New lipophenol antioxidants reduce oxidative damage in retina pigment epithelial cells.

Espérance Moine [1], Philippe Brabet [2], Laurent Guillou [2], Thierry Durand [1], Joseph Vercauteren [1] and Céline Crauste [1,*]

[1] Institute of Biomolecules Max Mousseron (IBMM), UMR 5247-CNRS-UM-ENSCM, Faculty of Pharmacy, 15 av. Charles Flahault, 34093 Montpellier, France, celine.crauste@umontpellier.fr
[2] Institute for Neurosciences of Montpellier, INSERM U1051-UM, Hospital St Eloi, 80 rue Augustin Fliche, 34091 Montpellier, France, philippe.brabet@inserm.fr
* Correspondence: celine.crauste@umontpellier.fr; Tel.: +33-4-11-75-95-66

Supplementary materials

Experimental procedures for lipophenols synthesis.

Figure S1: Graphical representation of *in vitro* evaluations of lipophenols.

Figure S2: Full NMR spectra characterization of derivatives from 2 to 18 (^{1}H and ^{13}C).

Experimental procedures for lipophenols synthesis.

3,5-bis(triisopropylsilyloxy)phenol (1): was synthesized according to the procedure described by Crauste et *al.* 2014 [26].

(9,12*Z*)-3,5-bis(triisopropylsilyloxy)phenyl-octadeca-9,12-dienoate (2): To a solution of linoleic acid (77 mg, 0.27 mmol), dicyclohexylcarbodiimide (62 mg, 0.30 mmol) and 4-dimethylaminopyridine (10 mg, 0.08 mmol) in anhydrous CH_2Cl_2 (2 mL) stirred under N_2, was added a solution of compound **1** (120 mg, 0.27 mmol) in anhydrous CH_2Cl_2 (2 mL). The resulting mixture was stirred at room temperature for 2 h and cooled to 4 °C for 1 h to afford filtration of the precipitate. The filtrate was washed with water and brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using hexane/EtOAc (99:1 v/v) as eluent to give compound **2** (120 mg, 62%) as colorless oil. R_f (hexane/EtOAc, 99:1) = 0.26. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.28 (t, *J* = 1.9 Hz, 1H, H4), 6.24 (d, *J* = 1.9 Hz, 2H, H2, H6), 5.44 – 5.27 (m, 4H, 2 × CH=CH), 2.78 (t, *J* = 6.6 Hz, 2H, H11'), 2.50 (t, *J* = 7.5 Hz, 2H, H2'), 2.12 – 1.99 (m, 4H, H8', H14'), 1.66 (qt, *J* = 7.5 Hz, 2H, H3'), 1.43 – 1.17 (m, 20H, H4', H5', H6', H7', H15', H16', H17', 6 × CHTIPS), 1.10 – 0.95 (m, 36H, 12 × CH_3TIPS), 0.89 (t, *J* = 6.8 Hz, 3H, H18'). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 157.1 (2C), 151.8, 130.2, 130.0, 128.1, 127.9, 109.3, 106.9, 34.4, 31.5, 29.6 (2C), 29.4 (2C), 29.2, 29.2, 29.1, 27.2, 25.6, 24.9, 22.6, 17.9 (12C), 14.1, 12.6 (6C). HRMS (ESI+I): calculated for $C_{42}H_{77}O_4Si_2$ $[M + H]^+$ 701.5355; found 701.5366.

(9Z,12Z)-3,5-dihydroxyphenyl octadeca-9,12-dienoate (phloro-LA, 3): To a solution of compound **2** (59 mg, 0.08 mmol) in anhydrous THF (4 mL) stirred under N_2, was added dropwise triethylamine trihydrofluoride (41 μL, 0.24 mmol). The resulting mixture was stirred at room temperature for 9 h, diluted in EtOAc and washed with water and brine. The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using hexane/EtOAc (80:20 v/v) as eluent to give compound **3** (30 mg, 92%) as colorless oil. R_f (hexane/EtOAc, 70:30) = 0.30. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (s, 3H, H2, H4, H6), 5.45 – 5.27 (m, 4H, 2 × CH=CH), 2.78 (t, *J* = 6.8 Hz, 2H, H11'), 2.57 (t, *J* = 7.5 Hz, 2H, H2'), 2.10 – 2.00 (m, 4H, H8', H14'), 1.75 (qt, *J* = 7.5 Hz, 2H, H3'), 1.46 – 1.22 (m, 14H, H4', H5', H6', H7', H15', H16', H17'), 0.89 (t, *J* = 6.8 Hz, 3H, H18'). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 157.4 (2C), 151.7, 130.3, 130.0, 128.1, 127.9, 102.0, 101.5, 34.4, 31.5, 29.6 (2C), 29.4 (2C), 29.2, 29.1, 29.1, 27.2, 25.7, 24.9, 22.6, 14.1. HRMS (ESI-I): calculated for $C_{24}H_{35}O_4$ $[M - H]^-$ 387.2535; found 387.2534.

(*E*)-4-(3,5-dihydroxystyryl)phenyl acetate (4): resveratrol (2,88 g, 12.61 mmol) was dissolved in 2-methylbutan-2-ol (280 mL) and vinyl acetate (72.40 mL, 756.70 mmol) in presence of the supported lipase *Candida Antarctica* (Novozyme 435, CalB, 14.40 g). The mixture was stirred with a rotary evaporator at 40°C during 4 days, protected from sunlight by aluminium foil. The lipase was then filtered off and washed with EtOAc and diethyl ether. The filtrate obtained was concentrated under reduced pressure and the residue obtained was purified by chromatography on silica gel using solid deposit using CH_2Cl_2/MeOH (99/1 to 98/2 v/v) as eluent to give the 4'-*O*-acetyl resveratrol **4** (2.89 mg, 85%) as white solid. R_f (CH_2Cl_2/MeOH, 95:5) = 0.3. Mp 199.1 °C. ^{1}H NMR (500 MHz, MeOD) δ 7.54 (d, *J* = 7.6 Hz, 2H, H2', H6'), 7.07 (d, *J* = 7.6 Hz, 2H, H3', H5'), 7.04 (d, *J* = 16.2 Hz, 1H, H8), 6.97 (d, *J* = 16.2 Hz, 1H, H7), 6.49 (s, 2H, H2, H6), 6.21-6.19 (m, 1H, H4), 2.27 (s, 3H, CH_3OCO). ^{13}C NMR (125 MHz, MeOD) δ 171.1, 159.7 (2C), 151.5, 140.6, 136.6, 130.2, 128.3, 128.3, 122.9 (2C), 122.9, 106.1 (2C), 103.2, 20.9. HRMS (ESI+I): calculated for $C_{16}H_{15}O_4$ $[M + H]^+$ 271.0964; found 271.0972.

(*E*)-4-(3,5-bis((triisopropylsilyl)oxy)styryl)phenyl acetate (5): 4'-*O*-acetyl resveratrol **4** (3.18 g, 11.78 mmol) was dissolved in dry THF (160 mL). DIPEA (4.20 mL, 24.70 mmol) and TIPS-OTf (6.70 mL, 24.70 mmol) were added dropwise to the solution and the reaction mixture was stirred at room temperature during 4.5h. Additional amount of DIPEA (1.0 mL, 5.90 mmol) and TIPS-OTf (1.6 mL,

5.90 mmol) were added to reach completion of the reaction. After 2.5 additional hours of reaction, the solvent was evaporated under reduced pressure. The residue obtained was dissolved in EtOAc and washed with water (x2) and brine. The organic phase was dried over $MgSO_4$ and concentrated under vacuum. The residue obtained was purified by chromatography on silica gel using pentane/EtOAc (99:1 to 70:30 v/v) as eluent to give the protected resveratrol **5** (6.85 g, 90%) as a colorless oil. R_f (pentane/EtOAc, 95:5) = 0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 2H, H2′, H6′), 7.09 (d, *J* = 8.0 Hz, 2H, H3′, H5′), 6.98 (d, *J* = 16.3 Hz, 1H, H8), 6.92 (d, *J* = 16.3 Hz, 1H, H7), 6.65 (s, 2H, H2, H6), 6.37 – 6.36 (m, 1H, H4), 2.31 (s, 3H, CH_3OCO), 1.26 (m, 6H, 6 × CHTIPS), 1.12 (d, *J* = 7.6 Hz, 36H, 12 × CH_3TIPS). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 157.3 (2C), 150.2, 139.0, 135.3, 129.3, 127.8, 127.7 (2C), 122.0 (2C), 111.6 (2C), 111.5, 21.4, 18.2 (6C), 12.9 (12C). HRMS (ESI+I): calculated for $C_{34}H_{55}O_4Si_2$ [M + H]$^+$ 583.3633; found 583.3640.

(*E*)-4-(3,5-bis((triisopropylsilyl)oxy)styryl)phenol (6): The protected resveratrol **5** (6.85 g, 10.59 mmol) was dissolved in dry MeOH (58 mL) and CH_2Cl_2 (28 mL). Sodium methoxide (191 mg, 3.53 mmol) was added to the solution and the reaction mixture was stirred at room temperature during 4.5h. Further, 0.3 eq of NaOMe (191 mg, 3.53 mmol) was added to drive the reaction to completion. After additional 2h, the solvent was evaporated under reduced pressure. The residue obtained was purified by chromatography on silica gel using pentane/EtOAc (96:4 to 90:10 v/v) as eluent to give the 4′-deprotected resveratrol **6** (6.04 g, 95%) as a colorless oil. R_f (hexane/EtOAc, 90:10) = 0.41. ^{1}H NMR (500 MHz; MeOD) δ 7.38 (d, *J* = 8.5 Hz, 2H, H2′, H6′), 6.95 (d, *J* = 16.2 Hz, 1H, H8), 6.84 (d, *J* = 16.2 Hz, 1H, H7), 6.77 (d, *J* = 8.5 Hz, 2H, H3′, H5′), 6.64 – 6.63 (m, 2H, H2, H6), 6.30 – 6.29 (m, 1H, H4), 1.30 – 1.22 (m, 6H, 6 × CHTIPS), 1.14 (d, *J* = 7.5 Hz, 36H, 12 × CH_3TIPS). ^{13}C NMR (125 MHz; MeOD) δ 158.5, 158.3 (2C), 141.3, 130.1, 129.9, 129.0 (2C), 126.5, 116.5 (2C), 112.1 (2C), 111.4, 18.4 (6C), 13.9 (12C). HRMS (ESI+I): calculated for $C_{32}H_{53}O_3Si_2$ [M + H]$^+$ 541.3527; found 541.3536.

(9,12*Z*)-4-((*E*)-3,5-bis((triisopropylsilyl)oxy)styryl)phenyl octadeca-9,12-dienoate (7): Compound **6** (1.00 g, 1.67 mmol) and linoleic acid (623 mg, 2,22 mmol) were dissolved in anhydrous CH_2Cl_2 (40 mL). Dicyclohexylcarbodiimide (573 mg, 2.78 mmol) and 4-dimethylaminopyridine (113 mg, 0.93 mmol) were added to the reaction and the resulting mixture was stirred at room temperature under under N_2 for 3 h before cooling to 4 °C for 1 h to afford filtration of the precipitate. The filtrate was washed with water and brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using pentane/EtOAc (99.5:0.5 to 99:1 v/v) as eluent to give compound **6** as a colorless oil (1.10 g, 74%). *Rf* (pentane/EtOAc, 95:5) = 0.7. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.5 Hz, 2H, H2′, H6′), 7.06 (d, *J* = 8.5 Hz, 2H, H3′, H5′), 6.97 (d, *J* = 16 Hz, 1H, H8), 6.91 (d, *J* = 16 Hz, 1H, H7), 6.64 (d, *J* =1.5 Hz, 2H, H2, H6), 6.3 (t, *J* = 1.5 Hz, 1H, H4), 5.41 – 5.33 (m, 4H, 2 × CH=CH), 2.78 (t, *J* = 6.5 Hz, 2H, H11′′), 2.55 (t, *J* = 7.5 Hz, 2H, H2′′), 2.07 – 2.03 (m, 4H, H8′′, H14′′), 1.75 (qt, *J* = 7.5 Hz, 2H, H3′′), 1.42 – 1.22 (m, 20H, H4′′, H5′′, H6′′, H7′′, H15′′, H16′′, H17′′, 6 × CHTIPS), 1.11 (d, *J* = 7.5 Hz, 36 H, 12 × CH_3TIPS), 0.89 (t, *J* = 7 Hz, 3H, H18′′). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 157.4 (2C), 150.4, 139.1, 135.3, 130.6, 130.3, 129.3, 128.4, 128.2, 127.9, 127.7 (2C), 122.1 (2C), 111.7 (2C), 111.6, 34.8, 31.8, 29.9, 29.7, 29.5, 29.4, 29.4, 27.5, 27.5, 26.0, 25.3, 22.9, 18.2 (6C), 14.4, 13.0 (12C). HRMS (ASAP+I): calculated for $C_{50}H_{83}O_4Si_2$ [M + H]$^+$ 803.5830; found 803.5815.

(9,12*Z*)-4-((*E*)-3,5-dihydroxystyryl)phenyl octadeca-9,12-dienoate (Resv-4′-LA, 8): To a solution of compound **7** (1.08 g, 1.35 mmol) in anhydrous THF (60 mL) stirred under N_2, was added dropwise triethylamine trihydrofluoride (1.32 mL, 8.08 mmol). The reaction was stirred at room temperature and further equivalents of triethylamine trihydrofluoride (2×0.66 mL, 2×4.04 mmol) were added at four and six hours of reaction time. Reaction was terminated after another two hours. The resulting mixture was evaporated and the residue was dissolved in EtOAc. Organic phases were washed with water and brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Crude product was purified by column chromatography on silica gel using pentane/EtOAc (70:30 to 60:40 v/v) as eluent to obtain the desired compound **8** (546 mg, 83%) as a white solid. R_f (pentane/EtOAc, 70:30) =

0.3. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.5 Hz, 2H, H2', H6'), 7.00 (d, *J* = 8.5 Hz, 2H, H3', H5'), 6.79 (d, *J* = 16.5 Hz, 1H, H8), 6.70 (d, *J* = 16.5 Hz, 1H, H7), 6.40 (d, *J* = 2.0 Hz, 2H, H2, H6), 6.23 (t, *J* = 2.0 Hz, 1H, H4), 5.99 (bs, 2H, 2 × OH), 5.41 – 5.32 (m, 4H, 2 × CH=CH), 2.77 (t, *J* = 6.5 Hz, 2H, H11''), 2.56 (t, *J* = 7.5 Hz, 2H, H2''), 2.06 – 2.03 (m, 4H, H8'', H14''), 1.75 (qt, *J* = 7.5 Hz, 2H, H3''), 1.42 – 1.25 (m, 14H, H4'', H5'', H6'', H7'', H15'', H16'', H17''), 0.88 (t, *J* = 7 Hz, 3H, H18''). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 157.0 (2C), 150.1, 139.7, 135.1, 130.4, 130.2, 128.4, 128.2, 128.2, 128.0, 127.7 (2C), 121.8 (2C), 106.3 (2C), 102.6, 34.6, 31.7, 29.7, 29.5, 29.3, 29.3, 29.2, 27.3, 27.3, 25.7, 25.0, 22.7, 14.2. HRMS (ASAP+I): calculated for $C_{32}H_{43}O_4$ $[M + H]^+$ 491.3161; found 491.3161.

(9*Z*,12*Z*)-(2*R*,3*S*)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-chroman-3-yl octadeca-9,12-dienoate (Cat-3-LA, 9): To a suspension of freshly prepared linoleyl chloride (103 mg, 0.34 mmol) in anhydrous CH_2Cl_2 (5 mL) stirred under N_2, was added trifluoroacetic acid (26 μL, 0.34 mmol) and dropwise a suspension of dried (+)-catechin (100 mg, 0.34 mmol) in anhydrous DMF (2 mL). The resulting mixture was stirred at room temperature for 22 h and at 40 °C for 6 h, diluted in EtOAc/MeOH (3:1 v/v) and evaporated under reduced pressure. The crude product was dissolved in EtOAc, washed with water, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using CH_2Cl_2/MeOH (98:2 to 96:4 v/v) as eluent to give compound **9** (4.9 mg, 2.6%) as colorless oil. R_f (CH_2Cl_2/MeOH, 80:20) = 0.80. ^{1}H NMR (500 MHz, MeOD) δ 6.80 (d, *J* = 2.0 Hz, 1H, H2'), 6.73 (d, *J* = 8.1 Hz, 1H, H5'), 6.68 (dd, *J* = 8.1, 2.0 Hz, 1H, H6'), 5.95 (d, *J* = 2.2 Hz, 1H, H8), 5.89 (d, *J* = 2.2 Hz, 1H, H6), 5.42 – 5.27 (m, 4H, 2 × CH=CH), 5.20 (dd, *J* = 12.4, 7.0 Hz, 1H, H3), 4.85 (d, *J* = 7.0 Hz, 1H, H2), 2.84 – 2.74 (m, 3H, H4β, H11''), 2.60 (dd, *J* = 16.3, 7.0 Hz, 1H, H4α), 2.20 (td, *J* = 7.3, 1.8 Hz, 2H, H2''), 2.06 (q, *J* = 6.9 Hz, 4H, H8'', H14''), 1.50 – 1.40 (m, 2H, H3''), 1.40 – 1.11 (m, 14H, H4'', H5'', H6'', H7'', H15'', H16'', H17''), 0.90 (t, *J* = 6.9 Hz, 3H, H18''). ^{13}C NMR (125 MHz, MeOD) δ 174.61, 158.17, 157.61, 156.60, 146.45, 146.31, 131.15, 130.98, 130.93, 129.09, 129.04, 119.53, 116.10, 114.79, 99.72, 96.49, 95.56, 79.68, 70.97, 35.22, 32.65, 30.68, 30.47, 30.17, 30.10, 29.90, 28.16, 28.14, 26.54, 26.00, 25.13, 23.61, 14.41. HRMS (ESI-I): calculated for $C_{36}H_{49}0_7$ $[M-H]^-$ 593.3478; found 593.3477.

(9*Z*,12*Z*)-2-(3,4-((9*Z*,12*Z*)-dioctadeca-9,12-dienoyloxy)phenyl)-4-oxo-4*H*-chromen-3,5,7-triyl trioctadeca-9,12-dienoate (10): To a solution of dried quercetin (0.1 g, 0.33 mmol) in 1,4-dioxan (8 mL) stirred under N_2, was added distilled triethylamine (0.35 mL, 2.48 mmol) and a suspension of freshly prepared linoleyl chloride (0.74 g, 2.48 mmol) in 1,4-dioxan (2 mL). The resulting mixture was stirred in the dark at room temperature for 19 h and evaporated under reduced pressure. The crude product was dissolved in CH_2Cl_2, washed with aqueous saturated $NaHCO_3$ solution and water, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using CH_2Cl_2/MeOH (100:0 to 99:1 v/v) as eluent to give compound **10** (236 mg, 75%) as colorless oil. R_f (CH_2Cl_2/MeOH, 99:1) = 0.67. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.6, 2.1 Hz, 1H, H6'), 7.66 (d, *J* = 2.1 Hz, 1H, H2'), 7.32 (d, *J* = 8.6 Hz, 1H, H5'), 7.31 (d, *J* = 2.1 Hz, 1H, H8), 6.84 (d, *J* = 2.1 Hz, 1H, H6), 5.47 – 5.25 (m, 20H, 10 × CH=CH), 2.81 – 2.75 (m, 10H, 5 × H11''), 2.73 (t, *J* = 7.6 Hz, 2H, H2''), 2.62 – 2.53 (m, 8H, 4 × H2''), 2.10 – 2.01 (m, 20H, 5 × H8'', 5 × H14''), 1.85 – 1.65 (m, 10H, 5 × H3''), 1.47 – 1.22 (m, 70H, 5 × H4'', 5 × H5'', 5 × H6'', 5 × H7'', 5 × H15'', 5 × H16'', 5 × H17''), 0.92 – 0.85 (m, 15H, 5 × H18''). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.01, 170.77, 170.62, 170.58, 170.53, 169.97, 156.84, 154.27, 153.60, 150.53, 144.45, 142.27, 134.07, 130.23, 130.22, 130.21, 130.19, 130.18, 130.07, 130.03, 129.94, 129.89, 129.88, 128.11, 128.10, 128.08, 127.98, 127.97, 127.90, 127.88, 127.85, 127.82 (2C), 127.75, 126.37, 123.83, 123.77, 114.79, 113.86, 108.85, 34.35, 34.09, 34.05, 33.99, 33.73, 31.49 (5C), 29.63 (2C), 29.61, 29.59 (2C), 29.56, 29.32 (4C), 29.31, 29.24, 29.23, 29.19, 29.16, 29.15, 29.12, 29.11 (2C), 29.10, 29.09, 29.08, 29.04, 28.98, 28.97, 27.21, 27.20, 27.17 (3C), 27.16 (3C), 27.15, 27.14, 25.62 (5C), 24.86, 24.83, 24.66, 24.56, 24.41, 22.56 (5C), 14.07 (5C).

(9*Z*,12*Z*,15*Z*)-2-(3,4-((9*Z*,12*Z*,15*Z*)-dioctadeca-9,12,15-trienoyloxy)phenyl)-4-oxo-4*H*-chromen-3,5,7-triyl trioctadeca-9,12,15-trienoate (11): To a solution of α-linolenic acid (ALA, 244 mg, 0.88 mmol), dicyclohexylcarbodiimide (181 mg, 0.88 mmol) and 4-dimethylaminopyridine (10 mg, 0.08 mmol) in

anhydrous CH_2Cl_2 (7 mL) stirred under N_2, was added a suspension of dried quercetin (50 mg, 0.17 mmol) in anhydrous CH_2Cl_2 (8 mL). The resulting mixture was stirred at room temperature for 4.5 h and cooled to 4 °C for 2 h to afford filtration of the precipitate. The filtrate was washed with water and brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using CH_2Cl_2 as eluent to give compound **11** (84 mg, 32%) as yellow oil. R_f (CH_2Cl_2/MeOH, 99:1) = 0.87. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.5, 2.1 Hz, 1H, H6'), 7.70 (d, *J* = 2.1 Hz, 1H, H2'), 7.34 (d, *J* = 8.5 Hz, 1H, H5'), 6.84 (d, *J* = 2.0 Hz, 1H, H8), 6.58 (d, *J* = 2.0 Hz, 1H, H6), 5.47 – 5.23 (m, 30H, 15 × CH=CH), 2.85 – 2.77 (m, 20H, 5 × H11'', 5 × H14''), 2.63 (t, *J* = 7.5 Hz, 2H, H2''), 2.60 – 2.54 (m, 8H, 4 × H2''), 2.13 – 2.02 (m, 20H, 5 × H8'', 5 × H17''), 1.81 – 1.69 (m, 10H, 5 × H3''), 1.48 – 1.28 (m, 40H, 5 × H4'', 5 × H5'', 5 × H6'', 5 × H7''), 1.02 – 0.92 (m, 15H, 5 × H18''). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.26, 171.08, 170.64 (2C), 170.60, 170.51, 161.67, 156.41, 155.91, 155.47, 144.71, 142.30, 132.19, 131.93 (2C), 131.92 (2C), 130.24 (2C), 130.17 (2C), 130.09 (2C), 130.08 (2C), 128.29 (2C), 128.25 (2C), 128.24 (2C), 128.21 (2C), 128.19 (2C), 128.15 (2C), 127.80 (2C), 127.75 (2C), 127.69, 127.47, 127.07, 126.46, 123.95, 123.93, 108.71, 105.44, 101.12, 34.37, 34.05 (2C), 34.00, 33.70, 29.60 (2C), 29.55 (2C), 29.23 (2C), 29.20 (2C), 29.12 (2C), 29.10 (2C), 29.08 (2C), 29.05 (2C), 29.00 (2C), 28.97 (2C), 27.20 (2C), 27.18 (3C), 25.59 (5C), 25.49 (5C), 24.84 (2C), 24.83, 24.73, 24.63, 20.52 (5C), 14.26 (5C).

(4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-2-(3,4-((4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-didocosa-4,7,10,13,16,19-hexaenoyloxy)phenyl)-4-oxo-4*H*-chromen-3,5,7-triyl tridocosa-4,7,10,13,16,19-hexaenoate (12): To a solution of *cis*-4,7,10,13,16,19-docosahexaenoic acid (300 mg, 0.91 mmol), dicyclohexylcarbodiimide (188 mg, 0.91 mmol) and 4-dimethylaminopyridine (11 mg, 0.09 mmol) in anhydrous CH_2Cl_2 (7 mL) stirred under N_2, was added a suspension of dried quercetin (52 mg, 0.17 mmol) in anhydrous CH_2Cl_2 (8 mL). The resulting mixture was stirred at room temperature for 19 h and cooled to 4 °C for 2 h to afford filtration of the precipitate. The filtrate was washed with water and brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using CH_2Cl_2 as eluent to give compound **12** (98 mg, 31%) as yellow oil. R_f (CH_2Cl_2) = 0.78. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 2H, H2', H6'), 7.35 (dd, *J* = 8.0, 0.9 Hz, 1H, H5'), 6.85 (d, *J* = 2.0 Hz, 1H, H8), 6.59 (d, *J* = 2.0 Hz, 1H, H6), 5.58 – 5.23 (m, 60H, 30 × CH=CH), 2.93 – 2.76 (m, 50H, 5 × H6'', 5 × H9'', 5 × H12'', 5 × H15'', 5 × H18''), 2.76 – 2.60 (m, 10H, 5 × H2''), 2.59 – 2.46 (m, 10H, 5 × H3''), 2.07 (qt, *J* = 7.5 Hz, 10H, 5 × H21''), 0.97 (t, *J* = 7.5 Hz, 15H, 5 × H22''). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.15, 170.36, 170.00 (2C), 169.95, 169.85, 161.69, 156.35, 155.89, 155.45, 144.64, 142.23, 132.21, 132.00 (5C), 130.05 (5C), 129.75 (5C), 128.50 (5C), 128.42 (5C), 128.28 (5C), 127.99 (5C), 127.81 (5C), 127.74 (5C), 127.48, 127.32 (5C), 127.09 (5C), 126.97 (5C), 126.54, 123.94 (2C), 108.74, 105.48, 101.11, 34.26, 33.91 (3C), 33.56, 25.60 (15C), 25.50 (10C), 22.52 (5C), 20.52 (5C), 14.25 (5C).

(9*Z*,12*Z*)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4*H*-chromen-3-yl octadeca-9,12-dienoate (Quer-3-LA, 13): To a solution of compound **10** (106 mg, 0.07 mmol) in *tert*-butylmethylether (7.5 mL) was added *n*-BuOH (0.3 mL) and supported lipozyme® from *Mucor miehei* (1:1 w/w, 106 mg). The resulting mixture was stirred at 45 °C for 6 days, supported enzyme was filtrated and rinsed several times with EtOAc and Et_2O. The filtrate was evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using CH_2Cl_2/MeOH (95:5 v/v) as eluent to give compound **13** (20 mg, 54%) as yellow solid. R_f (pentane/EtOAc, 50:50) = 0.25. Mp 193.8 °C. ^{1}H NMR (500 MHz, MeOD) δ 7.33 (d, *J* = 2.2 Hz, 1H, H2'), 7.28 (dd, *J* = 8.4, 2.2 Hz, 1H, H6'), 6.89 (d, *J* = 8.4 Hz, 1H, H5'), 6.43 (d, *J* = 2.1 Hz, 1H, H8), 6.24 (d, *J* = 2.1 Hz, 1H, H6), 5.41 – 5.27 (m, 4H, 2 × CH=CH), 2.77 (t, *J* = 6.5 Hz, 2H, H11''), 2.63 (t, *J* = 7.3 Hz, 2H, H2''), 2.12 – 2.00 (m, 4H, H8'', H14''), 1.70 (qt, *J* = 7.3 Hz, 2H, H3''), 1.43 – 1.24 (m, 14H, H4'', H5'', H6'', H7'', H15'', H16'', H17''), 0.89 (t, *J* = 6.8 Hz, 3H, H18''). ^{13}C NMR (125 MHz, MeOD) δ 177.22, 172.55, 166.30, 163.13, 158.68, 158.45, 150.37, 146.64, 131.43, 130.91, 130.90, 129.07, 129.06, 122.13, 121.97, 116.45, 116.18, 105.27, 100.14, 95.03, 34.61, 32.65, 30.63, 30.48, 30.19, 30.13, 29.98, 28.15, 28.12, 26.53, 25.80, 23.63, 14.42. HRMS (ESI-I): calculated for $C_{33}H_{39}O_8$ $[M-H]^-$ 563.2645; found 563.2654.

(9*Z*,12*Z*,15*Z*)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4*H*-chromen-3-yl octadeca-9,12,15-trienoate (Quer-3-ALA, 14): To a solution of compound **11** (46 mg, 29 μmol) in *tert*-butylmethylether (3.11 mL) was added *n*-BuOH (0.13 mL) and supported lipozyme® from *Mucor miehei* (1:1 w/w, 46 mg). The resulting mixture was stirred at 45 °C for 8 days, supported enzyme was filtrated and rinsed several times with EtOAc and Et_2O. The filtrate was evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using CH_2Cl_2/MeOH (95:5 v/v) as eluent to give compound **14** (16 mg, 96%) as yellow solid. R_f (CH_2Cl_2/MeOH, 95:5) = 0.25. Mp 180.0 °C. ^{1}H NMR (500 MHz, MeOD) δ 7.33 (d, *J* = 2.1 Hz, 1H, H2'), 7.28 (dd, *J* = 8.4, 2.1 Hz, 1H, H6'), 6.89 (d, *J* = 8.4 Hz, 1H, H5'), 6.43 (d, *J* = 1.9 Hz, 1H, H8), 6.23 (d, *J* = 1.9 Hz, 1H, H6), 5.42 – 5.18 (m, 6H, 3 × CH=CH), 2.85 – 2.75 (m, 4H, H11'', H14''), 2.63 (t, *J* = 7.1 Hz, 2H, H2''), 2.12 – 2.02 (m, 4H, H8'', H17''), 1.70 (qt, *J* = 7.1 Hz, 2H, H3''), 1.41 – 1.26 (m, 8H, H4'', H5'', H6'', H7''), 0.95 (t, *J* = 7.5 Hz, 3H, H18''). ^{13}C NMR (125 MHz, MeOD) δ 177.21, 172.56, 166.26, 163.12, 158.67, 158.42, 150.35, 146.63, 132.71, 131.45, 131.13, 129.23, 129.17, 128.82, 128.23, 122.16, 121.99, 116.46, 116.20, 105.30, 100.14, 95.05, 34.63, 30.63, 30.20, 30.14, 30.00, 28.14, 26.52, 26.40, 25.81, 21.48, 14.66. HRMS (ESI-I): calculated for $C_{33}H_{37}O_8$ $[M-H]^-$ 561.2488; found 561.2491.

(4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4*H*-chromen-3-yl docosa-4,7,10,13,16,19-hexaenoate (Quer-3-DHA, 15): To a solution of compound **12** (39 mg, 21 μmol) in *tert*-butylmethylether (2.7 mL) was added *n*-BuOH (0.1 mL) and supported lipozyme® from *Mucor miehei* (1:1 w/w, 39 mg). The resulting mixture was stirred at 45 °C for 8 days, supported enzyme was filtrated and rinsed several times with EtOAc and Et_2O. The filtrate was evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using CH_2Cl_2/MeOH (97:3 v/v) as eluent to give compound **15** (8 mg, 62%) as sticky yellow solid. R_f (CH_2Cl_2/MeOH, 95:5) = 0.20. Mp 191.3 °C. ^{1}H NMR (300 MHz, MeOD) δ 7.34 (d, *J* = 2.2 Hz, 1H, H2'), 7.28 (dd, *J* = 8.4, 2.2 Hz, 1H, H6'), 6.89 (d, *J* = 8.4 Hz, 1H, H5'), 6.43 (d, *J* = 2.1 Hz, 1H, H8), 6.24 (d, *J* = 2.1 Hz, 1H, H6), 5.51 – 5.16 (m, 12H, 6 × CH=CH), 2.89 – 2.74 (m, 10H, H6'', H9'', H12'', H15'', H18''), 2.70 (t, *J* = 7.3 Hz, 2H, H2''), 2.48 (q, *J* = 7.3 Hz, 2H, H3''), 2.04 (qt, *J* = 7.5 Hz, 2H, H21''), 0.94 (t, *J* = 7.5 Hz, 3H, H22''). ^{13}C NMR (75 MHz, MeOD) δ 177.15, 171.95, 166.27, 163.13, 158.67, 158.38, 150.38, 146.67, 132.73, 131.46, 130.61 (2C), 129.38 (3C), 129.12 (2C), 129.06, 128.89, 128.68, 128.18, 122.19, 121.96, 116.47, 116.20, 105.30, 100.14, 95.04, 34.68, 26.55 (4C), 26.39, 23.67, 21.46, 14.65. HRMS (ESI-I): calculated for $C_{37}H_{39}O_8$ $[M-H]^-$ 611.2645; found 611.2651.

3-(*tert*-butyldimethylsilyloxy)-2-(3,4-bis-(*tert*-butyldimethylsilyloxy)phenyl)-5,7-dihydroxy-4*H*-chromen-4-one (16): To a solution of dried quercetin (0.5 g, 1.65 mmol) in anhydrous CH_2Cl_2 (5 mL) stirred under N_2, was added distilled DBU (0.87 mL, 5.79 mmol) and TBDMSCl (0.77 g, 5.13 mmol). The resulting mixture was stirred at room temperature for 45 min, diluted in CH_2Cl_2 and washed several times with water. The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using CH_2Cl_2 as eluent to give compound **16** (240 mg, 22%) as yellow oil, isolated among penta- and tetra-derivatives. R_f (CH_2Cl_2/MeOH, 99:1) = 0.37. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, J = 8.5, 2.5 Hz, 1H, H6'), 7.33 (d, J = 2.5 Hz, 1H, H2'), 6.89 (d, *J* = 8.5 Hz, 1H, H5'), 6.35 (d, *J* = 2.0 Hz, 1H, H8), 6.26 (d, *J* = 2.0 Hz, 1H, H6), 1.81 (bs, 1H, OH), 1.00 (s, 9H, 3 × CH_3*t*Bu), 0.99 (s, 9H, 3 × CH_3*t*Bu), 0.83 (s, 9H, 3 × CH_3*t*Bu), 0.23 (s, 6H, 2 × CH_3Si), 0.20 (s, 6H, 2 × CH_3Si), 0.11 (s, 6H, 2 × CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.18, 162.03, 161.64, 156.68, 153.39, 149.24, 146.74, 135.49, 124.26, 123.28, 121.60, 120.76, 105.53, 98.53, 93.68, 25.89 (3C), 25.87 (3C), 25.64 (3C), 18.55, 18.53, 18.41, -4.09 (2C), -4.17 (2C), -4.20 (2C). HRMS (ESI-I): calculated for $C_{33}H_{51}O_7Si_3$ $[M-H]^-$ 643.2943; found 643.2949.

(9*Z*,12*Z*,15*Z*)-3-(*tert*-butyldimethylsilyloxy)-2-(3,4-bis-(*tert*-butyldimethylsilyloxy)phenyl)-5-hydroxy-4-oxo-4*H*-chromen-7-yl octadeca-9,12,15-trienoate (17): To a solution of α-linolenic acid (94 mg, 0.34 mmol), dicyclohexylcarbodiimide (77 mg, 0.37 mmol) and 4-dimethylaminopyridine (21 mg, 0.173 mmol) in anhydrous CH_2Cl_2 (5 mL) stirred under N_2, was added a solution of compound **16** (218 mg, 0.34 mmol) in anhydrous CH_2Cl_2 (4 mL). The resulting mixture was stirred at room temperature

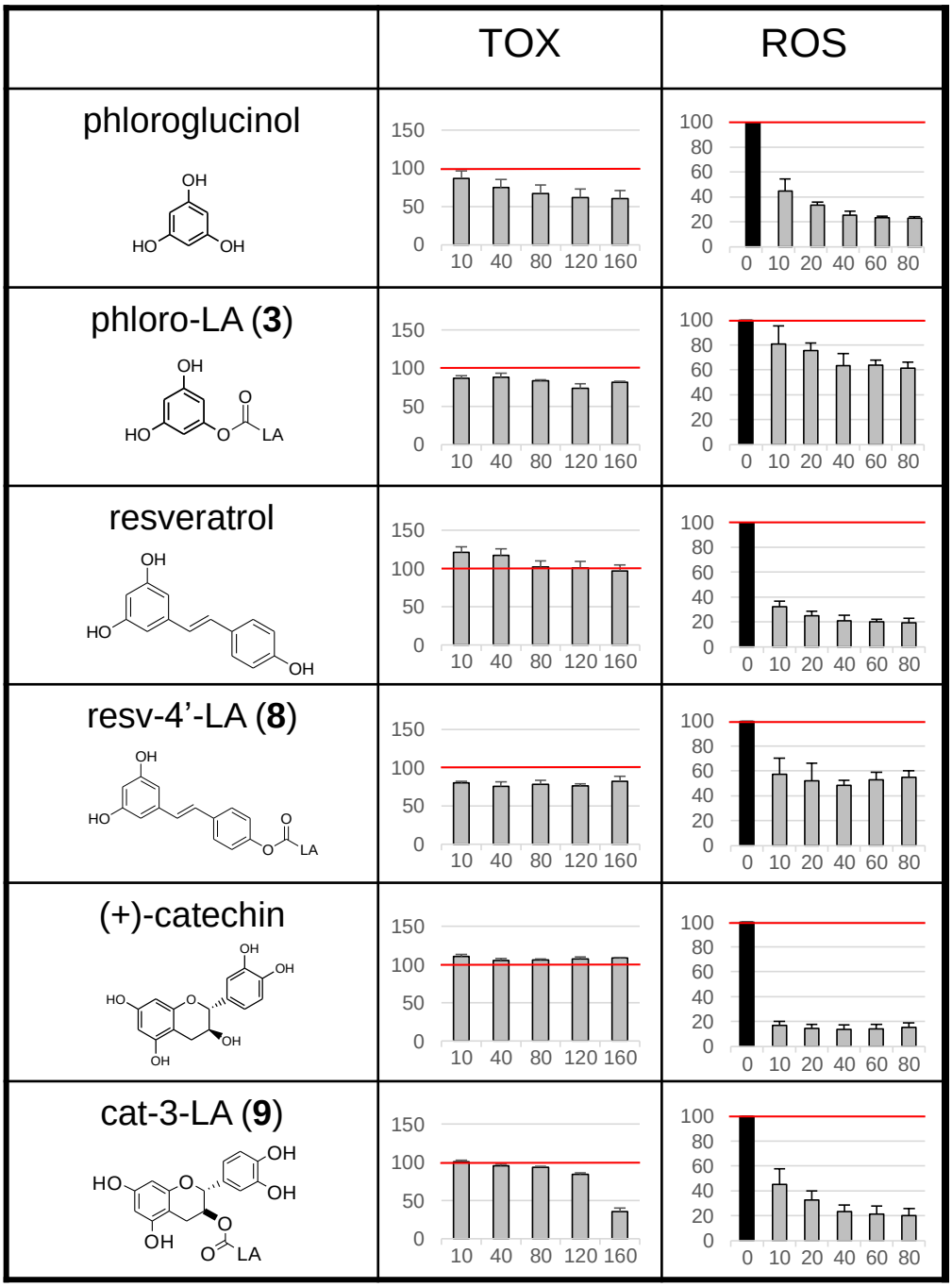
for 1 h and cooled to 4 °C for 1 h to afford filtration of the precipitate. The filtrate was washed with water and brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using pentane/EtOAc (99:1 v/v) as eluent to give compound **17** (126 mg, 41%) as yellow oil. R_f (pentane/EtOAc, 90:10) = 0.67. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 8.4, 2.2 Hz, 1H, H6'), 7.34 (d, *J* = 2.2 Hz, 1H, H2'), 6.90 (d, *J* = 8.4 Hz, 1H, H5'), 6.69 (d, *J* = 2.0 Hz, 1H, H8), 6.49 (d, *J* = 2.0 Hz, 1H, H6), 5.46 – 5.26 (m, 6H, 3 × CH=CH), 2.81 (t, *J* = 5.9 Hz, 4H, H11'', H14''), 2.58 (t, *J* = 7.5 Hz, 2H, H2''), 2.12 – 2.03 (m, 4H, H8'', H17''), 1.76 (qt, *J* = 7.5 Hz, 2H, H3''), 1.45 – 1.31 (m, 8H, H4'', H5'', H6'', H7''), 1.00 (s, 9H, 3 × CH_3*t*Bu), 1.00 (s, 9H, 3 × CH_3*t*Bu), 0.97 (t, *J* = 7.5 Hz, 2H, H18''), 0.83 (s, 9H, 3 × CH_3*t*Bu), 0.23 (s, 6H, 2 × CH_3Si), 0.20 (s, 6H, 2 × CH_3Si), 0.11 (s, 6H, 2 × CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.49, 171.46, 161.66, 155.52, 155.50, 154.23, 149.54, 146.82, 135.98, 131.95, 130.20, 128.28, 128.22, 127.77, 127.08, 123.99, 123.37, 121.75, 120.83, 108.84, 104.28, 100.66, 34.38, 29.55, 29.13, 29.07, 29.01, 27.17, 25.91 (3C), 25.88 (3C), 25.62 (3C), 25.60, 25.51, 24.79, 20.54, 18.58, 18.56, 18.41, 14.28, -4.06 (2C), -4.16 (2C), -4.17 (2C). HRMS (ASAP+I): calculated for $C_{32}H_{43}O_4$ $[M + H]^+$ 905.5239; found 905.5228.

(9*Z*,12*Z*,15*Z*)-2-(3,4-dihydroxyphenyl)-3,5-dihydroxy-4-oxo-4*H*-chromen-7-yl octadeca-9,12,15-trienoate (Quer-7-ALA, 18): To a solution of compound **17** (115 mg, 0.13 mmol) in anhydrous THF (9.5 mL) stirred under N_2, was added dropwise triethylamine trihydrofluoride (186 µL, 1.14 mmol). The resulting mixture was stirred at room temperature for 35 min, diluted in EtOAc and washed with water and brine. The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the residue was performed by silica column chromatography using pentane/EtOAc (90:10 to 80:20 v/v) as eluent to give compound **18** (30 mg, 61%) as bright yellow solid. R_f (pentane/EtOAc, 50:50) = 0.61. Mp 235.8 °C. ^{1}H NMR (500 MHz, MeOD) δ 7.77 (d, *J* = 2.0 Hz, 1H, H2'), 7.66 (dd, *J* = 8.5, 2.0 Hz, 1H, H6'), 6.88 (d, *J* = 8.5 Hz, 1H, H5'), 6.81 (d, *J* = 1.9 Hz, 1H, H8), 6.46 (d, *J* = 1.9 Hz, 1H, H6), 5.45 – 5.21 (m, 6H, 3 × CH=CH), 2.85 – 2.73 (m, 4H, H11'', H14''), 2.58 (t, *J* = 7.4 Hz, 2H, H2''), 2.13 – 2.01 (m, 4H, H8'', H17''), 1.72 (qt, *J* = 7.4 Hz, 2H, H3''), 1.48 – 1.30 (m, 8H, H4'', H5'', H6'', H7''), 0.96 (t, *J* = 7.5 Hz, 3H, H18''). ^{13}C NMR (125 MHz, MeOD) δ 177.63, 172.84, 161.97, 157.20, 156.76, 149.32, 149.21, 146.26, 138.03, 132.71, 131.05, 129.20, 129.18, 128.90, 128.23, 123.71, 122.01, 116.26, 116.23, 108.50, 104.83, 101.87, 35.02, 30.66, 30.23, 30.16, 30.09, 28.14, 26.52, 26.40, 25.80, 21.48, 14.67. HRMS (ESI-I): calculated for $C_{33}H_{37}O_8$ $[M-H]^-$ 561.2488; found 561.2490.

Figure S1 : Graphical representation of *in vitro* evaluations of lipophenols.

TOX = cytotoxicity assays represented in cell survival (%) depending on derivative concentration (µM). Results are normalized with non-treated control cells as 100% survival (red line).

ROS = Inhibition of ROS assays represented in ROS production (%) depending on derivative concentration (µM). Results are normalized with non-treated control cells exposed to stressor as 100% of ROS production (red line).



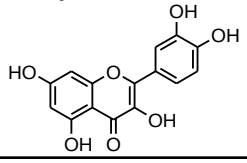
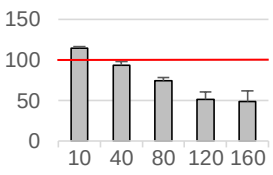
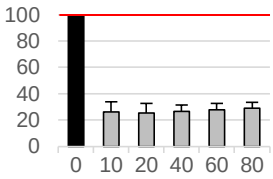
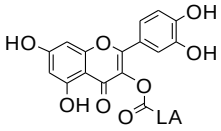
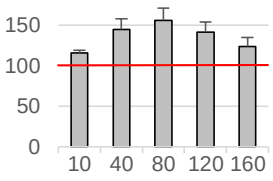
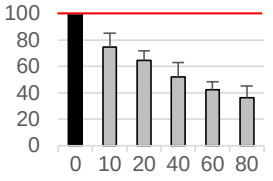
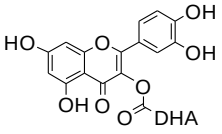
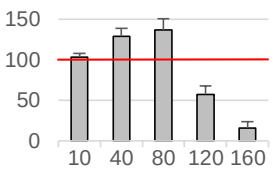
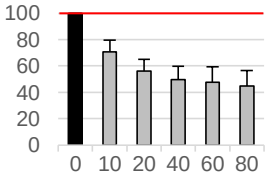
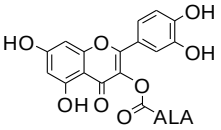
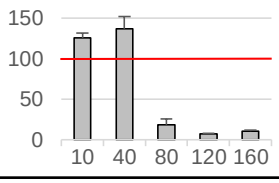
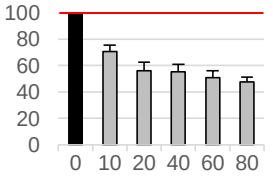
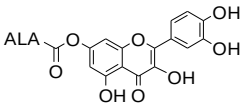
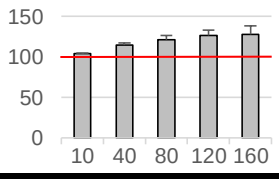
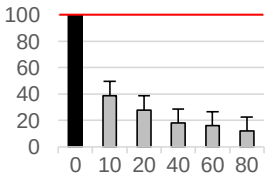
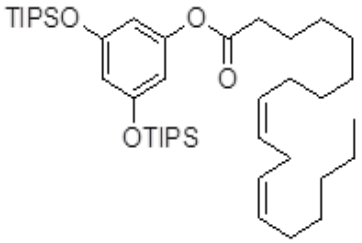
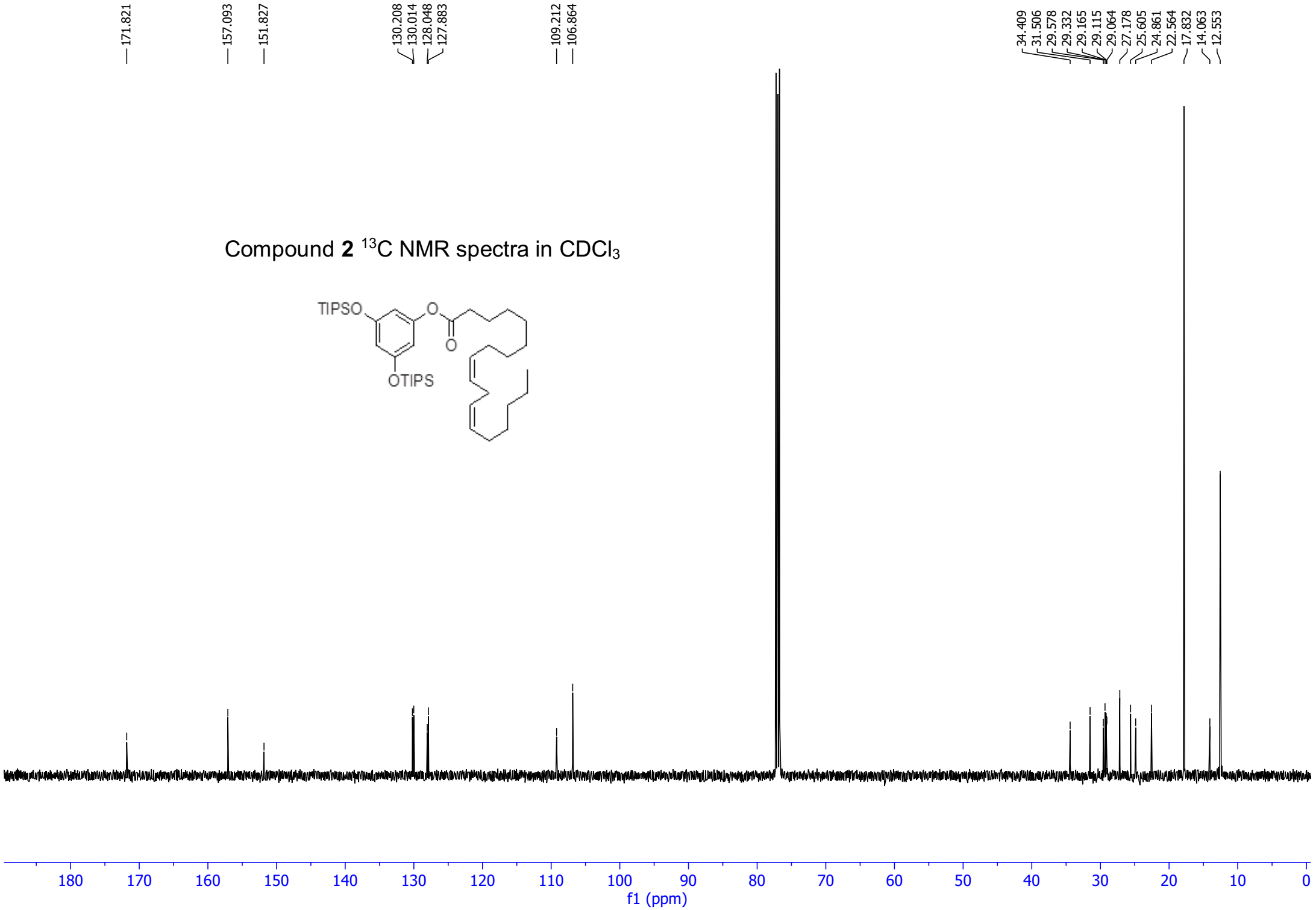
	TOX	ROS
quercetin 		
quer-3-LA (**13**) 		
quer-3-DHA (**15**) 		
quer-3-ALA (**14**) 		
quer-7-ALA (**18**) 		

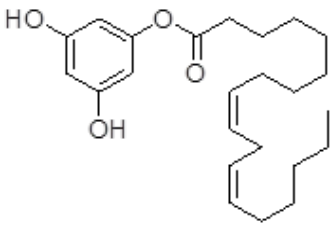
Figure S2: Full NMR spectra characterization of derivatives from 2 to 18 (^{1}H and ^{13}C).

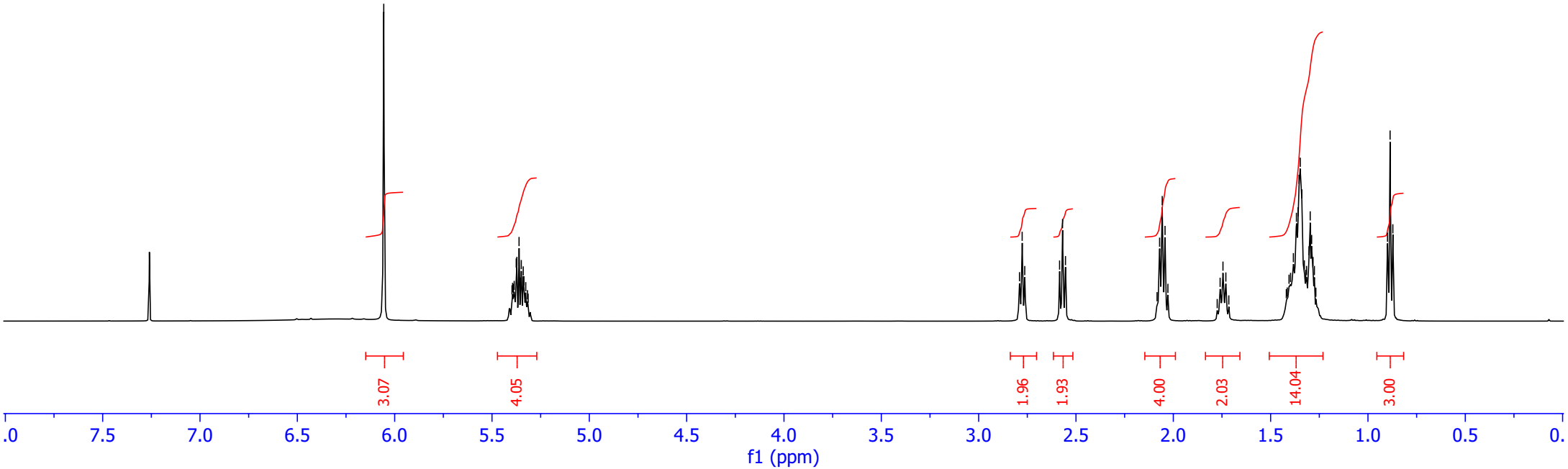
Compound **2** ^{1}H NMR spectra in $CDCl_3$




171.821
157.093
151.827
130.208
130.014
128.048
127.883
109.212
106.864
34.409
31.506
29.578
29.332
29.165
29.115
29.064
27.178
25.605
24.861
22.564
17.832
14.063
12.553
Compound 2 13C NMR spectra in CDCl3
TIPSO
O
O
OTIPS
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

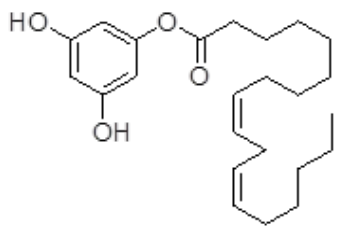
Phloro-LA (compound **3**) ^{1}H NMR spectra in $CDCl_3$

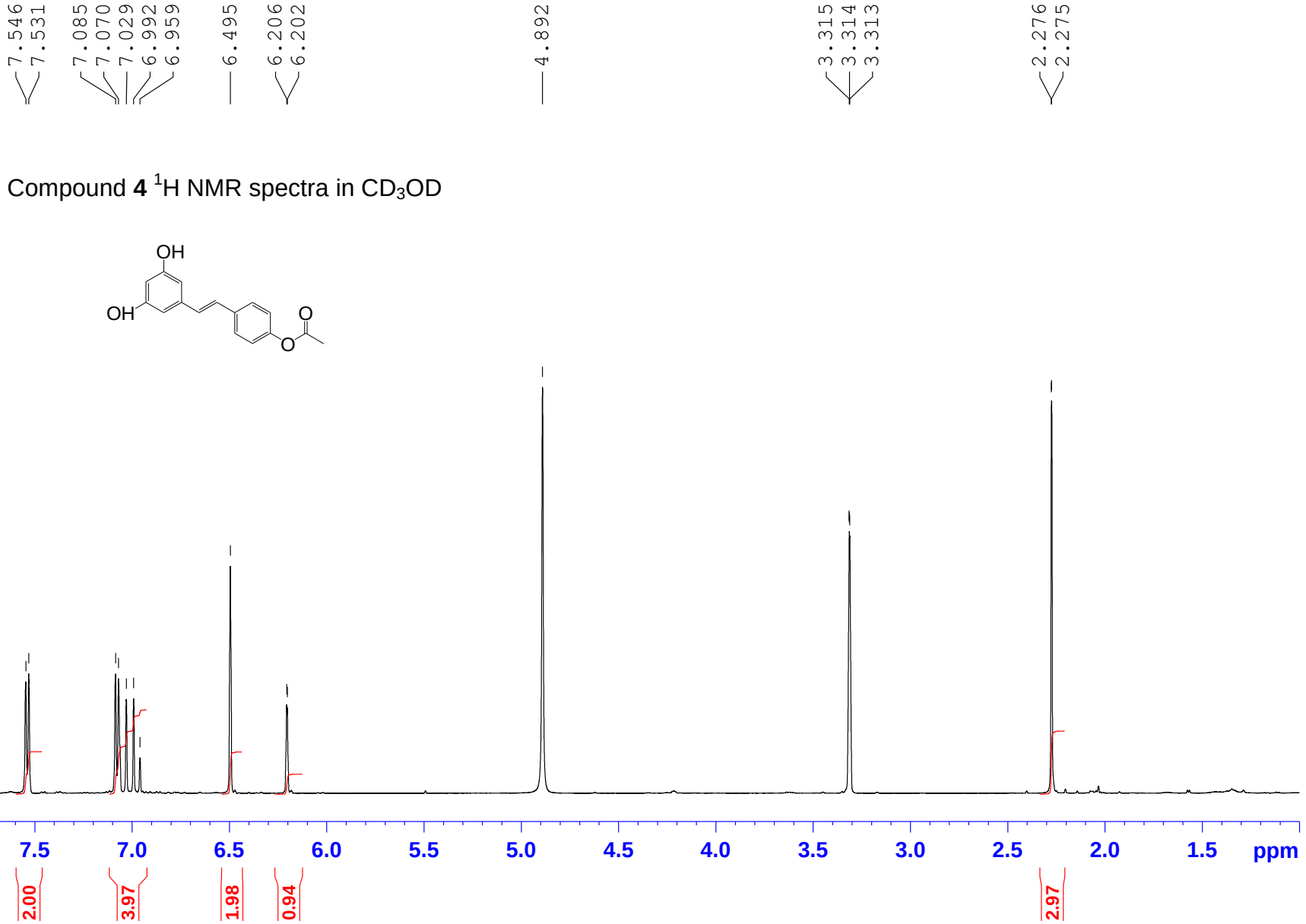




174.544
157.380
151.651
130.236
129.970
128.084
127.860
101.936
101.503
34.380
31.498
29.583
29.317
29.134
29.085
29.014
27.161
25.603
24.812
22.555
14.067

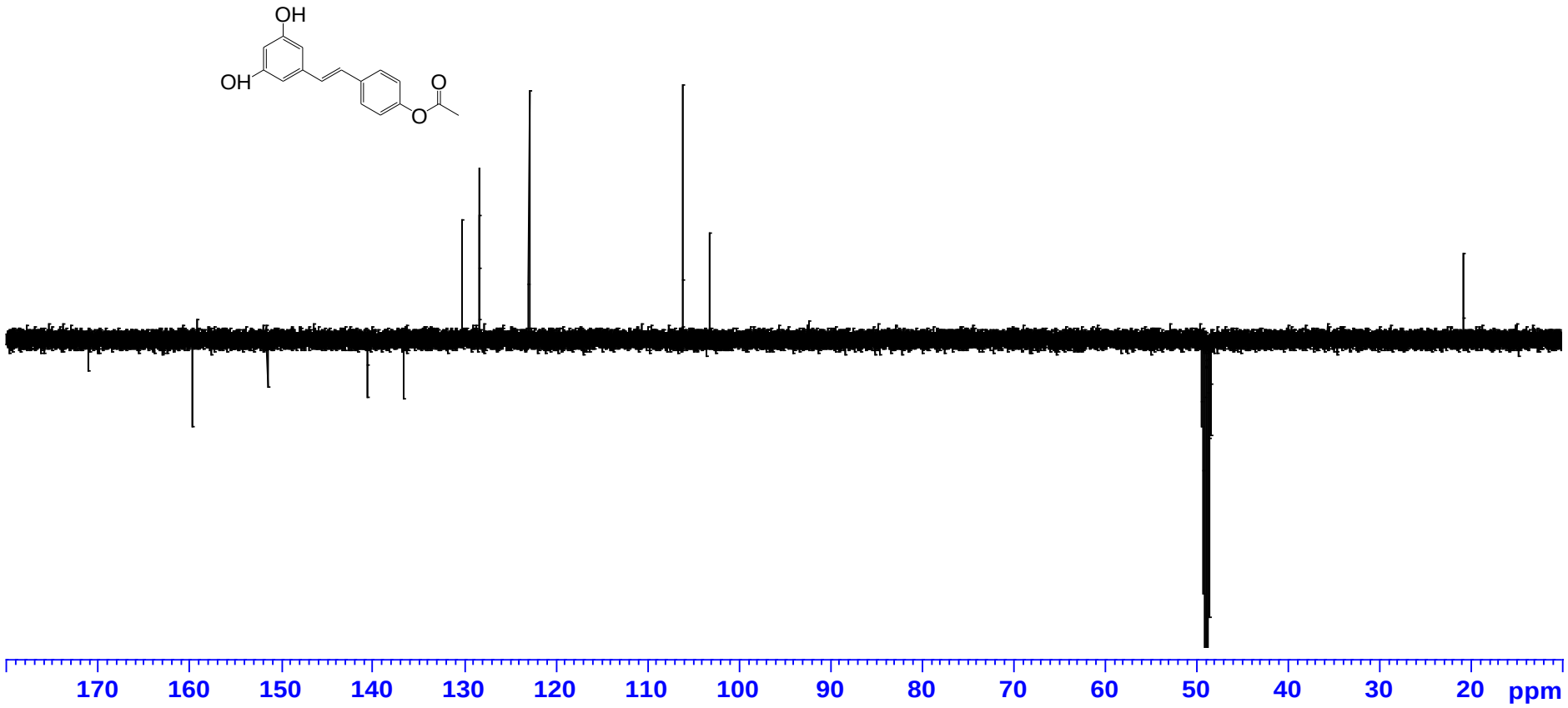
Phloro-LA (compound **3**) ^{13}C NMR spectra in $CDCl_3$



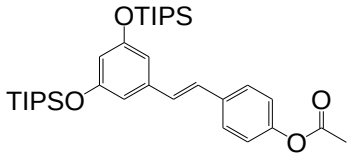


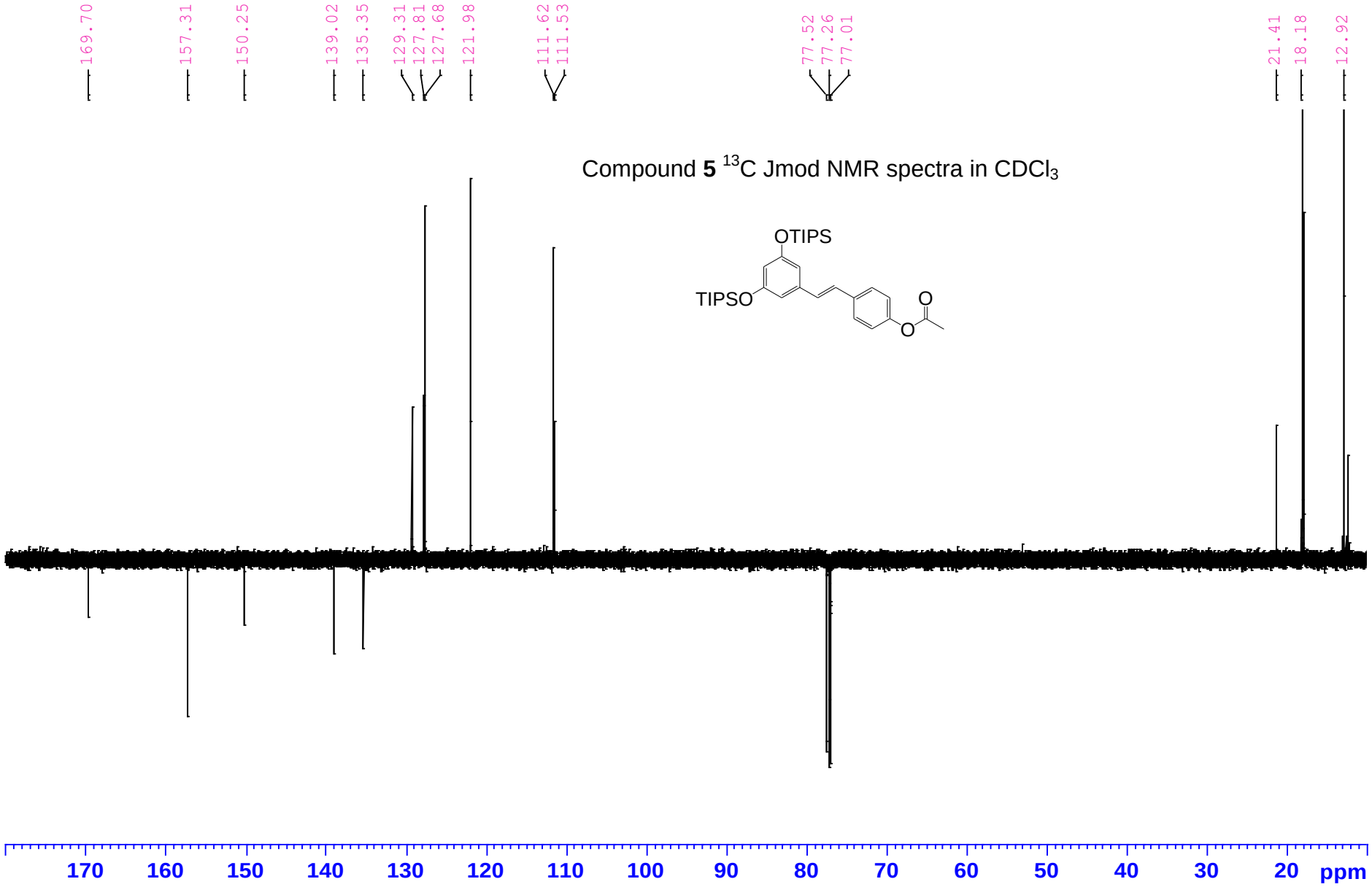
Compound **4** ^{1}H NMR spectra in CD_3OD

Compound **4** ^{13}C Jmod NMR spectra in CD_3OD

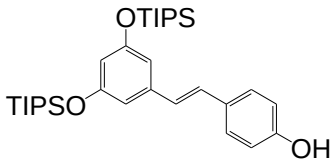


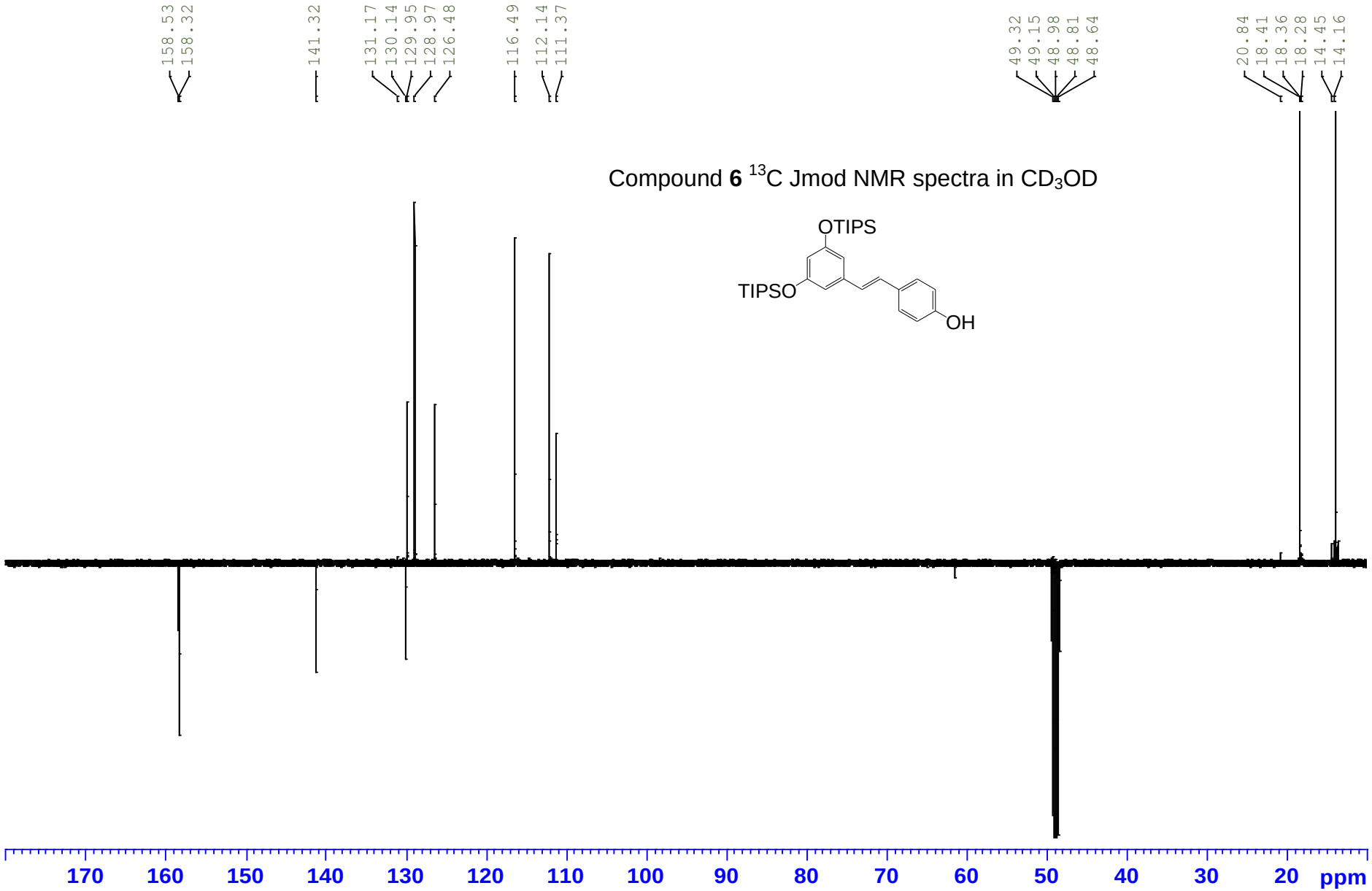
Compound **5** ^{1}H NMR spectra in $CDCl_3$



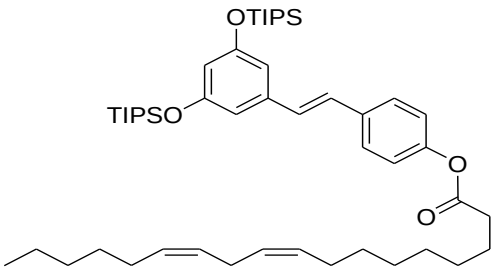

169.70
157.31
150.25
139.02
135.35
129.31
127.81
127.68
121.98
111.62
111.53
77.52
77.26
77.01
21.41
18.18
12.92
Compound 5 13C Jmod NMR spectra in CDCl3
OTIPS
TIPSO
O
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

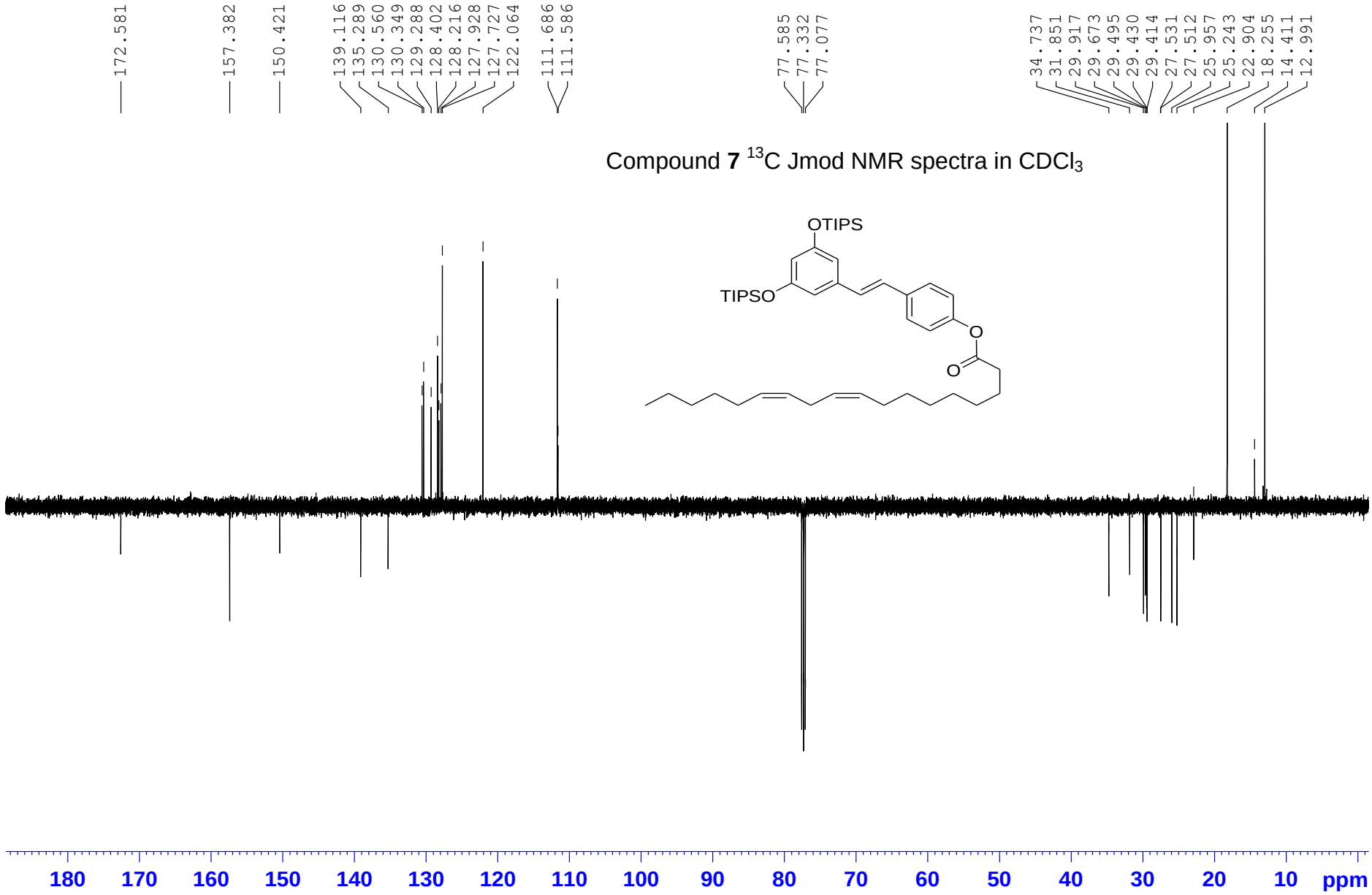
Compound **6** ^{1}H NMR spectra in CD_3OD

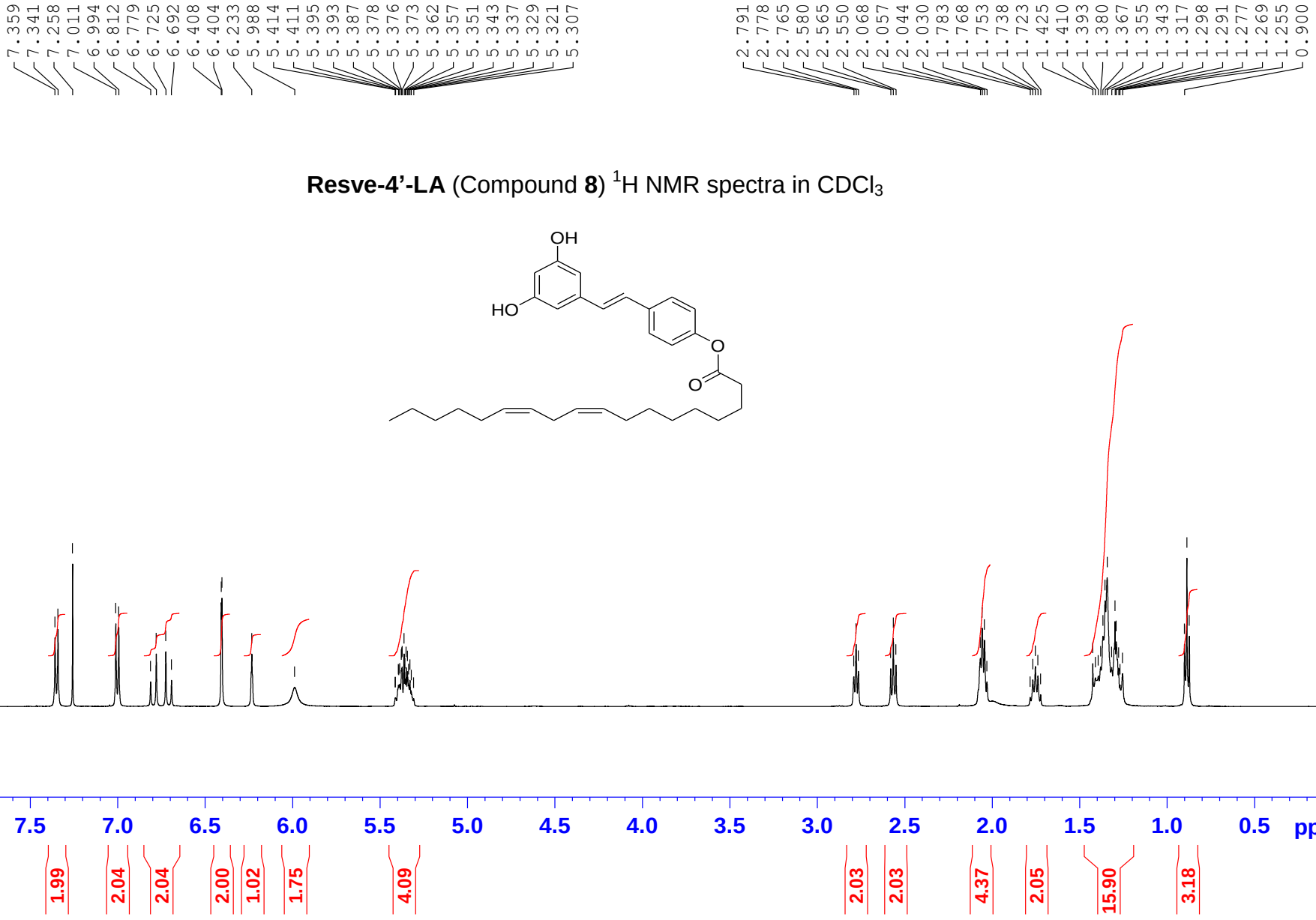



158.53
158.32
141.32
131.17
130.14
129.95
128.97
126.48
116.49
112.14
111.37
49.32
49.15
48.98
48.81
48.64
20.84
18.41
18.36
18.28
14.45
14.16
Compound 6 13C Jmod NMR spectra in CD3OD
OTIPS
TIPSO
OH
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

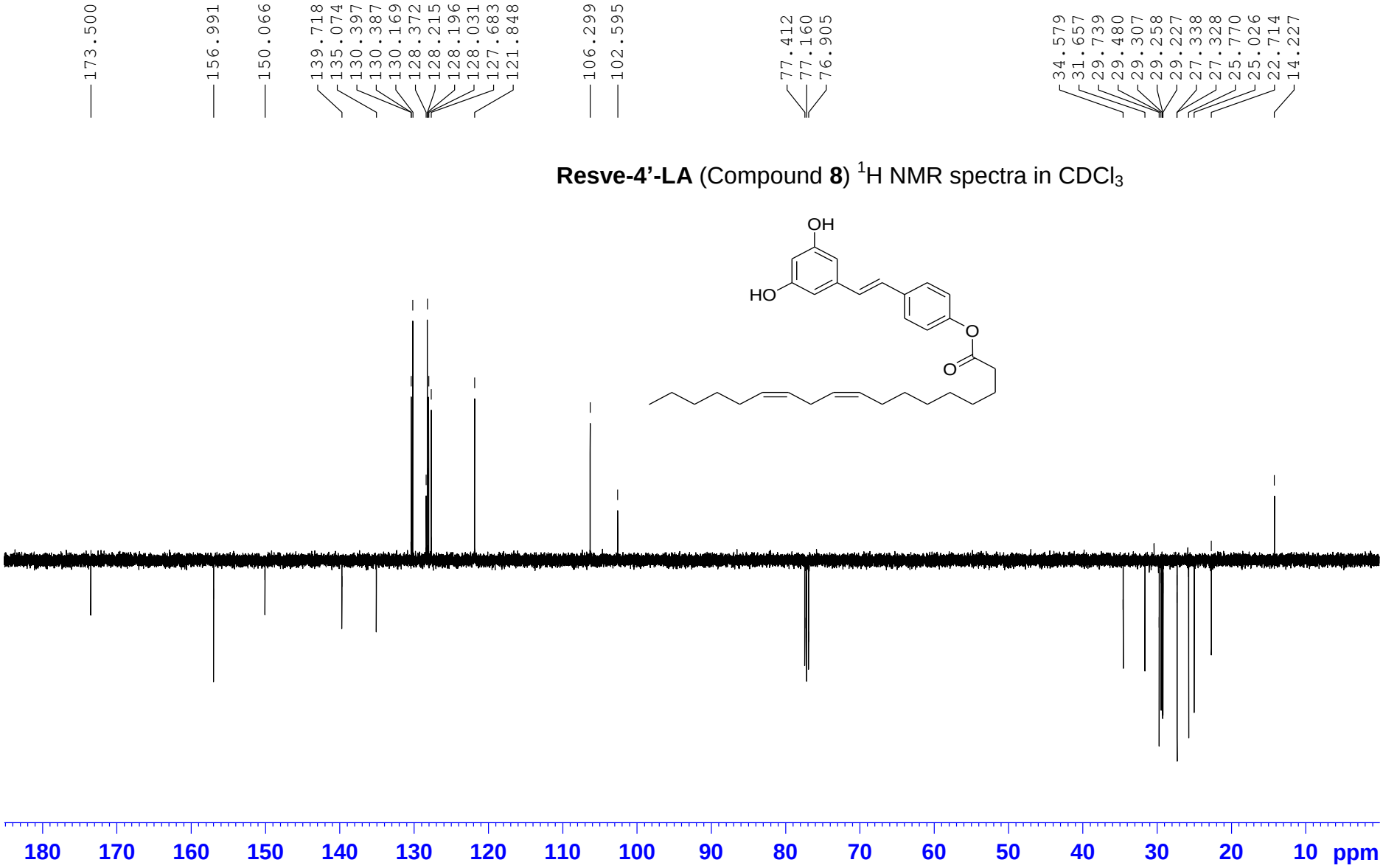
Compound **7** ^{1}H NMR spectra in $CDCl_3$




172.581
157.382
150.421
139.116
135.289
130.560
130.349
129.288
128.402
128.216
127.928
127.727
122.064
111.686
111.586
77.585
77.332
77.077
34.737
31.851
29.917
29.673
29.495
29.430
29.414
27.531
27.512
25.957
25.243
22.904
18.255
14.411
12.991
Compound 7 13C Jmod NMR spectra in CDCl3
OTIPS
TIPSO
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

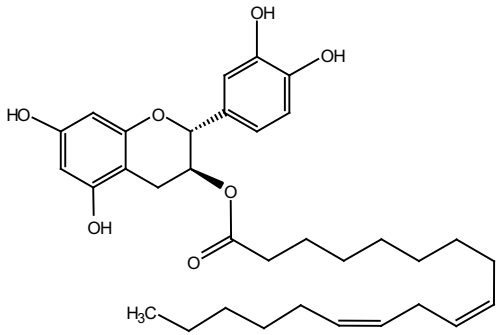


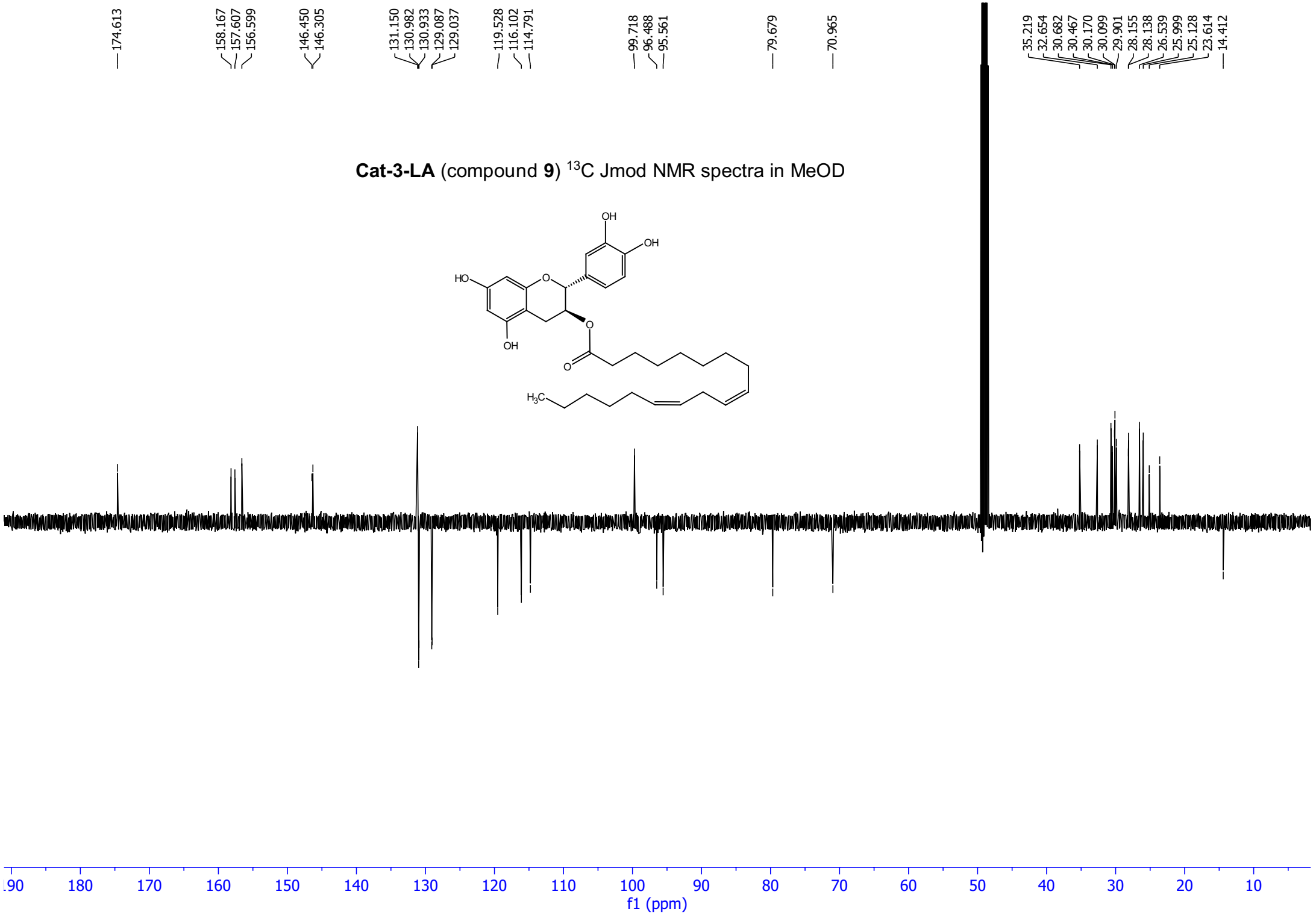
Resve-4'-LA (Compound **8**) ^{1}H NMR spectra in $CDCl_3$



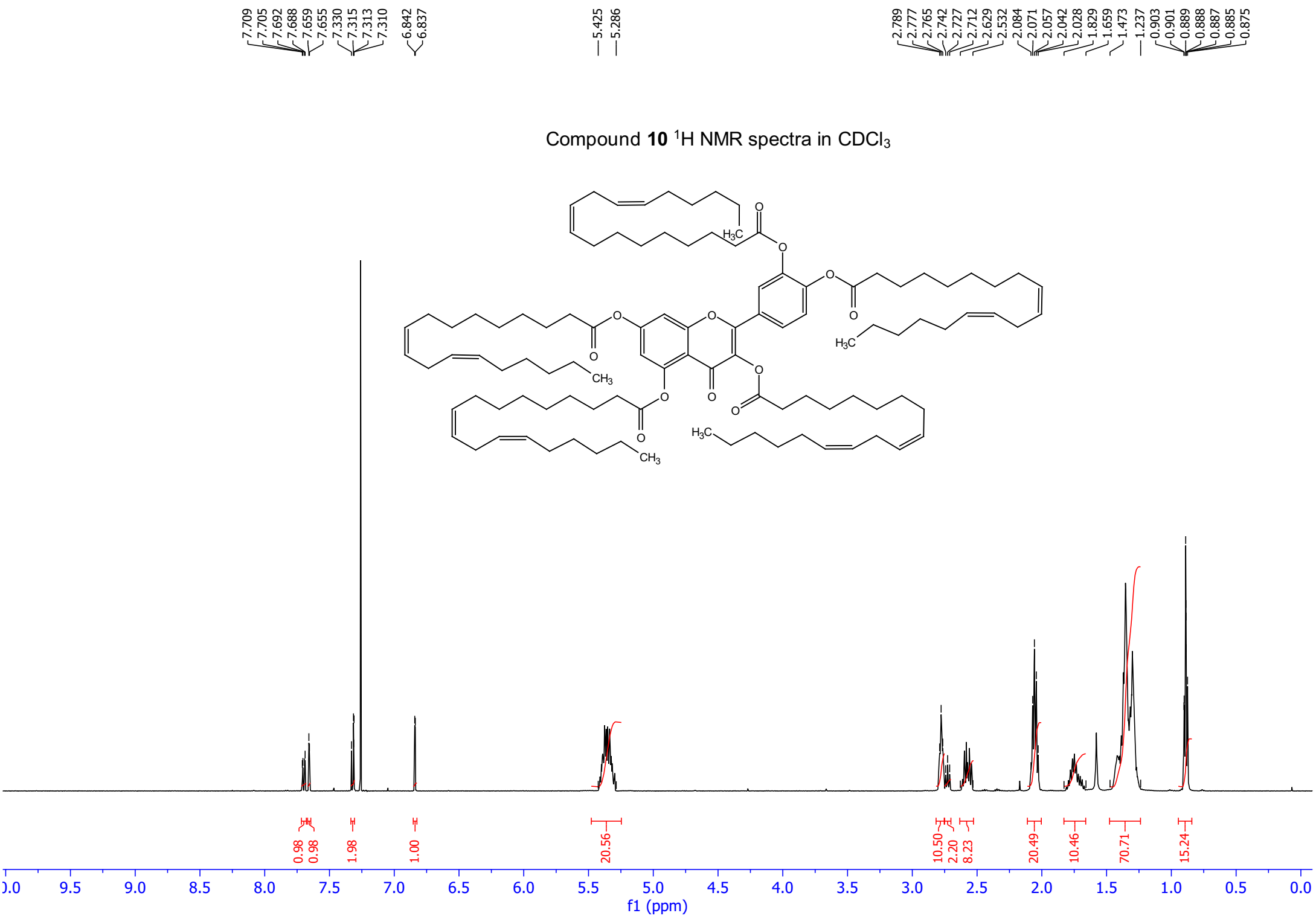
Resve-4'-LA (Compound **8**) ^{1}H NMR spectra in $CDCl_3$

Cat-3-LA (compound **9**) ^{1}H NMR spectra in MeOD



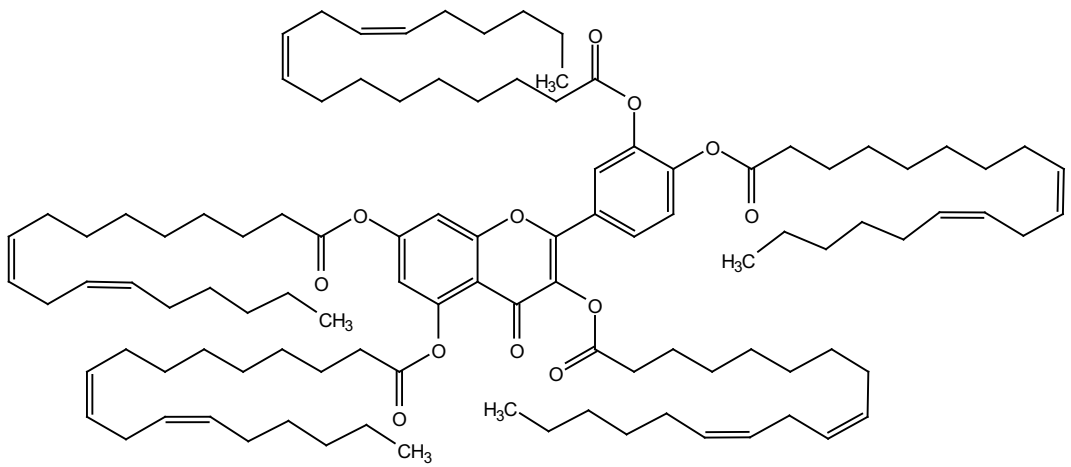

174.613
158.167
157.607
156.599
146.450
146.305
131.150
130.982
130.933
129.087
129.037
119.528
116.102
114.791
99.718
96.488
95.561
79.679
70.965
35.219
32.654
30.682
30.467
30.170
30.099
29.901
28.155
28.138
26.539
25.999
25.128
23.614
14.412
Cat-3-LA (compound 9) 13C Jmod NMR spectra in MeOD
OH
OH
HO
O
OH
O
O
H3C
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

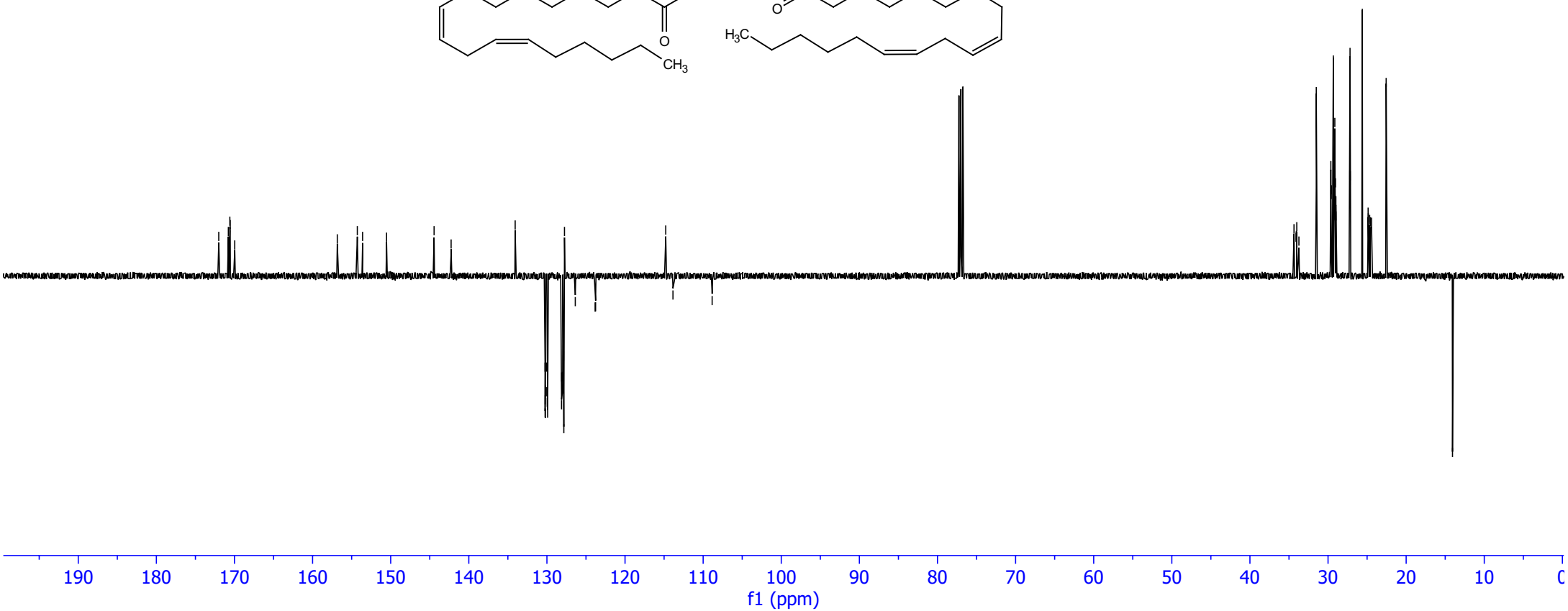
Compound **10** ^{1}H NMR spectra in $CDCl_3$



172.012
170.786
170.630
170.594
170.549
169.965
156.839
154.274
153.597
150.532
144.446
142.266
134.065
130.240
130.234
130.221
130.201
130.195
130.087
130.048
129.959
129.904
129.898
128.129
128.123
128.094
127.997
127.993
127.912
127.890
127.861
127.835
127.752
123.830
123.768
114.789
34.358
34.100
34.060
34.001
33.728
31.507
29.641
29.623
29.601
29.569
29.326
29.253
29.238
29.202
29.175
29.170
29.131
29.122
29.116
29.105
29.091
29.048
28.997
28.985
27.219
27.212
27.185
27.171
27.155
25.615
24.868
24.841
24.673
24.575
24.424
22.560

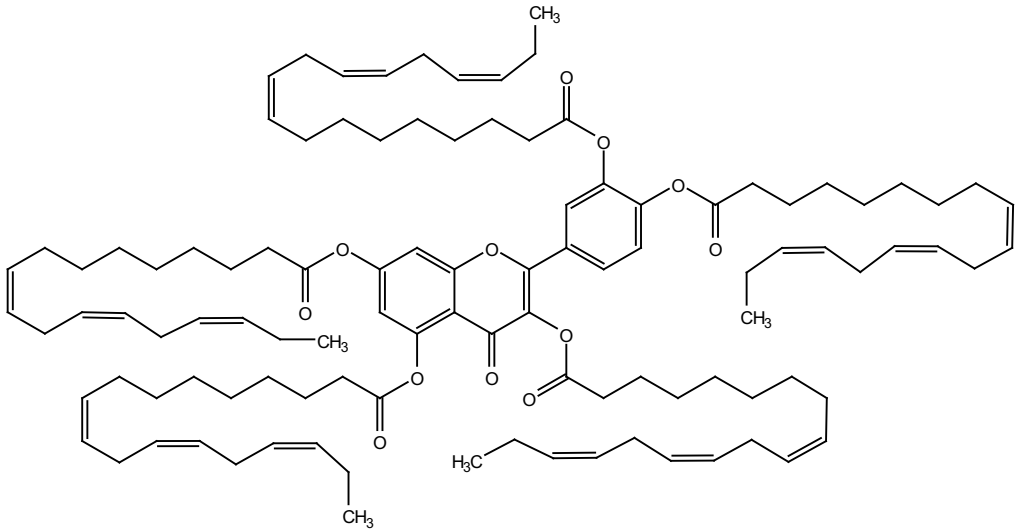
Compound **10** ^{13}C NMR spectra in $CDCl_3$

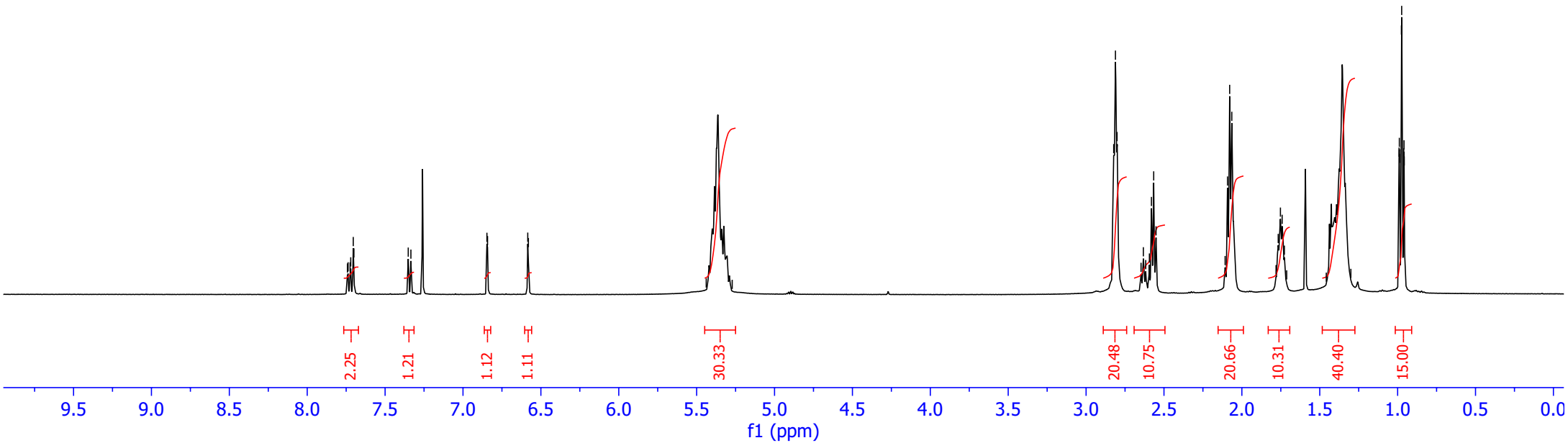




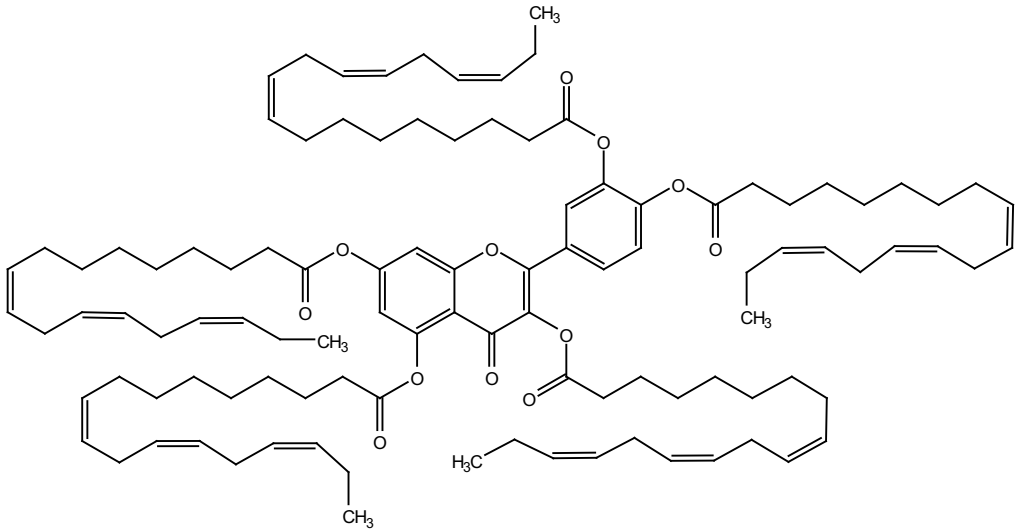
7.742
7.738
7.725
7.721
7.704
7.700
7.351
7.334
6.846
6.842
6.584
6.580
5.439
5.272
2.823
2.812
2.801
2.647
2.632
2.617
2.594
2.580
2.566
2.551
2.107
2.092
2.078
2.065
1.781
1.767
1.752
1.741
1.727
1.712
1.458
1.300
0.991
0.989
0.988
0.976
0.974
0.973
0.961
0.959
0.958

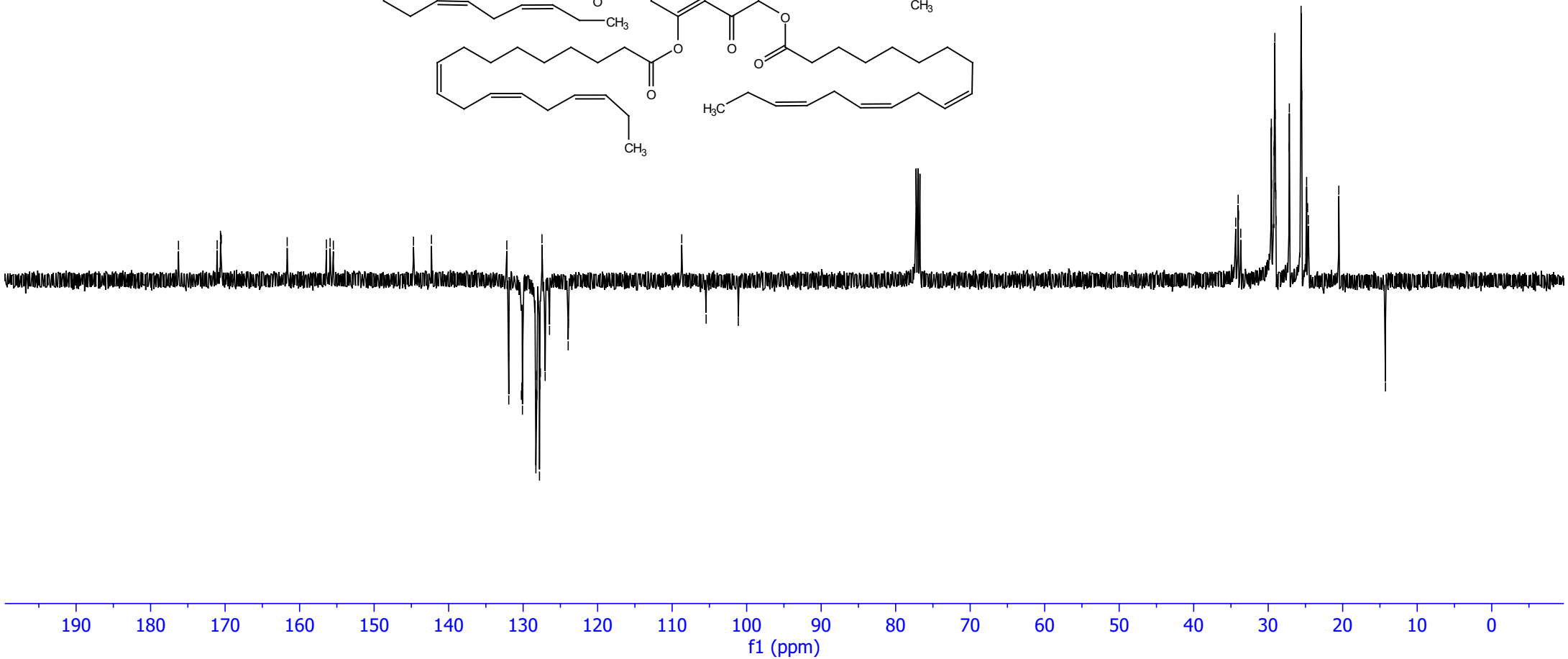
Compound **11** ^{1}H NMR spectra in $CDCl_3$



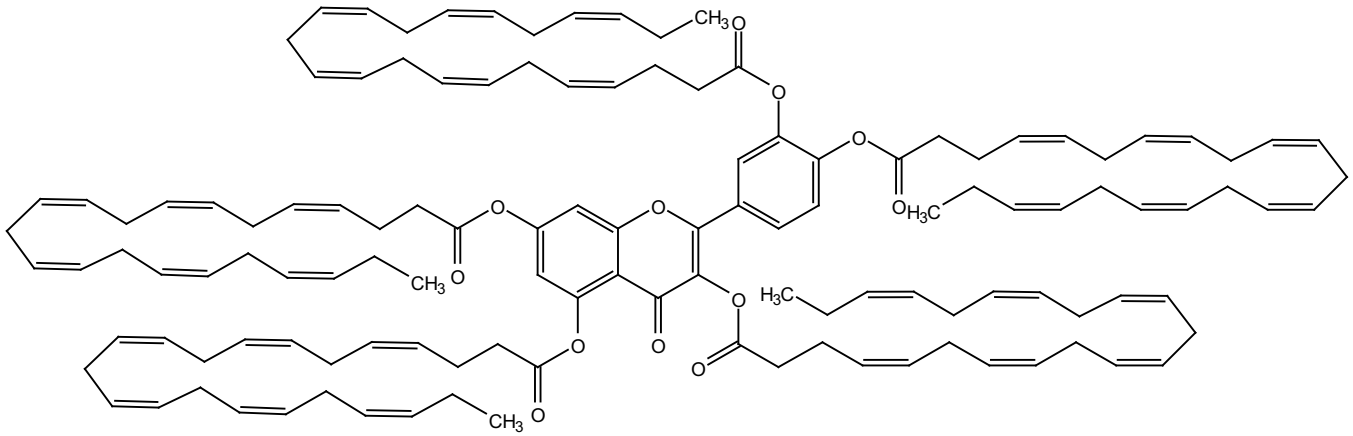


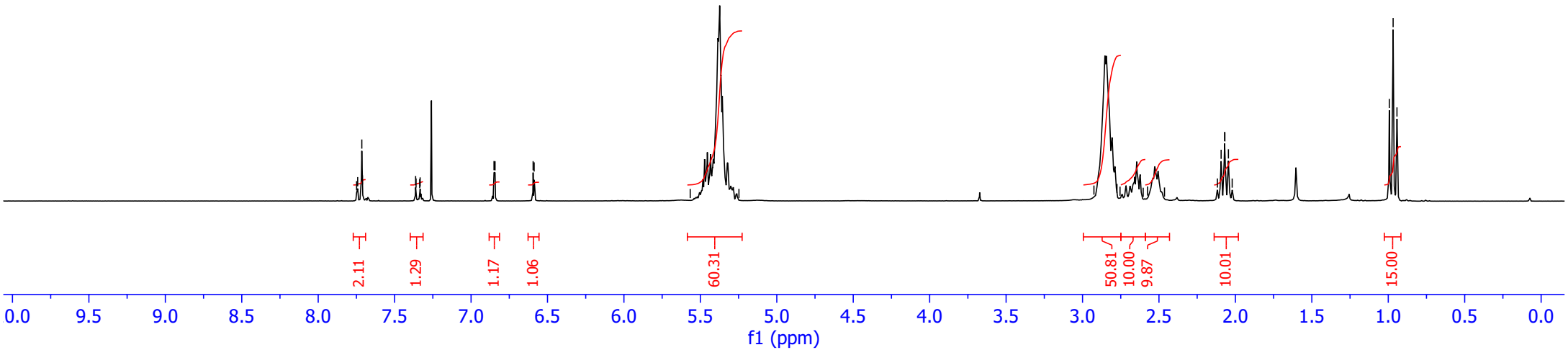
Compound **11** ^{13}C Jmod NMR spectra in $CDCl_3$

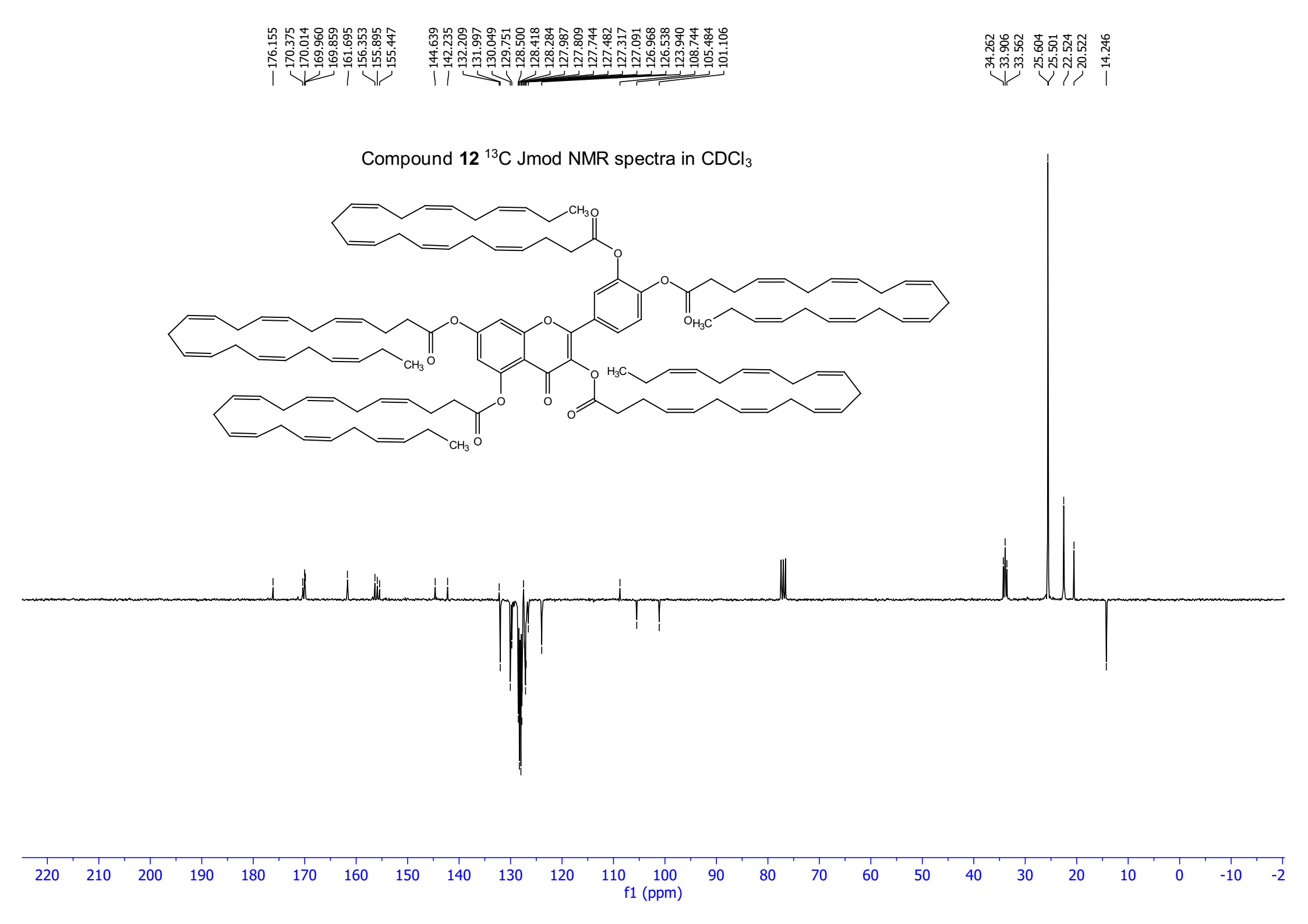




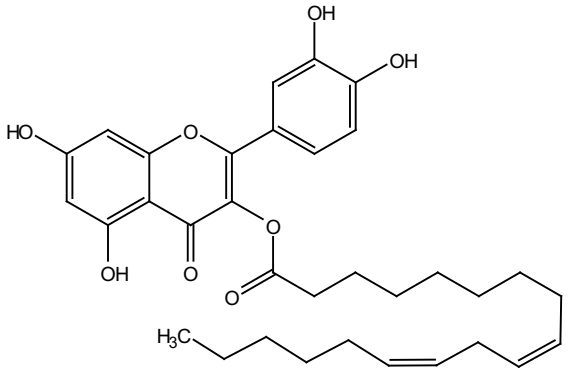
Compound **12** ^{1}H NMR spectra in $CDCl_3$

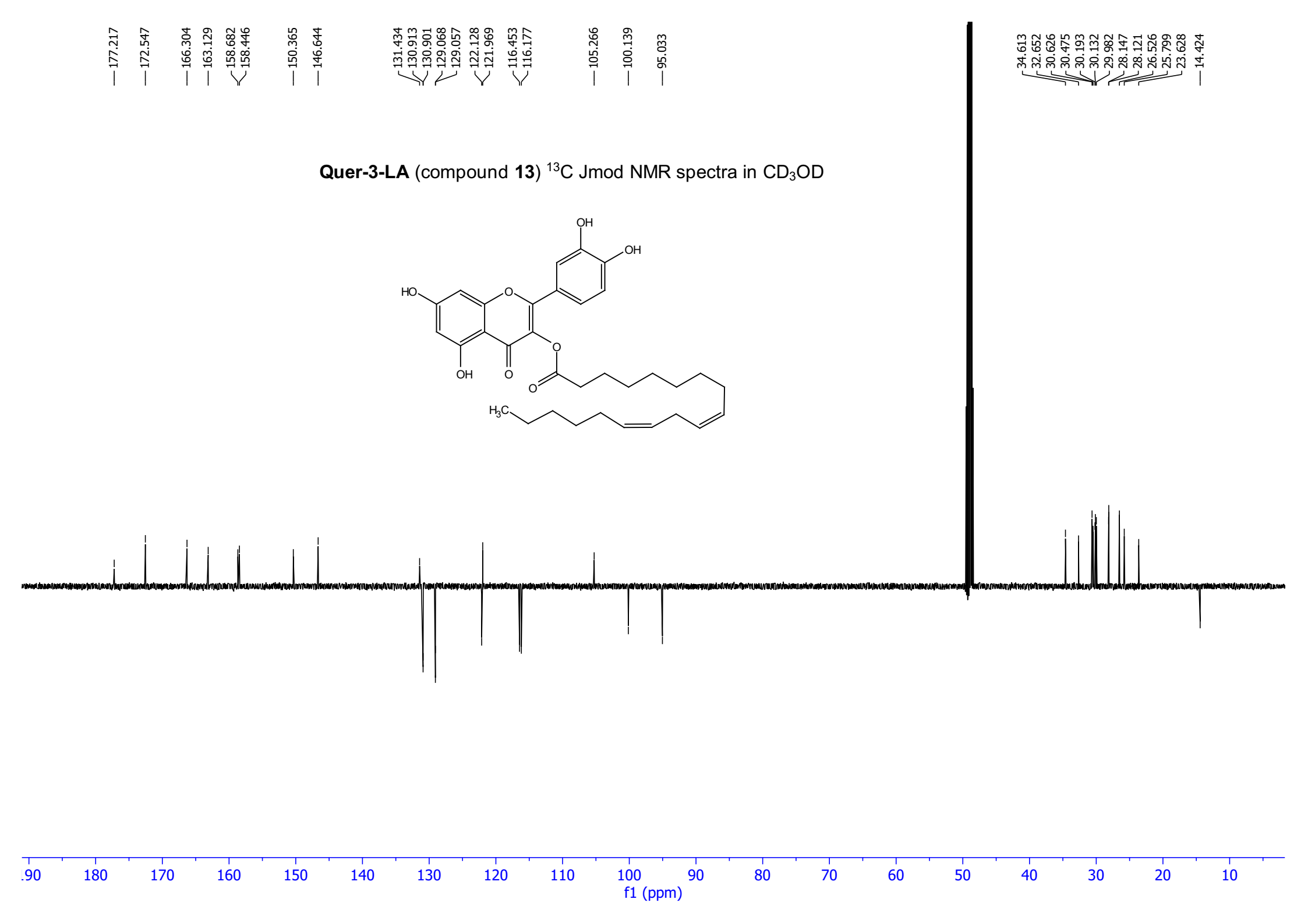




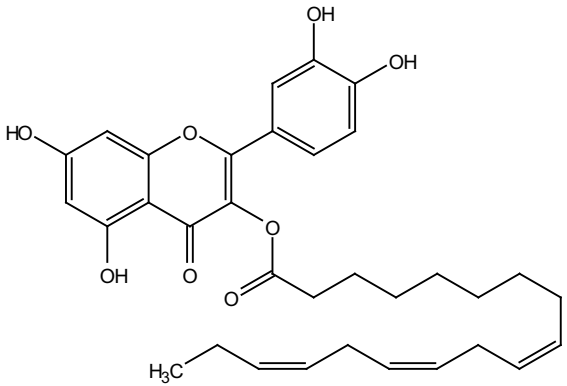

176.155
170.375
170.014
169.960
169.859
161.695
156.353
155.895
155.447
144.639
142.235
132.209
131.997
130.049
129.751
128.500
128.418
128.284
127.987
127.809
127.744
127.482
127.317
127.091
126.968
126.538
123.940
108.744
105.484
101.106
34.262
33.906
33.562
25.604
25.501
22.524
20.522
14.246
Compound 12 13C Jmod NMR spectra in CDCl3
f1 (ppm)

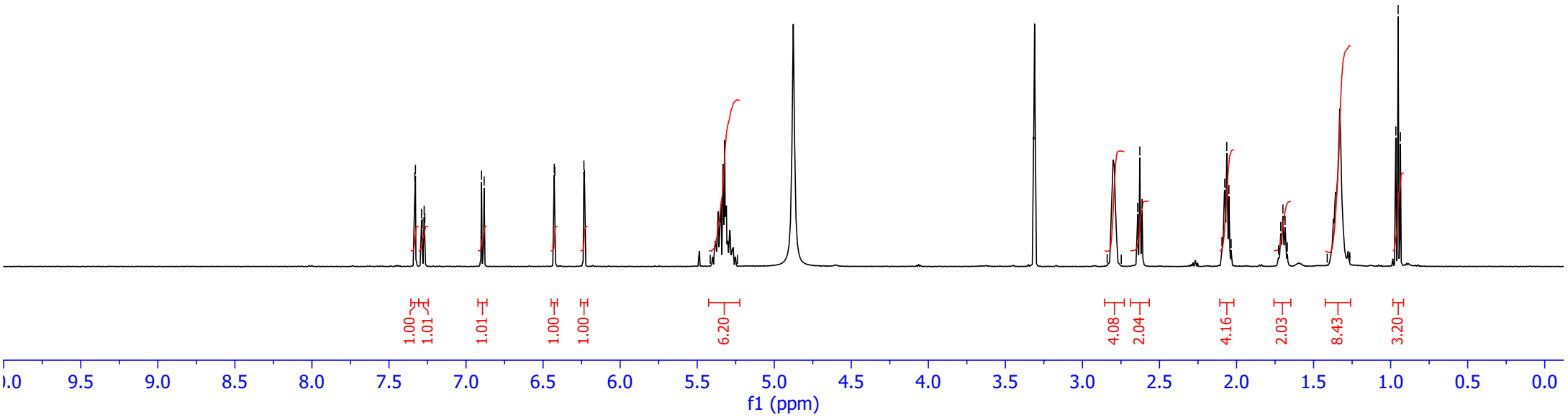
Quer-3-LA (compound **13**) ^{1}H NMR spectra in CD_3OD




177.217
172.547
166.304
163.129
158.682
158.446
150.365
146.644
131.434
130.913
130.901
129.068
129.057
122.128
121.969
116.453
116.177
105.266
100.139
95.033
34.613
32.652
30.626
30.475
30.193
30.132
29.982
28.147
28.121
26.526
25.799
23.628
14.424
Quer-3-LA (compound 13) 13C Jmod NMR spectra in CD3OD
OH
OH
HO
O
O
OH
O
O
H3C
f1 (ppm)

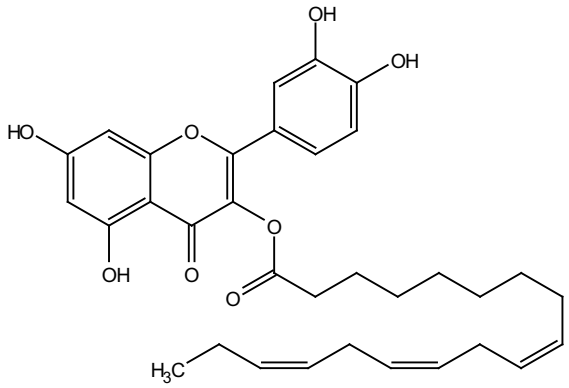
Quer-3-ALA (compound **14**) ^{1}H NMR spectra in CD_3OD

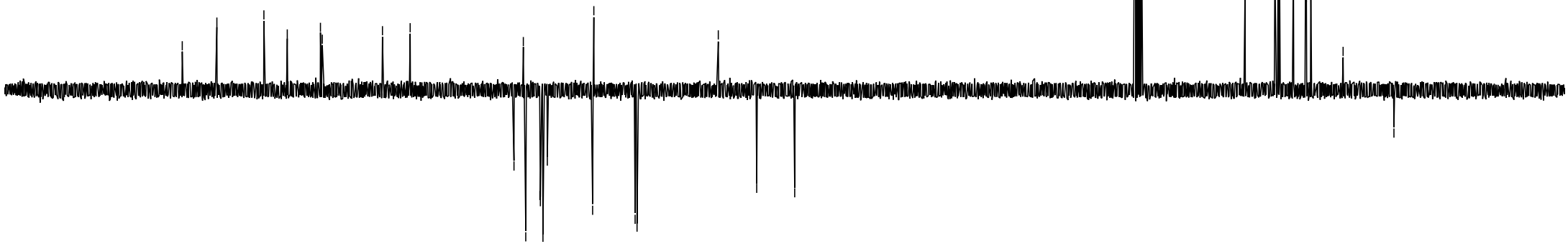


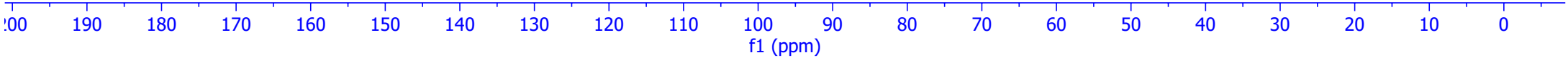


177.209
172.564
166.257
163.121
158.670
158.422
150.350
146.634
132.706
131.452
131.127
129.231
129.166
128.819
128.233
122.156
121.993
116.458
116.197
105.297
100.143
95.046
34.629
30.627
30.205
30.142
29.996
28.144
26.515
26.396
25.806
21.476
14.656

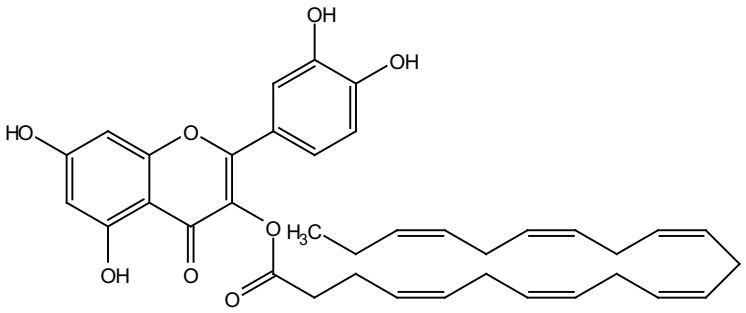
Quer-3-ALA (compound **14**) ^{13}C Jmod NMR spectra in CD_3OD



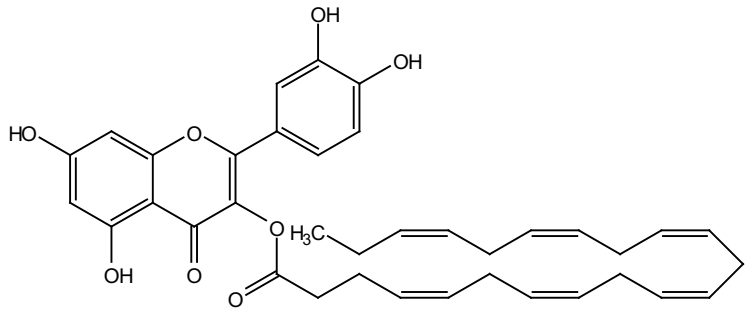




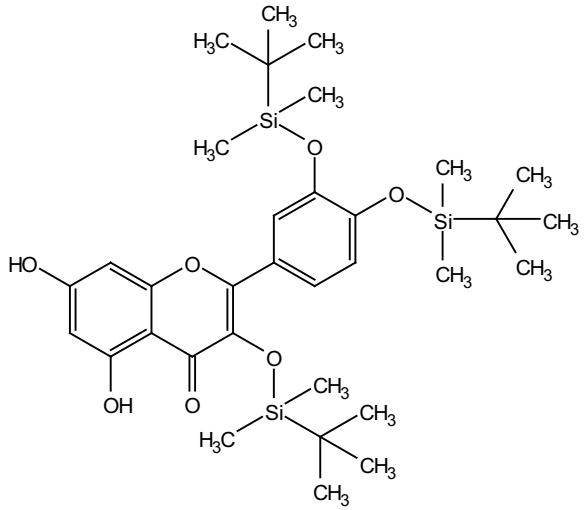
Quer-3-DHA (compound **15**) ^{1}H NMR spectra in CD_3OD



Quer-3-DHA (compound **15**) ^{13}C Jmod NMR spectra in CD_3OD

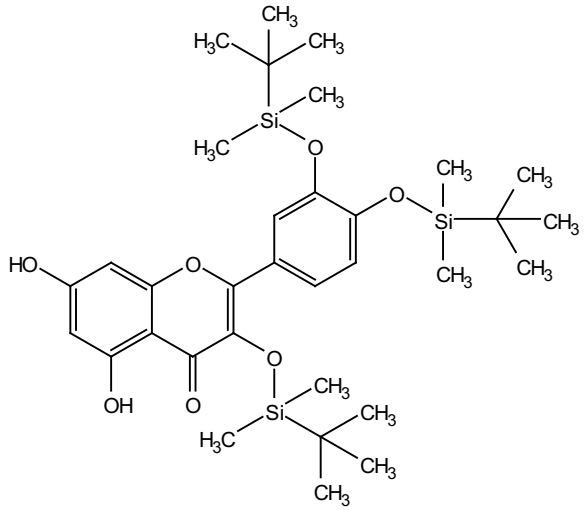


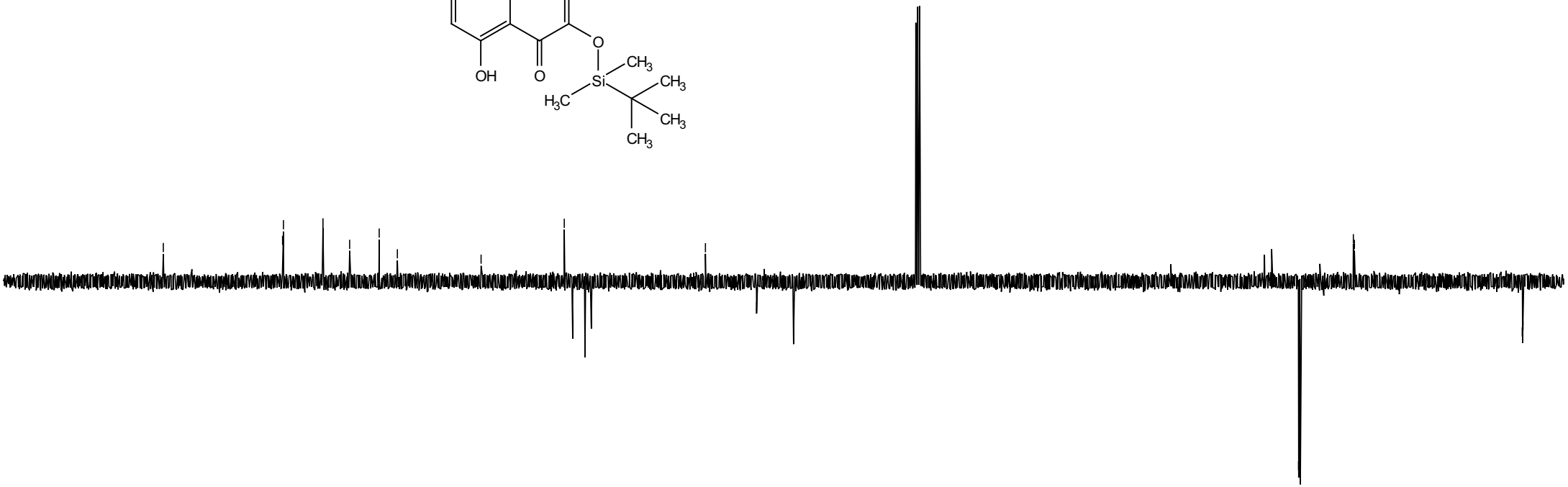
Compound **16** ^{1}H NMR spectra in $CDCl_3$

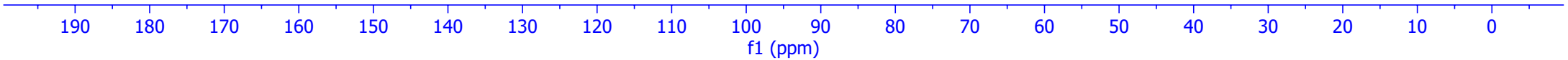


178.170
162.178
162.060
156.759
153.183
149.220
146.783
135.556
124.401
123.271
121.623
120.775
105.471
98.609
93.652
25.929
25.913
25.686
18.581
18.575
18.437
-4.067
-4.114
-4.164

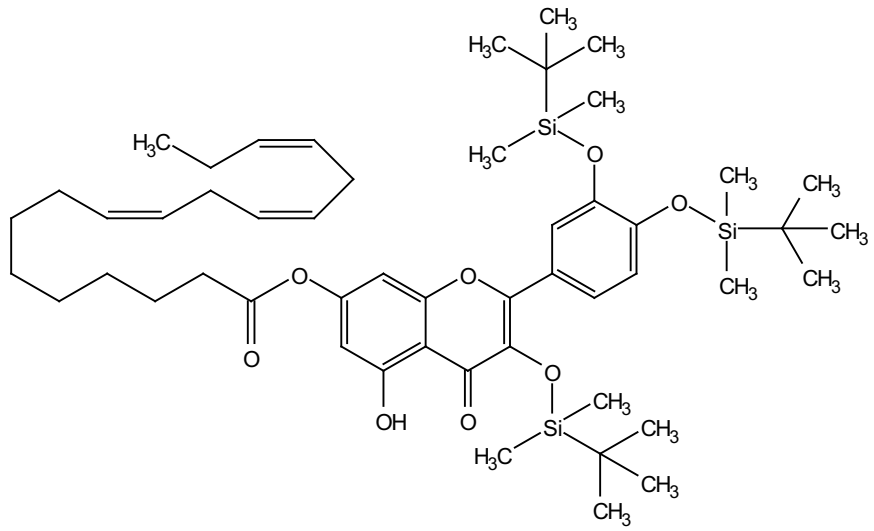
Compound **16** ^{13}C Jmod NMR spectra in $CDCl_3$





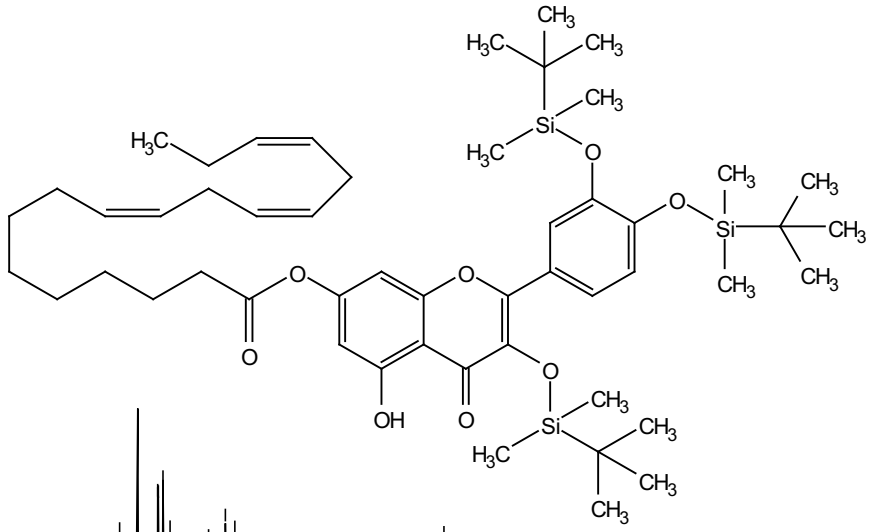


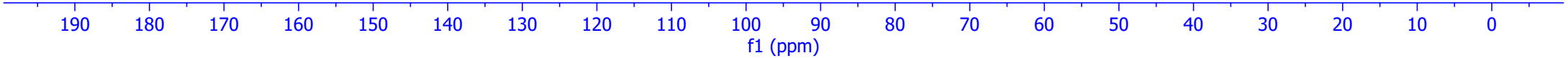
Compound **17** ^{1}H NMR spectra in $CDCl_3$



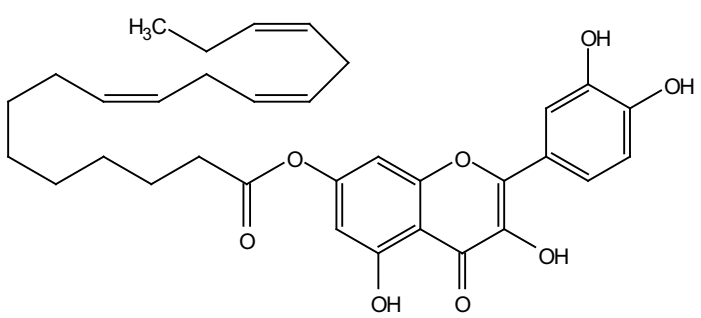
178.489
171.464
161.660
155.520
155.501
154.227
149.537
146.819
135.981
131.952
130.200
128.278
128.216
127.767
127.083
123.989
123.369
121.747
120.833
108.837
104.276
100.656
34.377
29.549
29.129
29.066
29.012
27.172
25.915
25.883
25.623
25.602
25.511
24.790
20.537
18.582
18.557
18.410
14.275
-4.059
-4.164
-4.175

Compound **17** ^{13}C Jmod NMR spectra in $CDCl_3$





Quer-7-ALA (compound **18**) ^{1}H NMR spectra in CD_3OD



177.632
172.839
161.969
157.200
156.761
149.321
149.214
146.264
138.035
132.712
131.049
129.196
129.180
128.898
128.229
123.715
122.015
116.258
116.232
108.500
104.828
101.870
35.017
30.658
30.231
30.160
30.090
28.138
26.523
26.402
25.799
21.485
14.671

Quer-7-ALA (compound **18**) ^{13}C Jmod NMR spectra in CD_3OD