Electronic Supplementary Material (ESI) for RSC Medicinal Chemistry.

Supplementary Material

An investigation of the antileishmanial properties of semi-synthetic saponins

Orlagh Anderson, Joseph Beckett, Carla C. Briggs, Liam A. Natrass, Charles F. Cranston, Elizabeth J. Wilkinson, Jack H. Owen, Rhodri Mir Williams, Angelos Loukaidis, Marc E. Bouillon, Deiniol Pritchard, Martina Lahmann, Mark S. Baird, Paul W. Denny

Experimental Section

Cell culture

Leishmania mexicana (MNYC/BZ/62/M379) were maintained at 26 °C in Schneider's Drosophila media (Sigma Aldrich) supplemented with heat inactivated foetal bovine sera (HIFBS; 15% for promastigotes, and 20% for amastigotes; Biosera). Promastigotes were transformed into axenic amastigotes by a pH and temperature shift as previously described.[1] *Mus musculus* leukaemia virus transformed macrophage (RAW267.4) cells (ATCC TIB-71) were cultured in Dulbecco's Modified Eagles Medium (DMEM; Fisher Scientific) supplemented with 10% HIFBS (Biosera). Cells were counted using a Neubauer Improved Haemocytometer.

Screening against axenic amastigote

For both primary and secondary dose response screens, analyses were performed in 96-well plates (Nunc) using alamarBlue® (Life Technologies) with some modifications to the published, optimized protocol[2]. Briefly, initial primary screening of the library (137 compounds) was carried at a single concentration (50 μM) in duplicate. Compounds were incubated with 100 μL axenic amastigote *L. mexicana* at $4x10^5$ mL^{-1} for 24 hours at 33 °C before the addition of alamarBlue® and incubation for a further for 24 hours at the same temperature, all in Parafilm (Fisher Scientific) sealed plates. Subsequently cell viability was assessed using a fluorescent plate reader (Biotek; 560EX nm/600EM nm), with amphotericin B as positive (50 μM) and DMSO as negative controls. Determination of the EC_{50} of the identified hits was then carried out using the same assay in duplicate, with three-fold compound dilutions for a concentration range 50 μM to 0.21 μM, on four separate occasions to ensure a robust data set was collected. Data were analysed using GraphPad Prism V7. Compounds demonstrating EC_{50} <10 μM were taken forward to toxicity screening using the murine macrophage line RAW267.4.

Cytotoxicity screening against RAW267.4 macrophages

For toxicity screening, plates were seeded with $2.5x10^5$ mL^{-1} RAW 267.4 cells in DMEM (10% HIFBS). Following 24 hours incubation at 37 °C, 5% CO_2, the cells were washed and the media replaced with reduced serum DMEM (2% HIFBS) and the plate incubated for further 24 hours as above. Following three washes with DMEM (2% HIFBS), compounds were added at the required concentration (100 μM to 0.41 μM) in the same media. After another 24 hours incubation at 37 °C, 5% CO_2, alamarBlue® was added to the plate and incubated for a further 4 hours. Subsequently, cell viability was assessed using a fluorescent plate reader (Biotek; 560EX nm/600EM nm), with cycloheximide as positive (50 μM) and DMSO as negative controls. Data were analysed using GraphPad Prism V7. The Selectivity Index (SI) was also calculated from these data (EC_{50} RAW267.4 / EC_{50} axenic amastigote *L. mexicana).*

Screening against infected macrophages

Efficacy against *L. mexicana* infected macrophages was tested as previously described[3-5]. The RAW264.7 cells were seeded in 96-well plates at $2.5x10^5$ mL^{-1} (200 μL/well) in DMEM (10% HIFBS) and incubated for 24 hours at 37 °C, 5% CO_2. Following washing with DMEM (2% HIFBS), *L. mexicana* axenic amastigotes were added at $25x10^5$ mL^{-1} (200 μL/well) in DMEM (2% HIFBS) and plate incubated for 24 hours at 37 °C, 5% CO_2. Subsequently, the infected RAW264.7 cells were washed carefully 5x with DMEM (2% HIFBS) before adding 100 μL/well of fresh DMEM (2% HIFBS) to each well. Isolated compounds and controls (10 μM amphotericin B and DMSO vehicle) were added at the required concentrations before a further incubation for 24 hours at 37 °C, 5% CO_2. Finally, the infected macrophages cells were washed 3x with Schneider's Insect medium (serum-free) and then lysed with 20 μL/well of SDS (0.05%, v/v in Schneider's) for 30 seconds before the addition of 180 μL/well of Schneider's Insect medium (pH7, 15% HIFBS). Plates were Parafilm sealed and incubated for 48 hours at 26 °C. Subsequently, alamarBlue® was added to each well before a 4 hour incubation at 26 °C prior to assessing parasite viability using a fluorescent plate reader (Biotek; 560EX nm / 600EM nm). All of the experiments described above were carried out on a three separate occasions in triplicate to ensure a robust data set was collected. Data were analysed using GraphPad Prism V7.

General Synthetic Methods

Chemicals used were obtained from commercial suppliers or prepared from them by methods described. Tetrahydrofuran (THF), dichloromethane (DCM) and diethyl ether (Et_2O) were dried with and stored over activated molecular sieves 4Å. Dimethylformamide (DMF) was purchased from Acros Organics as extra dry solvent in Acro-sealed® 1 L glass bottles. Diethyl ether for column chromatography was distilled under reduced pressure with a

rotary evaporator prior to usage. Petrol refers to petroleum spirit (PE, boiling point 40 – 60 ˚C). Reactions carried out under inert conditions, were carried out under a slow stream of nitrogen. Silica gel (Merck 7736) and silica plates used for column and thin layer chromatography were obtained from Aldrich. Ozone was generated with the ozone generator COM-AD-01 from Anseros Ltd. set to 4 g O_3 per hour at a flowrate of 100 litres per hour. Excess ozone passing the reaction vessel was destroyed with a sodium thiosulfate/potassium iodide solution. Organic solutions were dried over anhydrous magnesium sulfate. Infrared spectra were recorded with a Perkin Elmer Spectrum 100 FT-IR spectrometer as KBr disc (solid compounds) or thin films between NaCl plates (liquid compounds). ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER Ultrashield 400 Plus spectrometer ($CDCl_3$, C_6D_6, CD_3OD, or C_5D_5N) with tetramethylsilane as internal standard. NMR signal assignments are based on *H,H*-COSY, DEPTQ, HSQC and HMBC experiments. Optical rotations $[\alpha]_D$ were determined at a wavelength of 589.3 nm (sodium D line) using a 1 mL (0.25 dm) quartz cell with the Bellingham + Stanley ADP440 digital polarimeter at ambient temperature OR temperatures stated in degrees. High-resolution electrospray ionisation mass spectrometry (HR-ESI-MS) was performed with a Thermo Fisher Orbitrap Q Exactive Plus high-resolution mass spectrometer in positive ionisation mode. The analyses were done after upstream HPLC purification on a Thermo Scientific Vanquish UHPLC. The samples were dissolved in methanol or acetonitrile containing 0.1% formic acid. High-resolution mass spectroscopy was employed in lieu of elemental analysis, ^{1}H and ^{13}C NMR spectroscopy were used to determine the purity of synthesised compounds.

Some 137 compounds were analysed in the initial screen and their structures are provided in Supplementary **Table S1**.
Included below are the experimental details for the compounds taken to the final screen, except for **IVL16 - IVL18** and **IVL-75**, which will be described in full in a study of the isolation and synthesis of a wide class of anemoclemosides (Lahmann and Bouillon, unpublished results). Compound **IVL-1** was prepared as described earlier.[82] Full experimental details of all compounds not taken to the final screen are not included but can be obtained from the authors on request.

(((4a*R*,6a*R*,6b*S*,8a*S*,14b*R*)-2,2,4a,6a,6b,11,11,14b-Octamethyl-4a,5,6,6a,6b,7,8,9,10, 11,12,12a,14,14a,14b,15, 16,16a-octa-decahydro-4*H*-piceno[3,4-*d*][1,3]dioxin-8a(4b*H*)-yl)carbam-oyl)-L-proline (MC-033)

(i) To a stirred solution of 3,23-*O*-hederagenin acetonide (MC-014)[6] (0.50 g, 0.98 mmol) and diphenyl-diphosphorylazide (0.40g, 0.31mL, 1.47mmol) in anhydrous toluene (25 mL), triethylamine (0.17 g, 0.23 mL, 1.76 mmol) was added, and the mixture was then heated to 90°C under a nitrogen for 1h. The mixture was then adsorbed on silica and the material was applied directly to a silica column. Column chromatography (10:1 petrol: ethyl acetate; silica Et_3N neutralised) afforded (4a*R*,6a*R*,6b*S*,8a*S*,14b*R*)-8a-isocyanato-2,2,4a,6a,6b,11,11,14b-octamethyl4a,4b,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14,14a,14b,15, 16,16a-icosahydro-4*H*-piceno[3,4-*d*][1,3]dioxine (**MC-015**) as a white, crystalline solid (0.40 g; 80%): R_f(SiO_2; 6:1 petrol: ethyl acetate) = 0.49; $[\alpha]_D^{22.6}$: +63.5 (c 0.79, $CHCl_3$); IR (thin film from chloroform solution, cm^{-1}) 2936, 2862, 2246, 1462, 1380, 1364, 1256, 1207, 1194, 1164, 1109, 1065, 1042, 1026, 1007, 966, 954, 941, 862; ^{1}H NMR (400MHz, C_6D_6) δ_H: 5.21 (t, *J* = 3.6 Hz, 1H), 3.59 (d, *J* = 10.4 Hz, 1H), 3.43 (dd, *J* = 11.8, 3.8 Hz, 1H), 3.34 (d, *J* = 10.5 Hz, 1H), 2.40 – 2.30 (m, 1H), 2.00 (td, *J* = 13.4, 4.4 Hz, 1H), 1.89 – 1.59 (m, 5H), 1.59 – 0.97 (m, 13H), 1.54 (s, 3H), 1.34 (s, 3H), 1.19 (s, 3H), 1.08, (s, 3H), 1.03 (s, 3H), 0.92 (m, 1H), 0.87 – 0.76 (m, 1H), 0.85 (s, 3H), 0.80 (s, 3H), 0.79 (s, 3H), 0.74 – 0.68 (m, 1H); ^{13}C NMR (101MHz, C_6D_6) δ_C: 142.8, 124.5, 123.3, 99.0, 77.9, 72.8, 62.0, 52.0, 49.4, 48.1, 47.6, 41.8, 40.1, 39.2, 37.9, 37.5, 37.0, 35.7, 32.83, 32.75, 30.8, 30.4, 27.3, 27.1, 25.9, 24.1, 23.79, 23.74, 19.5, 17.9, 17.2, 16.7, 13.0; HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{33}H_{52}NO_3]^+$: 510.3947, Found: 510.3951.

(ii) A stirred mixture of isocyanate **MC-015** (0.031 g, 0.061mmol) and L-proline (0.035 g, 0.304 mmol) in absolute ethanol (1.3 mL) was heated briefly to reflux (1-2 mins) in order to effect the dissolution of the amino acid. The mixture was stirred vigorously for 19h at rt, then concentrated *in vacuo* and the residue was purified by column chromatography (10:1 chloroform: methanol) to afford the title urea derivative **MC-033** as a white, waxy solid (0.038 g; quant.): R_f(SiO_2; 10:1 chloroform: methanol) = 0.43; $[\alpha]_D^{22}$: -17.5 (c = 1.81, $CHCl_3$); IR (thin film from chloroform solution, cm^{-1}) 3435, 2946, 2872, 1743, 1644, 1524, 1463, 1380, 1363, 1341, 1257, 1207, 1195, 1166, 1110, 1066, 863; ^{1}H NMR (400MHz, C_5D_5N) δ_H: 5.41 – 5.31 (m, 1H), 5.01 – 4.71 (m, 2H), 3.72 – 3.59 (m, 3H), 3.59 – 3.42 (m, 2H), 2.74 – 2.62 (m, 1H), 2.61 – 2.47 (m, 2H), 2.29 – 1.60 (m, 12H), 1.59 – 0.82 (m, 11H), 1.53 (s, 3H), 1.48 (s, 3H), 1.20 (s, 3H), 1.19 (br. s, 6H), 0.96 (s, 3H), 0.94 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (101MHz, C_5D_5N) δ_C: 156.7, 144.7, 124.5, 99.5, 80.3, 78.1, 73.0, 60.4, 56.4, 51.9, 48.4, 47.7, 47.6, 46.8, 42.4, 40.6, 39.4, 37.9, 37.5, 36.2, 34.5, 33.5,

32.7, 31.4, 30.8, 30.6, 27.1, 26.6, 25.6, 24.6, 24.5, 24.3, 23.3, 20.1, 18.4, 17.6, 17.1, 13.4; HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{38}H_{61}N_2O_5]^+$: 625.4580, Found: 625.4583.

_N_-((4a_R_,6a_R_,6b_S_,8a_S_,14b_R_)-2,2,4a,6a,6b,11,11,14b-Octamethyl-4a,5,6,6a,6b,7,8,9,10,11,12,12a,14,14a,14b,15, 16,16a-octadeca-hydro-4_H_-piceno[3,4-_d_][1,3]dioxin-8a(4b_H_)-yl)pyrrolidine-1-carboxamide (MC-023)

A solution of isocyanate **MC-015** (0.045 g, 0.088mmol) and pyrrolidine (0.031g, 0.037mL, 0.44mmol) in anhydrous toluene (1.0mL) was stirred at room temperature for 18h. The reaction mixture was then concentrated *in vacuo* and the residue was purified by column chromatography (residue applied to silica in dichloromethane solution; 1:1 petrol: ethyl acetate → 10:1 chloroform: methanol) to afford the urea derivative **MC-023** as a white, resinous solid (0.045 g; 88%): Rf(SiO2; 1:1 petrol: ethyl acetate) = 0.44; $[\alpha]_D^{22.7}$+38.5 (c = 1.86, $CHCl_3$); IR (thin film from chloroform solution, cm^{-1}) 3436, 2946, 2870, 1642, 1511, 1486, 1461, 1378, 1363, 1339, 1289, 1256, 1195, 1166, 1110, 1065, 1043, 1027, 962, 941, 863, 821, 800; ^1H NMR (400MHz, C_6D_6) δ_H: 5.35 – 5.25 (m, 1H), 4.05 (s, 1H), 3.59 (d, *J* = 10.5 Hz, 1H), 3.44 (dd, *J* = 11.7, 3.8 Hz, 1H), 3.34 (d, *J* = 10.5 Hz, 1H), 3.29 – 3.11 (m, 4H), 2.91 (dt, *J* = 13.9, 3.4 Hz, 1H), 2.70-2.57 (m, 1H), 2.48 – 2.34 (m, 1H), 2.09 – 1.75 (m, 6H), 1.75 – 1.52 (m, 2H), 1.57 (s, 3H), 1.51 – 1.13 (m, 12H), 1.35 (s, 3H), 1.21 (s, 3H), 1.17 (s, 3H), 1.04 (s, 3H), 1.03-0.81 (m, 3H), 0.95 (s, 3H), 0.91 (s, 3H), 0.86 (s, 3H), 0.71 (dd, *J* = 11.6, 2.1 Hz, 1H); ^{13}C NMR (101MHz, C_6D_6) δ_C: 155.6, 144.5, 124.0, 99.0, 77.9, 72.7, 55.6, 51.9, 48.1, 47.9, 47.4, 45.8, 42.0, 40.1, 39.0, 37.4, 37.1, 35.8, 34.1, 33.2, 32.2, 31.0, 30.4, 26.7 26.0, 25.8, 24.2, 24.1, 23.8, 22.9, 19.5, 17.9, 17.1, 16.6, 13.0; HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{37}H_{61}N_2O_3]^+$: 581.4682, Found: 581.4679.

((3_S_,4_R_,6a_R_,6b_S_,8a_S_,14b_R_)-3-hydroxy-4,6a,6b,11,11,14b-hexa-methyl-8a-(pyrrolidine-1-carboxamido)-1,2,3,4,4a,5,6,6a,6b,7,8, 8a,9,10,11,12,12a,14,14a,14b-icosahydropicen-4-yl)methyl acetate (MC-057)

To a vigorously stirred solution of **MC-023** in dichloromethane (1.0 mL), water (0.05 mL) was added followed by HCl/Et_2O solution (2M solution; 0.05 mL). The mixture was stirred vigorously at room temperature for a period of 45 mins. Hydrochloric acid (2M aq. soln.; 5 drops) was now administered, and the reaction mixture was stirred vigorously for a further period of 1h at room temperature. The mixture was then concentrated *in vacuo* and the residue was purified by column chromatography (20:1 chloroform: methanol) to afford the intermediate urea **MC-055** as a white solid (0.046g; quant.): Rf(SiO_2; 10:1 chloroform: methanol) = 0.4; $[\alpha]_D^{22}$: +56.3 (c = 0.08, $CHCl_3$); IR (thin film from chloroform solution, cm^{-1}) 3433, 2947, 2928, 2870, 1635, 1516, 1486, 1462, 1433, 1385, 1362, 1341, 1195, 1087, 1049, 1012; ^1H NMR (400MHz, $CDCl_3$) δ_H: 5.30 (t, *J* = 2.3 Hz, 1H), 4.33 (s, 1H), 3.72 (d, *J* = 10.2 Hz, 1H), 3.67 – 3.60 (m, 1H), 3.42 (d, *J* = 10.2 Hz, 1H), 3.33 – 3.21 (m, 4H), 2.67 (br. s, 2H), 2.38 (dt, *J* = 13.7, 3.5 Hz, 1H), 2.23 – 2.10 (m, 2H), 1.96 – 1.82 (m, 7H), 1.81 – 1.54 (m, 7H), 1.52 – 1.10 (m, 7H), 1.13 (s, 3H), 1.05 – 0.74 (m, 3H), 0.96 (s, 3H), 0.94 (s, 3H), 0.90 (s, 3H), 0.89 (br. s, 6H); ^{13}C NMR (101MHz, $CDCl_3$) δ_C: 155.5, 143.5, 124.2, 77.0, 72.4, 56.3, 50.0, 47.7, 47.4, 46.9, 46.5, 41.9, 41.8, 39.7, 38.3, 37.0, 35.4, 33.4, 33.0, 32.2, 30.9, 26.7, 26.3, 25.9, 25.7, 24.1, 23.7, 22.6, 18.6, 17.1, 15.8, 11.6; HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{34}H_{57}N_2O_3]^+$: 541.4369, Found: 541.4374. To a stirred solution of intermediate **MC-055** (0.03 g, 0.06 mmol), Et_3N (0.007g, 0.009mL, 0.06mmol) and DMAP (0.0007g, 0.006mmol) in dry dichloromethane (1.2 mL), cooled to about +5 °C, a solution of acetyl chloride (0.0048 g, 0.0043 mL, 0.06 mmol) in dry dichloromethane (0.2 mL) was added dropwise over 2-3 min. The reaction mixture was then stirred at circa +5 °C for a period of 0.75 h. The mixture was concentrated *in vacuo,* and the residue was purified by column chromatography (1:1 → 2:3 petrol: ethyl acetate; silica Et_3N neutralised) to afford the urea **MC-057** as a white solid (0.018 g; 56%): Rf(SiO_2; 1:1 petrol: ethyl acetate) = 0.23; $[\alpha]_D^{22.6}$: +40.4 (c = 0.24, $CHCl_3$); IR (thin film from chloroform solution, cm^{-1}) 3435, 2949, 2909, 2873, 1743, 1726, 1636, 1516, 1485, 1461, 1383, 1364, 1341, 1285, 1241, 1196, 1036; ^1H NMR (400MHz, $CDCl_3$) δ_H: 5.30 (t, *J* = 2.3 Hz, 1H), 4.33 (s, 1H), 3.72 (d, *J* = 10.2 Hz, 1H), 3.67 – 3.60 (m, 1H), 3.42 (d, *J* = 10.2 Hz, 1H), 3.33 – 3.21 (m, 4H), 2.67 (br. s, 2H), 2.38 (dt, *J* = 13.7, 3.5 Hz, 1H), 2.23 – 2.10 (m, 2H), 1.96 – 1.82 (m, 7H), 1.81 – 1.54 (m, 7H), 1.52 – 1.10 (m, 7H), 1.13 (s, 3H), 1.05 – 0.74 (m, 3H), 0.96 (s, 3H), 0.94 (s, 3H), 0.90 (s, 3H), 0.89 (br. s, 6H); ^{13}C NMR (101MHz, $CDCl_3$) δ_C: 155.5, 143.5, 124.2, 77.0, 72.4, 56.3, 50.0, 47.7, 47.4, 46.9, 46.5, 41.9, 41.8, 39.7, 38.3, 37.0, 35.4, 33.4, 33.0, 32.2, 30.9, 26.7, 26.3, 25.9, 25.7, 24.1, 23.7, 22.6, 18.6, 17.1, 15.8, 11.6; HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{36}H_{59}N_2O_4]^+$: 583.4475, Found: 583.4471.

2-((2_R_,4a_R_,6a_R_,6b_S_,8a_S_,14b_R_,16a_S_)-8a-(Methoxycarbonyl)-4a, 6a,6b,11,11,14b-hexamethyl-4a,4b,5,6,6a,6b,7,8, 8a,9,10,11, 12,12a,14,14a,14b,15,16,16a-eicosahydro-4_H_-piceno[3,4-_d_][1,3]dioxin-2-yl)benzoic acid (MC-071)

(i) To a stirred solution of methyl-2-formylbenzoate (0.015 g, 0.09 mmol) in dry dichloromethane (0.35 mL), methyl hederagenate[7] was added in one portion followed by *p*-toluenesulfonic acid monohydrate (0.0016 g, 0.008 mmol), and the mixture was then stirred at rt for 1 h. Triethylamine (1-2 drops) was added and the mixture was then concentrated *in vacuo.* Column chromatography of the residue (10:1 petrol: ethyl acetate) afforded methyl (2*R*,4a*R*,6a*R*,6b*S*,8a*S*,14b*R*, 16a*S*)-2-(2-(methoxycarb-onyl)-phenyl)-4a,6a,6b,11,11,14b-hexamethyl-4a,5,6,6a,6b, 7,8,9,10,11,12,12a,14,14a,14b,15, 16,16a-octadecahydro-4*H*-piceno[3,4-*d*][1,3]dioxine-8a(4b*H*)-carboxylate (**MC-070**) as a white solid (0.055 g; quant.): Rf(SiO_2; 10:1 petrol: ethyl acetate) = 0.19; $[\alpha]_D^{22.9}$: +50.8 (c = 0.52, $CHCl_3$); IR (thin film from chloroform solution, cm^{-1}) 2947, 2878, 1727, 1460, 1433, 1376, 1262, 1206, 1191, 1153, 1115, 1069,

1032, 1017, 967; ^{1}H NMR (400MHz, C_6D_6) δ_H: 8.20 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.80 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.20 (td, *J* = 7.7, 1.4 Hz, 1H), 7.00 (td, *J* = 7.6, 1.3 Hz, 1H), 6.71 (s, 1H), 5.41 (t, *J* = 3.7 Hz, 1H), 3.87 (d, *J* = 10.2 Hz, 1H), 3.53 (s, 3H), 3.45 (s, 3H), 3.42 – 3.34 (m, 2H), 3.17 (dd, *J* = 13.9, 4.6 Hz, 1H), 2.05 – 1.93 (m, 1H), 1.92 – 1.50 (m, 10H), 1.41 – 1.26 (m, 4H), 1.26 – 1.04 (m, 6H), 1.23 (s, 3H), 1.02 – 0.88 (m, 1H), 0.96 (s, 3H), 0.92 (s, 3H), 0.85 (s, 3H), 0.83 (s, 3H), 0.82 – 0.72 (m, 1H), 0.67 – 0.60 (m, 1H); ^{13}C NMR (101MHz, C_6D_6) δ_C: 177.6, 167.8, 144.1, 140.2, 131.7, 130.2, 129.9, 128.4, 127.4, 122.9, 99.4, 86.1, 79.0, 51.7, 51.5, 51.3, 48.0, 47.0, 46.4, 42.0, 41.9, 39.9, 38.9, 37.4, 36.9, 34.2, 33.3, 32.9, 32.6, 30.9, 28.2, 26.3, 23.9, 23.8, 23.7, 23.5, 18.0, 17.2, 16.6, 13.9; HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{40}H_{57}O_6]^+$: 633.4155, Found: 633.4156.

(ii) To a stirred solution of **MC-070** (0.0275 g, 0.043mmol) in THF(0.4mL), methanol (0.1mL) and water (0.1mL) were added, and to the vigorously stirred mixture, $LiOH.H_2O$ (0.0029 g, 0.069 mmol) was added in one portion. The mixture was then heated to 62-65°C for a period of 1h, whereupon a further quantity of $LiOH.H_2O$ (0.0029 g, 0.069mmol) was added. The mixture was stirred for a further 1 h at 65 °C, then allowed to cool to rt, before being diluted with water (2 mL) and diethyl ether (5 mL). To the vigorously stirred mixture, glacial acetic acid (0.008 mL) was added and the mixture was stirred for a further 10 mins. The aq. phase was extracted with ethyl acetate (3 x 5 mL). The filtrate was concentrated *in vacuo* to afford a white solid **MC-071** (0.023 g; 86%), which was pure by TLC and NMR analysis and did not need for further purification: Rf(SiO_2; 10:1 chloroform: methanol) = 0.44; $[\alpha]_D^{22.1}$: +51.9 (c = 0.94, $CHCl_3$); IR (thin film from chloroform solution, cm^{-1}) 3662, 2946, 1724, 1604, 1584, 1460, 1433, 1387, 1303, 1263, 1234, 1207, 1153, 1114, 1069, 1032, 1014, 966; ^{1}H NMR (400MHz, C_6D_6) δ_H: 10.63 (br. s, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.25 – 7.17 (m, 1H), 7.07 – 6.97 (m, 1H), 6.62 (s, 1H), 5.44 – 5.36 (m, 1H), 3.85 (d, *J* = 10.2 Hz, 1H), 3.44 (s, 3H), 3.33 (d, *J* = 10.9 Hz, 2H), 3.15 (d, *J* = 13.0 Hz, 1H), 2.07 – 1.48 (m, 11H), 1.43 – 1.03 (m, 8H), 1.26 (s, 3H), 1.21 (s, 3H), 1.01 – 0.68 (m, 2H), 0.96 (s, 3H), 0.94 (s, 3H), 0.83 (br. s, 6H), 0.65 – 0.55 (m, 1H); ^{13}C NMR (101MHz, C_6D_6) δ_C: 177.7, 144.1, 140.3, 132.4, 130.9, 128.6, 127.6, 122.9, 99.3, 86.0, 78.9, 51.4, 47.9, 47.0, 46.4, 42.0, 41.9, 39.9, 38.8, 37.4, 36.9, 34.2, 33.4, 32.9, 32.6, 30.9, 28.2, 26.4, 23.8, 23.7, 23.65, 23.56, 17.9, 17.1, 16.6, 13.9; HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{39}H_{55}O_6]^+$: 619.3999, Found: 619.3994.

Gypsogenin (IVL-9)

Benzyl 3-*O*-acetyl-23-*O*-*tert*-butyldiphenylsilylhederagenate (6.746 g, 8.0 mmol, 1.0 equiv.) was dissolved in a mixture of acetic acid (5.033 mL, 88.0 mmol, 10.0 equiv.) and tetrabutylammonium fluoride solution (1 M in THF, 80 mL, 80 mmol, 10.0 equiv.) at rt. The mixture was stirred at 50 °C under an atmosphere of N_2. After 5 hours, additional acetic acid (5.033 mL, 88.0 mmol, 10.0 equiv.) and tetrabutylammonium fluoride solution (1 M in THF, 80 mL, 80 mmol, 10.0 equiv.) were added, and stirring was continued overnight at 50 °C under N_2. After 24 hours, TLC (EtOAc/PE, 25/75) indicated incomplete conversion and solid TBAF trihydrate (12.6 g, 40 mmol, 5 equiv.) was added. The mixture was stirred under reflux at 100 °C for a further 24 hours. After 48 h, the reaction was stopped, although TLC still showed the presence of starting material. The mixture was diluted with EtOAc (400 mL) and washed with water (160 mL), sat. $NaHCO_3$ solution (160 mL) and phosphate buffer pH 7 (160 mL). The organic phase was concentrated under reduced pressure yielding a pale-yellow syrup. The residue was dissolved in DCM (8 ml), adsorbed on silica (16 g) and purified by column chromatography (∅ = 6 cm, h_C = 14 cm, V_{Fr} = 200 mL, EtOAc/PE, 5/95 to 25/75). After chromatography, benzyl 3-*O*-acetyl hederagenate was obtained (1.30 g, 2.14 mmol, 27%). In addition benzyl 23-*O*-acetyl hederagenate (2.06 g, 3.40 mmol, 43%) was isolated due to acetyl migration. To a solution of benzyl 3-*O*-acetyl hederagenate[8] (1210 mg, 1.0 mmol, 1.0 equiv.) in dry DCM (10 mL), TEMPO (32 mg, 0.2 mmol, 0.1 equiv.) and BAIB (805 mg, 2.5 mmol, 1.25 equiv.) were added at 0 °C. The mixture was stirred under an atmosphere of N_2 at 0 °C for 5 min and then at rt until TLC (EtOAc/PE, 25/75) control indicated full conversion of the starting material. After 24 hrs, the mixture was quenched by the addition of 2 M $Na_2S_2O_3$ solution (10 mL) and diluted with Et_2O (50 mL). The phases were separated, and the organic phase was washed with sat. $NaHCO_3$ solution (10 mL) and 1 M phosphate buffer pH 7 (10 mL), concentrated under reduced pressure to yield the crude product as pale-amber solid. The crude product was dissolved in DCM (2 mL), adsorbed on silica (4 g). Chromatography (∅ = 3 cm, h_C = 12 cm dry, V_{Fr} = 42 mL, Et_2O/PE, 10/90 to 15/85) provided benzyl 3-*O*-acetyl gypsogenate (**7**), the protected gypsogenin (813 mg, 1.35 mmol, 67%). Benzyl 3-*O*-acetyl gypsogenate (**9**, 700 mg, 1.16 mmol) was dissolved in a mixture of DME/THF/H_2O (1:1:1). NaOH (aqueous) was added and the reaction stirred at rt overnight. After chromatography the 3-OH gypsogenate was isolated (324 mg, 0.578 mmol, 83%); $Pd(OH)_2$/C (50 mg) was added to a solution of this (300 mg, 0.535 mmol) in MeOH/EtOAc, placed under a H_2 atmosphere and stirred overnight at room temperature. After 24 hours the catalyst was removed by filtration through a pad of Supercel®, and the filter cake was washed with MeOH. The solvents were removed under reduced pressure to yield the crude saponin. After chromatography, gypsogenin (**IVL-9**, 238 mg, 0.508 mmol, 80%) were obtained. The analytical data was in agreement with the data obtained from the natural product.[9] ^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm]: 0.74 (s, 3H, H_3-26), 0.91 (s, 3H, H_3-29), 0.93 (s, 3H, H_3-30), 0.96 (s, 3H, H_3-25), 1.00 (m, 1H, H_A-6), 1.05 (m, 2H, H_A-1, H_A-15), 1.06 (s, 3H, H_3-24), 1.15 (s, 3H, H_3-27), 1.15 (m, 1H, H_A-19), 1.21 (m, 1H, H_A-21), 1.24 (m, 1H, H_A-7), 1.28 (m, 1H, H-5), 1.34 (dt, J_1 = 3.4 Hz, J_2 = 13.6 Hz, 1H, H_B-21), 1.47 (m, 1H, H_B-7), 1.49 (m, 1H, H_B-6), 1.56 (m, 1H, H_A-22), 1.61 (m, 1H, H_A-

16), 1.62 (m, 1H, H_B-19), 1.63 (m, 1H, H_A-2), 1.64 (m, 1H, H-9), 1.68 (m, 1H, H_B-1), 1.69 (m, 1H, H_B-15), 1.71 (m, 1H, H_B-2), 1.76 (dt, J_1 = 4.2 Hz, J_2 = 13.7 Hz, 1H, H_B-22), 1.90 (m, 2H, H_2-11), 1.97 (dt, J_1 = 3.6 Hz, J_2 = 13.2 Hz, 1H, H_B-16), 2.82 (dd, J_1 = 3.4 Hz, J_2 = 13.4 Hz, 1H, H-18), 3.78 (dd, J_1 = 4.4 Hz, J_2 = 11.0 Hz, 1H, H-3), 5.28 (t, J = 3.1 Hz, 1H, H-12), 9.40 (s, 1H, H-23). ^{13}C NMR (100 MHz, $CDCl_3$) δ [ppm]: 8.9 (CH_3, C-24), 15.6 (CH_3, C-25), 17.1 (CH_3, C-26), 20.7 (CH_2, C-6), 22.8 (CH_2, C-16), 23.3 (CH_2, C-11), 23.6 (CH_3, C-30), 26.0 (CH_3, C-27), 26.1 (CH_2, C-2), 27.6 (CH_2, C-15), 30.7 (C_q, C-20), 32.0 (CH_2, C-7), 32.4 (CH_2, C-22), 33.1 (CH_3, C-29), 33.8 (CH_2, C-21), 36.0 (C_q, C-10), 38.0 (CH_2, C-1), 39.6 (C_q, C-8), 41.0 (CH, C-18), 41.6 (C_q, C-14), 45.8 (CH_2, C-19), 46.5 (C_q, C-17), 47.5 (CH, C-9), 48.2 (CH, C-5), 55.2 (C_q, C-4), 71.9 (CH, C-3), 122.2 (CH, C-12), 143.6 (C_q, C-13), 184.2 (CO, C-28), 207.1 (CHO, C-23).

Hederagenin 2-(1'-deoxy-L-fucofuranos-1'-yl)acetacetal (IVL-104)

Ozone was bubbled through a solution of 1-C-allyl-2,3,5-tribenzyl-L-fucofuranoside (**5**)[81] (928 mg, 2.0 mmol, 1 equiv.) in DCM (20 mL) at -75℃ until a pale bule colour appeared (9 min). Excess ozone was purged with O_2 until the blue colour disappeared. Triphenyl phosphine (630 mg, 2.4 mmol, 1.2 equiv.) was added in one portion and stirred overnight and allowed to warm up to room temperature. The solvent was evaporated under reduced pressure giving a yellow oil. The oil was diluted with DCM (1 mL), adsorbed on silica (2 g) and purified by chromatography (hexane/EtOAc, 9:1 to 8:2) to yield a colourless syrup of 2-(1'-deoxy-2',3',5'-tri-*O*-benzyl-L-fucofuranos-1'-yl)acetalaldehyde (**6**) (932 mg, 2.02 mmol, 75%) as an inseparable pseudo anomeric mixture; IR(neat) $\tilde{\nu}$ [cm^{-1}]: 2869 (s), 1724 (vs).

To a solution of **6** (830 mg, 1.8 mmol, 1 equiv.) in dry DCM (18 mL), benzyl hederagenate (1520 mg, 2.7 mmol, 1.5 equiv.) and PTSA (70 mg, 0.36 mmol, 0.2 equiv.) was added in one portion. The mixture was stirred under a nitrogen atmosphere for 17 hrs. The solvent was evaporated under reduced pressure and the syrupy residue was purified by column chromatography (hexane/ethyl acetate, 9:1 to 8:2) yielding the inseparable pseudo anomeric mixture of benzyl hederagenate 2-(1'-deoxy-2',3',5'-tri-*O*-benzyl-L-fucofuran-os-1'-yl)acetoacetate as white foam-like solid (1.721 g, 1.71 mmol) in 95% yield; IR(neat) $\tilde{\nu}$ [cm^{-1}]: 3031(s), 2942(vs), 2863(vs), 1725(vs). Pearlman's catalyst (20%$Pd(OH)_2$/C, 170 mg) was added to a solution of benzyl hederagenate 2-(1'-deoxy-2',3',5'-tri-O-benzyl-L-fucofuranos-1'-yl)acetacetal (1.721g, 1.71 mmol) in MTBE/MeOH (1:1, 20 mL). The reaction mixture was placed under a H_2 atmosphere and stirred overnight at room temperature. After 24 hours the catalyst was removed by filtration through a pad of Supercel®, and the filter cake was washed with MeOH. The solvents were removed under reduced pressure to yield the crude saponin as a white foamy solid. The solid was dissolved in MeOH (3.4 mL), adsorbed on silica (6.8 g) and subjected to column chromatography (∅ = 4 cm, h_c = 16 cm, V_{Fr} = 100 ml, TCM/MeOH/H_2O (95:5:0.5 to 92.5:7.5:0.75 to 90:10:1) to yield hederagenin 2-(1'-deoxy-L-fucofuranos-1'-yl)acetacetal (**IVL-104**) (884 mg, 1.37 mmol, 80%) as a 1:1 mixture of pseudo anomers a white solid; ^{1}H NMR (400 MHz, C_5D_5N, TMS) δ [ppm]: 5.49 ("s", 1H, H-12), 5.24 – 5.16 (m, 2H, H-1"α, H-1"β), 4.92 (m, 1H, H-1'β), 4.85 (t, J = 5.4 Hz, 1H, H-3'α), 4.78 (s, 1H, H-3'β), 4.72 (dd, J = 12.9, 5.8 Hz, 1H, H-1'α), 4.57 (t, J = 5.7 Hz, 1H, H-2'α), 4.52 (d, J = 2.3 Hz, 1H, H-2'β), 4.41 – 4.33 (m, 2H, H-5'α, H-5'β), 4.32 (q, J = 5.5 Hz, 1H, H-4'α), 4.24 (dd, J = 3.4, 2.7 Hz, 1H, H-4'β), 3.88 (d, J = 10.3 Hz, 1H, H_B-23β), 3.83 (d, J = 10.3 Hz, 1H, H_B-23α), 3.35 – 3.14 (m, 5H, H-18, H_A-23α, H_A-23β, H-3α, H-3β), 2.66 (ddd, J = 11.8, 8.0, 3.8 Hz, 1H, H_B-2"β), 2.59 (dd, J = 13.2, 7.1 Hz, 1H, H_A-2"β), 2.56 – 2.45 (m, 2H, H_2-2"α), 2.17 – 2.08 (m, 2H, H_B-15, H_B-16), 2.05 (td, J = 13.9, 3.8 Hz, 1H, H_B-22), 1.97 (m, 1H, H_A-16), 1.90 (dd, J = 8.3, 2.7 Hz, 2H, H_2-11), 1.83 (m, 1H, H_A-22), 1.82 (m, 1H, H_B-19), 1.75 – 1.62 (m, 2H, H_B-2, H-9), 1.59 (d, J = 5.2 Hz, 3H, H_3-6'α), 1.58 (d, J = 6.1 Hz, 3H, H_3-6'β), 1.50 (m, 1H, H_A-2), 1.48 (m, 1H, H_B-1), 1.46 (m, 1H, H_B-21), 1.40 (m, 1H, H_B-7), 1.32 (m, 1H, H_A-19), 1.29, 1.28 (2s, 3H, H_3-27), 1.26, (m, 1H, H_B-6), 1.26 – 1.15 (m, 2H, H_A-7, H_A-21), 1.16 (m, 1H, H_A-15), 1.15, 1.14 (2s, 3H, H_3-24), 1.06 (m, 1H, H_A-6), 1.03 (s, 3H, H_3-30), 0.98 (s, 3H, H_3-26), 0.97 (s, 3H, H_3-29), 0.95 (m, 1H, H_A-1), 0.84 (s, 3H, H_3-25), 0.76 (t, J = 11.6 Hz, 1H, H-5). ^{13}C NMR (100 MHz, C_5D_5N, TMS) δ [ppm]: 180.0 (CO, C-28), 144.8 (C_q, C-13), 122.3 (CH, C-12), 101.6 (CH, C-1"β), 101.1 (CH, C-1"α), 90.7 (CH, C-4'β), 88.2 (CH, C-4'α), 85.5 (CH, C-3β), 85.3 (CH, C-3α), 82.9 (CH, C-2'α), 80.9 (CH, C-3'β), 80.1 (CH, C-1'α), 79.6 (CH, C-3'α), 79.3 (CH, C-2'β), 78.23 (CH, C-1'β), 78.18 (CH_2, C-23α), 78.14 (CH_2, C-23β), 68.3 (CH, C-5'), 51.59, 51.55 (CH, C-5), 47.99, 47.96 (CH, C-9), 46.61 (C_q, C-17), 46.5 (CH_2, C-19), 42.2 (C_q, C-14), 42.0 (CH, C-18), 40.5 (CH_2, C-2"α), 39.8 (C_q, C-8), 38.92, 38.90 (CH_2, C-1), 37.39, 37.37 (C_q, C-10), 36.83, 36.78 (C_q, C-4), 35.6 (CH_2, C-2"β), 34.2 (CH_2, C-21), 33.3 (CH_3, C-29), 33.2 (CH_2, C-22), 32.7 (CH_2, C-7), 31.0 (C_q, C-20), 28.3 (CH_2, C-15), 26.1 (CH_3, C-27), 23.8 (1 × CH_2 & 1 × CH_3, C-2 & C-30), 23.7, 23.6 (2 × CH_2, C-11 & C-16), 20.6 (CH_3, C-6'β), 20.3 (CH_3, C-6'α), 17.9 (CH_2, C-6), 17.3 (CH_3, C-26), 16.47, 16.44 (CH_3, C-25), 13.75, 13.73 (CH_3, C-24). HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{38}H_{61}O_8]^+$: 645.4361, Found: 645.4359.

Hederagenin (1'-*O*-methyl-5'-dehydro-α-D-xylos-5'-yl) formacetal (IVL-106)

To a solution of methyl 2,3,4-tri-*O*-benzyl-α-D-gluco-hexodialdo-1,5-pyranoside[10] (**3**, 3.85 g, 8.33 mmol, 1.0 equiv.) in dry DCM (83 mL), benzyl hederagenate (7.04 g, 12.5 mmol, 1.5 equiv.) and pTSA (0.32 g, 1.67 mmol, 0.2 equiv.) were added. The reaction mixture was stirred at room temperature under a nitrogen atmosphere for 36 hours. The solvent was consequently evaporated under reduced pressure and the syrupy residue was purified by column chromatography (EtOAc/hexane, gradient 10:90 to 50:50) to afford benzyl hederagenate (1'-O-methyl-2',3',4'-tri-

O-benzyl-5'-dehydro-α-D-xylos-5'-yl) formacetal (**4**, 6.56 g, 6.51 mmol, 78%) as a foamy white solid. 1H NMR (400 MHz, C6D6) δ (ppm) = 7.38 - 7.03 (m, 20H, HAr), 5.42 (t, 3J(H,H) = , 1H, H12), 5.12 - 4.78 (m, 12H, PhCH2), 4.44 (q, 3J(H,H) = 33.4 Hz, 1H, H3', H4'), 4.34 (t, 3J(H,H) = , 1H, H1''), 4.18 - 4.05 (m, 2H, H23α, H23β), 3.60 (dd, 3J(H,H) = 9.5 Hz, 1H, H2') 3.31 (s, 3H, H5*α, H5*β, H5*γ), 3.03 (d, 3J(H,H) = 10.2 Hz, 1H, H1'), 2.98 (m, 1H, H3), 2.00 - 0.53 (m, 21H, H2α, H2β, H5, H6α, H6β, H7α, H7β, H9, H11α, H11β, H15α, H15β, H16α, H16β, H18, H19α, H19β, H21α, H21β, H22α, H22β), 1.28 (s, 3H, H24α, H24β, H24γ), 1.18 (s, 3H, H27α, H27β, H27γ), 0.93 (s, 3H, H29α, H29β, H29γ), 0.89 (s, 3H, H30α, H30β, H30γ), 0.77 (s, 3H, H25α, H25β, H25γ), 0.73, (s, 3H, H26α, H26β, H26γ); 13C NMR (101 MHz, CDCl3) δ (ppm): 177.4 (C=O), 143.7 (C13), 138.9 (C-C, Ph-C), 138.5 (C-C, Ph-C), 138.3 (C-C, Ph-C), 136.4 (C-C, Ph-C), 128.4 (C-H, Ph-H), 128.1 (C-H, Ph-H), 128.0 (C-H, Ph-H), 127.9 (C-H, Ph-H), 127.93 (C-H, Ph-H), 127.8 (C-H, Ph-H), 127.6 (C-H, Ph-H), 127.5 (C-H, Ph-H), 122.3 (C12), 100.0 (C1''), 97.9 (C3), 86.3 (C5'), 82.7 (C3'), 79.4 (C4'), 78.8 (C2'), 77.4 (C1'), 77.3 (C4*), 77.0 (C3*), 76.7 (C2*), 73.2 (C23), 65.9 (C28'), 55.0 (C5*), 51.5 (C18), 47.6 (C5, C9), 45.9 (C4), 41.7 (C14), 39.4 (C1), 38.8 (C17), 37.2 (C19), 36.8 (C8), 33.8 (C10), 33.1 (C20), 32.3 (C21), 32.2 (C7), 30.7 (C22), 27.6 (C15), 25.9 (C29, C30), 23.6 (C27), 23.33 (C2), 23.2 (C16), 23.0 (C11), 17.7 (C6), 16.8 (C26), 16.4 (C25), 13.3 (C24). To a solution of the above acetal (**4**, 1914 mg, 1.9 mmol) in MTBE/MeOH (1:1) (10 mL), Pearlman catalyst (20% $Pd(OH)_2$/C, 190 mg) was added. The reaction mixture was set under hydrogen atmosphere and stirred at room temperature overnight. After 24 hrs, the catalyst was removed by filtration over a pad of Supercel®, and the remaining filter cake was washed thoroughly with hot MeOH. Removal of the solvents under reduced pressure yielded the crude product as an off-white foamy solid. Purification by column chromatography ($CHCl_3$/MeOH/H_2O, 95:5:0.5), yielded the title compound **IVL-106** (1311 mg, 1.75 mmol, 92%) as a white foamy solid. ^{1}H NMR (500 MHz, C_5D_5N, TMS) δ [ppm]: 5.53 (d, *J* = 1.3 Hz, 1H, H-1''), 5.48 (t, *J* = 3.4 Hz, 1H, H-12), 5.23 (d, *J* = 3.6 Hz, 1H, H-1'), 4.58 (t, *J* = 9.1 Hz, 1H, H-3'), 4.45 (dd, *J* = 9.9, 8.8 Hz, 1H, H-4'), 4.30 (dd, *J* = 10.0, 1.2 Hz, 1H, H-5'), 4.14 (dd, *J* = 9.5, 3.7 Hz, 1H, H-2'), 4.01 (d, *J* = 10.3 Hz, 1H, H_B-23), 3.51 (s, 3H, H_3-1'*), 3.40 (d, *J* = 10.3 Hz, 1H, H_A-23), 3.35 (dd, *J* = 12.2, 3.5 Hz, 1H, H-3), 3.32 (dd, *J* = 12.4, 4.1 Hz, 1H, H-18), 2.14 (m, 1H, H_B-15), 2.05 (td, *J* = 13.9, 4.2 Hz, 1H, H_B-22), 2.11 (m, 1H, H_B-16), 1.96 (m, 1H, H_A-16), 1.88 (dd, *J* = 8.8, 3.3 Hz, 2H, H_2-11), 1.83 (m, 1H, H_A-22), 1.82 (m, 1H, H_B-19), 1.71 (m, 1H, H_B-2), 1.68 (t, *J* = 8.9 Hz, 1H, H-9), 1.50 (m, 1H, H_A-2), 1.46 (m, 1H, H_B-21), 1.45 (m, 1H, H_B-1), 1.39 (td, *J* = 12.5, 3.7 Hz, 1H, H_B-7), 1.32 (m, 1H, H_A-19), 1.28 (s, 3H, H_3-27), 1.27 (s, 3H, H_3-24), 1.26 (m, 1H, H_B-6), 1.22 (m, 1H, H_A-21), 1.20 (m, 1H, H_A-7), 1.17 (m, 1H, H_A-15), 1.08 ("d", *J* = 13.4 Hz, 1H, H_A-6), 1.03 (s, 3H, H_3-30), 0.98 (s, 3H, H_3-29), 0.97 (s, 3H, H_3-26), 0.96 (m, 1H, H_A-1), 0.80 (s, 3H, H_3-25), 0.79 (d, *J* = 13.7 Hz, 1H, H-5); ^{13}C NMR (100 MHz, C_5D_5N, TMS) δ [ppm]: 180.0 (CO, C-28), 144.7 (C_q, C-13), 122.3 (CH, C-12), 101.5 (CH, C-1'), 101.4 (CH, C-1''), 86.0 (CH, C-3), 78.6 (CH_2, C-23), 75.3 (CH, C-3'), 73.4 (CH, C-2'), 72.7 (CH, C-5'), 71.4 (CH, C-4'), 55.1 (CH_3, C-1'*), 51.5 (CH, C-5), 47.9 (CH, C-9), 46.6 (C_q, C-17), 46.5 (CH_2, C-19), 42.1 (C_q, C-14), 42.0 (CH, C-18), 39.8 (C_q, C-8), 38.9 (CH_2, C-1), 37.4 (C_q, C-10), 37.1 (C_q, C-4), 34.2 (CH_2, C-21), 33.3 (CH_3, C-29), 33.1 (CH_2, C-22), 32.6 (CH_2, C-7), 31.0 (C_q, C-20), 28.3 (CH_2, C-15), 26.1 (CH_3, C-27), 23.8 (CH_2, C-2), 23.8 (CH_3, C-30), 23.7, 23.6 (2 × CH_2, C-11 & C-16), 17.9 (CH_2, C-6), 17.3 (CH_3, C-26), 16.4 (CH_3, C-25), 13.7 (CH_3, C-24).; IR (KBr): ν (cm^{-1}): 3465 (O-H). HMRS *m*/*z*: $[M+H]^+$ Calcd. $[C_{37}H_{59}O_9]^+$: 647.4154, Found: 647.4149.

Anemoclemoside A tetraacetate (IVL-81)

To a solution of anemoclemoside A[6] (200 mg, 0.33 mmol, 1.0 equiv.) in dry pyridine (3 mL) acetic anhydride (1.6 mL, 16.5 mmol, 50.0 equiv.) was added at room temperature. The mixture was heated to 90 °C and stirred for 1 hour under an atmosphere of N_2. Upon full conversion of the starting material (2 hours) the mixture was cooled to room temperature, diluted with toluene (6 mL) and evaporated to dryness. The co-evaporation was repeated twice (2 x 6 mL) to give the crude product as an orange honey. The residue was dissolved in DCM (1 mL), adsorbed onto silica (1 g) and submitted to column chromatography (EtOAx/Hex 30:70) to yield after chromatography **IVL-81** (242 mg, 0.313 mmol, 95%) as a foamy white solid. Optical Rotation: $[\alpha]_D^{19.5}$ = +43.0° (*c* = 4 g /100 mL TCM); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ [ppm]: 5.55 (dd, *J* = 8.5, 2.8 Hz, 1H, H-3'), 5.26 ("s", 1H, H-12), 5.24 (dd, *J* = 4.8, 3.0 Hz, 1H, H-2'), 5.15 (ddd, *J* = 8.3, 5.6, 2.7 Hz, 1H, H-4'), 4.61 (d, *J* = 4.9 Hz, 1H, H-1'), 4.25 (dd, *J* = 12.4, 2.6 Hz, 1H, H_B-5'), 4.11 (dd, *J* = 12.4, 5.6 Hz, 1H, H_A-5'), 3.79 (d, *J* = 10.5 Hz, 1H, H_B-23), 3.21 – 3.11 (m, 2H, H-3, H_A-23), 2.81 (dd, *J* = 13.6, 3.7 Hz, 1H, H-18), 2.10 (s, 3H, Ac-CH_3), 2.08 (s, 3H, Ac-CH_3), 2.06 (s, 3H, Ac-CH_3), 2.05 (s, 3H, Ac-CH_3), 1.96 (td, *J* = 12.8, 3.1 Hz, 1H, H_B-16), 1.91 – 1.83 (m, 2H, H_2-11), 1.75 (td, *J* = 13.9, 4.3 Hz, 1H, H_B-22), 1.67 (m, 1H, H_B-15), 1.66 (m, 1H, H_B-2), 1.65 (m, 1H, H_B-1), 1.60 (m, 2H, H_A-16, H_B-19), 1.56 (m, 1H, H-9), 1.55 (m, 1H, H_A-22), 1.53 (m, 1H, H_A-2), 1.37 (m, 2H, H_B-6, H_B-7), 1.33 (m, 1H, H_B-21), 1.23 (m, 1H, H_A-7), 1.20 (m, 1H, H_A-21), 1.14 (m, 1H, H_A-19), 1.12 (s, 3H, H_3-27), 1.11 (m, 1H, H_A-6), 1.04 (m, 1H, H_A-15), 1.03 (s, 3H, H_3-24), 0.98 (m, 1H, H_A-1), 0.94 (s, 3H, H_3-25), 0.92 (s, 3H, H_3-30), 0.90 (s, 3H, H_3-29), 0.73 (d, *J* = 11.1 Hz, 1H, H-5), 0.71 (s, 3H, H_3-26). ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ [ppm]: 184.1 (CO, C-28), 170.7, 169.98, 169.89, 169.42 (4 × Ac-CO), 143.5 (C_q, C-13), 122.4 (CH, C-12), 100.0 (CH, C-1'), 86.2 (CH, C-3), 78.3 (CH_2, C-23), 69.9 (CH, C-2'), 68.3 (CH, C-3'), 68.1 (CH, C-4'), 62.0 (CH_2, C-5'), 51.4 (CH, C-5), 47.6 (CH, C-9), 46.5 (C_q, C-17), 45.8 (CH_2, C-19), 41.6 (C_q, C-14), 40.9 (CH, C-18), 39.4 (C_q, C-8), 38.7 (CH_2, C-1), 37.2 (C_q, C-10), 36.8 (C_q, C-4), 33.8 (CH_2, C-21), 33.1 (CH_3, C-29), 32.4 (CH_2, C-22), 32.1 (CH_2, C-7), 30.7 (C_q, C-20), 27.6 (CH_2, C-15), 25.9 (CH_3, C-27), 23.6 (CH_3, C-30), 23.2 (CH_2, C-11), 23.1 (CH_2, C-2), 22.8 (CH_2, C-16), 20.9 (Ac-CH_3), 20.8 (2 × Ac-CH_3),

20.7 (Ac-CH_3), 17.6 (CH_2, C-6), 16.9 (CH_3, C-26), 16.4 (CH_3, C-25), 13.3 (CH_3, C-24).HMRS *m/z*: $[M+H]^+$ Calcd. $[C_{43}H_{65}O_{12}]^+$: 773.4471, Found: 773.4465.

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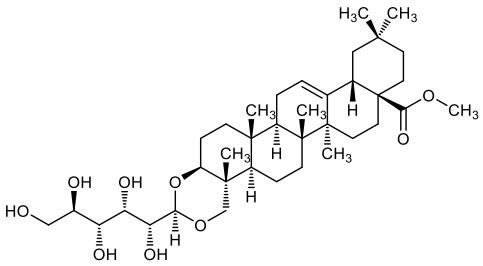
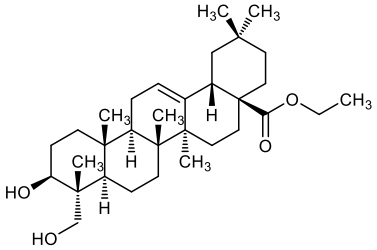
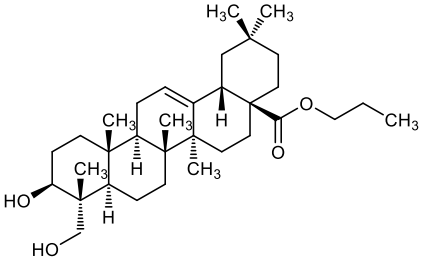
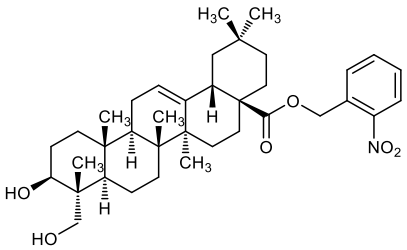
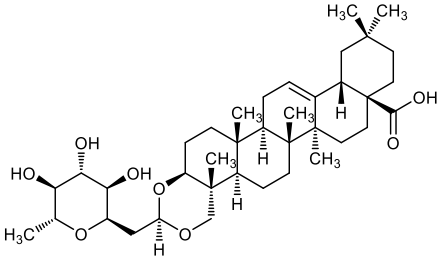
Table S1

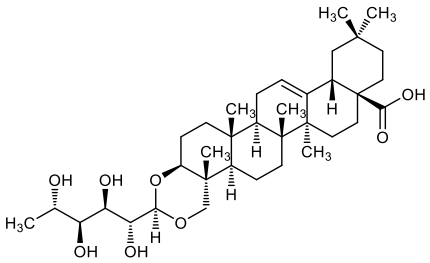
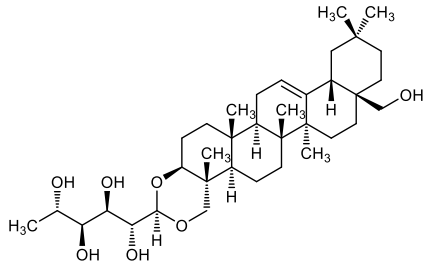
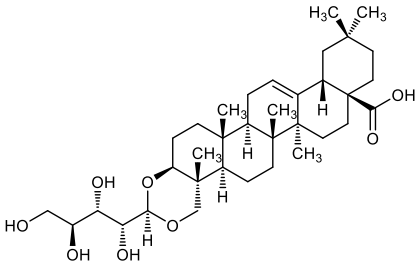
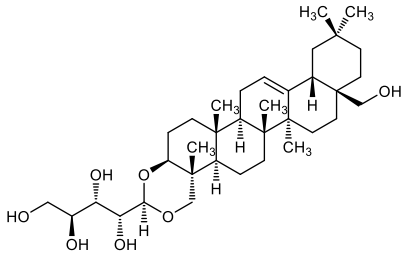
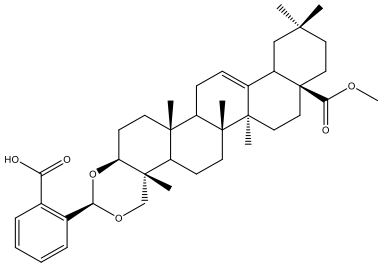
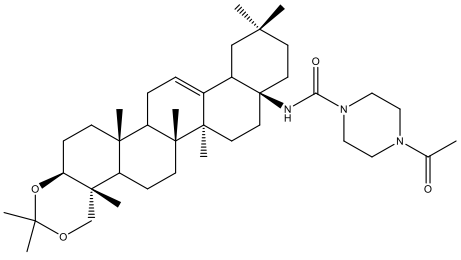
Compound codes for all molecules included in the study, together with results in initial and secondary screens

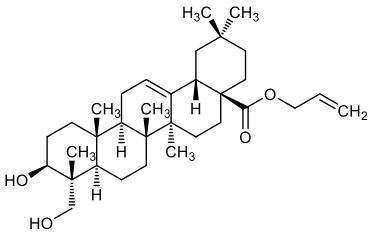
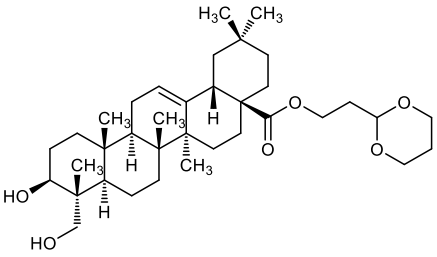
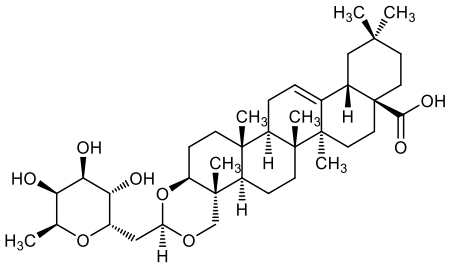
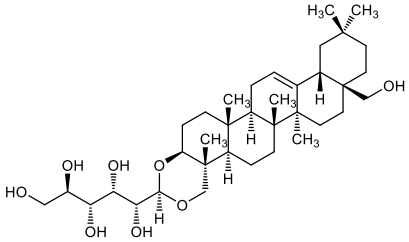
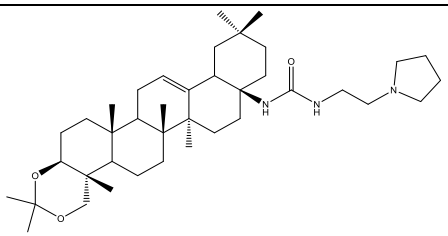
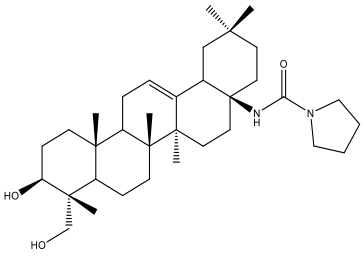
Yellow (58) are molecules selected for further study from the initial screen, in order of response. Red (60) gave intermediate responses the initial screen, in order of compound reference number. Blue (19) gave no response in initial assay.

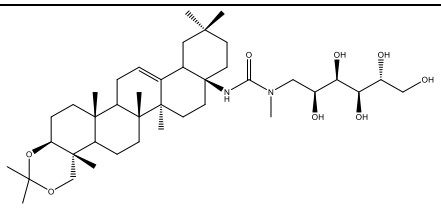
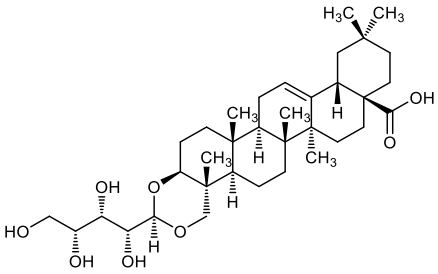
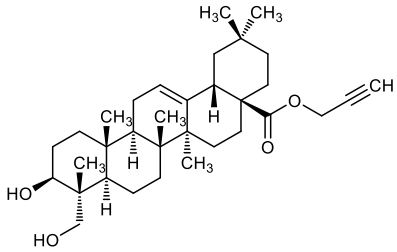
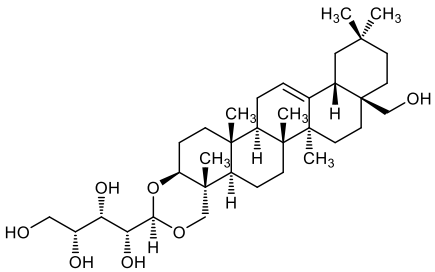
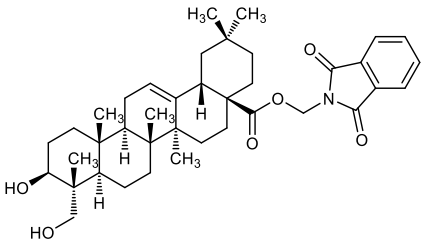
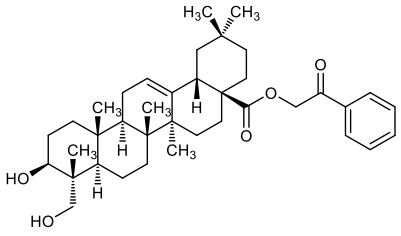
The compounds in the library have been divided according to their functionality into sub-groups:

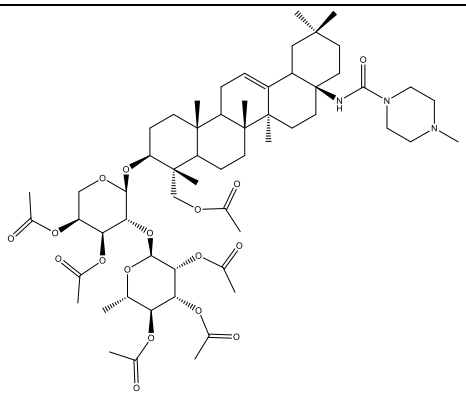
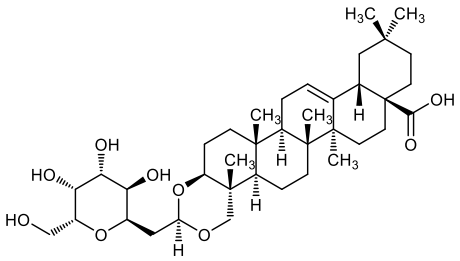
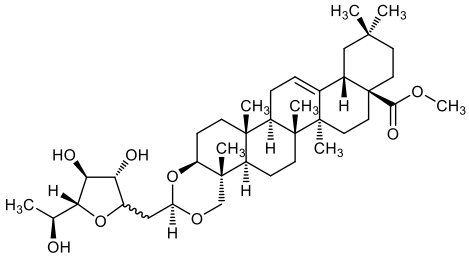
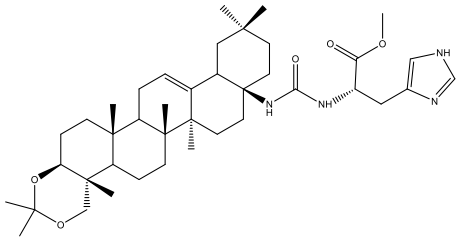
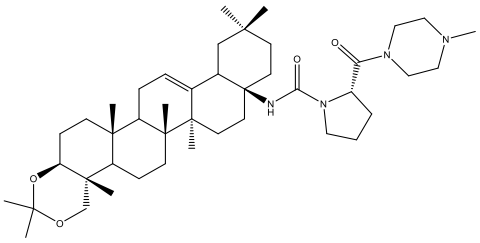
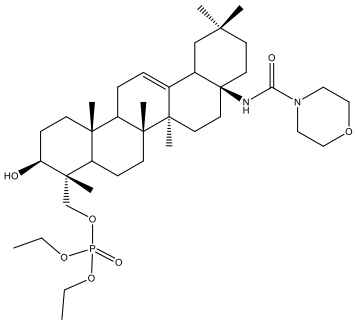
1. Molecules isolated from *Hedera helix*. (9)
2. Anemoclemosides. (28)
3. Other hederagenin 3,23-acetals and 3,23-diprotected compounds. (15)
4. Hederagenin 28-esters (19)
5. Hederagenin 3,23-protected 28-esters. (12)
6. Hederagenin 28-ureas (46)
7. Hederagenin disuccinate (1)
8. Others (7)

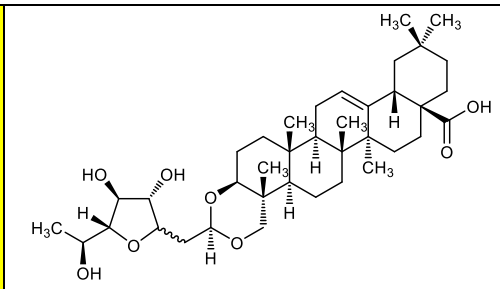
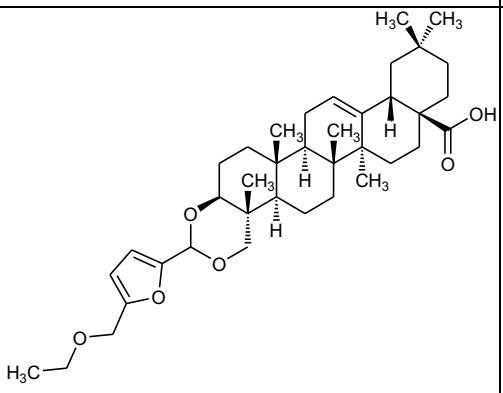
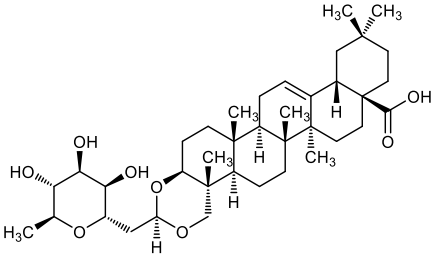
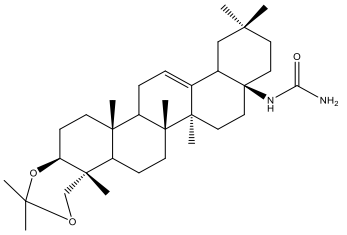
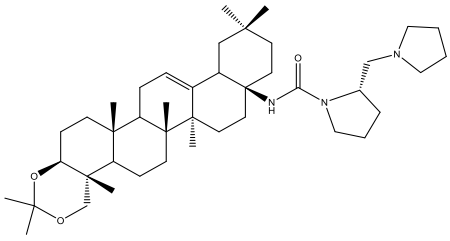
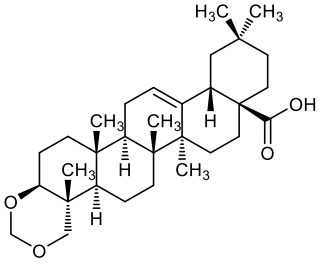
Compound code	Molecular structure	Sub-group	% inhibition Primary screen	AMA ED_{50} (µM) Secondary screen
IVL-18		2	**100**	**9.5**
IVL-22		4	**100**	**>50**
IVL-40		4	**100**	**43.6**
IVL-53		4	**100**	**>50**
IVL-73		3	**100**	**>50**

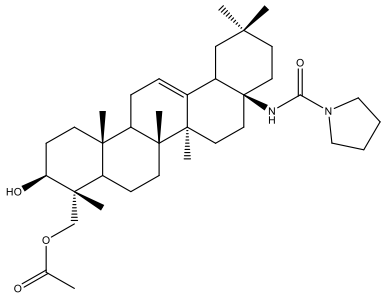
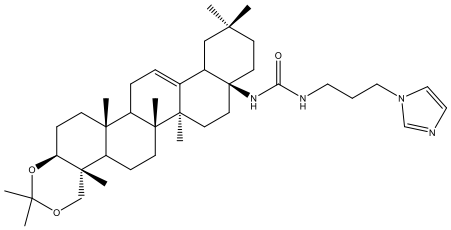
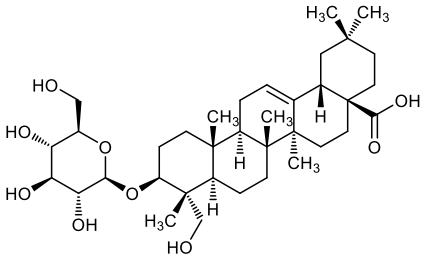
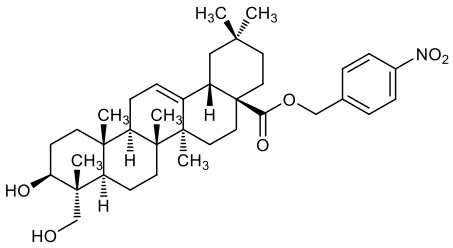
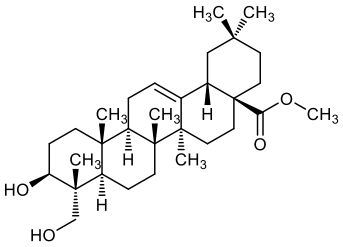
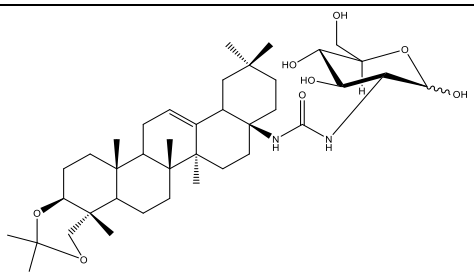
IVL-74 Anemoclemoside E		2	**100**	**21.2**
IVL-77 Anemoclemoside E2		2	**100**	**26.9**
IVL-78 Anemoclemoside A		1	**100**	**14.6**
IVL-80 Anemoclemoside A2		2	**100**	**>50**
MC-071		5	**100**	**10.0**
MC-084		6	**100**	**26.4**

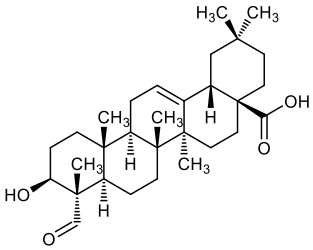
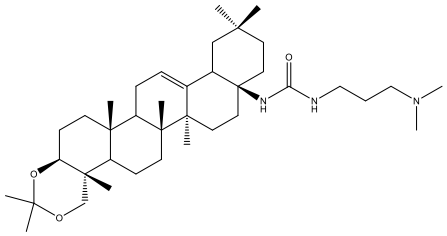
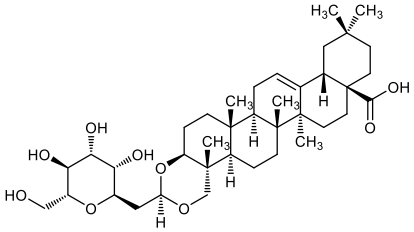
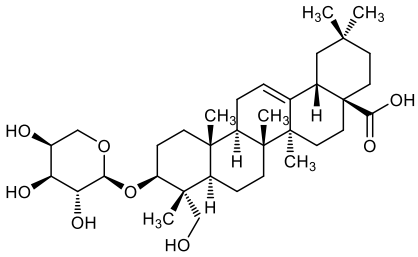
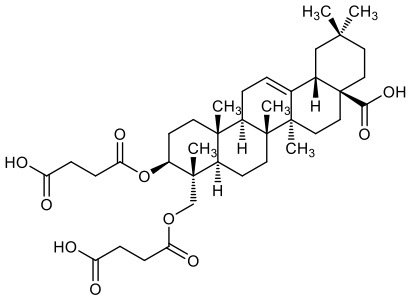
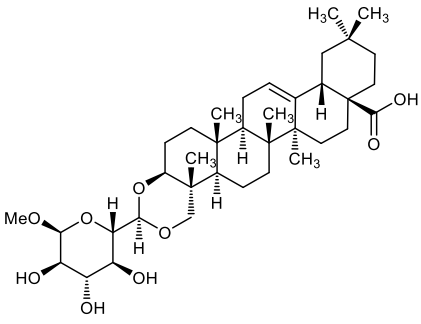
IVL-23		4	**99.9**	**22.7**
IVL-58		4	**99.6**	**>50**
IVL-72		3	**99.2**	**19.4**
IVL-19 Anemoclemoside C2		2	**99.1**	**>50**
MC-096		6	**99.1**	**>50**
MC-055		6	**99**	**15.3**

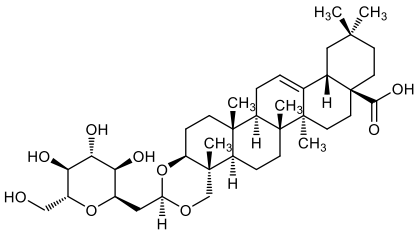
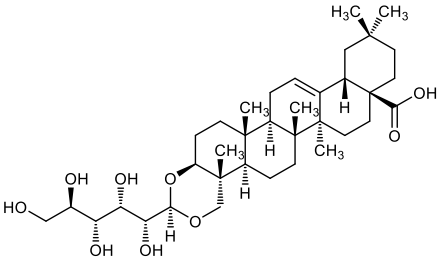
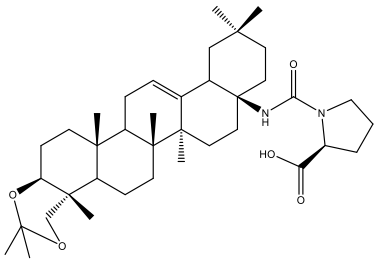
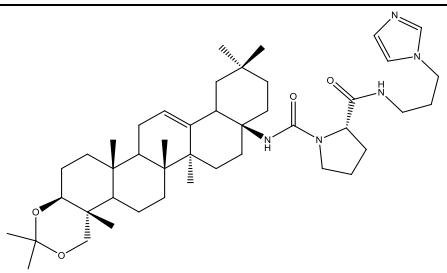
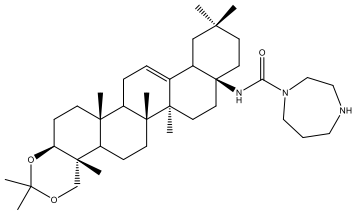
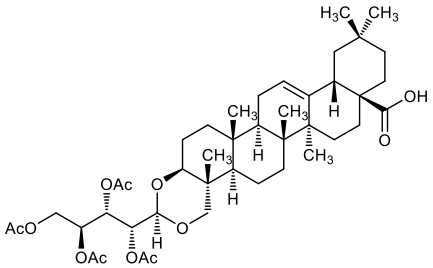
MC-059		6	**99**	**19.9**
IVL-75 Anemoclemoside X		2	**98.9**	**9.7**
IVL-68		4	**98.7**	**15.1**
IVL-90 Anemoclemoside X2		2	**98.7**	**>50**
IVL-56		4	**98.6**	**17.8**
IVL-57		4	**98.4**	**45.9**

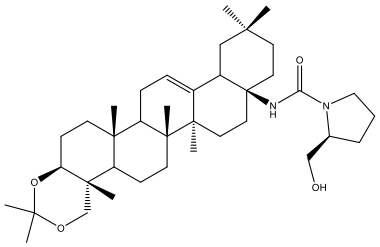
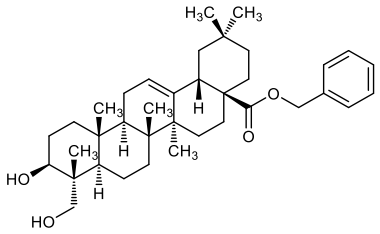
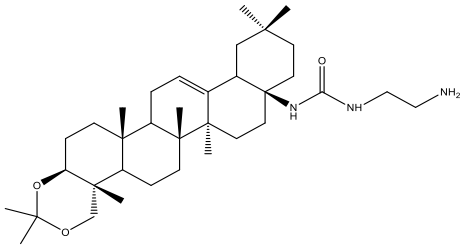
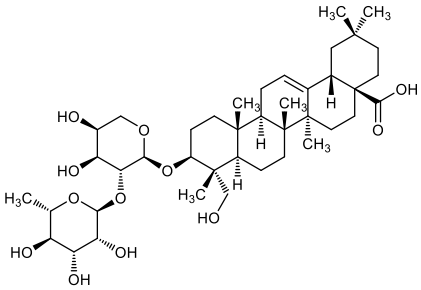
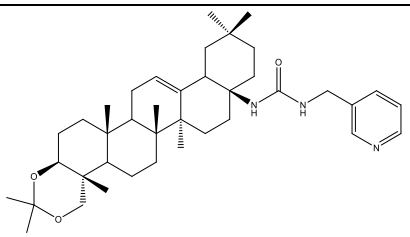
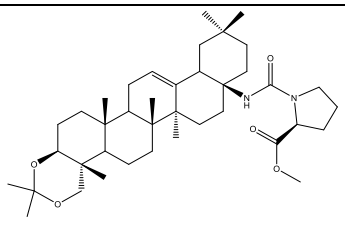
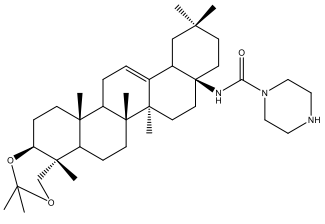
MC-118		6	**98.3**	**19.9**
IVL-71		3	**98.1**	**21.7**
IVL-105		5	**98**	**>50**
MC-048		6	**98**	**20.9**
MC-097		6	**97.9**	**32.4**
MC-114		6	**97.9**	**19.3**

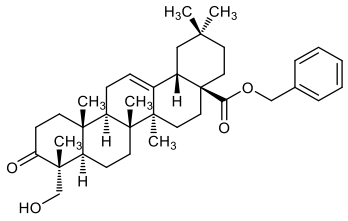
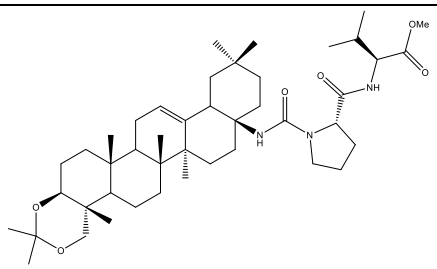
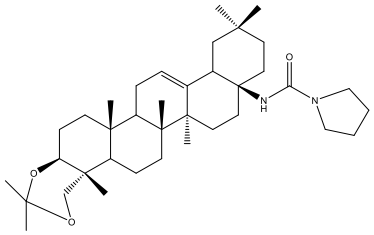
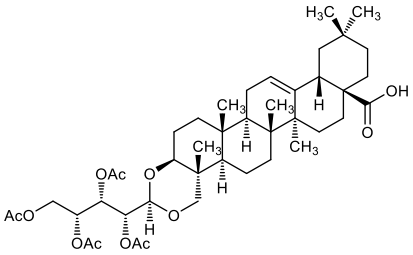
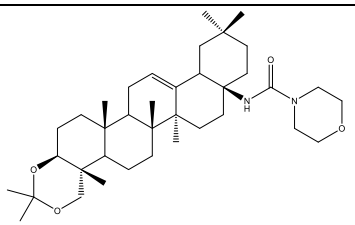
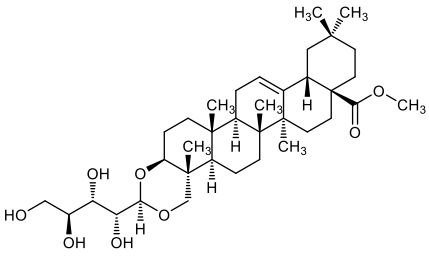
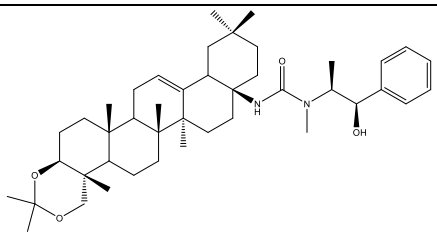
IVL-104		3	**97.8**	**10.3**
IVL-4		3	**97.6**	**19.2**
IVL-101		3	**97.6**	**13.9**
MC024		6	**97.6**	**19.6**
MC-095		6	**97.6**	**>50**
IVL-24		3	**97.5**	**14.9**

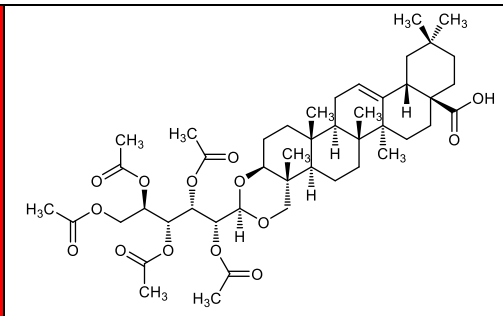
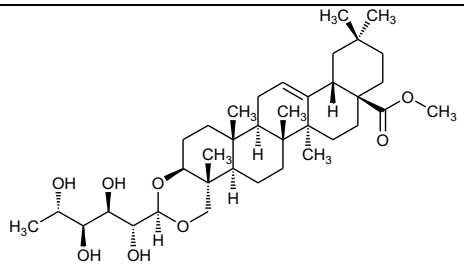
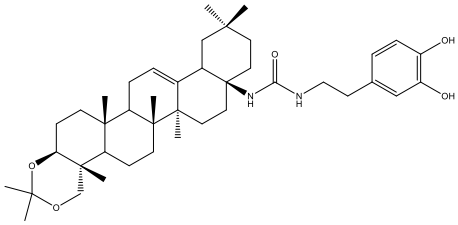
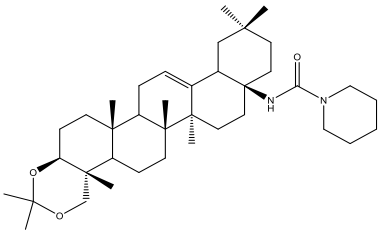
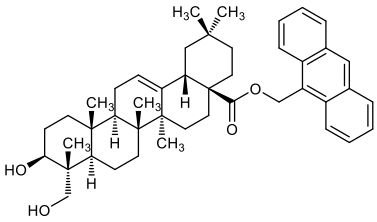
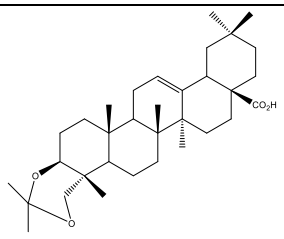
MC-057		6	**97.4**	**10.4**
MC-093		6	**97.3**	**37.6**
IVL-12 Hederoside B		1	**97.3**	**>50**
IVL-54		4	**97.3**	**36.2**
IVL-21		4	**97.2**	**12.0**
MC-028		6	**97.2**	**>50**

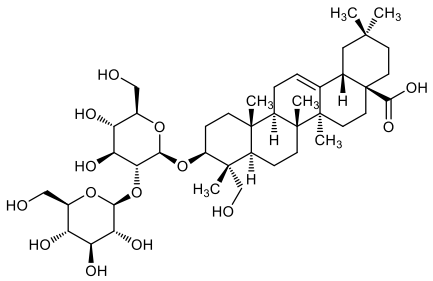
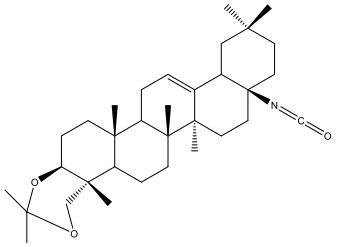
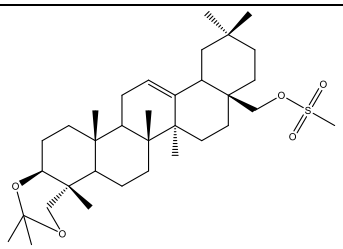
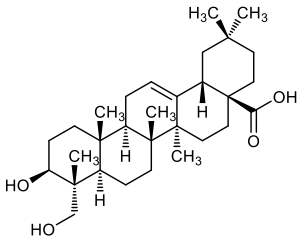
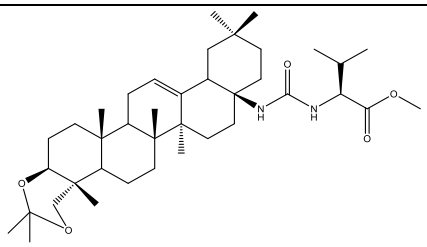
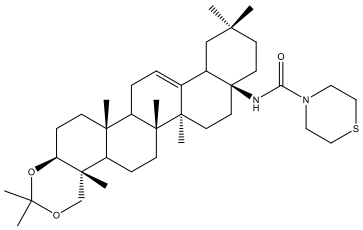
IVL-9 Gypsogenin		1	**97.1**	**9.6**
MC-108		6	**97.1**	**17.5**
IVL-100		4	**97**	**>50**
IVL-13 -Hederin		1	**96.9**	**>50**
IVL-1		7	**96.7**	**2.3**
IVL-106		3	**96.6**	**6.0**

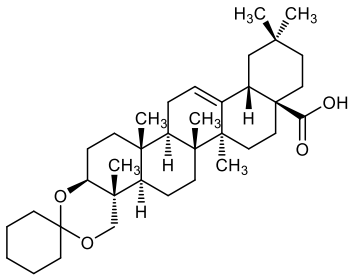
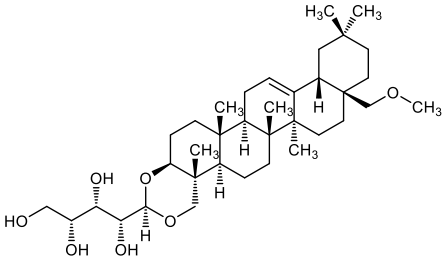
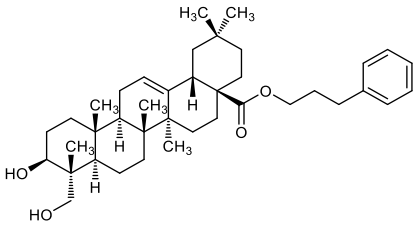
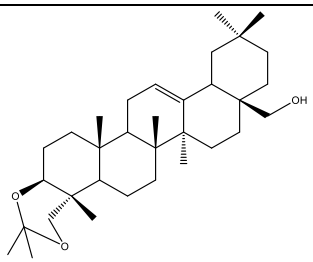
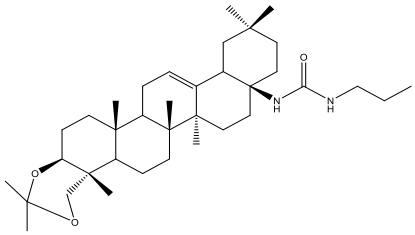
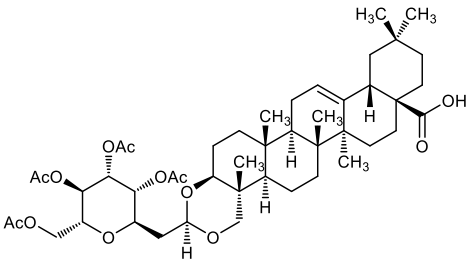
IVL-16		3	**96.3**	**7.5**
IVL-17 Anemoclemoside C		2	**96.2**	**4.5**
MC-033		6	**96**	**0.9**
MC-098		6	**96**	**20.2**
MC-043		6	**95.9**	**>50**
IVL-81 Anemoclemoside A tetraacetate		2	**95.8**	**7.2**

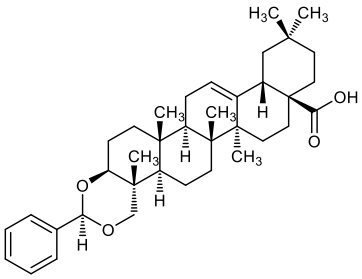
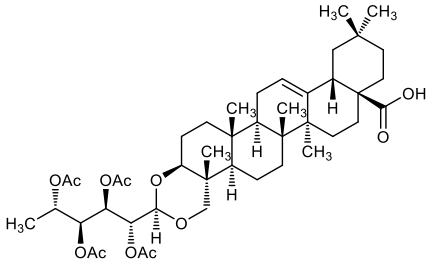
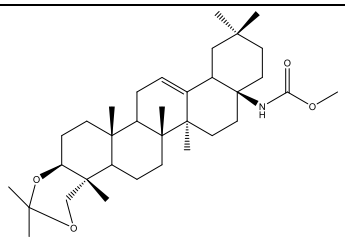
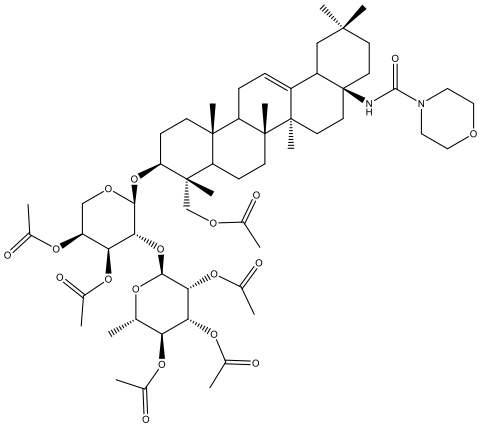
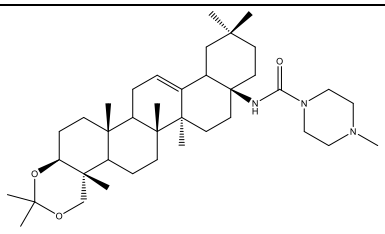
MC-092		6	**95.8**	**26.2**
IVL-5		4	**95.4**	**>50**
MC-046		6	**95.3**	**>50**
IVL-11		1	**95.1**	**19.6**
MC-106		6	**95**	**17.5**
MC-091		6	94.8	
MC-035		6	94.5	

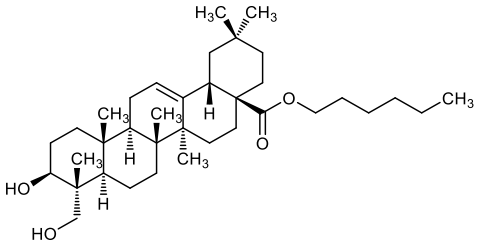
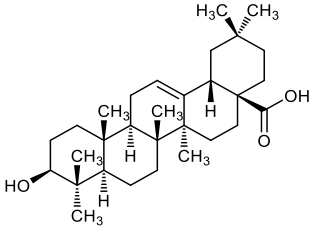
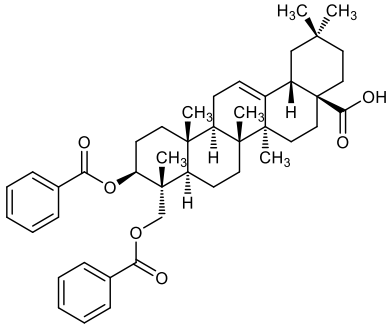
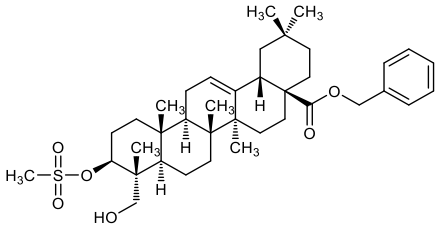
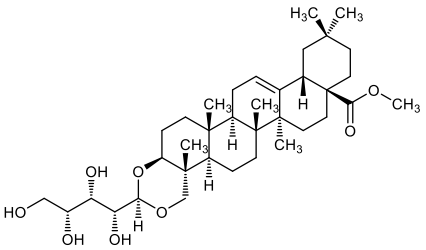
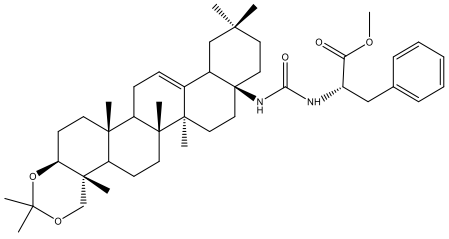
IVL-60		8	92.9	
MC-101		6	92.3	
MC-023		6	92	
IVL-93 Anemoclemoside X tetraacetate		2	91.2	
MC-042		6	91.2	
IVL-79 Anemoclemoside A1		2	90.2	
MC-085		6	90.2	

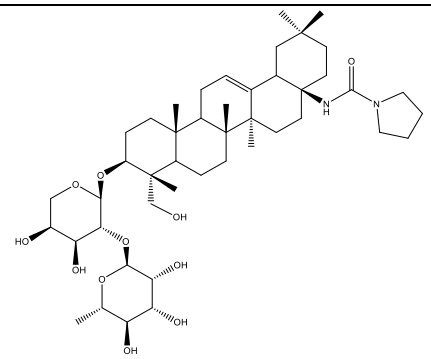
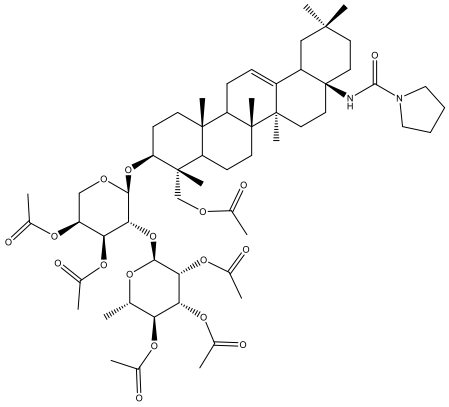
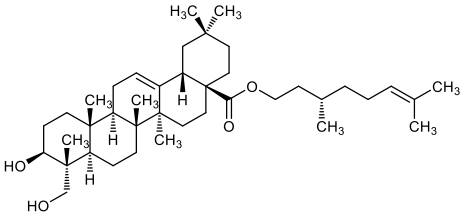
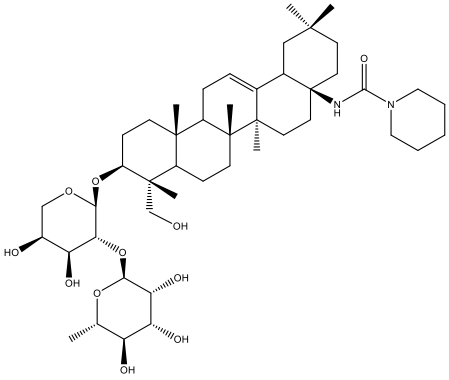
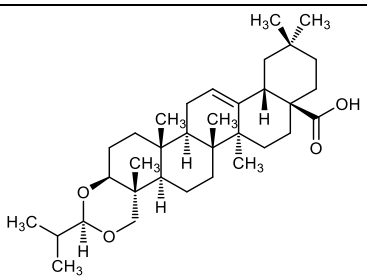
IVL-20 Anemoclemoside C pentaacetate		2	90.1	
IVL-76 Anemoclemoside E1		2	87.7	
MC-086		6	86.8	
MC-089		6	85.1	
IVL-63		4	84.4	
MC-014		3	83.6	

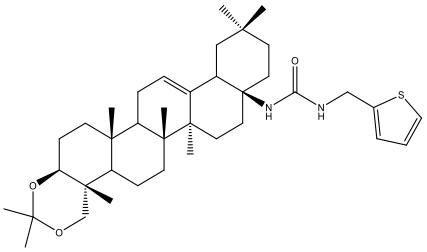
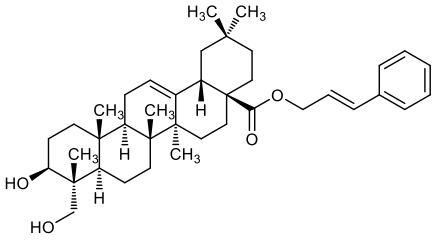
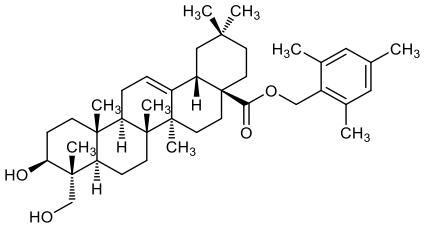
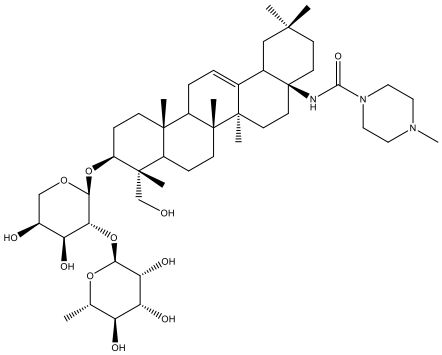
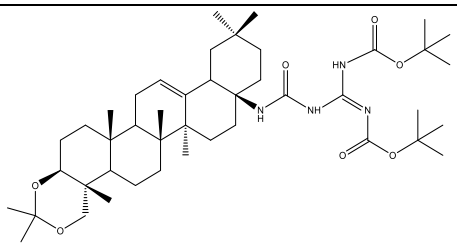
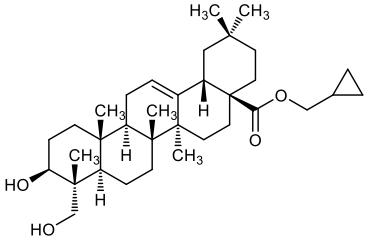
IVL-14 Hederoside F		1	82.4	
MC-015		8	81.1	
MC-034		8	81.1	
IVL-7 Hederagenin		1	79.8	
MC-027		6	78	
MC-134		6	75	

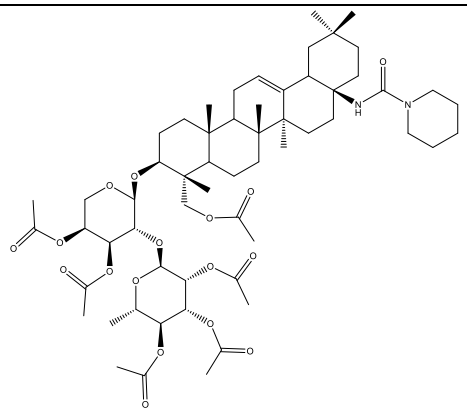
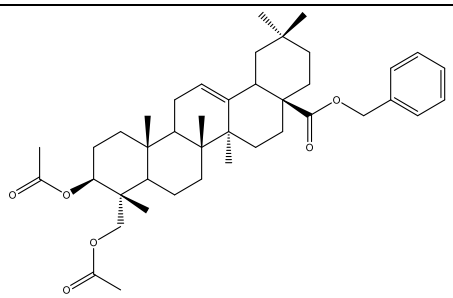
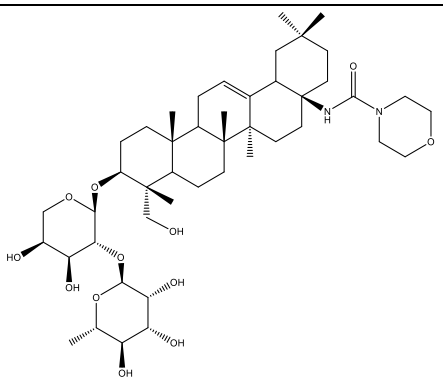
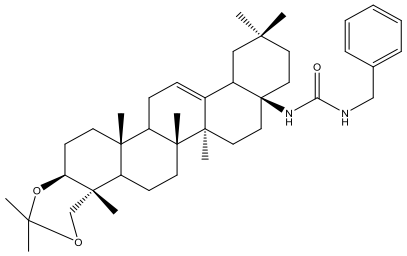
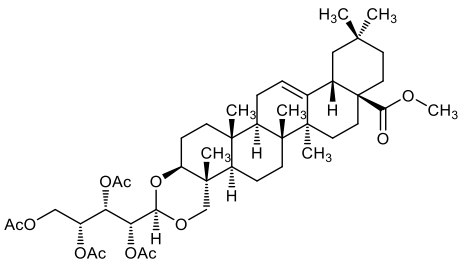
IVL-25		3	74	
IVL-92		2	69.4	
IVL-44		4	65.3	
MC-029		3	65.1	
MC-022		6	64.5	
IVL-107		2	63.8	

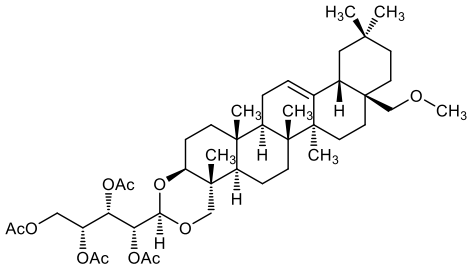
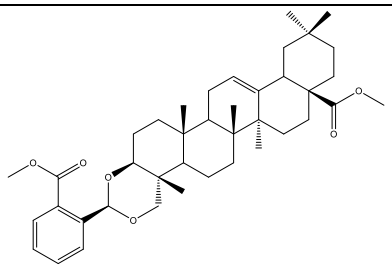
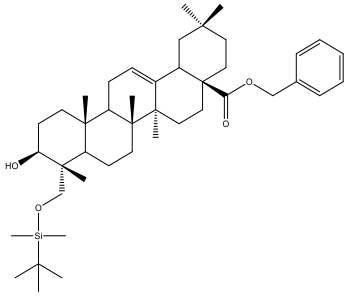
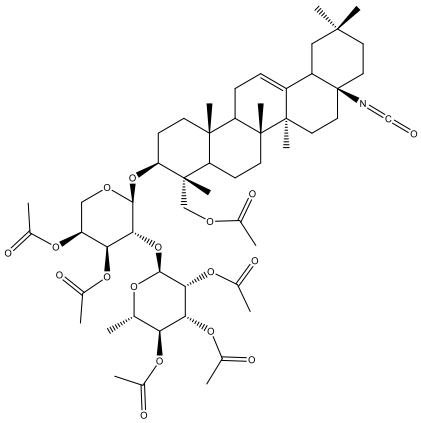
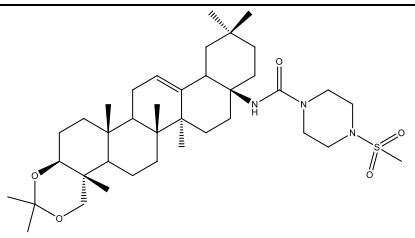
IVL-26		3	62.5	
IVL-86 Anemoclemoside E tetraacetate		2	62	
MC-016		8	61.7	
MC-102		6	56.4	
MC-062		6	56.1	

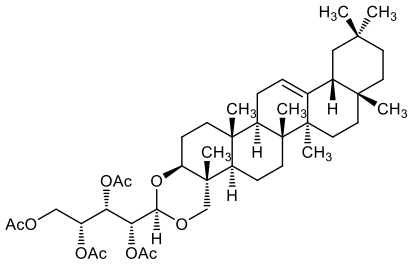
IVL-66		4	54.6	
IVL-8 Oleanolic acid		1	53.2	
IVL-39		3	48.3	
IVL-61		8	47.9	
IVL-89 Anemoclemoside X1		2	45.2	
MC-045		6	43.3	

MC-107		6	38.6	
MC-105		6	36	
IVL-67		4	35.3	
MC-116		6	35.2	
IVL-33		3	31.5	

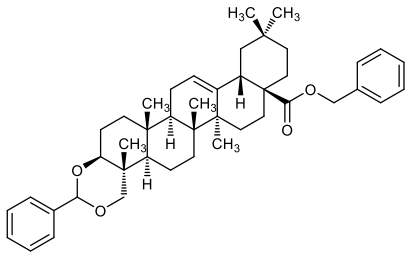
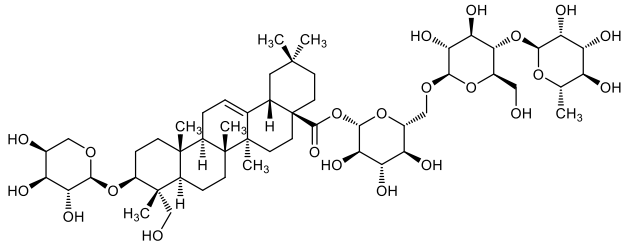
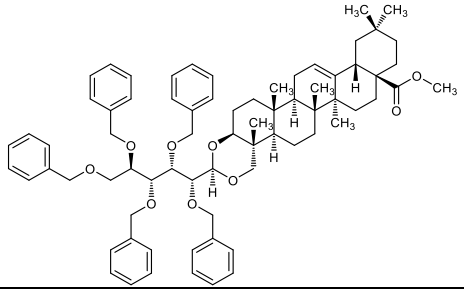
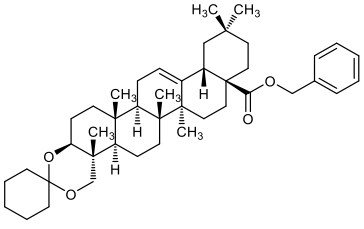
MC-094		6	26.1	
IVL-43		4	25.3	
IVL-55		4	24.2	
MC-119		6	24.1	
MC-044		6	18.6	
IVL-65		4	18.3	

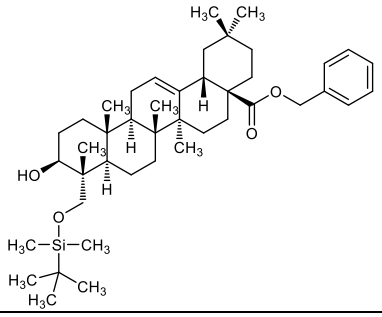
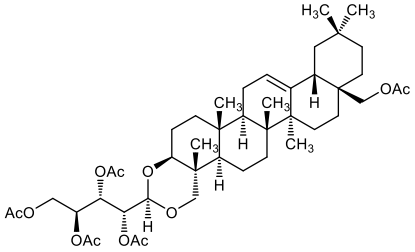
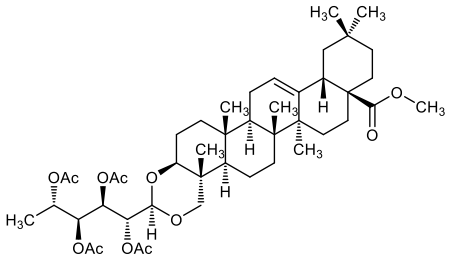
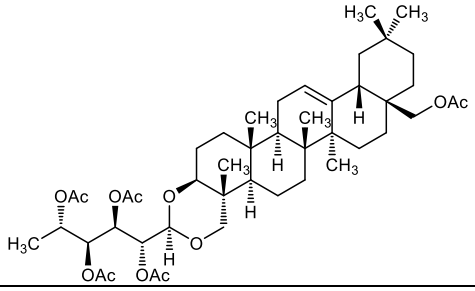
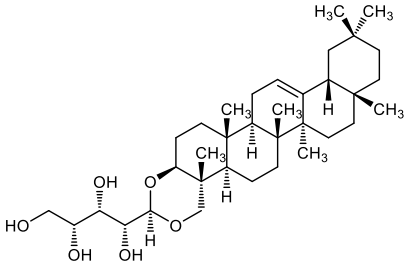
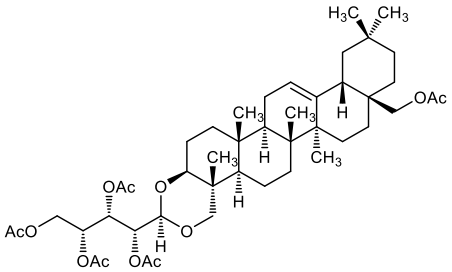
MC-115		6	17.3	
MC-066		5	13.7	
MC-104		6	12.2	
MC-017		6	11.9	
IVL-94 Anemoclemoside X1 tetraacetate		2	9.6	

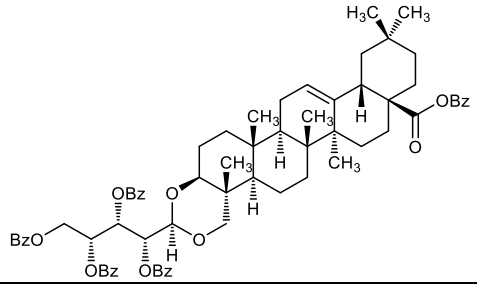
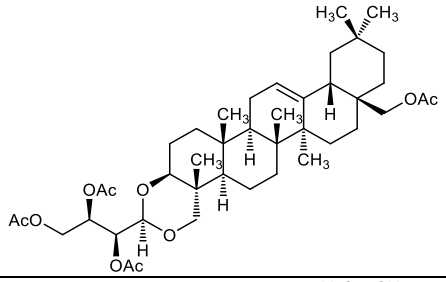
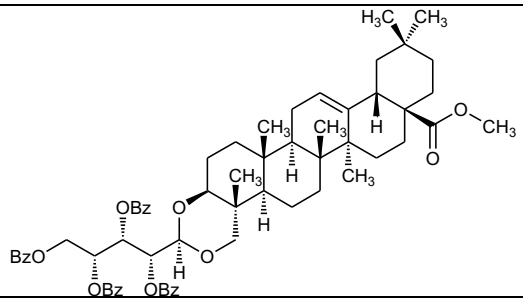
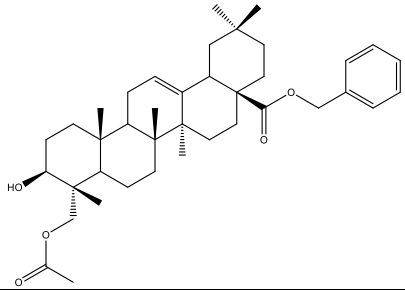
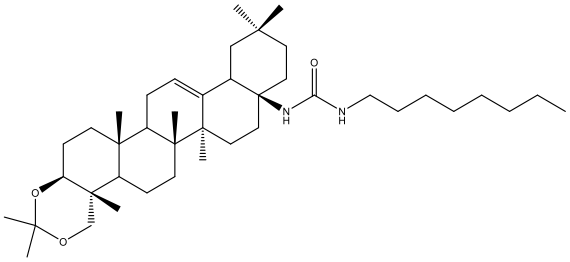
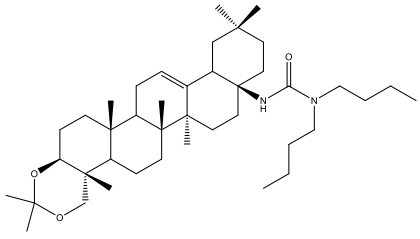
IVL-97 28-Methoxy Anemoclemoside X3 tetraacetate		2	9.4	
MC-070		5	2.9	
MC-068		5	1.7	
MC-103		8	7.1	
MC-083		6	0.9	

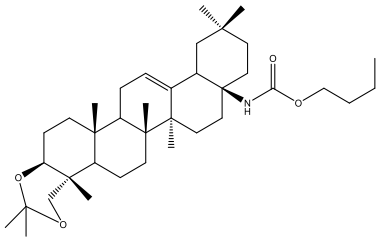
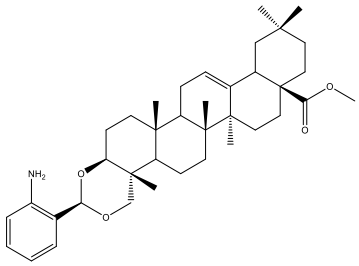
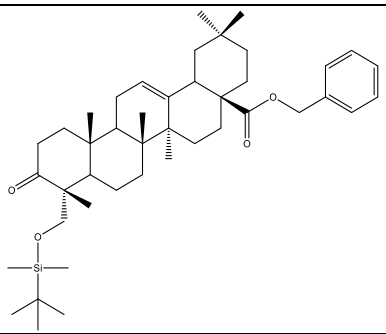
IVL-96		2	0.9	

Saponins derivatives giving no response in primary screening assay

Compound code	Molecular structure	Sub-group	% inhibition Primary screen
IVL-6		5	0
IVL-15 Hederacoside D		1	0
IVL-28		5	0
IVL-45		5	0

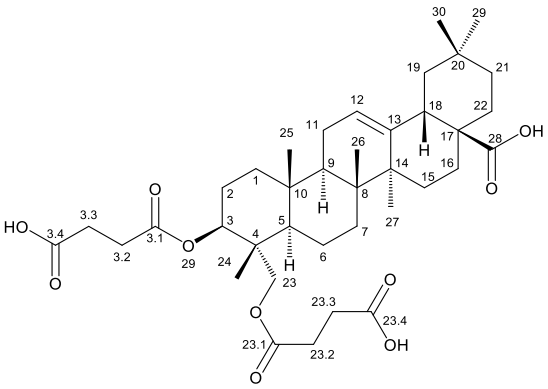
IVL-62		5	0
IVL-83		2	0
IVL-87		2	0
IVL-88		2	0
IVL-91		2	0
IVL-95		2	0

IVL-98		2	0
IVL-99		2	0
IVL-108		2	0
MC-065		5	0
MC-081		6	0
MC-082		6	0

MC019		8	0
MC-073		5	0
MC-069		5	0

NMR data

Hederagenin 3,23-di-*O*-succinate (IVL-1)



^{1}H NMR (400 MHz, CD_3OD) δ [ppm]: 0.82 (s, 3H, H_3-26), 0.86 (s, 3H, H_3-24), 0.91 (s, 3H, H_3-29), 0.94 (s, 3H, H_3-30), 1.01 (s, 3H, H_3-25), 1.03 – 1.17 (m, 3H, H_A-1, H_A-15, H_A-19), 1.19 (s, 3H, H_3-27), 1.21 – 1.33 (m, 2H, H_A-7, H_A-21), 1.34 – 1.48 (m, 3H, H_2-6, H_B-21), 1.49 – 1.82 (m, 9H, H_B-1, H_2-2, H_B-7, H_B-15, H_A-16, H_B-19, H_A-22, H_B-22), 1.86 – 1.96 (m, 2H, H_2-11), 1.96 – 2.07 (m, 1H, H_B-16), 2.57 (s, 4H, H_2-3.2, H_2-23.2), 2.60 (s, 4H, H_2-3.3, H_2-23.3), 2.85 (dd, *J* = 3.9, 13.7 Hz, 1H, H-18), 3.76 (d, *J* = 11.6 Hz, 1H, H_A-23), 3.92 (d, *J* = 11.6 Hz, 1H, H_B-23), 4.80 (m, 1H, H-3), 5.24 (t, *J* = 3.1 Hz, 1H, H-12).

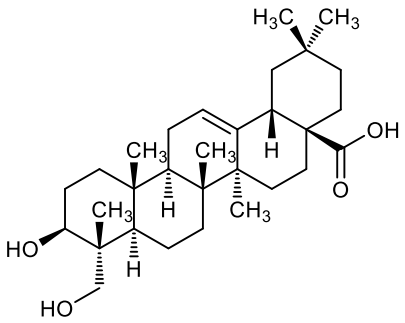
^{13}C NMR (100 MHz, CD_3OD) δ [ppm]: 13.55 (CH_3, C-24), 16.34 (CH_3, C-25), 17.70 (CH_3, C-26), 18.99 (CH_2, C-5), 23.87 (CH_2, C-2), 24.01 (CH_3, C-30), 24.05 (CH_2, C-16), 24.50 (CH_2, C-11), 26.45 (CH_3, C-27), 28.77 (CH_2, C-15), 29.81, 29.82 (2 × CH_2, C-3.3 & C-23.3), 30.24 (CH_2, C-23.2), 30.47 (CH_2, C-3.2), 31.60 (C_q, C-20), 33.50 (CH_2, C-7), 33.59 (CH_3, C-29), 33.77 (CH_2, C-22), 34.88 (CH_2, C-21), 37.93 (C_q, C-10), 38.90 (CH_2, C-1), 40.50 (C_q, C-8), 41.96 (C_q, C-4), 42.68 (CH, C-18), 42.91 (C_q, C-14), 47.18 (CH_2, C-19), 47.58 (C_q, C-17), 47.18 (CH_2, C-19), 47.58 (C_q, C-17), 48.96, 48.98 (2 × CH, C-5 & C-9), 66.24 (CH_2, C-23), 76.07 (CH, C-3), 123.40 (CH, C-12), 145.24 (C_q, C-13), 173.67, 173.69 (2 × CO, C-3.1 & C-23.1), 175.65, 175.86 (2 × CO, C-3.4 & C-23.4), 181.75 (CO, C-28).

NMR spectra for all 12 compounds taken through to toxicity screening and all novel compounds generated

^{1}H NMR

400 MHz

pyridine-d_5

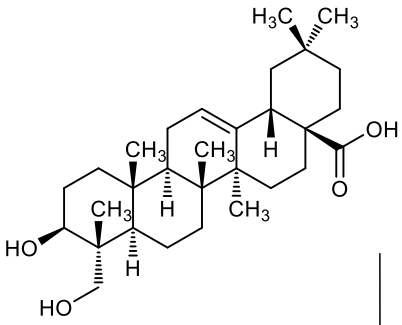


Hederagenin (**IVL-7**)

^{13}C NMR (DEPTQ)

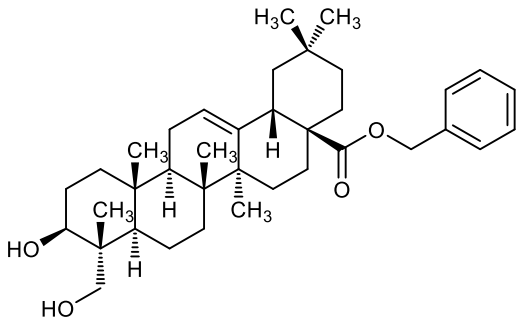
100 MHz

pyridine-d_5



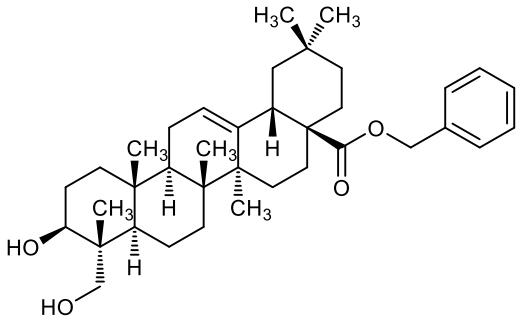
Hederagenin (**IVL-7**)

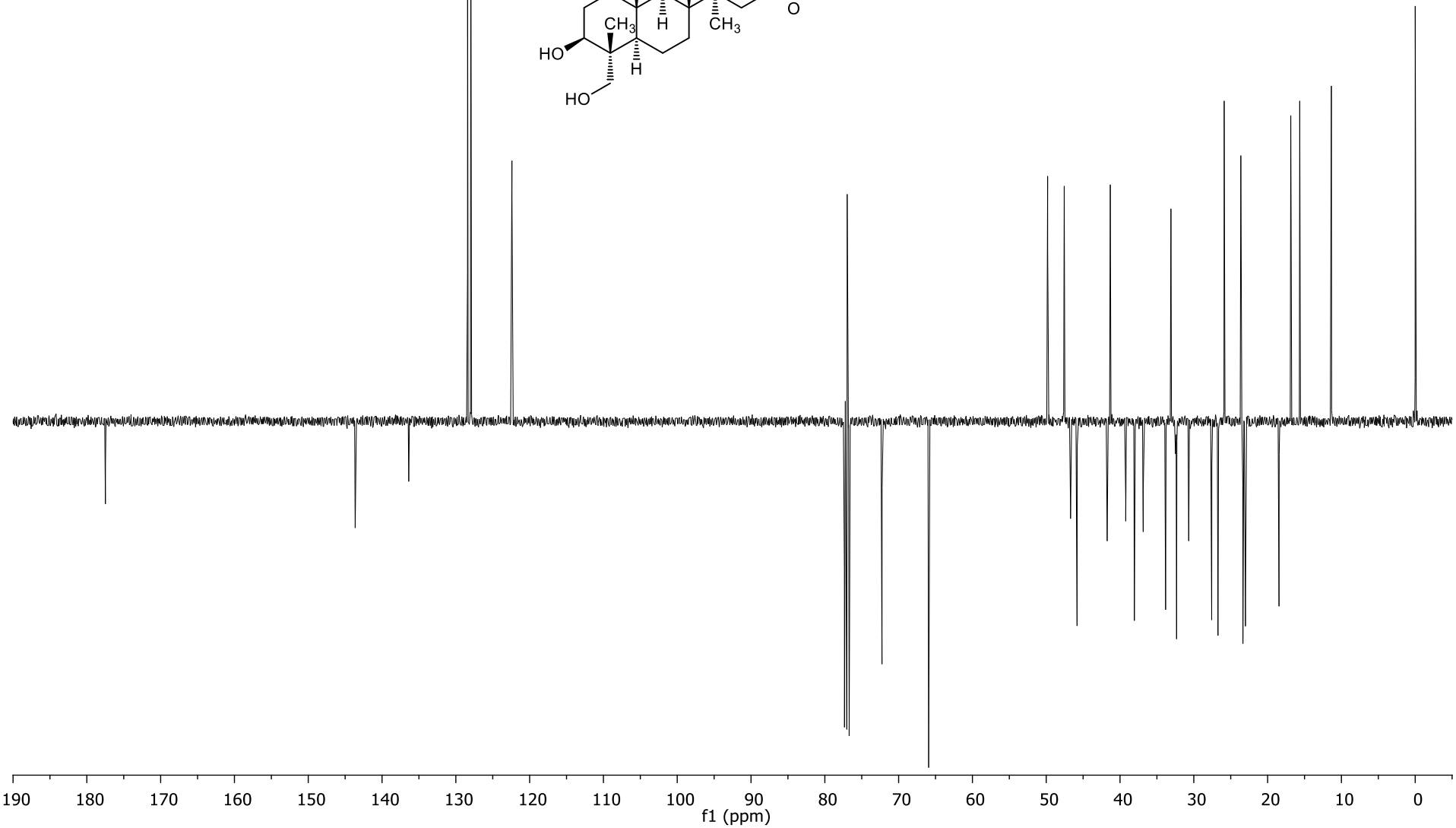
^{1}H NMR
400 MHz
chloroform-d$_{1}$



Benzyl hederagenate (**IVL-5**)

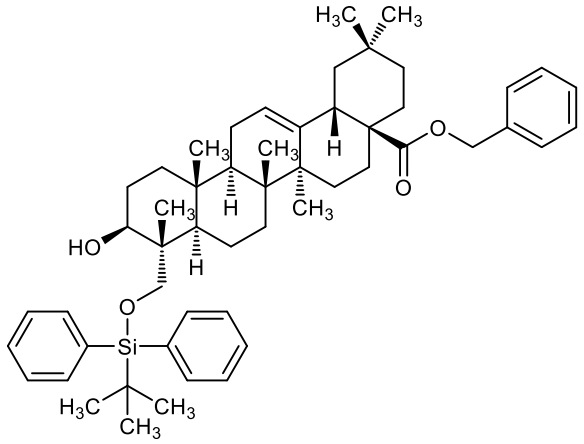
^{13}C NMR (DEPTQ)
100 MHz
chloroform-d$_1$





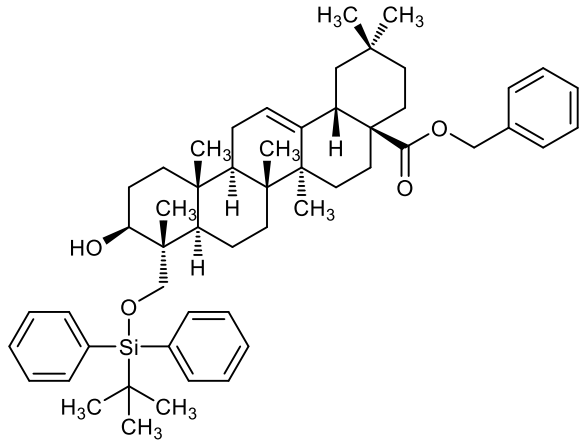
Benzyl hederagenate (**IVL-5**)

^{1}H NMR
400 MHz
chloroform-d$_{1}$



Benzyl 23-*O*-*tert*-butyldiphenylsilylhederagenate **(8)**

^{13}C NMR (DEPTQ)
100 MHz
chloroform-d_1

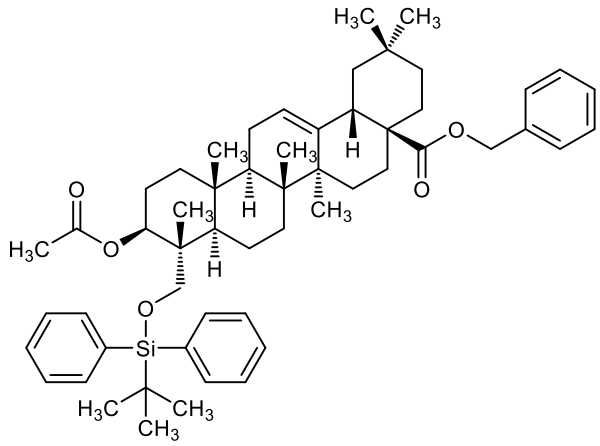


Benzyl 23-*O*-*tert*-butyldiphenylsilylhederagenate **(8)**

^{1}H NMR

400 MHz

chloroform-d$_{1}$

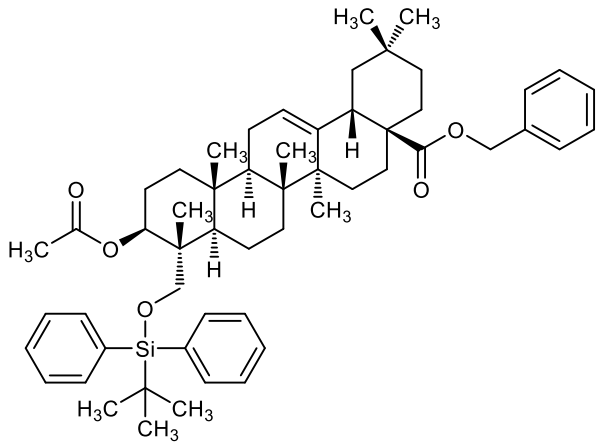


Benzyl 3-*O*-acetyl-23-*O*-*tert*-butyldiphenylsilylhederagenate

^{13}C NMR (DEPTQ)

100 MHz

chloroform-d_1

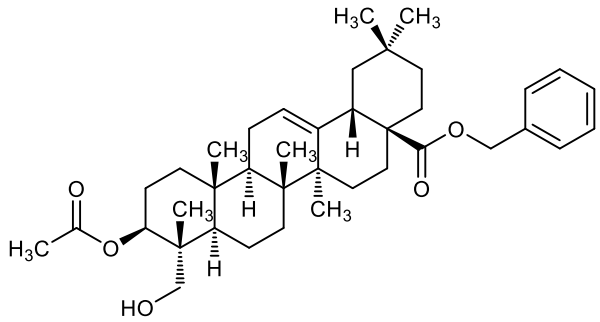


Benzyl 3-*O*-acetyl-23-*O*-*tert*-butyldiphenylsilylhederagenate

^{1}H NMR

400 MHz

chloroform-d$_{1}$

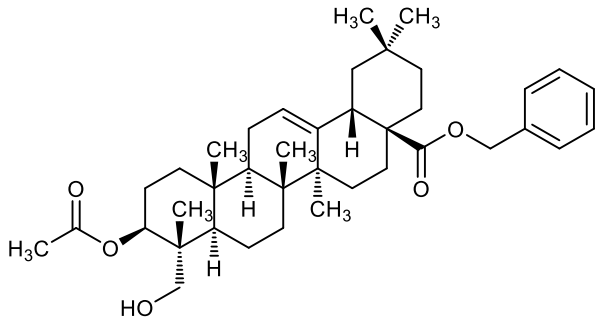


Benzyl 3-*O*-acetylsilylhederagenate

^{13}C NMR (DEPTQ)

100 MHz

chloroform-d_1

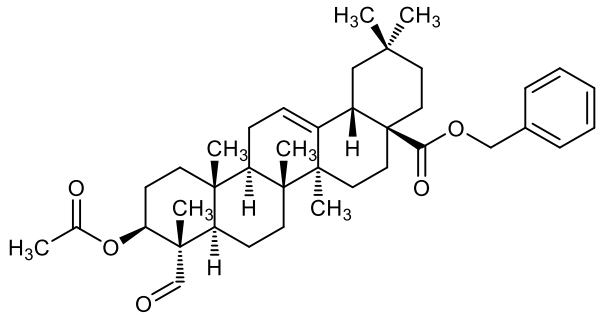


Benzyl 3-*O*-acetylsilylhederagenate

^{1}H NMR

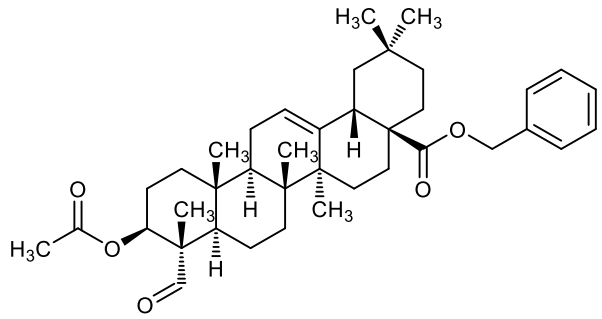
400 MHz

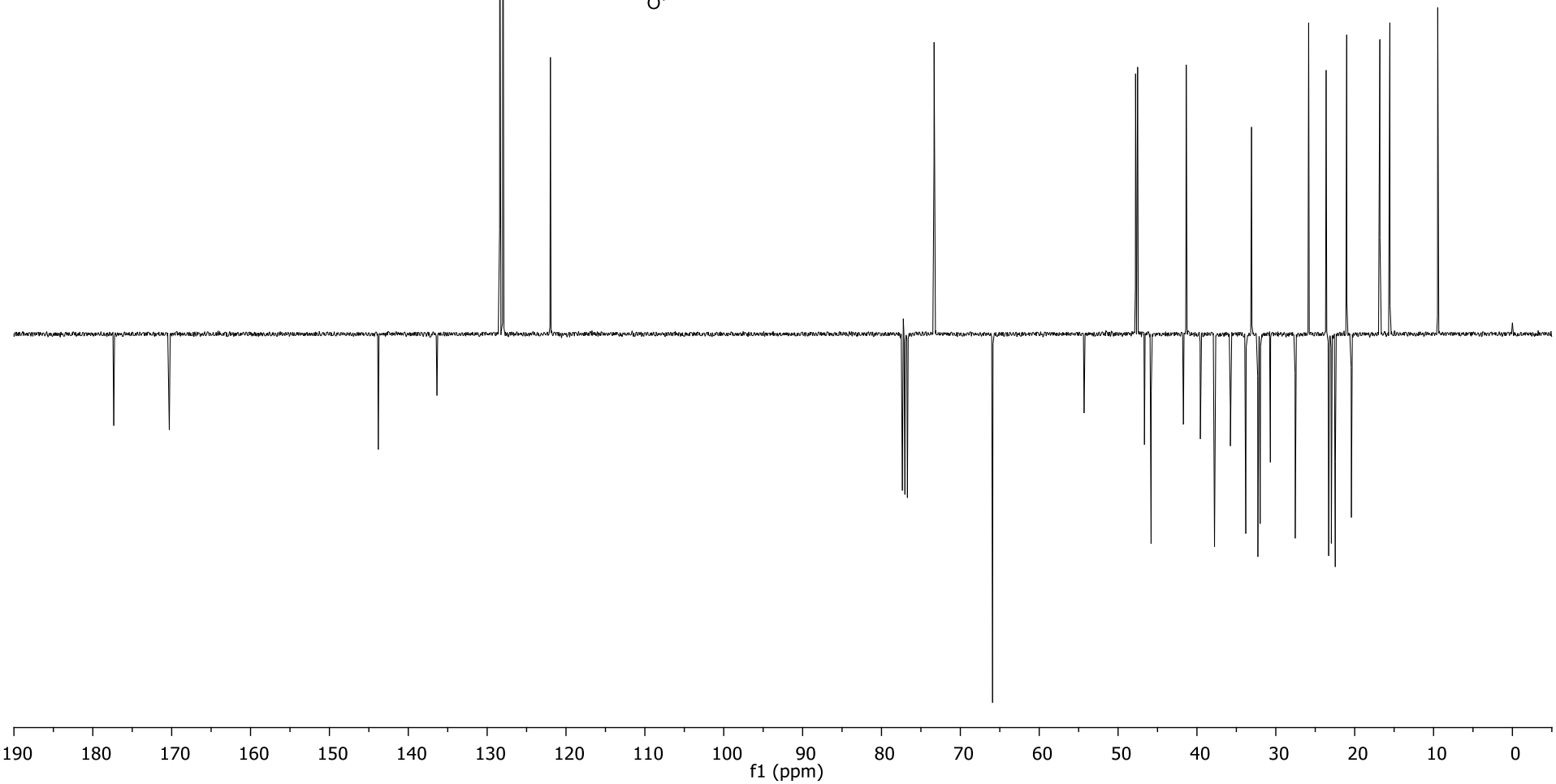
chloroform-d_1



Benzyl 3-*O*-acetylgypsogenate **(9)**

^{13}C NMR (DEPTQ)
100 MHz
chloroform-d_1



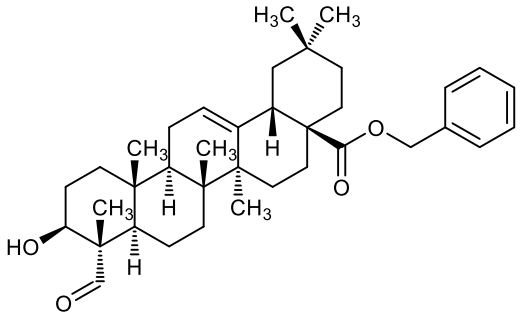


Benzyl 3-*O*-acetylgypsogenate **(9)**

^{1}H NMR

400 MHz

chloroform-d_1

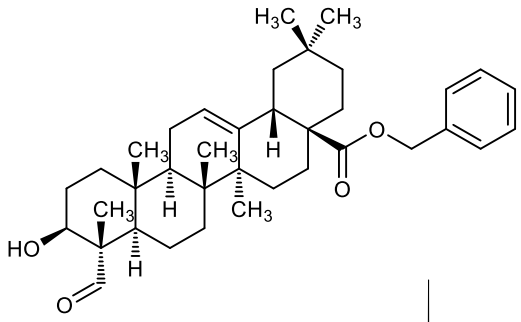


Benzyl gypsogenate

^{13}C NMR (DEPTQ)

100 MHz

chloroform-d_1

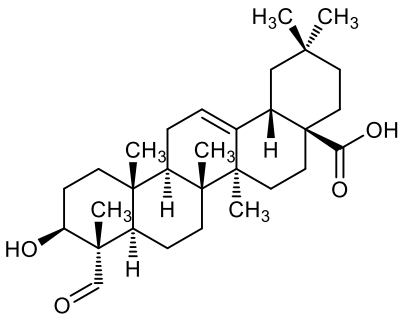


Benzyl gypsogenate

^{1}H NMR

400 MHz

chloroform-d_1

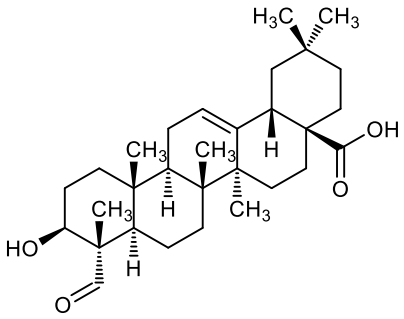


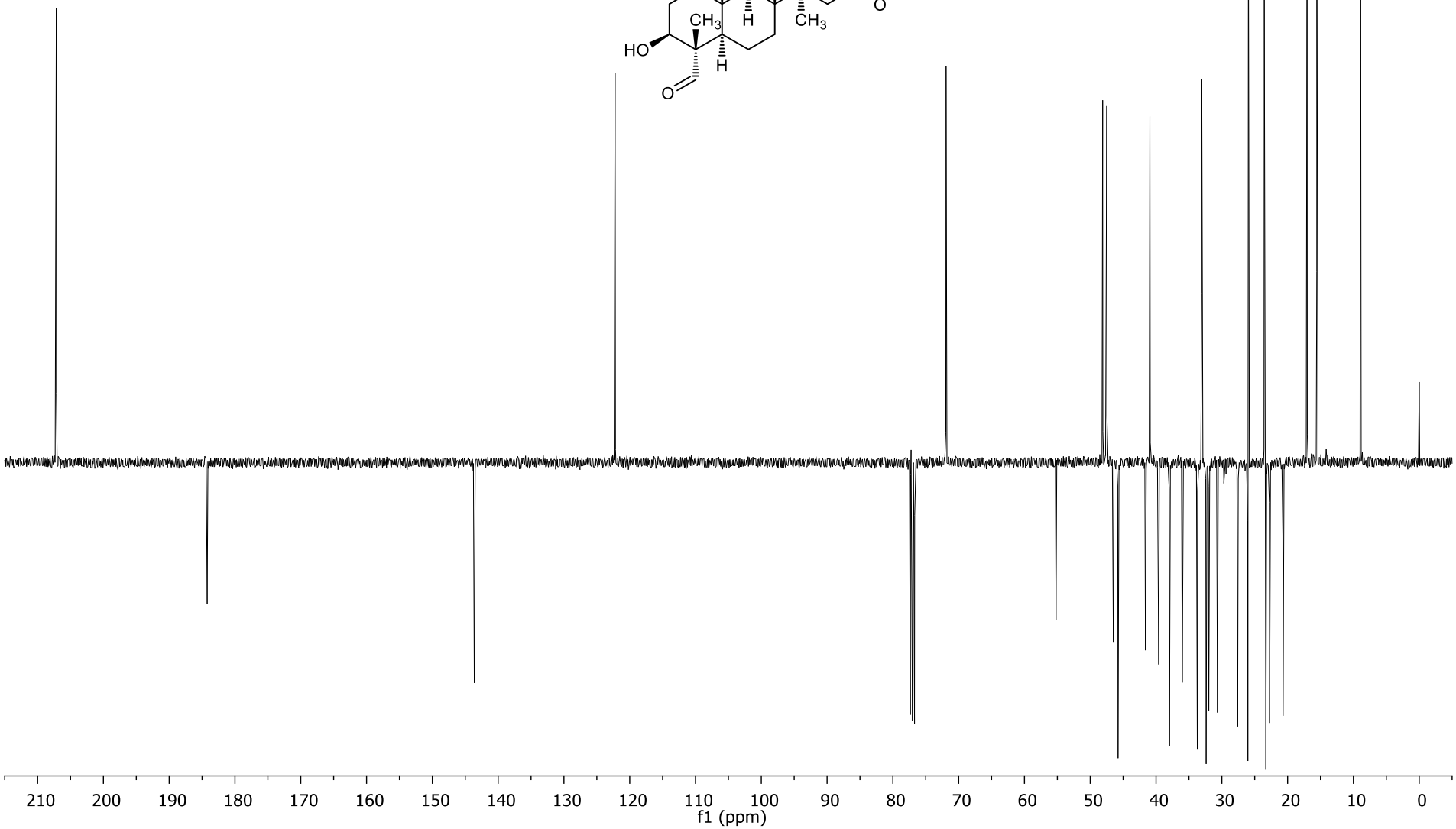
Gypsogenin (**IVL-9**)

^{13}C NMR (DEPTQ)

100 MHz

chloroform-d_1



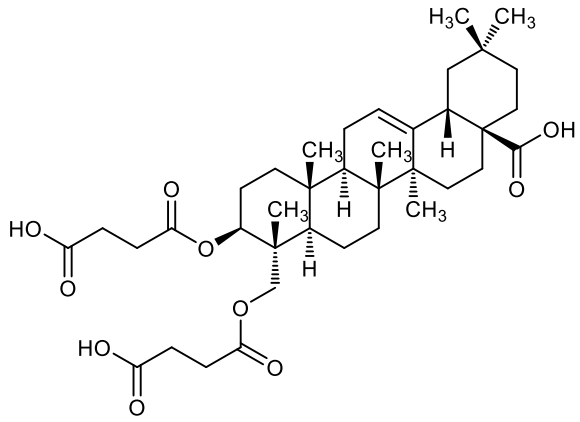


Gypsogenin (**IVL-9**)

^{1}H NMR

400 MHz

methanol-d_4

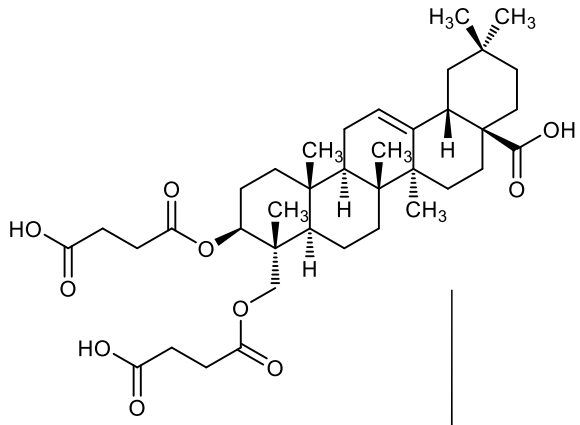


Hederagenin disuccinate (**IVL-1**)

^{13}C NMR (DEPTQ)

100 MHz

methanol-d_4

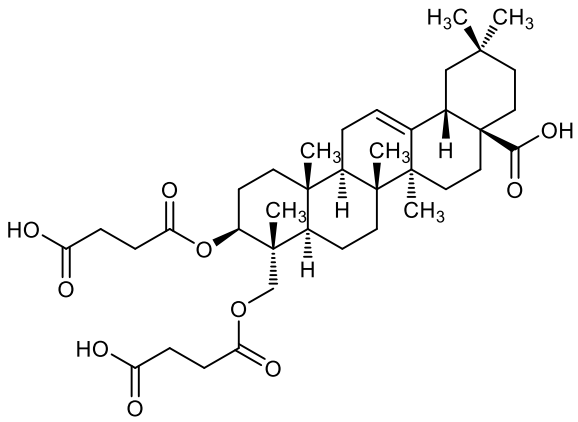


Hederagenin disuccinate (**IVL-1**)

^{1}H NMR

400 MHz

pyridine-d_5

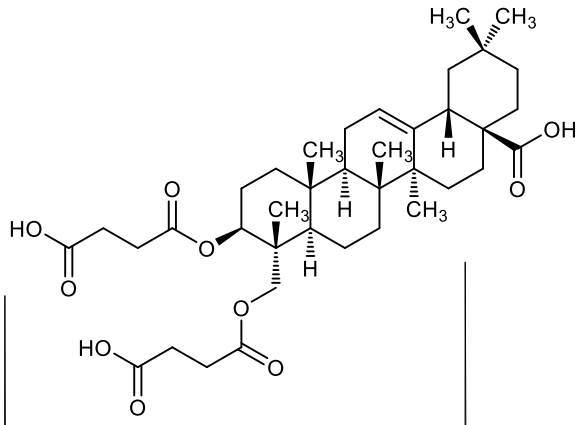


Hederagenin disuccinate (**IVL-1**)

^{13}C NMR (DEPTQ)

100 MHz

pyridine-d_5

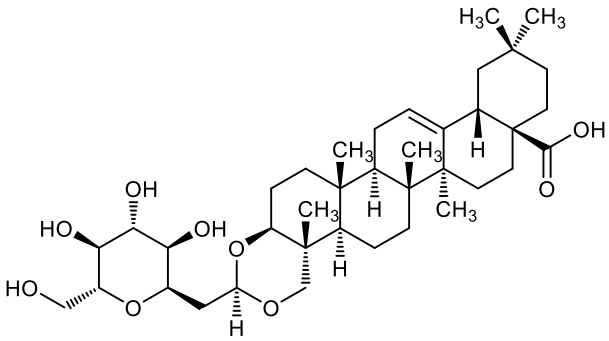


Hederagenin disuccinate (**IVL-1**)

^{1}H NMR

400 MHz

pyridine-d_5

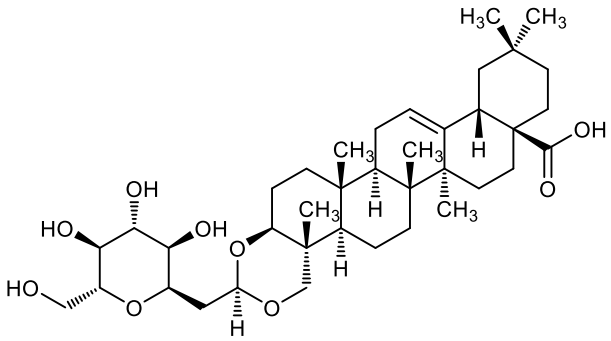


Hederagenin 2-(1'-deoxy-α-D-glucopyranos-1'-yl)acetacetal (**IVL-16**)

^{13}C NMR (DEPTQ)

100 MHz

pyridine-d_5

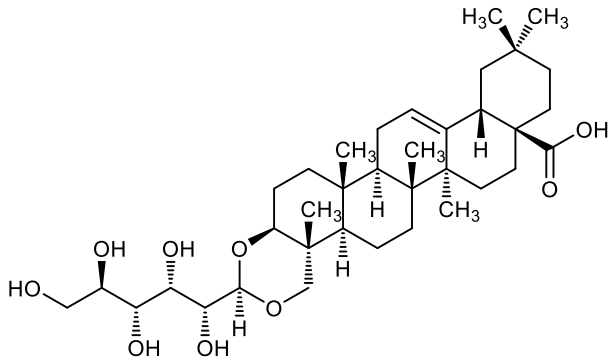


Hederagenin 2-(1'-deoxy-α-D-glucopyranos-1'-yl)acetacetal (**IVL-16**)

^{1}H NMR

400 MHz

pyridine-d_5

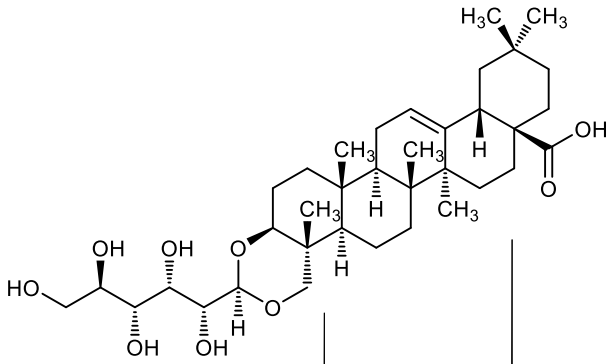


Hederagenin D-glucosylidene acetal (**IVL-17**)

^{13}C NMR (DEPTQ)

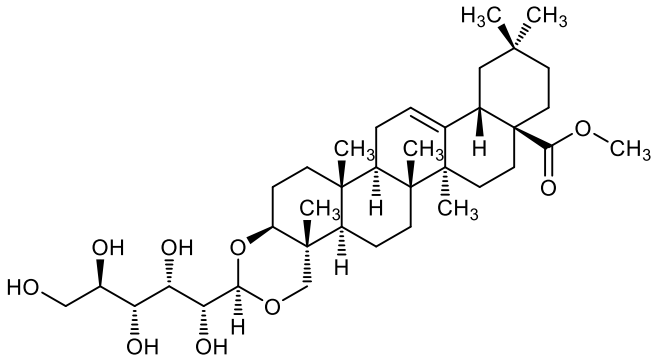
100 MHz

pyridine-d_5



Hederagenin D-glucosylidene acetal (**IVL-17**)

^{1}H NMR
400 MHz
pyridine-d_5

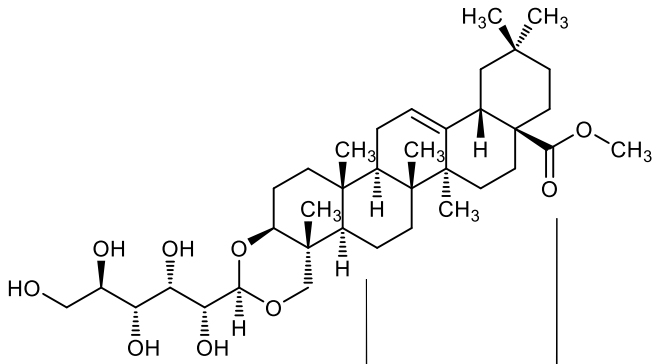


Methyl hederagenate D-glucosylidene acetal (**IVL-18**)

^{13}C NMR (DEPTQ)

100 MHz

pyridine-d_5

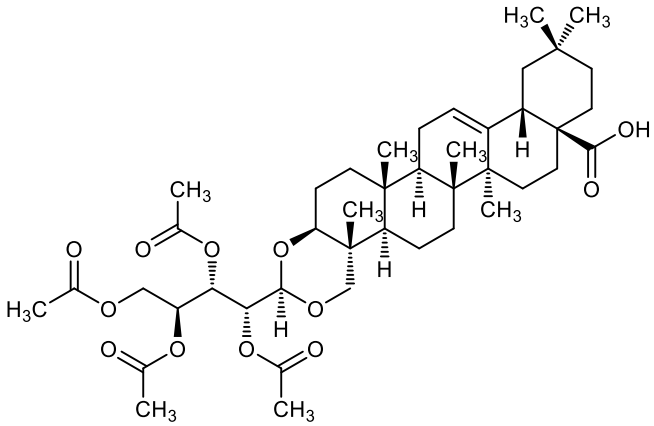


Methyl hederagenate D-glucosylidene acetal (**IVL-18**)

^{1}H NMR

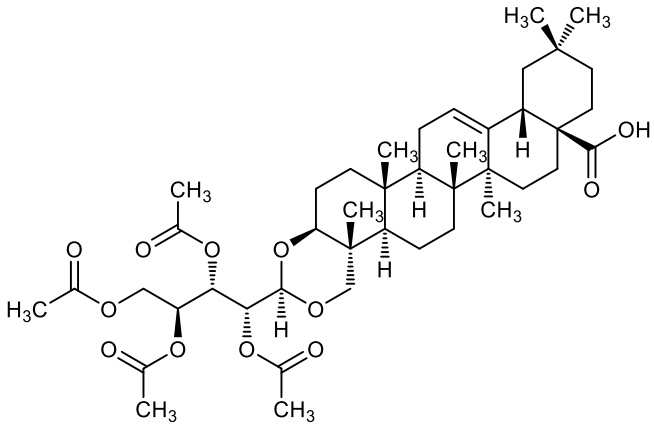
400 MHz

chloroform-d_1



Hederagenin 2',3',4',5'-tetra-*O*-acetyl-L-arabinosylidene acetal / Anemoclemoside A tetraacetate (**IVL-81**)

^{13}C NMR (DEPTQ)
100 MHz
chloroform-d_1

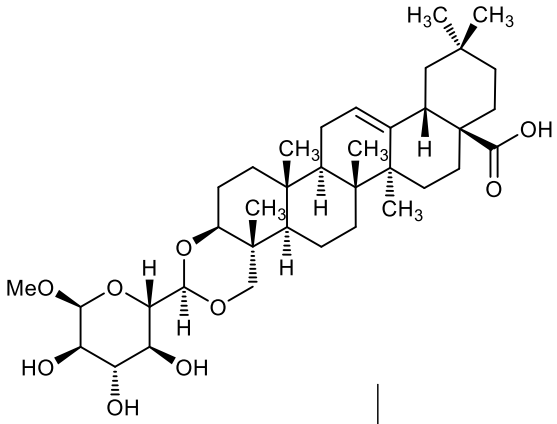


Hederagenin 2',3',4',5'-tetra-*O*-acetyl-L-arabinosylidene acetal / Anemoclemoside A tetraacetate (**IVL-81**)

^{1}H NMR

400 MHz

pyridine-d_5

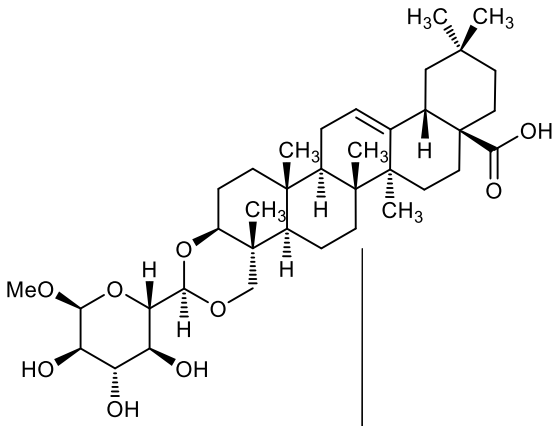


Hederagenin (1'-*O*-methyl-5'-dehydro-α-D-xylopyranos-5'-yl)formacetal (**IVL-106**)

^{13}C NMR (DEPTQ)

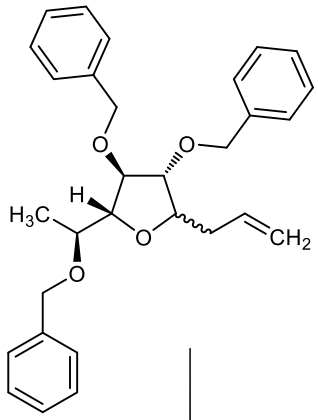
100 MHz

pyridine-d_5



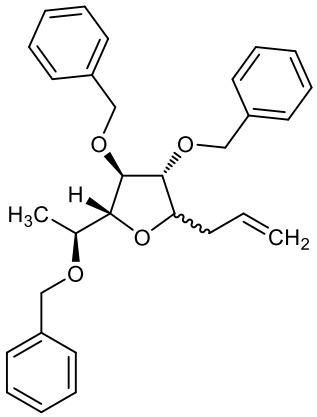
Hederagenin (1'-*O*-methyl-5'-dehydro-α-D-xylopyranos-5'-yl)formacetal (**IVL-106**)

^{1}H NMR
400 MHz
chloroform-d_1



1-Deoxy-1-*C*-allyl-2,3,5-tri-*O*-benzyl-α/β-L-fucofuranose **(5)**

^{13}C NMR (DEPTQ)
100 MHz
chloroform-d_1

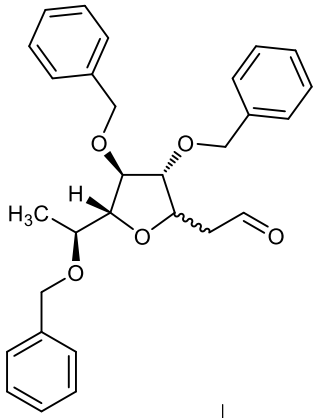


1-Deoxy-1-*C*-allyl-2,3,5-tri-*O*-benzyl-α/β-L-fucofuranose **(5)**

^{1}H NMR

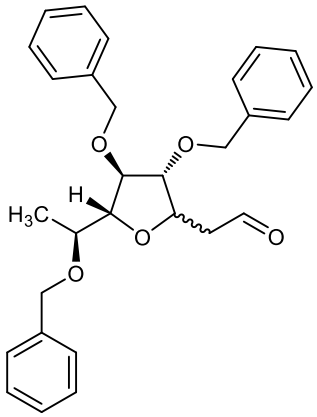
400 MHz

chloroform-d_1



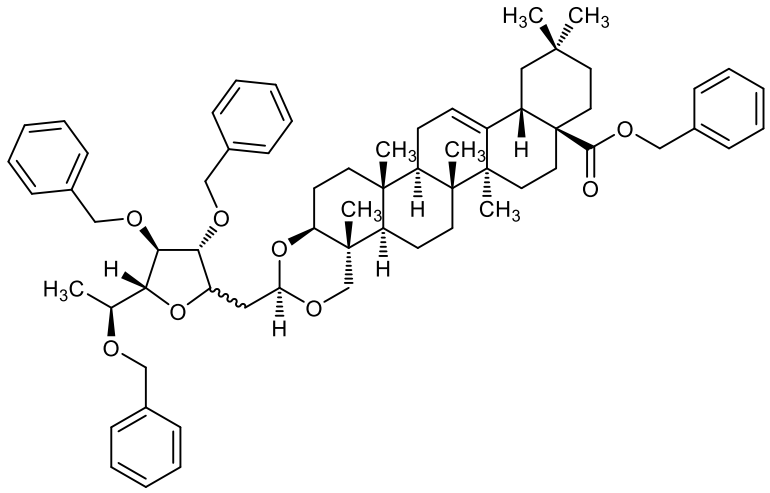
2-(1'-Deoxy-2',3',5'-tri-O-benzyl-α/β-L-fucofuranos-1'-yl)acetaldehyde **(6)**

^{13}C NMR (DEPTQ)
100 MHz
chloroform-d_1



2-(1'-Deoxy-2',3',5'-tri-O-benzyl-α/β-L-fucofuranos-1'-yl)acetaldehyde **(6)**

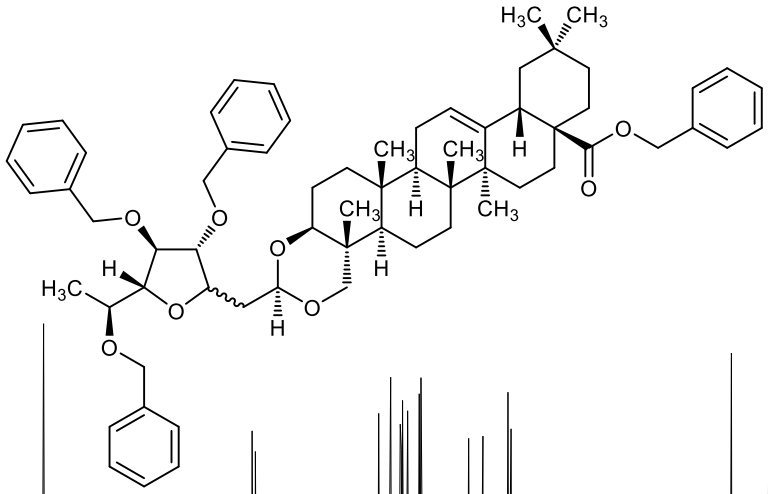
^{1}H NMR
400 MHz
chloroform-d_1



(6)

Benzyl hederagenate 2-(1'-deoxy-2',3',4'-tri-*O*-benzyl-α/β-L-fucofuranos-1'-yl)acetacetal **(7)**

^{13}C NMR (DEPTQ)
100 MHz
chloroform-d_1

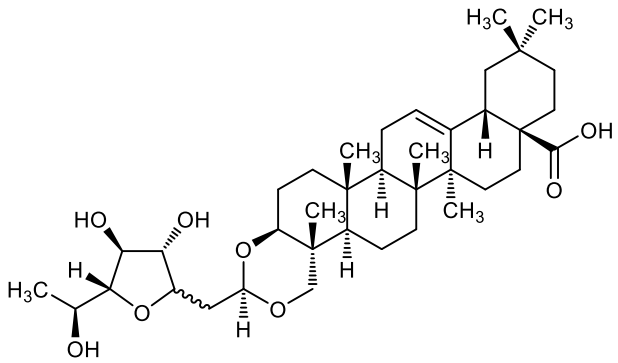


Benzyl hederagenate 2-(1'-deoxy-2',3',4'-tri-*O*-benzyl-α/β-L-fucofuranos-1'-yl)acetacetal **(7)**

^{1}H NMR

400 MHz

pyridine-d_5

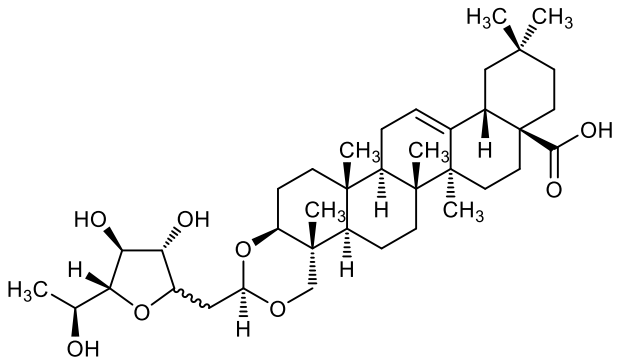


Hederagenin 2-(1'-deoxy-α/β-L-fucofuranos-1'-yl)acetacetal (**IVL-104**)

^{13}C NMR (DEPTQ)

100 MHz

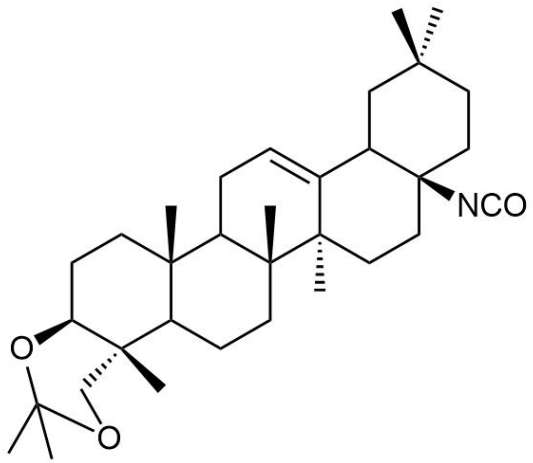
pyridine-d_5



Hederagenin 2-(1'-deoxy-α/β-L-fucofuranos-1'-yl)acetacetal (**IVL-104**)

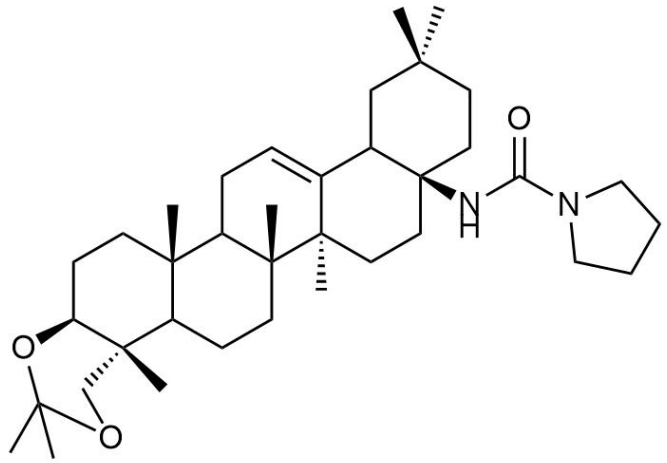
MC-015

proton, 400 MHz, C_6D_6



MC-023

proton, 400 MHz, C_6D_6



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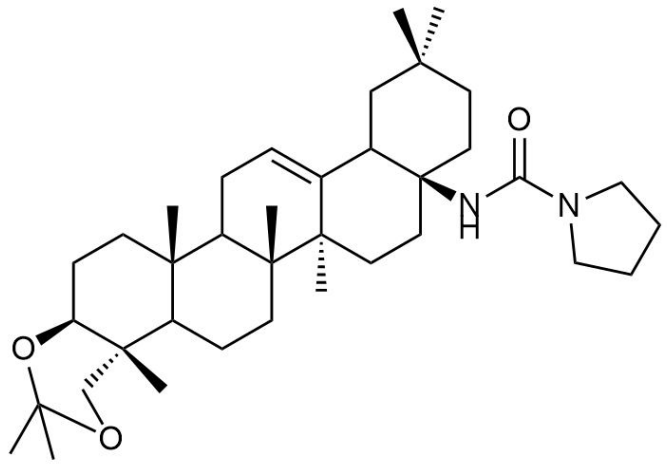
MC-023

DEPTq, 100 MHz, C_6D_6



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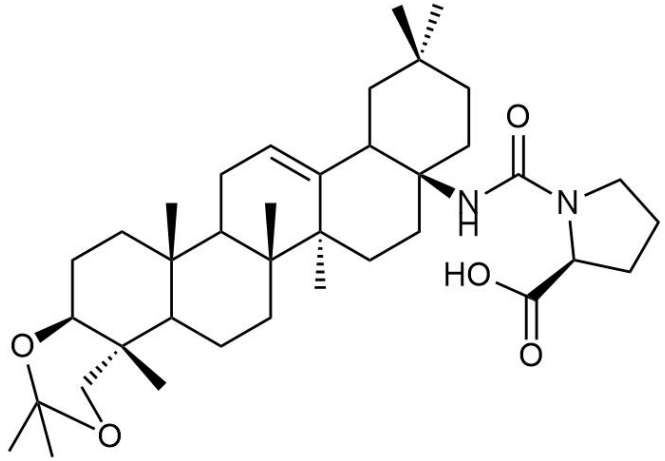
MC-033

proton, 400 MHz, py-d_5



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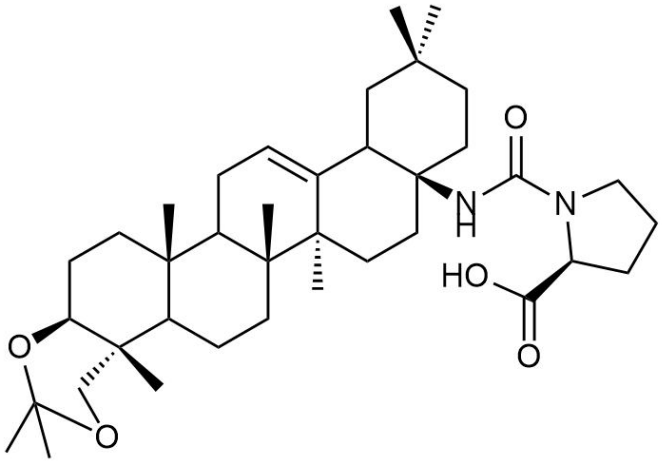
MC-033

DEPTq, 100 MHz, py-d_5



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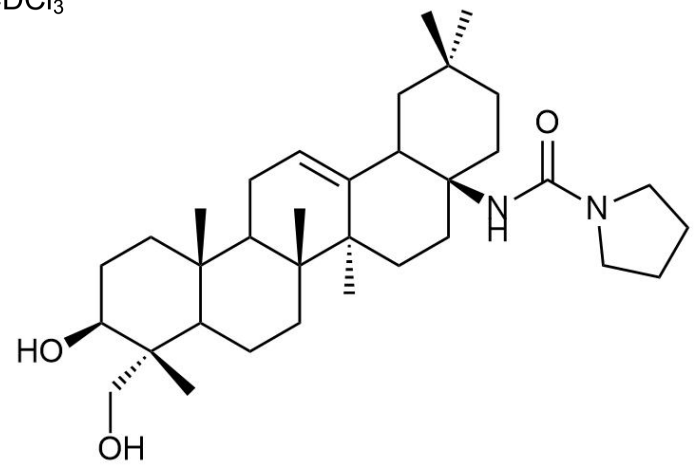
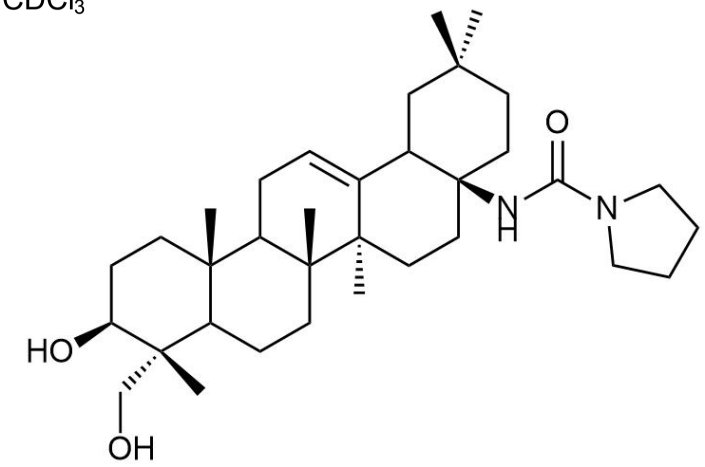
MC-055

proton, 400 MHz, $CDCl_3$



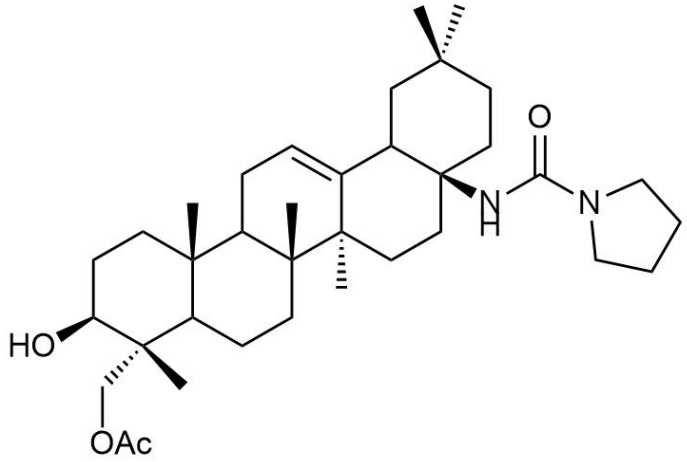
MC-055

DEPTq, 100 MHz, $CDCl_3$



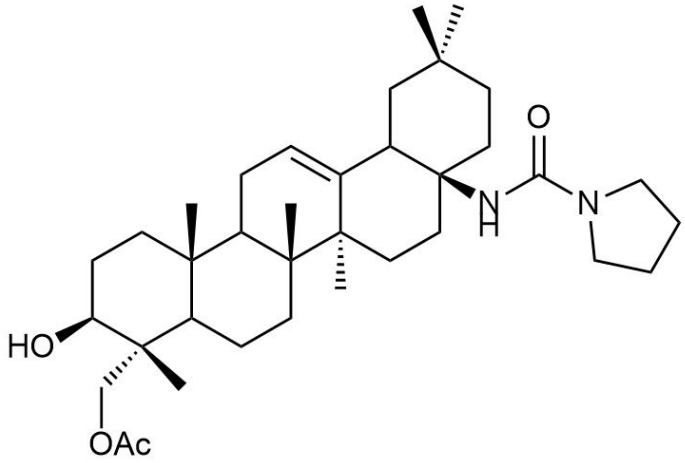
MC-057

proton, 400 MHz, C_6D_6



MC-057

DEPTq, 100 MHz, C_6D_6



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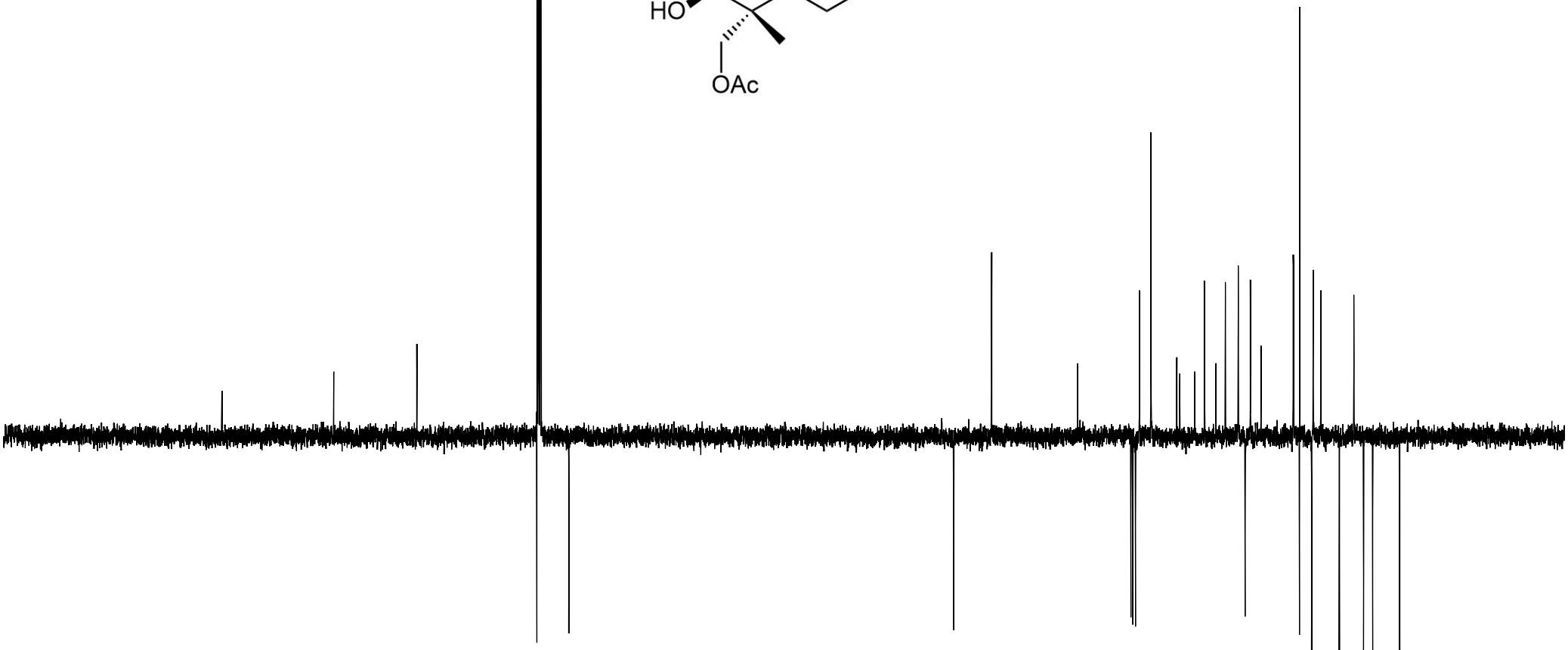
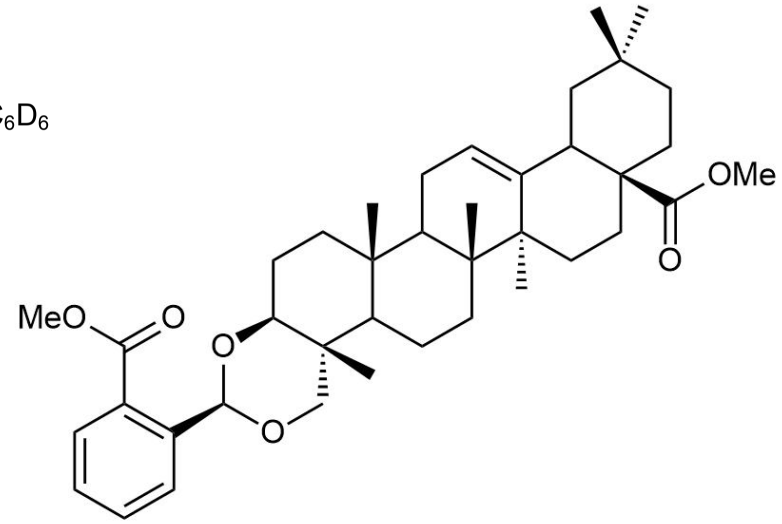


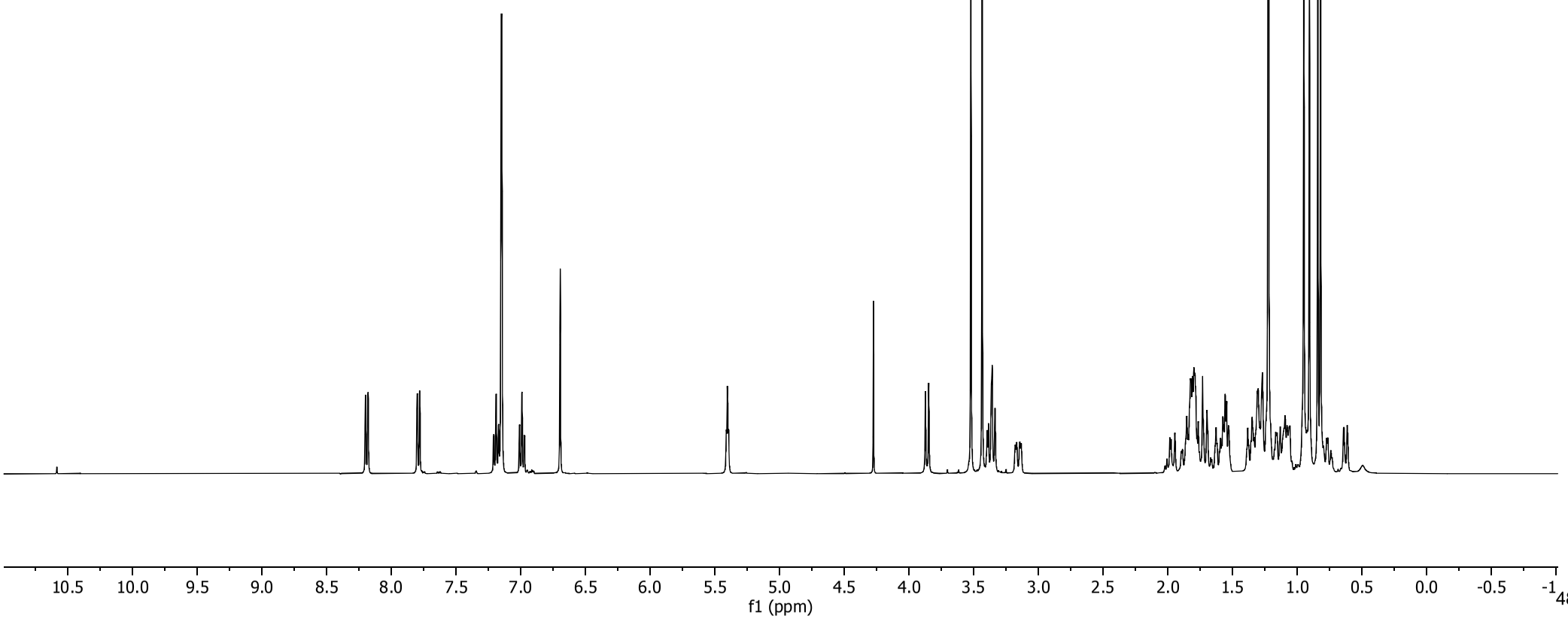
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

f1 (ppm)

MC-070

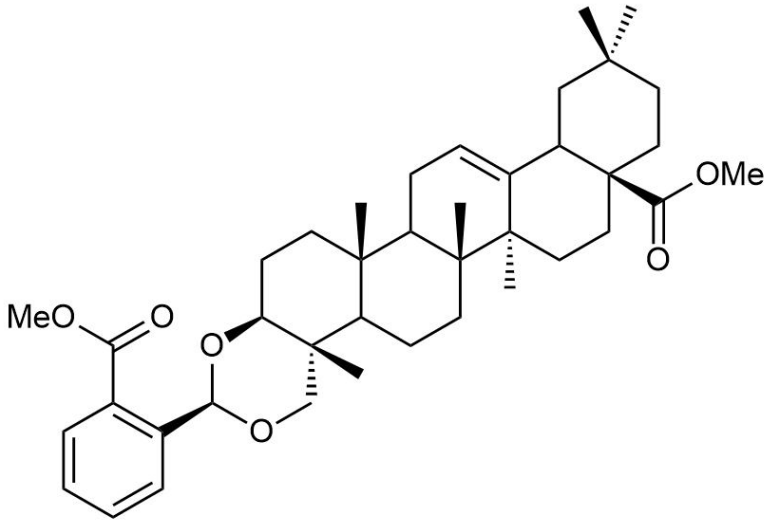
proton, 400 MHz, C_6D_6





MC-070

DEPTq, 100 MHz, C_6D_6



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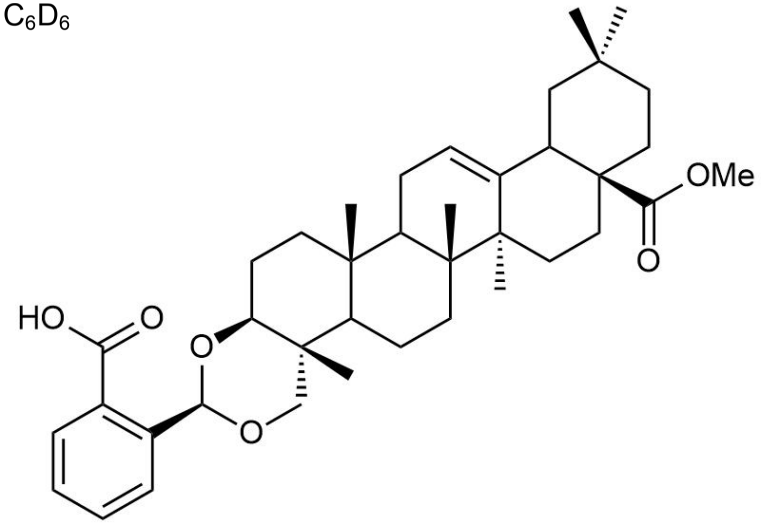
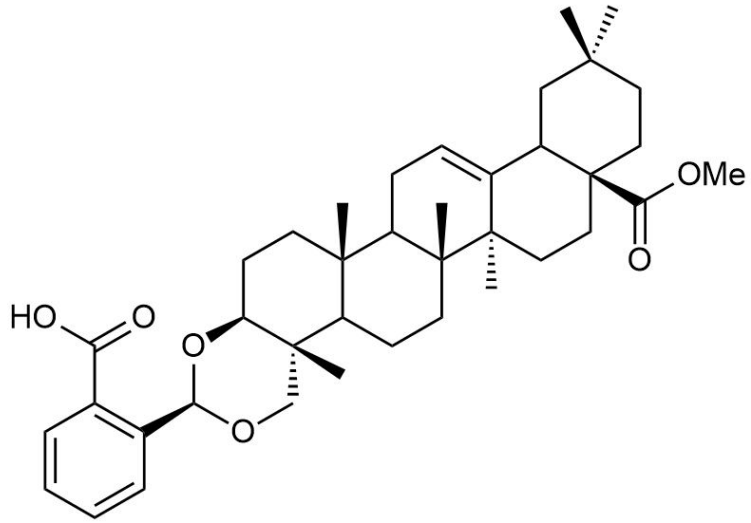
MC-071

proton, 400 MHz, C_6D_6



MC-071

DEPTq, 100 MHz, C_6D_6



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