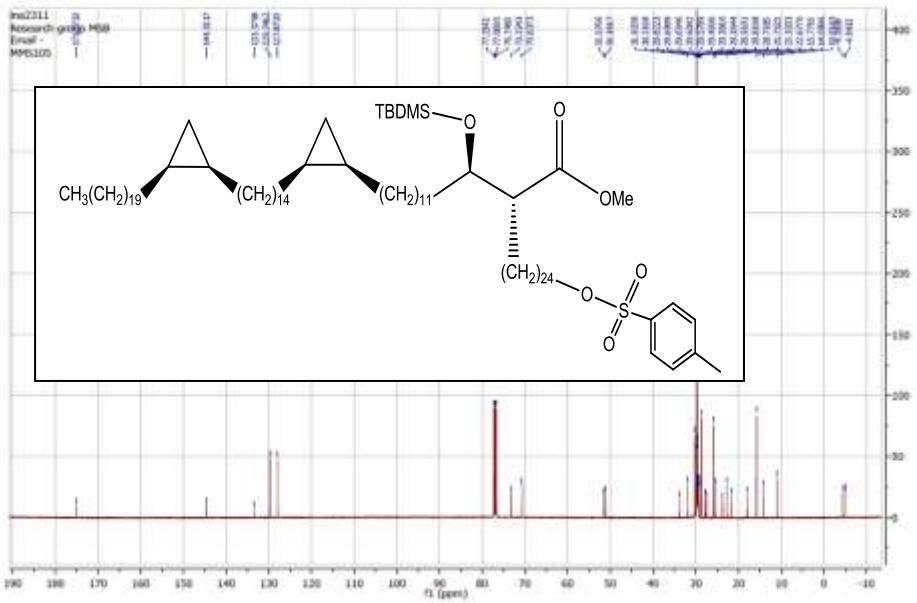
(*R*)-methyl-2-((*R*)-1-(tert-butyldimethylsilyloxy)-12-((*1R*,2*S*)-2-(14-((1*R*,2*S*)-2-icosylcy-clopropyl)tetradecyl)cyclopropyl)dodecyl)-26-(pivaloyloxy)hexacosanoate



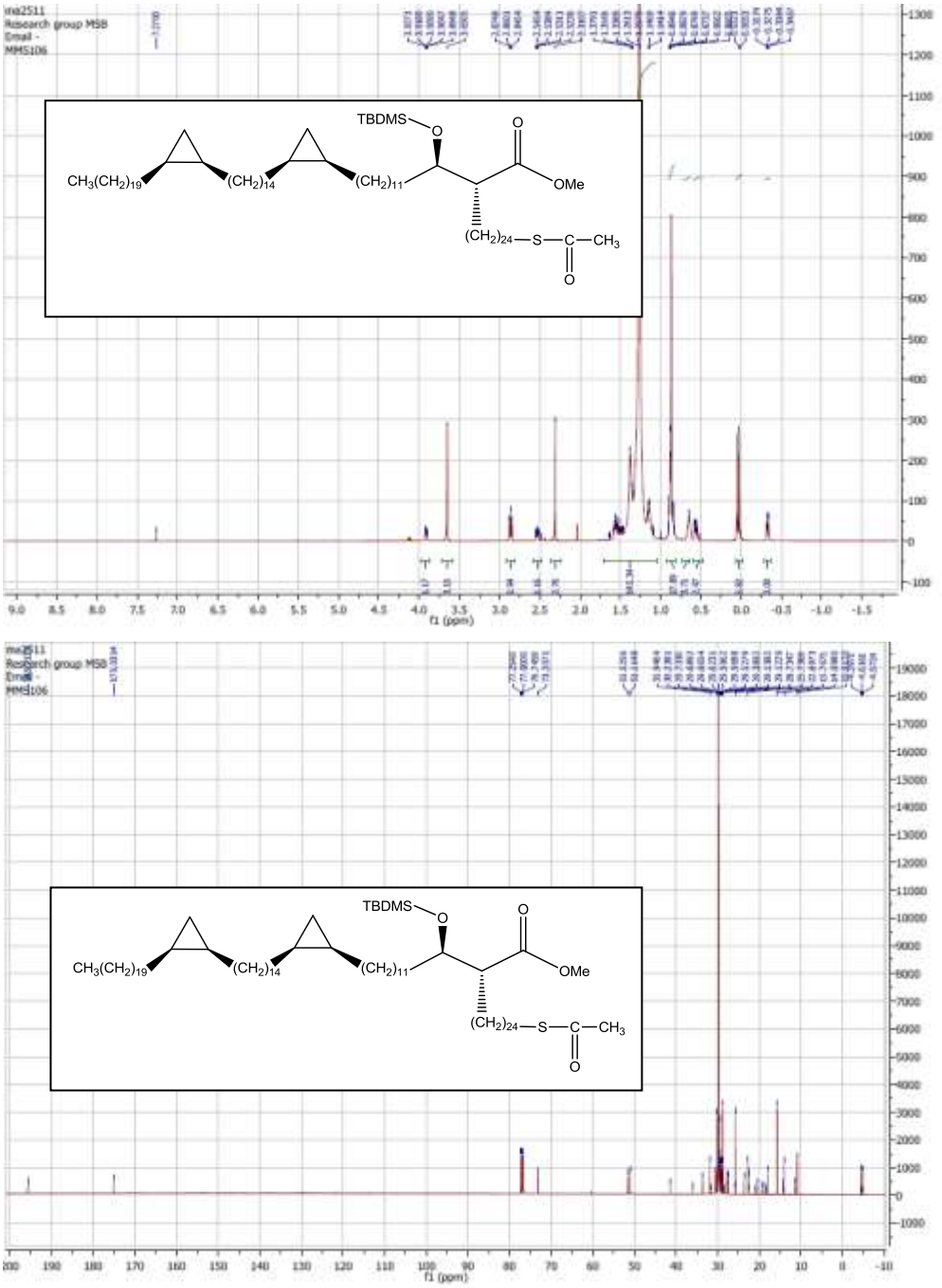


(*R*)-methyl-2-((*R*)-1-(tert-butyldimethylsilyloxy)-12-((1*R*,2*S*)-2-(14-((1*R*,2*S*)-2-icosylcyclopropyl)tetradecyl)cyclopropyl)dodecyl)-26-hydrox yhexacosanoate

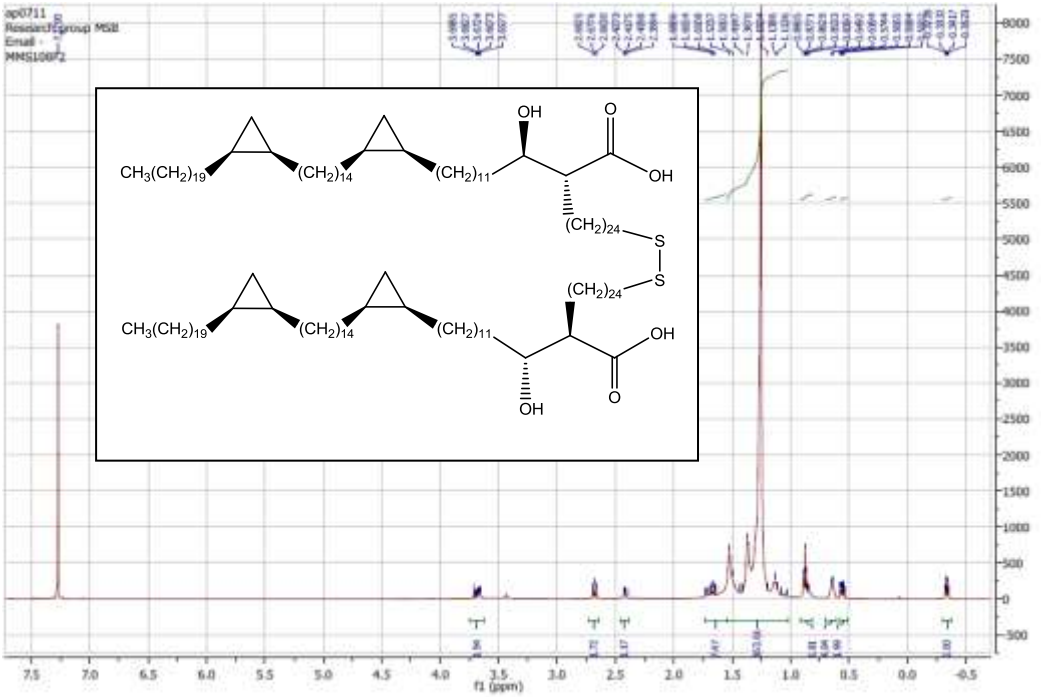


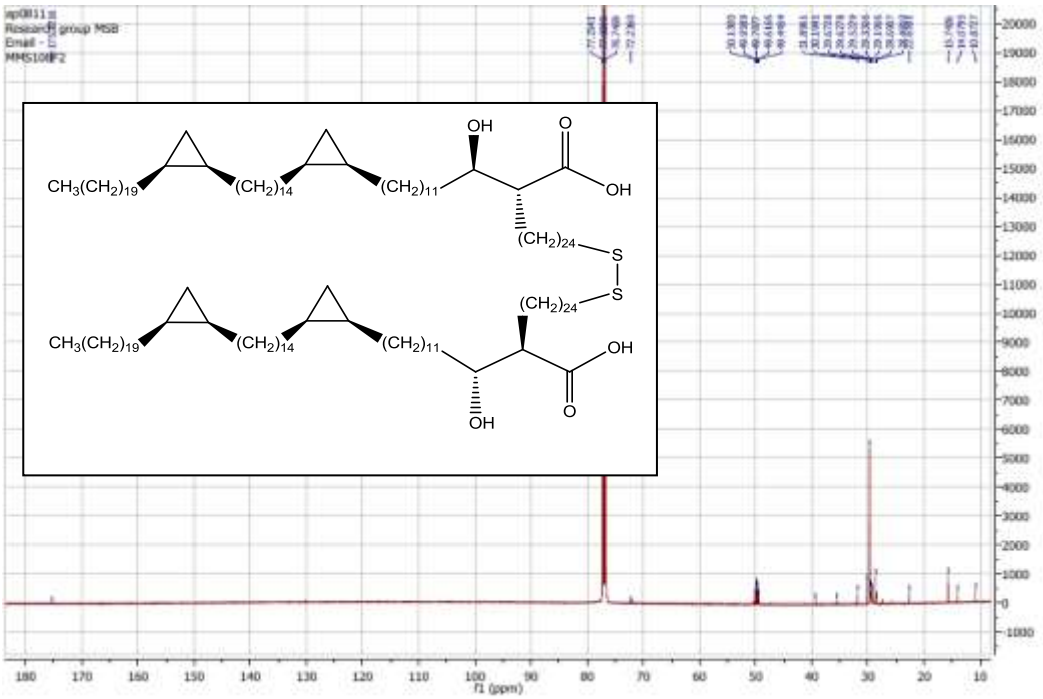


(*R*)-methyl-2-((*R*)-1-(tert-butyldimethylsilyloxy)-12-((1*R*,2*S*)-2-(14-((1*R*,2*S*)-2-icosylcyclopropyl)tetra-decyl)cyclopropyl)dodecyl)-26-(tosyloxy)hexacosanoate

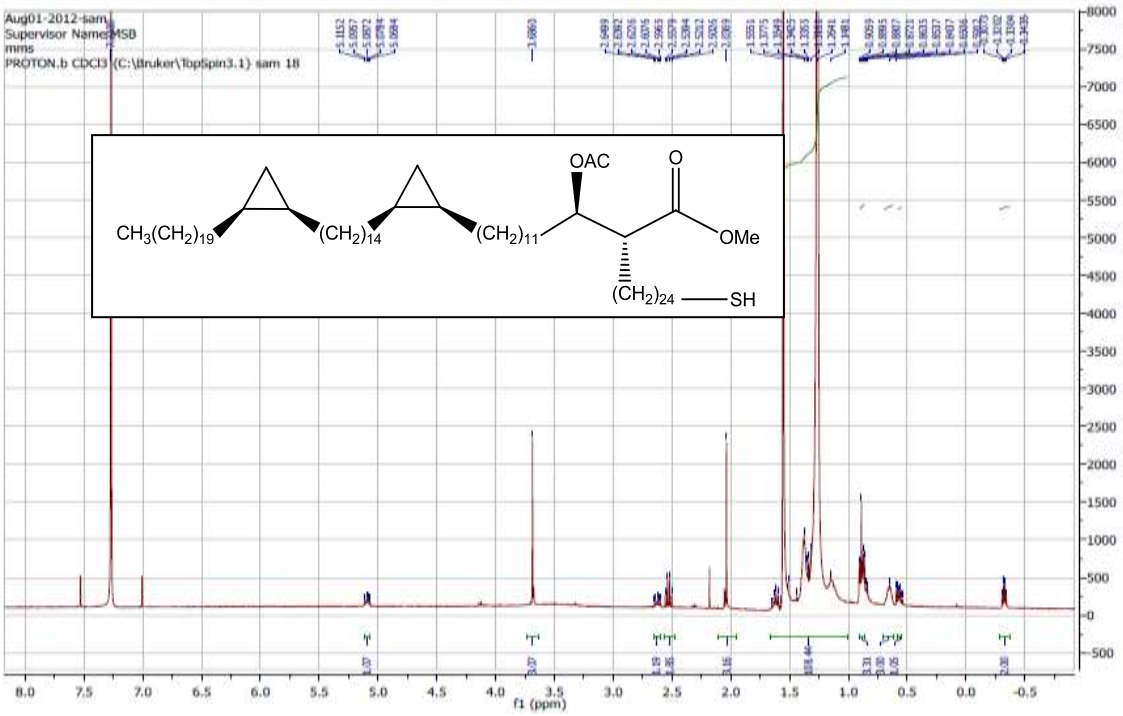


(*R*)-methyl-26-(acetylthio)-2-((*R*)-1-(tert-butyldimethylsilyloxy)-12-((1*R*,2*S*)-2-(14-((1*R*,2*S*)-2-icosylcyclopropyl)tetradec- yl)cyclopropyl)dodecyl)hexacosanoate





(*S*,*R*,*S*,*R*,*R*,2*R*,2'*R*)-26,26'-disulfanediylbis(2-((*R*)-1-hydroxy-12-((1*R*,2*S*)-2-(14-((1*R*,2*S*)-2-icosylcyclopropyl)tetradecyl) cyclopropyl)dodecyl)hexacosanoic acid)



(*R*)-methyl-2-((*R*)-1-acetoxy-12-((1*R*,2*S*)-2-(14-((1*R*,2*S*)-2-icosylcyclopropyl)tetradecyl)cyclopropyl)dodecyl)-26-mercaptohexacosanoate

Additional experimental data

(1-Phenyl-1*H*-tetrazole-5-ylsulfanyl) heptanol

1-Phenyl-1*H*-tetrazole-5-thiol (10.55 g, 59.23 mmol), was added to a stirred solution of 7-bromoheptan-1-ol (10.5 g, 53.84 mmol) and anhydrous potassium carbotonate (16.30 g, 118.46 mmol) in acetone (250 ml) at room temperature. The mixture was vigorously stirred for 18 hours at room temperature. TLC analysis indicated that the reaction was completed. Water (500 ml) was added to the mixture and the product was extracted with dichloromethane (1 x 200 ml, 2 x 100 ml). The combined organic phases were washed with brine (2 x 200 ml), dried and evaporated. The crude product was purified by column chromatography eluting petrol/ethyl acetate (5:1) to give a colourless oil of (1-phenyl-1*H*-tetrazole-5-ylsulfanyl)heptanol, (14 g, 89%) {Found $[M+Na]^+$: 315.1256; $C_{14}H_{20}ON_4SNa$ requires 315.1255}, δ_H: (500MHz, $CDCl_3$): 7.61-7.52 (5H, m), 3.6 (2H, t, *J* 6.6 Hz), 3.4 (2H, t, *J* 7.6 Hz), 1.82 (2H, pent, *J* 7.6 Hz), 1.5 (1H, s), 1.42 (2H, pent, *J* 6.6 Hz), 1.29-1.21 (6H, m); δc: 153.52, 133.71, 130.00, 129.72, 123.81, 62.93, 33.37, 32.72, 29.51, 29.35, 28.93, 28.61, 25.70; ν_{max}: 3401, 2929, 2857, 1461 cm^{-1}.

(1-Phenyl-1*H*-tetrazol-5-ylsulfonyl)heptanol

A solution of ammonium molybdate (VI) tetra hydrate (29.60 g, 23.95 mmol) in 35% H_2O_2 (50 ml), prepared and cooled in an ice bath was added to a stirred solution of (1-phenyl-1*H*-tetrazol-5-thiol)heptanol (14 g, 47.90 mmol) in THF(150 ml) and IMS (150 ml) at 10 ˚C. The reaction mixture was stirred at room temperature for 2 h, a further solution of ammonium molybdate (VI) tetra hydrate (14.80 g, 11.75mmol) in 35% H_2O_2 (25 ml) was added and the mixture was stirred at room temperature for 18 hours. The mixture was poured into water (1 L) and extracted with dichloromethane (1 x 250 ml, 3 x 150 ml). The combined organic phases were washed with water (500 ml), dried and the solvent was evaporated. The crude product was purified by column chromatography eluting petrol/ethyl acetate (5:1) and then (1:1) to give a yellow oil of (1-phenyl-1*H*-tetrazol-5-ylsulfonyl)heptanol (14 g, 90%) {Found $[M+Na]^+$ 347.1172; $C_{14}H_{20}O_3N_4SNa$ requires 347.1153}, δ_H: (500MHz, $CDCl_3$): 7.69-7.66 (2H, m), 7.62-7.54 (3H, m), 3.72 (2H, t, *J* 6.95 Hz), 3.61 (2H, t, *J* 6.6 Hz), 1.86 (2H, pent, *J* 6.95 Hz), 1.62 (1H, s), 1.54 (2H, pent, *J* 6.95 Hz), 1.39-1.21 (6H, m); δc: 153.49, 133.04, 131.48, 129.73, 125.08, 62.76, 55.95, 32.71, 29.56, 28.75, 28.07, 25.84; ν_{max}: 3401, 2929, 2857, 1596, 1463, 1338,1152,764 cm^{-1}.

7-Bromo-(1-phenyl-*1H*-tetrazole-5-sulfonyl)heptane

N-Bromosuccinimide (9.99 g, 56.13 mmol) was added in portion to a stirred solution of (1-phenyl-*1H*-tetrazole-5-sulfonly)heptanol (14 g, 43.18 mmol) and triphenylphosphine (14.72 g, 54.34 mmol) in dichloromethane (300 ml) at 0 ˚C over 10 min. The mixture was allowed to reach room temperature and stirred at room temperature for 75 min, TLC showed no starting material was left then sat. aq. sodium meta bisulfate (60 ml) was added and the organic layer was separated. The aqueous layer was re-extracted with dichloromethane (2 x 200 ml) and the combined organic layers were dried and evaporated to give a residue which was treated with petrol/ethyl acetate (5:1, 300 ml) and stirred for 30 min. The triphenylphosphonium oxide was filtered and washed with petrol/ethyl acetate (5:1, 100 ml) then the solvent was evaporated. The crude product was purified by column chromatography eluting with

petrol/ethyl acetate (5:1) to give a colourless oil, 7-bromo-(1-phenyl-*1H*-tetrazole-5-sulfonyl)heptane (14 g, 83%) {Found $[M+Na]^+$: 409.0311; $C_{14}H_{19}O_2N_4SNaBr$ requires 409.0309}, δ_H: (500MHz, $CDCl_3$): 7.69-7.67 (2H, m), 7.64-7.59 (3H, m), 3.74 (2H, t, *J* 7.95 Hz), 3.40 (2H, t, *J* 6.95 Hz), 1.96 (2H, *J* 7.9 Hz), 1.86 (2H, *J* 6.65), 1.56-1.39 (6H, m); δc: 153.42, 132.99, 131.44, 129.69, 125.02, 55.86, 33.59, 32.44, 28.02, 27.91, 27.65, 21.88; ν_{max}: 2934, 2859, 1739, 1596, 1497, 1466, 1341, 1152, 764 cm^{-1}.

(*R*)-2-[(*R*)-10-Bromo-1-(tert-butyl-dimethyl-silanyloxy)-decyl]-26-(2,2-dimethylpropionyloxy) hexacosanoic acid methyl ester

Lithium bis(trimethylsilyl)amide (5.85 ml, 4.77 mmol,) was added to a stirred solution of (*R*)-2-[(*R*)-1-(*tert*-butyl-dimethyl-silanyloxy)-3-oxo-propy]-26-(2,2-dimethyl-propionyloxy)-hexacosanoic acid methyl ester **17** (2.46 g, 3.67 mmol) and 7-bromo-(1-phenyl-1*H*-tetrazole-5-sulfonyl)heptane (1.84 g, 4.77 mmol) in dry THF(100 ml) under nitrogen at -10 ˚C. The reaction turned bright yellow and was left to reach r.t. and stirred for one hour under nitrogen atmosphere. Then TLC showed no starting material was left. The reaction was quenched with sat. Solution of NH_4Cl (20 ml). The product was extracted with petrol / ethyl acetate (20:1) (3x 150 ml) dried over $MgSO_4$, filtered and evaporated. The crude prodect was purified by column chromotography over silica eluting solvent with petrol/ethyl acetate (20:1) to give a colourless oil, (*R*)-2-[(*E*/*Z*)-(*R*)-10-bromo-1-(*tert*-butyl-dimethyl-silanyloxy)-dec-3-enyl]-26-(2,2-dimethylpropionyloxy)hexacosanoic acid methyl ester, (2.30 g, 76%) in ratio (2:1). Palladium on carbon (10%), (0.3 g) was added to a stirred solution of (*R*)-2-[(*E*/*Z*)-(*R*)-10-bromo-1-(tert-butyl-dimethyl-silanyloxy)-dec-3-enyl]-26-(2,2-dimethylpropionyloxy)hexacosanoic acid methyl ester (2.30 g, 2.68 mmol) in IMS/THF (1:1, 100 ml) under hydrogen atmosphere. Hydrogenation was carried out for 1 hour. The mixture was filtered over a bed of celite and the solvent was evaporated. The crude product was purified by column chromatography eluting with petrol/ethyl acetate (10:1) to give a colourless oil, (*R*)-2-[(*R*)-10-bromo-1-(*tert*-butyl-dimethyl-silanyloxy)-decyl]-26-(2,2dimethylpropionyloxy)-hexacosanoic acid methyl ester (2.0 g, 81%), $[\alpha]_D^{22}$ = -17.56 (c 1.4, $CHCl_3$) {Found $[M+Na]^+$: 881.5904, $C_{48}H_{95}O_5SiBrNa$ requires 881.6024}; δ_H: (500MHz, $CDCl_3$); 4.03 (2H, t, *J* 6.6 Hz),

3.91-3.88 (1H, m), 3.64 (3H, s), 3.39 (2H, t, *J* 6.9 Hz), 2.51 (1H, ddd, *J* 3.8, 7.25, 11.05 Hz), 1.84 (2H, pent, *J* 6.95 Hz), 1.60 (2H, pent, *J* 6.6 Hz), 1.30-1.14 (67H, m, including singlet at δ 1.18), 0.86 (9H, s), 0.03 (3H, s), 0.02 (3H,s); δc: 178.56, 175.05, 73.14, 64.41, 60.32, 51.52, 51.17, 41.31, 38.67, 36.03, 33.60, 32.79, 31.87, 29.78, 29.68, 29.55, 29.49, 29.31, 29.19, 29.01, 28.69, 28.58, 28.13, 27.79, 27.44, 27.16, 25.87, 25.71, 23.64, 22.64, 20.98, 17.92, 14.16, -4.40, -4.97; ν_{max}: 2923, 2853, 1732, 1463, 1366, 1284, 1254, 1159, 1070, 836, 775 cm^{-1}.

Methyl (*R*)-2-((*R*)-1-(*tert*-butyldimethylsilyloxy)-10-(1-phenyl-1*H*-tetrazol-5-ylsulfanyl) decyl)-26-(pivaloyloxy) hexacosanoate

1-Phenyl-1*H*-tetrazole-5-thiol (0.41 g, 2.29 mmol) was added to a stirred solution of (*R*)-2-[(*R*)-10-bromo-1-(*tert*-butyl-dimethyl-silanyloxy)-decyl]-26-(2,2-dimethylpropionyloxy)hexacosanoic acid methyl ester (1.8 g, 2.093 mmol) and anhydrous potassium carbotonate (0.63 g, 4.60 mmol) in acetone and THF (30 : 15 ml) at room temperature. The reaction mixture was refluxed for 2 and then TLC showed no starting material was left. Water (50 ml) was added and the product was extracted with dichloromethane (1 x 100 ml, 2 x 75 ml). The combined organic layers were washed with brine (2 x 100 ml), dried and evaporated. The crude product was purified by column chromatography eluting with petrol/ethyl acetate (5:1) to give a colourless oil, (*R*)-methyl2-((*R*)-1-(*tert*-butyldimethylsilyloxy)-10-(1-phenyl-1*H*-tetrazol-5-ylsulfanyl)decyl)-26-(pivaloyloxy)hexacosanoate (1.70 g, 85%), $[\alpha]_D^{22}$ = -3.84 ; {Found $[M+Na]^+$: 979.7046; $C_{55}H_{100}O_5SiNSNa$ requires 979.7076}; δ_H: (500MHz, $CDCl_3$): 7.58-7.53 (5H, m), 4.04 (2H, t, *J* 6.65 Hz), 3.91-3.88 (1H, m), 3.65 (3H, s), 3.39 (2H, t, *J* 7.5 Hz), 2.52 (1H, ddd, 3.8, 7.25, 10.75 Hz), 1.82 (2H, pent, *J* 7.6 Hz), 1.60 (2H, pent, *J* 6.9 Hz), 1.35-1.13 (67H, m, including a singlet at δ 1.19), 0.86 (9H, s), 0.04 (3H, s), 0.02 (3H, s); δc: 178.65, 175.10, 154.49, 133.75, 130.03, 129.78, 123.83, 73.16, 64.45, 51.57, 51.22, 38.71, 33.62, 33.34, 29.77, 29.69, 29.57, 29.46, 29.36, 29.20, 29.07, 28.99, 28.64, 27.83, 27.44, 27.19, 25.89, 25.74, 23.71, 22.63, 17.95, 14.09, 11.41, -4.38, -4.93; ν_{max}: 2928, 2854, 1731, 1500, 1463, 1284, 1250, 1160, 1073, 836, 775 cm^{-1}.

Methyl (*R*)- 2-((*R*)-1-(*tert*-butyldimethylsilyloxy)-10-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl) decyl)-26-(pivaloyloxy) hexacosanoate

A solution of ammonium molybdate (VI) tetra hydrate (1.05 g, 0.85 mmol) in 35% H_2O_2 (15 ml), prepared and cooled in an ice bath was added to a stirred solution of (*R*)-methyl-2-((*R*)-1-(tert-butyldimethylsilyloxy)-10-(1-phenyl-1*H*-tetrazol-5-ylsulfan -yl) decyl)-26-(pivaloyloxy)hexacosanoate (1.63 g, 1.70 mmol) in THF/ IMS (15:20 ml) at 10 ˚C and stirred at room temperature for 2 h. A further solution of ammonium molybdate (VI) tetra hydrate (0.52 g, 0.42 mmol) in 35% H_2O_2 (10 ml) was added and the mixture was stirred at room temperature for 18 hours. The mixture was poured into water (250 ml) and the product was extracted with petrol/ethyl acetate (5:2) (200 ml). The combined organic layers were washed with water (100 ml), dried and evaporated. The crude product was purified by column chromatography eluting with petrol/ethyl acetate (5:1) and then (1:1) to give a colourless oil, (*R*)-methyl-2-((*R*)-1-(tert-butyldimethylsilyloxy)-10-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl)decyl)-26-(pivaloyloxy)hexacosanoate (**33**) (1.28 g, 76%), $[\alpha]_D^{23}$ -7.64 (*c* 1.0, $CHCl_3$) {Found $[M+Na]^+$: 1011.6958; $C_{55}H_{100}O_7SiN_4SNa$ requires 1011.6974}; δ_H: (500MHz, $CDCl_3$): 7.71-7.69 (2H, m), 7.62-7.60 (3H, m), 4.04 (2H, t, *J* 6.6 Hz), 3.92-3.88 (1H, m), 3.73 (2H, t, *J* 7.85 Hz), 3.65 (3H, s), 2.52 (1H, ddd, *J* 3.45, 6.9, 10.7 Hz), 1.95 (2H, pent, *J* 7.6 Hz), 1.61 (2H, pent, *J* 6.9 Hz), 1.53-1.15 (67H, m, including a singlet at δ 1.19), 0.86 (9H,s), 0.04 (3H, s), 0.02 (3H, s); δc : 178.66, 175.08, 153.48,133.03, 131.43, 129.70, 125.04, 73.15, 64.46, 55.99, 51.58, 51.23, 38.71, 33.61, 29.55, 29.44, 29.39, 29.21, 28.87, 28.59, 28.13, 27.84, 27.43, 27.19, 25.89, 25.74, 23.73, 21.94, 17. 96, -4.37, -4.93; ν_{max}: 2925, 2853, 1731, 1463, 1344, 1284, 1254, 1154, 1099, 1074, 836, 775 cm^{-1}

Methyl (2*R*,3*R*)-5-(benzyloxy)-3-(*tert*-butyldimethylsilyloxy)-2-(2-oxoethyl) pentanoate (5)

2,6-Lutidine (1.64 g, 15.28 mmol, 1.77 ml) and osmium tetroxide 2.5 % in 2-methyl-2-propanol (1.72 ml, 0.14 mmol), followed by $NaIO_4$ (6.52 g, 30.48 mmol) were added to a stirred solution of methyl (*R*)-2-((*R*)-3-(benzyloxy)-1-(*tert*-butyldimethyl-silyloxy)-propyl)pent-4-enoate (3.0 g, 7.63 mmol) in 1,4-dioxane/water (3:1, 150 ml) at room temperature. After stirring for ~2.5 hrs the mixture was quenched with water (200 ml) and extracted with dichloromethane (1 x 200 ml, 2 x 50 ml). The combined

organic layers were washed with brine (150 ml), dried, filtered and evaporated. Column chromatography (petrol/ethyl acetate, 5:2) gave methyl (2*R*,3*R*)-5-(benzyl-oxy)-3-(*tert*-butyldimethyl-silyloxy)-2-(2-oxoethyl)pentanoate **(5)** (2.31 g, 77 %) [Koza, 2009] as a colourless oil. This showed δ_H: 9.81 (1H, s), 7.28-7.36 (5H, m), 4.50 (1H, d, *J* 11.7 Hz), 4.47 (1H, d, *J* 12.0 Hz), 4.26 (1H, dt, *J* 4.1, 8.1 Hz), 3.68 (3H, s, OCH_3), 3.52 (2H, m), 3.23 (1H, ddd, *J* 3.5, 7.9, 10.4 Hz), 2.98 (1H, dd, *J* 10.6, 18.1 Hz), 2.71 (1H, dd, *J* 3.3, 18.1 Hz), 1.68 (2H, m), 0.86 (9H, s), 0.08 (3H, s) and 0.07 (3H, s); δ_C: 200.5, 172.4, 128.4, 127.6, 127.5, 72.9, 68.8, 66.6, 52.0, 45.3, 40.0, 33.7, 25.7, 22.6, 19.4, 17.9, -4.7, -4.8; ν_{max}(film)/cm^{-1}: 3031, 2955, 2857, 1729 and 1462

1-Phenyl-5-(12-(tetrahydro-2*H*-pyran-2-yloxy)dodecylthio)-1*H*-tetrazole.

2-(12-Bromododecyloxy)tetrahydro-2*H*-pyran (12.38 g, 35.47 mmol) was added with vigorous stirring to 1-phenyl-1*H*-tetrazole-5-thiol (6.32 g, 35.47 mmol) and anhydrous potassium carbonate (9.80 g, 70.94 mmol) in acetone (150 ml). The mixture was heated under reflux overnight. The inorganic solids were filtered off and washed with acetone (100 ml). The organic filtrate was evaporated to give a residue to which dichloromethane (150 ml) and water (300 ml) were added. The solution was extracted with dichloromethane (3 x 300 ml) and the combined organic extracts were dried, filtered and evaporated. Column chromatography (petrol/ethyl acetate, 5:1) gave 1-phenyl-5-(12-(tetrahydro-2*H*-pyran-2-yloxy)dodecylthio)-1*H*-tetrazole (14.26 g, 90 %) as a colorless oil. {Found $(M+Na)^+$: 469.2618, $C_{24}H_{38}O_2N_4SNa$ requires 469.2613}.This showed δ_H: 7.58 (5H, m), 4.57 (1H, t, *J* 3.5 Hz), 3.87 (1H, ddd, *J* 3.3, 7.7, 11.0 Hz), 3.73 (1H, dt, *J* 7.0, 9.5 Hz), 3.50 (1H, m), 3.39 (3H, m), 1.81 (3H, m), 1.72 (1H, m), 1.57 (8H, m), 1.44 (2H, m) and 1.26 (12H, m); δ_C: 154.5, 133.8, 130.1, 129.8, 123.9, 98.9, 67.7, 62.4, 33.4, 30.8, 29.8, 29.6, 29.54, 29.51, 29.48, 29.43, 29.40, 29.1, 29.03, 29.00, 28.6, 26.2, 25.5, 19.7; ν_{max}(film)/cm^{-1}: 2927, 2853, 1597, 1500 and 1463.

1-Phenyl-5-(12-(tetrahydro-2*H*-pyran-2-yloxy)dodecylsulfonyl)-1*H*-tetrazole (6)

A solution of ammonium molybdate (VI) tetrahydrate (19.54 g, 0.016 mol) in ice cold hydrogen peroxide (35 %, w/w, 50 ml) was added with stirring to 1-phenyl-5-(12-(tetrahydro-2*H*-pyran-2-yloxy)dodecylthio)-1*H*-tetrazole (14.1 g, 0.032 mol) in THF

(200 ml) and IMS (400 ml) at 12 °C. After 2 hrs at 15-20 °C, further ammonium molybdate (VI) tetrahydrate (7.90 g, 6.4 mmol) in ice cold hydrogen peroxide (35 %, w/w, 20 ml) was added and the mixture was stirred at room temperature for 18 hours. The solution was then poured into water (1 L), extracted with dichloromethane (3 x 250 ml), and the combined organic extracts were dried, filtered and evaporated. Column chromatography (petrol/ethyl acetate, 10:3) gave 1-phenyl-5-(12-(tetrahydro-2*H*-pyran-2-yloxy)dodecylsulfonyl)-1*H*-tetrazole **(6)** (11.60 g, 77 %) as a white solid, m.p. 30-32 °C {Found $(M+Na)^+$: 501.2524, $C_{24}H_{38}O_4SNa$ requires 501.2511}. This showed δ_H: 7.67 (2H, m), 7.59 (3H, m), 4.55 (1H, dd, *J* 3.0, 4.3 Hz) 3.86 (1H, ddd, *J* 3.4, 7.6, 11.1 Hz), 3.72 (3H, m), 3.49 (1H, m), 3.38 (1H, dt, *J* 6.7, 9.6 Hz), 1.92 (2H, m), 1.81 (1H, m), 1.68 (1H, m), 1.52 (8H, m) and 1.29 (14H, m); δ_C: 153.5, 133.1, 131.4, 129.7, 125.1, 98.8, 67.7, 62.3, 56.0, 30.8, 29.7, 29.52, 29.48, 29.45, 29.42, 29.2, 28.9, 28.1, 26.2, 25.5, 21.9, 19.7; ν_{max}(film)/cm^{-1}: 2920, 2853, 1592, 1497, 1457.

Methyl (2*R*,3*R*)-2-(14-bromotetradecyl)-3-(*tert*-butyldimethylsilyloxy) heneicosanoate (10)

N-Bromosuccinimide (51 mg, 0.23 mmol) was added in portions to a stirred solution of alcohol **(8)** (129 mg, 0.19 mmol) and triphenylphosphine (74 mg, 0.23 mmol) in dichloromethane (10 ml) at 0 °C. The solution was allowed to warm to room temperature and stirred for 1 hr, then quenched with sat.aq. $Na_2S_2O_5$ (20 ml). The aqueous layer was re-extracted with dichloromethane (2 x 20 ml). The combined organic layers were washed with water (10 ml), dried, filtered and evaporated. The residue was treated with petrol/ethyl acetate (1:1, 20 ml) and heated under reflux for 30 minutes. The solution was filtered, washed with petrol/ethyl acetate (1:1) and the solvent evaporated. Column chromatography (petrol/ethyl acetate, 10:1) gave methyl (2*R*,3*R*)-2-(14-bromotetradecyl)-3-(*tert*-butyldimethylsilyloxy)henicosanoate **(10)** (102 mg, 72 %) as a colourless oil, $[\alpha]_D^{23}$ -0.89 (*c* 1.13, $CHCl_3$). This showed δ_H: 3.91 (1H, dt, *J* 4.7, 6.6 Hz), 3.66 (3H, s), 3.41 (2H, t, *J* 7.0 Hz), 2.53 (1H, ddd, *J* 3.7, 7.2, 11.0 Hz), 1.85 (2H, pent., *J* 7.2 Hz), 1.54 (2H, m), 1.42 (2H, m), 1.26 (54H, m), 0.88 (3H, t, *J* 6.9 Hz), 0.87 (9H, s), 0.05 (3H, s) and 0.02 (3H, s); δ_C: 174.1, 72.2, 50.6, 50.2, 32.9, 32.7, 31.9, 30.9, 28.8, 28.73, 28.69, 28.65, 28.60, 28.58, 28.53, 28.43,

28.35, 27.8, 27.2, 26.8, 26.5, 24.7, 22.7, 21.7, 17.0, 13.1, -5.4 and -5.9; ν_{max}(film)/cm^{-1}: 2925, 2853, 1740 and 1463.

Attempted preparation of thiol (12)

(i) A solution of thiourea (1.5 mg, 0.020 mmol) and bromide **(10)** (10 mg, 0.013 mmol) in ethanol (1 ml) was heated under reflux for 2.5 hrs. The solvent was evaporated and 5 M NaOH (1 ml) was added slowly whilst stirring and the reaction mixture was heated under reflux for another 2 hrs, then cooled in an ice bath, acidified with dilute HCl and extracted with ethyl acetate (3 x 10 ml). The combined organic layers were dried, filtered and evaporated. The residue, which contained numerous spots on TLC, gave a complicated 1H NMR spectrum.

(ii) The reaction was repeated using thiourea (1.5 mg, 0.020 mmol), bromide (10) (10 mg, 0.013 mmol) and ethanol (1 ml) which were heated under reflux overnight. The residueof this reaction, which contained numerous spots on TLC, gave a complicated ^{1}H NMR spectrum.

(iii) A solution of thiourea (7.5 mg, 0.099 mmol) and bromide (10) (10 mg, 0.013 mmol) in ethanol (1 ml) was heated to 80 °C for 16 hrs. A 5 M solution of NaOH (1 ml) was added and the mixture was stirred for a further 5 mins at ambient temperature. The solution was then neutralised with dilute H2SO4 and stirring continued for 20 mins. The mixture was extracted with dichloromethane (3 x 10 ml) and the combined organic layers were dried, filtered and evaporated. The residue gave a complicated 1H NMR spectrum and showed numerous spots on TLC

(2*R*,2'*R*,3*R*,3'*R*)-2,2'-Disulfanediyl*bis*(tetradecane-14,1-diyl))*bis*(3-hydroxy heneicosanoic acid (13): attempted alternative methods

(i) Lithium hydroxide (15 eq, 49 mg, 1.17 mmol) was added to ester **(11)** (50 mg, 0.079 mmol) in a mixture of THF (5 ml), methanol (0.5 ml) and water (0.5 ml) and stirred at 45 °C overnight. The reaction was diluted by addition of petrol/ethyl acetate (1:1, 10 ml) and brought to pH 1 by dropwise addition of dil. HCl. The product was extracted with petrol/ethyl acetate (5:1, 5 x 15 ml) and the combined organic extracts were dried and evaporated. The residue gave a very complicated ^{1}H NMR spectrum and showed numerous spots by TLC.

(ii) Lithium hydroxide (4 eq, 8 mg, 0.187 mmol) dissolved in water (1.5 ml) was added dropwise to **(11)** (30 mg, 0.047 mmol) in isopropanol (3 ml) and THF (0.5 ml) at 40 °C under N_2 (g). The mixture was stirred at 23 °C for 1 hr, then added to water (50 ml) and the pH adjusted to pH 5 with dilute HCl. The solution was extracted with ethyl acetate (3 x 20 ml) and the combined organic extracts were dried, filtered and evaporated. This gave the starting material, **(11)**.

(iii) Lithium hydroxide (2 eq, 1.3 mg, 0.031 mmol) was added to **(11)** (10 mg, 0.016 mmol) in THF (2 ml), water (0.2 ml) and methanol (0.2 ml) and the mixture was stirred at 45 °C overnight. The reaction was diluted by the addition of petrol/ethyl acetate (1:1, 10 ml) and brought to pH 1 by the dropwise addition of dil. HCl. The product was extracted with petrol/ethyl acetate (5:1, 5 x 10 ml) and the combined organic extracts were dried and evaporated. A suspected mixture of (2*R*,2'*R*,3*R*,3'*R*)-2,2'-(disulfanediyl*bis*(tetradecane-14,1-diyl))*bis*(3-hydroxyheneicosanoic acid **(13)** and dimethyl (2*R*,2'*R*,3*R*,3'*R*)-2,2'-(disulfanediyl*bis*(tetradecane-14,1-diyl))*bis*(3-hydroxyhenicosanoate was produced, which could not be separated.

(iv) The reaction was repeated using lithium hydroxide (3 eq, 2.0 mg, 0.048 mmol) and **(11)** (10 mg, 0.016 mmol) in THF/water/methanol (2 ml/0.2 ml/0.2 ml). A mixture of disulfide **(11)** and the above methyl ester disulfide that could not be separated was believed to be produced. Significant peaks in the crude ^{1}H NMR spectrum included two triplets at 2.69 ppm and a singlet at 3.72 ppm.

2, 2-Dimethyl-propionic acid 12-bromo-dodecyl ester

Trimethylacetyl chloride (22.19 ml, 0.181 mol) in dichloromethane (25 ml) was added to a stirred solution of 12-bromododecan-1-ol (40 g, 150 mmol) and triethylamine (0.74 g, 5.92 mmol) dichloromethane (200 ml) over 15 min at 0˚C under nitrogen. The mixture was stirred 18 h then quenched with dil. hydrochloric acid (100 ml). The aqueous layer was re-extracted with dichloromethane (2 x 50 ml). The combined organic layers were washed with brine dried and evaporated to give a crude product which was purified by column chromatography eluting with petrol/ethyl acetate (1:1), to give a colorless oil, 2,2-dimethylpropionic acid 12-bromododecyl ester (42 g, 80%) {Found $(M+Na)^+$: 371.1552, $C_{17}H_{33}O_2BrNa$ requires 371.1561}, δ_H: (500 MHz, $CDCl_3$): 4.03 (2H, t, *J* 6.65 Hz), 3.39 (2H, t, *J* 7.0 Hz), 1.83 (2H, pent, *J* 7.0 Hz), 1.60 (2H, pent, *J* 6.6 Hz), 1.41 (2H, pent, *J* 7.0 Hz), 1.30-1.22 (14H, m), 1.18 (9H, s); δc:

178.5, 64.4, 38.7, 33.9, 32.8, 29.4, 29.36, 29.2, 29.0, 28.7, 28.6, 28.0, 27.1, 26.4; ν_{max}: 2928, 2855, 1729, 1480, 1461, 1284, 1158, 1042, 1005, 852 cm^{-1}.

2,2- Dimethylpropionic acid 12-(1-phenyl-1*H*-tetrazol-5-ylsulfanl)-dodecyl ester

1-Phenyl-*1H*-tetrazole-5-thiol (23.57 g, 132 mmol), 2,2-dimethylpropionic acid 12-bromododecyl ester (42 g, 0.12mol) and anhydrous potassium carbonate (36.44 g, 260 mmol) in acetone (250 ml) were mixed at room temperature and vigorously stirred for 18 h. Water (1 L) was added and the product was extracted with dichloromethane (1 x 200 ml, 2 x 100 ml). The combined organic layers were washed with brine (2 x 200 ml), dried and evaporated. The product was purified by column chromatography eluting with petrol/ethyl acetate (5:1) to give a colorless oil, 2,2-dimethylpropionic acid 12-(1-phenyl-1H-tetrazol-5-ylsulfanyl)-dodecyl ester (49 g, 91%) {Found $(M+Na)^+$: 469.2615, $C_{24}H_{38}O_2N_4SNa$ requires : 469.2613}, δ_H: (500 MHz, $CDCl_3$): 7.55-7.49 (5H, m), 3.90 (2H, t, *J* 6.6 Hz), 3.56 (2H, t, *J* 7.2 Hz), 1.83 (2H, pent, *J* 7.0 Hz), 1.63 (2H, pent, *J* 7.0 Hz), 1.46-142 (2H, m), 1.32-1.26 (14H, m), 1.20 (9H, s); δ_C: 178.6, 154.5, 133.8, 131.1, 129.7, 125.1, 63.1, 56.1, 32.7, 29.5, 29.4, 29.3, 29.1, 28.8, 28.1, 25.7; ν_{max}: 2927, 2854, 1726, 1500, 1462, 1387, 1284, 1159, 761 cm^{-1}.

2,2-Dimethylpropionic acid 12-(1-phenyl-1*H*-tetrazole-5-ylsulfonyl)dodecyl ester

Ammonium molybdate (VI) tetrahydrate (67.8 g, 54.8 mmol) in 35 % H_2O_2 (100 ml), prepared and cooled in an ice bath was added to a stirred solution of 2,2-dimethylpropionic acid 12-(1-phenyl-1*H*-tetrazol-5-ylsulfanyl)-dodecyl ester (49 g, 109.7m mol) in THF (150) IMS (300 ml) at 10 ˚C and stirred at room temperature for 2 h. Further ammonium molybdate (VI) tetrahydrate (33.88 g, 27.0 mmol) in 35% (50 ml) was added and the mixture was stirred for 18 hrs, then poured into water (1.2 L) and extracted with dichloromethane (1 x 250 ml, 3 x 150 ml). The combined organic phases were washed with water (500 ml), dried and the solvent was evaporated. The product was purified by column chromatography eluting with petrol/ethyl acetate (5:1, then 1:1) to give a yellow oil, 2,2-dimethyl-propionic acid 12-(1-phenyl-1*H*-tetrazole-5-ylsulfonyl)dodecyl ester (46 g, 88 %) {Found $(M+Na)^+$: 501.2526, $C_{24}H_{38}O_4N_4SNa$ requires 501.2511}, δ_H: (500 MHz, $CDCl_3$): 7.70-7.68 (2H, m), 7.61-7.59 (3H,m), 4.04 (2H, t, *J* 6.6 Hz), 3.73 (2H, t, *J* 7.9 Hz), 1.95 (2H, pent, *J* 7.5 Hz), 1.61 (2H, pent, *J* 6.65 Hz), 1.49 (2H, pent, *J* 7.0 Hz), 1.34-123 (14H, m), 1.19 (9H, s); δc: 178.6, 153.4, 133.0, 131.1, 129.7, 125.1, 64.4, 56.0, 38.7, 29.5, 29.4, 29.3, 29.1,

28.8, 28.1, 25.8, 21.9; ν_{max}: 2930, 2857, 1725, 1498, 1480, 1342, 1285, 1154, 735 cm^{-1}.

2,2–Dimethylpropanoic acid (22–bromo) docosyl ester

Lithium bis(trimethylsilyl)amide (70 ml, 74.6 mmol) was added dropwise with stirring to 10-bromodecanal (9.0 g, 38.2 mol) [Furber, 1986] and 2,2-dimethylpropionic acid 12-(phenyl-1-H-tetrazole-5-ylsulfonyl)-dodecyl ester (21.98 g, 45.9 mmol) in dry THF (200 ml) under nitrogen at 0 ˚C. The mixture was allowed to reach room temperature and stirred for 40 min, and then quenched with sat. aq. NH_4Cl at 0 ˚C and extracted with petrol/ethyl acetate (10:1, 50 ml). The organic layer was separated and the aqueous layer was extracted with petrol/ethyl acetate (10:1, 3x100 ml). The combined organic layers were dried and evaporated. The product was purified by column chromatography eluting with petrol/ethyl acetate (20:1) to give (*E/Z*)-22-bromodocos-12-enyl pivalate (12.60 g, 68%), in ratio (2:1). Palladium on 10% carbon (1 g) was added to a stirred solution of alkene (12.60 g, 25.81 mmol) in IMS/THF (1:1) under hydrogen. Hydrogenation was carried out for 1 h, then the mixture was filtered through a bed of celite and the solvent was evaporated. The crude product was purified by column chromatography eluting with petrol/ethyl acetate (10:1) to give a white solid, 22-bromodocosyl pivalate (11 g, 87%), mp 37-38 ˚C {Found $(M+Na)^+$: 511.3125, $C_{27}H_{53}BrO_2Na$ requires: 511.3121}; δ_H: (500 MHz, $CDCl_3$): 4.05 (2H, t, *J* 6.65 Hz), 3.41 (2H, t, *J* 6.95 Hz), 1.86 (2H, pent, *J* 6.65 Hz), 1.61 (2H, *J* 6.6 Hz), 1.45-1.26 (36H,br., m), 1.20 (9H, s); δc:178.7, 67.9, 64.5, 58.3, 33.9, 32.8, 29.6, 29.57, 29.55, 29.50, 29.47, 29.45, 29.4, 29.2, 28.7, 28.6, 28.1, 27.1, 25.8, 25.5, 18.3; ν_{max}: 2914, 2328, 1719, 1476, 1286, 1159, 1034, 889 cm^{-1}.