Electronic supplementary information

Novel antimycobacterial C-21 amide derivatives of the antibiotic fusidic acid: Synthesis, pharmacological evaluation and rationalization of media-dependent activity using molecular docking studies in the binding site of human serum albumin

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1.0 Experimental procedures

All chemicals and reagents were sourced from commercial vendors. Fusidic acid was purchased from AvaChem Scientific. All other reagents (starting materials) were purchased from Sigma-Aldrich or Combi-Blocks. Solvents and reagents used to prepare the mobile phase for LCMS analyses were of HPLC-grade and were obtained Sigma-Aldrich (ammonium acetate as an additive), Merck (glacial acetic acid) and Microsep (acetonitrile and methanol). Bulk solvents used for extraction and purification purposes were obtained from Scienceworld Chemicals and were of CP or AR grade. Reactions were monitored using aluminum silica pre-coated thin layer chromatography (TLC) plates (60 F_{254} from Merck or Al foils 60 Å medium pore diameter from Merck). Visualization of TLC spots were accomplished with the aid of either ultraviolent light (UV) at 245 nm or by using $Ce(SO_4)_2$ stain (15% aqueous sulfuric acid saturated with ceric sulfate). Purification of synthesized compounds was achieved by preparative TLC (Silica gel GF254, 2000 µm on glass from Analtech). Melting points (uncorrected) were determined using a Stuart Automatic Melting Point Apparatus, SMP40 (Bibby Scientific). Low Resolution-ESI-MS was acquired on an Agilent 1260 Infinity HPLC system (Agilent® 1260 Infinity Binary Pump, Agilent® 1260 Infinity Diode Array Detector (DAD), Agilent® 1290 Infinity Column Compartment, and Agilent® 1260 Infinity Standard Auto sampler) coupled to Agilent 6120 Quardrupole MS system and Peak Scientific® Genius 1050 Nitrogen Generator. Phenomenex Kinetex® 2.6 µm EVO C18 100 Å (30 x 2.1 mm) reverse phase analytical column was used. The chromatographic method included a column temperature of 40 ^{o}C, an injection volume of 2 µL, flow rate of 0.7 mL/min and maximum column back pressure set at 600 bars. The mass spectra were acquired using electrospray ionisation (ESI) and/or atmospheric pressure chemical ionization (APCI) in the positive ionization mode. Characterization of synthesized compounds was achieved by analyses of their MS and 1D NMR data. The NMR data was acquired on either a Bruker UltraShield-Plus (400 MHz and 101 MHz for ^{1}H and ^{13}C nuclei, respectively) spectrometer or on a BRUKER Ascend 600 cryoprobe prodigy (600 MHz and 151 MHz for ^{1}H and ^{13}C nuclei, respectively).

2.0 Chemistry

2.0.1 General Synthetic Procedure for compounds 1.1 - 1.22 and 1.24 - 1.28

To a mixture of fusidic acid (**1.0**) (1 eq.) and the respective amine (1.5 eq.) in DCM (1 mL) was added triethylamine (3 eq.) dropwise at 25 ^{o}C. T3P solution (3.0 eq., 50% w/v in EtOAc, d=0.534 g/mL) was added dropwise. The temperature of the reaction mixture was increased to 35 ^{o}C and left to stir until reaction was complete (5 – 24 h depending on amine). The progress of the reaction was followed by TLC and LCMS. On completion, the reaction mixture was diluted with DCM (20 mL) and the by-products were extracted with water (15 mL x2) in a separating funnel. The organic layer was dried with anhydrous sodium sulfate, filtered and concentrated *in vacuo* to obtain the crude product. Further purification was accomplished by normal phase preparative TLC using DCM-EtOAc mixture or DCM-MeOH mixture as eluent depending on the

amine. Bands were detected under UV-254 nm, scraped and extracted with EtOAc or acetone. After extraction of the compounds, the silica was filtered off and the filtrate was concentrated *in vacuo* to obtain the target compounds as amorphous solids.

_N_-((_S_)-1-(phenyl)ethyl)fusidic acid amide (1.1)

White powder (0.080 g obtained from 0.100 g of **1.0**, 65%); *R*f 0.6 (60% EtOAc:DCM); Mp 182-184 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.16 (m, 5H), 5.72 (d, *J* = 7.5 Hz, 1H), 5.67 (d, *J* = 8.2 Hz, 1H), 5.01 (m, 1H), 5.00-4.93 (m, 1H), 4.28 (m, 1H), 3.69 (m, 1H), 2.94 (m, 1H), 2.48-2.37 (m, 1H), 2.35-2.29 (m, 1H), 2.27-2.24 (m, 1H), 2.17-1.97 (m, 5H), 1.90 (s, 3H), 1.85-1.61 (m, 4H), 1.58 (s, 3H), 1.56-1.48 (m, 4H), 1.47 (s, 3H), 1.41 (d, *J* = 6.9 Hz, 3H), 1.33 (s, 3H), 1.30-1.24 (m, 1H), 1.13-0.99 (m, 2H), 0.93 (s, 3H), 0.90 (s, 3H), 0.87 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 170.4, 143.3, 141.2, 135.9, 132.4, 128.7 (2C), 127.4, 126.2 (2C), 123.3, 74.1, 71.4, 68.3, 49.3, 49.1, 48.6, 43.3, 39.5, 39.4, 37.0, 36.3, 36.1, 35.7, 32.3, 30.2, 30.0, 29.6, 28.0, 25.6, 24.0, 22.8, 21.4, 21.1, 20.8, 17.8, 17.7 and 15.9; LC-MS (ESI): *m/z* 642 $[M+Na]^+$, 560 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.11 min.)

_N_-((_R_)-1-(phenyl)ethyl)fusidic acid amide (1.2)

White powder (0.074 g obtained from 0.100 g of **1.0**, 60%); *R*f 0.5 (60% EtOAc:DCM); Mp 181-183 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.18 (m, 5H), 5.79 (d, *J* = 7.6 Hz, 1H), 5.51 (d, *J* = 8.0 Hz, 1H), 5.09 (m, 1H), 5.03 (m, 1H), 4.31 (m, 1H), 3.72 (m, 1H), 2.97 (m, 1H), 2.56-2.43 (m, 1H), 2.38-2.31 (m, 1H), 2.30-2.22 (m, 1H), 2.18-2.00 (m, 5H), 1.78 (s, 3H), 1.85-1.61 (m, 4H), 1.66 (s, 3H), 1.58 (s, 3H), 1.56-1.48 (m, 4H), 1.48 (d, *J* = 6.9 Hz, 3H), 1.34 (s, 3H), 1.30-1.24 (m, 1H), 1.15-1.00 (m, 2H), 0.96 (s, 3H), 0.92-0.88 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 170.3, 142.8, 141.4, 135.8, 132.5, 128.8 (2C), 127.5, 126.4 (2C), 123.4, 74.5, 71.4, 68.3, 49.3, 49.1, 48.5, 43.2, 39.6, 37.0, 36.3, 36.1, 35.8, 32.3, 30.2, 30.0, 29.8, 28.1, 25.7, 24.0, 22.8, 21.8, 21.0, 20.8, 18.0, 17.8 and 15.9; LC-MS (ESI): *m/z* 642 $[M+Na]^+$, 560 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.07 min.)

_N_-((_S_)-1-(4-fluorophenyl)ethyl)fusidic acid amide (1.3)

White powder (0.032 g obtained from 0.100 g of **1.0**, 25%); *R*f 0.6 (60% EtOAc:DCM); Mp 171-173 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.23 (m, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 5.71 (d, *J* = 8.1 Hz, 1H), 5.65 (d, *J* = 7.5 Hz, 1H), 5.02 (m, 1H), 5.00-4.94 (m, 1H), 4.32 (m, 1H), 3.74 (m, 1H), 2.98 (m, 1H), 2.53-2.40 (m, 1H), 2.36-2.29 (m, 1H), 2.30-2.23 (m, 1H), 2.21-1.96 (m, 5H), 1.96 (s, 3H), 1.89-1.64 (m, 4H), 1.62 (s, 3H), 1.60-1.52 (m, 4H), 1.50 (s, 3H), 1.43 (d, *J* = 6.9 Hz, 3H), 1.36 (s, 3H), 1.30-1.24 (m, 1H), 1.15-1.00 (m, 2H), 0.96 (s, 3H), 0.93 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 170.3, 162.0 (d, *J* = 245.6 Hz), 141.3, 139.2 (d, *J* = 3.2 Hz), 135.8, 132.5, 127.8 (d, *J* = 8.0 Hz), 123.2, 115.4 (d, *J* = 21.4 Hz), 74.0, 71.4, 68.3, 49.3, 48.6, 48.4, 43.3, 39.5, 39.4, 37.1, 36.2 (2C), 35.7, 32.4, 30.3, 30.0, 29.6, 27.9, 25.6, 24.1, 22.7, 21.4, 21.1, 20.8, 17.9, 17.7 and 15.9; LC-MS (ESI): *m/z* 578 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.22 min.)

_N_-((_R_)-1-(4-fluorophenyl)ethyl)fusidic acid amide (1.4)

White powder (0.026 g obtained from 0.100 g of **1.0**, 20%); *R*f 0.5 (60% EtOAc:DCM); Mp 182-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.23 (m, 2H), 7.05-6.99 (t, *J* = 8.7 Hz, 2H), 5.68 (d, *J* = 7.5 Hz, 1H), 5.52 (d, *J* = 8.0 Hz, 1H), 5.08 (m, 1H), 5.00 (dq, *J* = 6.9, 7.0 Hz, 1H), 4.31 (m, 1H), 3.73 (m, 1H), 2.97 (m, 1H), 2.53-2.43 (m, 1H), 2.38-2.29 (m, 1H), 2.30-2.23 (m, 1H), 2.21-2.03 (m, 5H), 1.80 (s, 3H), 1.89-1.61 (m, 4H), 1.66 (s, 3H), 1.58 (s, 3H), 1.56-1.48 (m, 4H), 1.46 (d, *J* = 6.9 Hz, 3H), 1.34 (s, 3H), 1.30-1.24 (m, 1H), 1.15-1.00 (m, 2H), 0.96 (s, 3H), 0.93-0.88 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 170.3, 162.0 (d, *J* = 245.6 Hz), 141.5, 138.6 (d, *J* = 3.2 Hz), 135.8, 132.5, 128.1 (d, *J* = 8.0 Hz), 123.3, 115.5 (d, *J* = 21.3 Hz), 74.0, 71.4, 68.3, 49.3, 48.6, 48.5, 43.2, 39.6, 39.3, 37.1, 36.2 (2C), 35.7, 32.5, 30.3, 30.0, 29.8, 28.1, 25.7, 24.1, 22.7, 21.4, 21.1, 20.8, 17.9, 17.7 and 15.9; LC-MS (ESI): *m/z* 578 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.21 min.)

***N*-((*S*)-1-(2-chlorophenyl)ethyl)fusidic acid amide (1.5)**

White powder (0.043 g obtained from 0.100 g of 1.0, 33%); *R*f 0.6 (60% EtOAc:DCM); Mp 237-239 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.13 (m, 4H), 5.81 (d, *J* = 7.0 Hz, 1H), 5.75 (d, *J* = 8.2 Hz, 1H), 5.31-5.21 (m, 1H), 5.04 (m, 1H), 4.33 (m, 1H), 3.75 (m, 1H), 3.00 (m, 1H), 2.50-2.40 (m, 1H), 2.36-2.28 (m, 1H), 2.27-2.23 (m, 1H), 2.22-2.00 (m, 5H), 1.99 (s, 3H), 1.91-1.66 (m, 4H), 1.63 (s, 3H), 1.64-1.55 (m, 4H), 1.52 (s, 3H), 1.46 (d, *J* = 6.9 Hz, 3H), 1.38 (s, 3H), 1.30-1.24 (m, 1H), 1.20-1.05 (m, 2H), 0.97 (s, 3H), 0.91-0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 170.1, 141.3, 140.6, 135.8, 132.8, 132.4, 130.2, 128.5, 127.3, 127.2, 123.3, 73.9, 71.4, 68.4, 49.3, 48.6, 47.4, 43.3, 39.5, 39.4, 37.1, 36.3, 36.2, 35.6, 32.6, 30.4, 30.0, 29.7, 27.9, 25.6, 24.2, 22.7, 21.1, 20.7, 20.5, 17.9, 17.7 and 15.9; LC-MS (ESI): *m/z* 594 [M-OAc]+; purity (LC-MS): 98% (t_R = 3.25 min.)

***N*-((*R*)-1-(2-chlorophenyl)ethyl)fusidic acid amide (1.6)**

White powder (0.011 g obtained from 0.100 g of 1.0, 8%); *R*f 0.5 (60% EtOAc:DCM); Mp 178-180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 1.7, 7.3 Hz, 1H), 7.28-7.17 (m, 3H), 6.10 (d, *J* = 8.4 Hz, 1H), 5.51 (d, *J* = 8.1 Hz, 1H), 5.48-5.38 (m, 1H), 5.10 (m, 1H), 4.33 (m, 1H), 3.74 (m, 1H), 2.99 (m, 1H), 2.55-2.46 (m, 1H), 2.40-2.32 (m, 1H), 2.31-2.24 (m, 1H), 2.21-2.00 (m, 5H), 1.90-1.70 (m, 4H), 1.68 (s, 3H), 1.67 (s, 3H), 1.60-1.52 (m, 4H), 1.59 (s, 3H), 1.48 (d, *J* = 6.9 Hz, 3H), 1.36 (s, 3H), 1.30-1.24 (m, 1H), 1.15-1.00 (m, 2H), 0.96 (s, 3H), 0.91-0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 170.1, 141.5, 140.1, 135.7, 132.6, 132.4, 130.4, 128.6, 128.1, 127.3, 123.4, 74.4, 71.4, 68.4, 49.3, 48.5, 47.5, 43.1, 39.5, 39.3, 37.1, 36.2 (2C), 35.8, 32.4, 30.3, 30.0, 29.8, 28.2, 25.7, 24.1, 22.7, 21.4, 20.8 (2C), 18.0, 17.8 and 15.9; LC-MS (ESI): *m/z* 594 [M-OAc]+; purity (LC-MS): 98% (t_R = 3.26 min.)

***N*-((*R*)-2-(phenyl)methylacetyl)fusidic acid amide (1.7)**

White powder (0.006 g obtained from 0.050 g of **1.0**, 9%); *R*f 0.6 (60% EtOAc:DCM); Mp 238-240 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.27 (m, 5H), 6.59 (d, *J* = 7.5 Hz, 1H), 5.73 (d, *J* = 8.0 Hz, 1H), 5.50 (d, *J* =7.3 Hz, 1H), 5.06 (m, 1H), 4.33 (m, 1H), 3.75 (s, 3H), 3.71 (m, 1H), 3.02 (m, 1H), 2.54-2.44 (m, 1H), 2.39-2.30 (m, 1H), 2.29-2.23 (m, 1H), 2.21-2.00 (m, 5H), 1.84 (s, 3H), 1.85-1.65 (m, 4H), 1.64 (s, 3H), 1.61-1.54 (m, 4H), 1.53 (s, 3H), 1.37 (s, 3H), 1.35-1.24 (m, 1H), 1.18-0.99 (m, 2H), 0.97 (s, 3H), 0.93 (s, 3H), 0.92 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

171.0, 170.5, 170.1, 142.8, 136.8, 135.1, 132.5, 128.9 (2C), 128.4, 127.1 (2C), 123.2, 73.9, 71.4, 68.4, 56.2, 52.9, 49.3, 48.7, 43.4, 39.6, 39.3, 37.1, 36.3, 36.1, 35.7, 32.5, 30.3, 30.0, 29.5, 27.9, 25.6, 24.2, 22.6, 20.8, 20.7, 18.0, 17.7 and 15.9; LC-MS (ESI): *m/z* 604 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.21 min.)

***N*-((*R*)-2-(phenyl)acetamido)fusidic acid amide (1.8)**

White powder (0.022 g obtained from 0.100 g of **1.0**, 17%); *R*f 0.4 (EtOAc); Mp 181-183 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.28 (m, 5H), 6.95 (d, *J* = 6.8 Hz, 1H), 5.77 (d, *J* = 7.9 Hz, 1H), 5.39 (d, *J* =6.8 Hz, 1H), 5.05 (m, 1H), 4.32 (m, 1H), 3.74 (m, 1H), 3.02 (m, 1H), 2.53-2.41 (m, 1H), 2.39-2.30 (m, 1H), 2.32-2.22 (m, 1H), 2.20-1.99 (m, 5H), 1.79 (s, 3H), 1.88-1.63 (m, 4H), 1.64 (s, 3H), 1.62-1.54 (m, 4H), 1.51 (s, 3H), 1.37 (s, 3H), 1.35-1.24 (m, 1H), 1.16-1.01 (m, 2H), 0.97 (s, 3H), 0.93 (s, 3H), 0.92 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 170.5, 170.2, 142.9, 138.1, 135.2, 132.5, 129.1 (2C), 128.4, 127.4 (2C), 123.2, 74.1, 71.4, 68.4, 56.8, 49.3, 48.7, 43.5, 39.6, 39.3, 37.1, 36.3, 36.2, 35.7, 32.5, 30.3, 30.0, 29.6, 27.9, 25.6, 24.1, 22.6, 20.9, 20.7, 18.1, 17.7 and 15.9; LC-MS (ESI): *m/z* 589 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.10 min.)

***N*-(1-(4-methylphenyl)ethyl)fusidic acid amide (1.9)**

White powder (0.073 g obtained from 0.100 g of **1.0**, 58%); *R*f 0.5, 0.6 (60% EtOAc:DCM); a 2:1 mixture of diastereomers; **Major produc**t: ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 5.75 (m, 1H), 5.50 (d, *J* = 8.0 Hz, 1H), 5.08 (m, 1H), 4.97 (m, 1H), 4.30 (m, 1H), 3.70 (m, 1H), 2.95 (m, 1H), 2.56-2.46 (m, 1H), 2.42-2.34 (m, 1H), 2.32 (s, 3H), 2.30-2.22 (m, 1H), 2.20-2.00 (m, 5H), 1.81 (s, 3H), 1.91-1.67 (m, 4H), 1.65 (s, 3H), 1.62-1.45 (m, 4H), 1.57 (s, 3H), 1.45 (d, *J* = 6.8 Hz, 3H), 1.33 (s, 3H), 1.28-1.23 (m, 1H), 1.16-1.01 (m, 2H), 0.95 (s, 3H), 0.92-0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 170.3, 141.3, 139.7, 137.1, 135.9, 132.4, 129.4 (2C), 126.3 (2C), 123.4, 74.5, 71.4, 68.3, 49.4, 48.9, 48.5, 43.2, 39.6, 39.3, 37.0, 36.4, 36.0, 35.8, 32.2, 30.2, 30.0, 29.8, 28.1, 25.7, 23.8, 22.9, 21.7, 21.0 (2C), 20.9, 18.0, 17.8 and 15.9; **Minor product**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 5.68 (m, 1H), 5.50 (d, *J* = 8.0 Hz, 1H), 5.08 (m, 1H), 4.97 (m, 1H), 4.30 (m, 1H), 3.70 (m, 1H), 2.95 (m, 1H), 2.56-2.46 (m, 1H), 2.42-2.34 (m, 1H), 2.30 (s, 3H), 2.30-2.22 (m, 1H), 2.20-2.00 (m, 5H), 1.92 (s, 3H), 1.91-1.67 (m, 4H), 1.61 (s, 3H), 1.62-1.45 (m, 4H), 1.50 (s, 3H), 1.42 (d, *J* = 6.9 Hz, 3H), 1.35 (s, 3H), 1.28-1.23 (m, 1H), 1.16-1.01 (m, 2H), 0.95 (s, 3H), 0.92-0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 170.3, 141.1, 140.3, 137.0, 135.9, 132.3, 129.3 (2C), 126.1 (2C), 123.4, 74.1, 71.4, 68.3, 49.4, 48.8, 48.6, 43.3, 39.5, 39.3, 37.0, 36.4, 36.0, 35.7, 32.2, 30.2, 30.0, 29.7, 28.0, 25.6, 23.9, 22.9, 21.4, 21.1, 21.0, 20.8, 17.8, 17.7 and 15.9; LC-MS (ESI): *m/z* 574 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.30 min.)

***N*-(1-(4-fluorophenyl)ethyl)fusidic acid amide (1.10)**

White powder (0.051 g obtained from 0.100 g of **1.0**, 40%); *R*f 0.5 (60% EtOAc:DCM); a 3:2 mixture of diastereomers; **Major produc**t: ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.20 (m, 2H), 7.07-6.94 (m, 2H), 5.74 (d, *J* = 7.6 Hz, 1H), 5.51 (d, *J* = 8.0 Hz, 1H), 5.08 (m, 1H), 5.05-4.93 (m, 1H), 4.31 (m, 1H), 3.72 (m, 1H), 2.97 (m, 1H), 2.55-2.44 (m, 1H), 2.40-2.31 (m, 1H), 2.29-2.20 (m, 1H),

2.18-2.00 (m, 5H), 1.89-1.67 (m, 4H), 1.79 (s, 3H), 1.66 (s, 3H), 1.62-1.45 (m, 4H), 1.57 (s, 3H), 1.45 (d, *J* = 6.8 Hz, 3H), 1.33 (s, 3H), 1.28-1.23 (m, 1H), 1.16-1.01 (m, 2H), 0.95 (s, 3H), 0.92-0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 170.3, 162.1 (d, *J* = 245.7 Hz), 141.5, 138.6 (d, *J* = 3.1 Hz), 135.7, 132.5, 128.1 (d, *J* = 8.1 Hz), 123.3, 115.5 (d, *J* = 21.4 Hz), 74.3, 71.4, 68.3, 49.3, 48.6, 48.4, 43.2, 39.5, 39.3, 37.0, 36.3 (2C), 35.7, 32.3, 30.2, 30.0, 29.7, 28.1, 25.7, 24.0, 22.8, 21.9, 21.0, 20.8, 18.0, 17.8 and 15.9; **Minor produc**t: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.20 (m, 2H), 7.07-6.94 (m, 2H), 5.71 (d, *J* = 7.6 Hz, 1H), 5.70 (d, *J* = 8.0 Hz, 1H), 5.08 (m, 1H), 5.05-4.93 (m, 1H), 4.31 (m, 1H), 3.72 (m, 1H), 2.97 (m, 1H), 2.52-2.38 (m, 1H), 2.36-2.31 (m, 1H), 2.29-2.20 (m, 1H), 2.18-2.00 (m, 5H), 1.95 (s, 3H), 1.89-1.67 (m, 4H), 1.61 (s, 3H), 1.62-1.45 (m, 4H), 1.49 (s, 3H), 1.42 (d, *J* = 6.8 Hz, 3H), 1.35 (s, 3H), 1.28-1.23 (m, 1H), 1.16-1.01 (m, 2H), 0.95 (s, 3H), 0.92-0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 170.3, 162.0 (d, *J* = 245.7 Hz), 141.2, 139.2 (d, *J* = 3.2 Hz), 135.7, 132.4, 127.8 (d, *J* = 8.0 Hz), 123.2, 115.4 (d, *J* = 21.4 Hz), 74.0, 71.4, 68.3, 49.3, 48.6, 48.4, 43.3, 39.5, 39.4, 37.0, 36.0 (2C), 35.6, 31.9, 30.2, 30.0, 29.7, 27.9, 25.6, 24.0, 22.8, 21.4, 21.1, 20.8, 17.8, 17.7 and 15.9; LC-MS (ESI): *m/z* 578 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.25 min.)

***N*-(1-(3,4-dichlorophenyl)ethyl)fusidic acid amide (1.11)**

White powder (0.034 g obtained from 0.100 g of **1.0**, 25%); *R*f 0.6 (60% EtOAc:DCM); a 1:1 mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 2.2 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.37 (d, *J* = 2.2 Hz, 1H), 7.16-7.11 (m, 2H), 5.75-5.66 (m, 3H), 5.54 (d, *J* = 8.0 Hz, 1H), 5.09 (m, 1H), 5.03 (m, 1H), 5.00-4.94 (m, 1H), 4.94-4.87 (m, 1H), 4.32 (m, 2H), 3.74 (m, 2H), 2.98 (m, 2H), 2.53-2.40 (m, 2H), 2.36-2.29 (m, 2H), 2.30-2.23 (m, 2H), 2.21-1.96 (m, 10H), 1.98 (s, 3H), 1.89-1.64 (m, 8H), 1.80 (s, 3H), 1.67 (s, 3H), 1.63 (s, 3H), 1.60-1.52 (m, 8H), 1.58 (s, 3H), 1.51 (s, 3H), 1.44 (d, *J* = 6.9 Hz, 3H), 1.41 (d, *J* = 7.0 Hz, 3H), 1.37 (s, 3H), 1.34 (s, 3H), 1.30-1.24 (m, 2H), 1.15-1.00 (m, 4H), 0.97 (s, 3H), 0.96 (s, 3H), 0.94 (s, 3H), 0.95-0.86 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 170.4, 170.3, 170.2, 143.9, 143.2, 142.0, 141.6, 135.5 (2C), 132.7 (2C) 132.6 (2C), 131.5, 131.2, 130.8, 130.6, 128.5, 128.1, 126.0, 125.7, 123.2, 123.1, 74.3, 73.8, 71.4 (2C), 68.3 (2C), 49.3 (2C), 48.6 (2C) 48.2, 48.1, 43.4, 43.3, 39.6, 39.5, 39.4, 39.3, 37.1 (2C), 36.2 (3C), 36.1, 35.7, 35.6, 32.5 (2C), 30.3 (2C), 30.0 (2C), 29.7 (2C), 28.1, 27.9, 25.7, 25.6, 24.1 (2C), 22.7, 22.6, 21.7, 21.3, 21.1, 21.0, 20.7 (2C), 18.1, 17.8, 17.8, 17.7 and 15.9 (2C); LC-MS (ESI): *m/z* 628 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.31 min.)

***N*-(1-(3-pyridinyl)ethyl)fusidic acid amide (1.12)**

White powder (0.028 g obtained from 0.050 g of **1.0**, 48%); *R*f 0.3 (EtOAc); a 1:1 mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72-8.45 (m, 4H), 7.75-7.67 (m, 2H), 7.39-7.33 (m, 1H), 7.32-7.27 (m, 1H), 6.24 (d, *J* = 7.6 Hz, 1H), 6.14 (d, *J* = 7.6 Hz, 1H), 5.74 (d, *J* = 8.2 Hz, 1H), 5.53 (d, *J* = 8.2 Hz, 1H), 5.14-4.97 (m, 4H), 4.31 (m, 2H), 3.72 (m, 2H), 2.95 (m, 2H), 2.53-2.40 (m, 2H), 2.39-2.30 (m, 2H), 2.33-2.23 (m, 2H), 2.23-1.96 (m, 10H), 1.97 (s, 3H), 1.89-1.64 (m, 8H), 1.74 (s, 3H), 1.65 (s, 3H), 1.60 (s, 3H), 1.57 (s, 3H), 1.59-1.53 (m, 8H), 1.48 (s, 3H), 1.53-1.49 (m, 6H), 1.34 (s, 3H), 1.32 (s, 3H), 1.30-1.24 (m, 2H), 1.18-1.04 (m, 4H), 0.96 (s, 6H), 0.95 (s, 3H), 0.94-0.90 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 170.7, 170.5, 170.3, 147.7, 147.5, 147.2,

147.1, 141.9, 141.7, 135.7, 135.3 (2C), 135.0, 132.6, 132.5, 124.1, 123.8, 123.3 (2C), 123.2 (2C), 74.3, 73.9, 71.3 (2C), 68.3 (2C), 49.4, 49.3, 48.6, 48.5, 47.0, 46.9, 43.4, 43.3, 39.5 (2C), 39.4, 39.3, 37.0 (2C), 36.3 (2C), 36.1, 36.0, 35.7, 35.6, 32.3, 32.2, 30.2 (2C), 30.0 (2C), 29.7 (2C), 28.1, 28.0, 25.7, 25.6, 24.0, 23.9, 22.9 (2C), 21.7, 21.1 (2C), 20.9, 20.8 (2C), 17.9, 17.8 (2C), 17.7 and 15.9 (2C); LC-MS (ESI): *m/z* 644 $[M+H+Na]^+$, 561 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.06 min.)

N-(1-(4-pyridinyl)ethyl)fusidic acid amide (1.13)

White powder (0.028 g obtained from 0.050 g of **1.0**, 48%); *R*f 0.5 (EtOAc); a 1:1 mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61-8.52 (m, 4H), 7.37-7.30 (m, 4H), 6.29-6.18 (m, 2H), 5.77 (d, *J* = 8.2 Hz, 1H), 5.58 (d, *J* = 8.0 Hz, 1H), 5.11-5.00 (m, 3H), 4.98-4.88 (m, 1H), 4.32 (m, 2H), 3.73 (m, 2H), 2.98 (m, 2H), 2.50-2.38 (m, 2H), 2.39-2.30 (m, 2H), 2.33-2.23 (m, 2H), 2.23-1.96 (m, 10H), 1.98 (s, 3H), 1.88-1.68 (m, 8H), 1.73 (s, 3H), 1.66 (s, 3H), 1.63 (s, 3H), 1.58 (s, 3H), 1.59-1.53 (m, 8H), 1.51 (s, 3H), 1.46 (d, *J* = 7.0 Hz, 3H), 1.44 (d, *J* = 7.0 Hz, 3H), 1.34 (s, 3H), 1.33 (s, 3H), 1.30-1.24 (m, 2H), 1.16-1.02 (m, 4H), 0.98 (s, 6H), 0.95 (s, 3H), 0.94-0.87 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 170.8, 170.6, 170.5, 154.6, 154.0, 148.5 (2C), 142.0 (2C), 135.2, 135.1, 132.6 (2C), 132.5, 123.3 (2C), 123.2 (2C), 122.2 (2C), 121.8., 74.5, 73.8, 71.3 (2C), 68.3, 68.2, 49.4, 49.3, 48.6, 48.5, 47.0, 46.9, 43.4, 43.3, 39.5 (2C), 39.4, 39.3, 37.0 (2C), 36.3 (2C), 36.1, 36.0, 35.7, 35.6, 32.3, 32.2, 30.2 (2C), 30.0 (2C), 29.7 (2C), 28.1, 28.0, 25.7, 25.6, 24.0, 23.9, 22.9 (2C), 21.7, 21.1 (2C), 20.9, 20.8 (2C), 17.9, 17.8 (2C), 17.7 and 15.9 (2C); LC-MS (ESI): *m/z* 644 $[M+H+Na]^+$, 561 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.06 min.)

***N*-(1-(pyrazin-2-yl)ethyl)fusidic acid amide (1.14)**

White powder (0.047 g obtained from 0.100 g of **1.0**, 40%); *R*f 0.3 (EtOAc); a 3:2 mixture of diastereomers; **Major produc**t: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62-8.43 (m, 3H), 6.80 (d, *J* = 8.2 Hz, 1H), 5.47 (d, *J* = 8.2 Hz, 1H), 5.23 (m, 1H), 5.11 (m, 1H), 4.32 (m, 1H), 3.73 (m, 1H), 2.99 (m, 1H), 2.55-2.40 (m, 1H), 2.41-2.32 (m, 1H), 2.32-2.22 (m, 1H), 2.21-1.93 (m, 5H), 1.89-1.67 (m, 4H), 1.77 (s, 3H), 1.59 (s, 3H), 1.60-1.48 (m, 4H), 1.50-1.42 (m, 6H), 1.35 (s, 3H), 1.21-1.15 (m, 1H), 1.15-1.00 (m, 2H), 0.95 (s, 3H), 0.95-0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 170.0, 156.1, 143.7, 143.3, 143.1, 141.7, 135.5, 132.4, 123.4, 74.0, 71.3, 68.3, 49.3, 48.5, 47.1, 43.2, 39.5, 39.2, 37.1, 36.3, 36.1, 35.7, 32.3, 30.3, 30.0, 29.5, 28.0, 25.7, 24.0, 22.8, 20.8 (2C), 20.7, 17.9, 17.8 and 15.9; **Minor produc**t: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62-8.43 (m, 3H), 6.56 (d, *J* = 7.6 Hz, 1H), 5.74 (d, *J* = 8.2 Hz, 1H), 5.15 (m, 1H), 5.02 (m, 1H), 4.32 (m, 1H), 3.73 (m, 1H), 2.99 (m, 1H), 2.55-2.40 (m, 1H), 2.41-2.32 (m, 1H), 2.32-2.22 (m, 1H), 2.21-1.93 (m, 5H), 1.96 (s, 3H), 1.89-1.67 (m, 4H), 1.66 (s, 3H), 1.60-1.48 (m, 4H), 1.50-1.42 (m, 6H), 1.37 (s, 3H), 1.33-1.27 (m, 1H), 1.15-1.00 (m, 2H), 0.96 (s, 3H), 0.95-0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 170.7, 157.0, 143.9, 143.7, 143.3, 141.7, 135.5, 132.3, 123.3, 74.1, 71.3, 68.3, 49.3, 48.6, 47.7, 43.4, 39.5, 39.4, 37.1, 36.3, 36.1, 35.7, 32.4, 30.3, 30.0, 29.5, 27.9, 25.6, 24.0, 22.8, 21.5, 21.2, 20.8, 17.8, 17.7 and 15.9; LC-MS (ESI): *m/z* 644 $[M+Na]^+$, 562 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.10 min.)

***N*-(1-(phenyl)cyclopropyl)fusidic acid amide (1.15)**

White powder (0.017 g obtained from 0.050 g of **1.0**, 28%); *R*f 0.6 (60% EtOAc:DCM); Mp 199-201 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.31 (m, 2H), 7.29-7.23 (m, 2H), 7.21-7.15 (m, 1H), 6.13 (s, 1H), 5.59 (d, *J* = 7.8 Hz, 1H), , 5.07 (m, 1H), 5.00-4.94 (m, 1H), 4.32 (m, 1H), 3.74 (m, 1H), 2.98 (m, 1H), 2.53-2.40 (m, 1H), 2.36-2.29 (m, 1H), 2.30-2.23 (m, 1H), 2.21-1.96 (m, 5H), 1.86-1.69 (m, 4H), 1.80 (s, 3H), 1.66 (s, 3H), 1.62-1.47 (m, 4H), 1.55 (s, 3H), 1.36 (s, 3H), 1.34-1.00 (m, 3H), 0.97 (s, 3H), 0.94-0.78 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 170.7, 142.4, 141.3, 136.3, 132.5, 128.4 (2C), 126.8 (2C), 126.7, 123.3, 74.3, 71.4, 68.4, 49.2, 48.5, 43.4, 39.5, 39.4, 37.2, 36.3, 36.1, 35.7, 35.3, 32.6, 30.4, 30.0, 29.9, 28.1, 25.7, 24.2, 22.6, 21.1, 20.7, 18.1, 17.8, 17.0, 16.2 and 15.9; LC-MS (ESI): *m/z* 572 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.07 min.)

_N_-((_S_)-1-(cyclohexyl)ethyl)fusidic acid amide (1.16)

White powder (0.043 g obtained from 0.100 g of **1.0**, 35%); *R*f 0.6 (60% EtOAc:DCM); Mp 159-161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.58 (d, *J* = 8.1 Hz, 1H),5.28 (d, *J* = 8.8 Hz, 1H), 5.08 (m, 1H), 4.31 (m, 1H), 3.79-3.71 (m, 1H), 3.74 (m, 1H), 2.96 (m, 1H), 2.50-2.40 (m, 1H), 2.36-2.29 (m, 1H), 2.29-2.25 (m, 1H), 2.28-2.00 (m, 5H), 1.99 (s, 3H), 1.91-1.68 (m, 6H), 1.66 (s, 3H), 1.64-1.55 (m, 4H), 1.58 (s, 3H), 1.49 (m, 1H), 1.36 (s, 3H), 1.35 (m, 1H), 1.30-1.24 (m, 1H), 1.23-1.05 (m, 6H), 1.05-0.93 (m, 3H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.95 (s, 3H), 0.92 (s, 3H), 0.89 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 170.5, 140.4, 136.4, 132.3, 123.3, 74.0, 71.4, 68.3, 49.5, 49.3, 48.5, 43.2, 42.9, 39.5, 39.4, 37.0, 36.3, 36.1, 35.6, 32.4, 30.3, 30.0, 29.7, 29.3, 28.6, 28.0, 26.4, 26.2 (2C), 25.7, 24.0, 22.8, 21.3, 20.8, 17.8, 17.8, 16.8 and 15.9; LC-MS (ESI): *m/z* 648 $[M+Na]^+$, 566 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.21 min.)

_N_-((_R_)-1-(cyclohexyl)ethyl)fusidic acid amide (1.17)

White powder (0.026 g obtained from 0.050 g of **1.0**, 43%); *R*f 0.5 (60% EtOAc:DCM); Mp 182-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.58 (d, *J* = 8.1 Hz, 1H),5.28 (d, *J* = 8.8 Hz, 1H), 5.08 (m, 1H), 4.31 (m, 1H), 3.79-3.71 (m, 1H), 3.74 (m, 1H), 2.96 (m, 1H), 2.50-2.40 (m, 1H), 2.36-2.29 (m, 1H), 2.29-2.25 (m, 1H), 2.28-2.00 (m, 5H), 1.99 (s, 3H), 1.91-1.68 (m, 6H), 1.66 (s, 3H), 1.64-1.55 (m, 4H), 1.58 (s, 3H), 1.49 (m, 1H), 1.36 (s, 3H), 1.35 (m, 1H), 1.30-1.24 (m, 1H), 1.24-1.08 (m, 6H), 1.05-0.93 (m, 3H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.95 (s, 3H), 0.92 (s, 3H), 0.89 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 170.5, 141.0, 136.5, 132.4, 123.4, 74.8, 71.4, 68.4, 49.5, 49.3, 48.6, 43.2, 42.7, 39.6, 39.4, 37.1, 36.2 (2C), 35.8, 32.4, 30.3, 30.1, 30.0, 29.6, 28.4, 28.1, 26.4, 26.3, 26.1, 25.7, 24.1, 22.7, 21.3, 20.8, 18.2, 17.8, 17.3 and 15.9; LC-MS (ESI): *m/z* 648 $[M+Na]^+$, 566 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.22 min.)

_N_-(2-methoxyphenyl)fusidic acid amide (1.18)

White powder (0.061 g obtained from 0.250 g of **1.0**, 20%); *R*f 0.6 (60% EtOAc:DCM); Mp 322-324 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 1.7, 7.9 Hz, 1H), 7.75 (s, 1H), 7.01 (td, *J* = 1.7, 7.7 Hz, 1H), 6.92 (td, *J* = 1.4, 7.7 Hz, 1H), 6.85 (dd, *J* = 1.4, 8.0 Hz, 1H), 5.74 (d, *J* = 8.6 Hz, 1H), 5.11 (m, 1H), 4.36 (m, 1H), 3.88 (s, 3H), 3.75 (m, 1H), 3.06 (m, 1H), 2.63-2.51 (m, 1H), 2.45-2.39 (m, 1H), 2.36-2.28 (m, 1H), 2.26-2.05 (m, 5H), 1.93-1.71 (m, 4H), 1.68 (s, 3H), 1.65 (s, 3H), 1.63-1.49 (m, 4H), 1.59 (s, 3H), 1.41 (s, 3H), 1.28-1.22 (m, 1H), 1.17-1.06 (m, 2H), 0.98 (s, 3H), 0.94 (s,

3H), 0.92 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 169.3, 147.8, 142.2, 135.5, 132.5, 127.7, 123.5, 123.3, 121.0, 119.3, 110.0, 73.8, 71.3, 68.4, 55.8, 49.4, 48.5, 43.1, 39.5, 39.4, 37.1, 36.3, 36.2, 35.7, 32.5, 30.3, 30.0, 29.4, 28.1, 25.6, 24.2, 22.8, 20.8, 20.5, 17.8, 17.7 and 15.9; LC-MS (ESI): *m/z* 644 $[M+Na]^+$ 562 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.24 min.)

***N*-(3-methoxyphenyl)fusidic acid amide (1.19)**

White powder (0.058 g obtained from 0.250 g of **1.0**, 19%); *R*f 0.6 (60% EtOAc:DCM); Mp 322-324 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 1.9, 2.4 Hz, 1H), 7.18 (t, *J* = 8.1 Hz, 1H), 7.12 (s, 1H), 6.96 (dd, *J* = 1.9, 7.8 Hz, 1H), 6.64 (dd, *J* = 2.4, 8.2 Hz, 1H), 5.75 (d, *J* = 8.6 Hz, 1H), 5.11 (m, 1H), 4.36 (m, 1H), 3.79 (s, 3H), 3.75 (m, 1H), 3.05 (m, 1H), 2.63-2.51 (m, 1H), 2.47-2.37 (m, 1H), 2.34-2.26 (m, 1H), 2.26-2.05 (m, 5H), 1.91-1.71 (m, 4H), 1.76 (s, 3H), 1.67 (s, 3H), 1.63-1.49 (m, 4H), 1.60 (s, 3H), 1.39 (s, 3H), 1.28-1.22 (m, 1H), 1.17-1.06 (m, 2H), 0.98 (s, 3H), 0.95 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 169.4, 160.1, 142.5, 139.1, 135.3, 132.7, 129.6, 123.2, 111.7, 110.1, 105.2, 73.8, 71.4, 68.3, 55.3, 49.4, 48.7, 43.1, 39.5, 39.3, 37.1, 36.3, 36.2, 35.7, 32.4, 30.3, 30.0, 29.4, 28.1, 25.7, 24.1, 22.8, 20.9, 20.8, 17.9, 17.8 and 15.9; LC-MS (ESI): *m/z* 644 $[M+Na]^+$ 562 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.22 min.)

***N*-(4-methoxyphenyl)fusidic acid amide (1.20)**

White powder (0.062 g obtained from 0.250 g of **1.0**, 21%); *R*f 0.5 (60% EtOAc:DCM); Mp 262-264 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.9 Hz, 2H), 7.08 (s, 1H), 6.83 (d, *J* = 8.9 Hz, 2H), 5.77 (d, *J* = 8.5 Hz, 1H), 5.12 (m, 1H), 4.35 (m, 1H), 3.77 (s, 3H), 3.74 (m, 1H), 3.03 (m, 1H), 2.62-2.51 (m, 1H), 2.50-2.37 (m, 1H), 2.34-2.26 (m, 1H), 2.26-2.07 (m, 5H), 1.91-1.71 (m, 4H), 1.76 (s, 3H), 1.67 (s, 3H), 1.64-1.47 (m, 4H), 1.60 (s, 3H), 1.39 (s, 3H), 1.28-1.22 (m, 1H), 1.17-1.06 (m, 2H), 0.98 (s, 3H), 0.94 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 169.2, 156.3, 142.1, 135.5, 132.6, 131.0, 123.3, 121.3 (2C), 114.1 (2C), 73.8, 71.4, 68.3, 55.4, 49.4, 48.7, 43.1, 39.5, 39.3, 37.1, 36.3, 36.1, 35.7, 32.4, 30.3, 30.0, 29.4, 28.1, 25.7, 24.0, 22.8, 20.9, 20.8, 17.9, 17.8 and 15.9; LC-MS (ESI): *m/z* 644 $[M+Na]^+$ 562 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.22 min.)

***N*-(4-methylphenyl)fusidic acid amide (1.21)**

White powder (0.010 g obtained from 0.050 g of **1.0**, 16%); *R*f 0.6 (60% EtOAc:DCM); Mp 322-324 °C; ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 5.80 (d, *J* = 8.6 Hz, 1H), 5.16 (m, 1H), 4.32 (m, 1H), 3.66 (m, 1H), 3.09 (m, 1H), 2.72-2.63 (m, 1H), 2.38-2.34 (m, 1H), 2.33-2.19 (m, 1H), 2.28 (s, 3H), 2.19-2.09 (m, 5H), 1.91-1.70 (m, 4H), 1.67 (s, 3H), 1.64 (s, 3H), 1.61-1.44 (m, 4H), 1.59 (s, 3H), 1.40 (s, 3H), 1.22-1.16 (m, 1H), 1.17-1.07 (m, 2H), 1.00 (s, 3H), 0.95 (s, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, MeOH-d_4) δ 172.6, 172.5, 143.7, 137.3, 135.8, 134.9, 133.3, 130.1 (2C), 124.5, 121.3 (2C), 75.5, 72.4, 68.6, 50.8, 49.9, 44.4, 40.7, 40.3, 38.3, 37.8, 37.4, 36.8, 32.9, 31.0 (2C), 30.6, 28.8, 25.9, 23.8 (2C), 22.4, 21.0, 20.9, 17.9 (2C) and 16.4; LC-MS (ESI): *m/z* 629 $[M+Na]^+$ 546 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 3.27 min.)

***N*-(4-fluorophenyl)fusidic acid amide (1.22)**

White powder (0.021 g obtained from 0.050 g of **1.0**, 35%); *R*f 0.5 (60% EtOAc:DCM); Mp 322-324 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 5.4, 8.6 Hz, 2H), 7.13 (s, 1H), 6.99 (t, *J* = 8.7 Hz, 2H), 5.78 (d, *J* = 8.5 Hz, 1H), 5.12 (m, 1H), 4.36 (m, 1H), 3.76 (m, 1H), 3.06 (m, 1H), 2.64-2.53 (m, 1H), 2.49-2.38 (m, 1H), 2.35-2.27 (m, 1H), 2.26-2.01 (m, 5H), 1.91-1.71 (m, 4H), 1.74 (s, 3H), 1.67 (s, 3H), 1.64-1.47 (m, 4H), 1.60 (s, 3H), 1.40 (s, 3H), 1.28-1.22 (m, 1H), 1.17-1.06 (m, 2H), 0.99 (s, 3H), 0.95 (s, 3H), 0.93 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 169.3, 159.1 (d, *J* = 244.4 Hz), 142.6, 135.2, 133.9, 132.8, 123.2, 121.2 (d, *J* = 7.7 Hz), 115.6 (d, *J* = 22.4 Hz), 73.8, 71.4, 68.3, 49.4, 48.7, 43.2, 39.5, 39.3, 37.1, 36.3, 36.2, 35.7, 32.4, 30.3, 30.0, 29.4, 28.1, 25.7, 24.1, 22.8, 20.8, 20.7, 17.9, 17.8 and 15.9; LC-MS (ESI): *m/z* 550 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.23 min.)

_N_-(benzyl)fusidic acid amide (1.24)

White powder (0.042 g obtained from 0.050 g of **1.0**, 70%); R*f* 0.6 (60% EtOAc:DCM); Mp 182-184 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.73 (d, *J* = 8.0 Hz, 1H), 5.39 (dd, *J* = 4.7, 5.6 Hz, 1H), 5.07 (m, 1H), 4.59 (dd, *J* = 6.4, 14.4 Hz, 1H), 4.32 (m, 1H), 4.11 (dd, *J* = 4.2, 14.4 Hz, 1H), 3.73 (m, 1H, H-3), 2.97 (m, 1H), 2.56-2.46 (m, 1H), 2.43-2.31 (m, 1H), 2.29-2.21 (m, 1H), 2.18-1.99 (m, 5H), 1.98 (s, 3H), 1.89-1.67 (m, 4H), 1.63 (s, 3H), 1.62-1.45 (m, 4H), 1.55 (s, 3H), 1.36 (s, 3H), 1.30-1.25 (m, 1H), 1.17-1.03 (m, 2H), 0.97 (s, 3H), 0.94 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 170.8, 141.8, 137.9, 135.6, 132.4, 128.8 (2C), 128.1 (2C), 127.6, 123.3, 73.7, 71.4, 68.3, 49.3, 48.7, 43.9, 43.2, 39.5, 39.3, 37.1, 36.2, 36.2, 35.7, 32.4, 30.3, 30.0, 29.4, 28.0, 25.6, 24.0, 22.7, 21.0, 20.8, 17.8, 17.8 and 15.9; LC-MS (ESI): *m/z* 628 $[M+Na]^+$, 546 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (tr = 3.23 min.)

_N_-(4-fluorobenzyl)fusidic acid amide (1.25)

White powder (0.031 g obtained from 0.050 g of **1.0**, 50%); *R*f 0.5 (60% EtOAc:DCM); Mp 182-184 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 2H), 7.00 (t, *J* = 8.6 Hz, 2H), 5.74 (d, *J* = 8.5 Hz, 1H), 5.39 (m, 1H), 5.06 (m, 1H), 4.55 (dd, *J* = 6.5, 14.3 Hz, 1H), 4.32 (m, 1H), 4.07 (dd, *J* = 4.2, 14.4 Hz, 1H), 3.73 (m, 1H), 2.97 (m, 1H), 2.55-2.44 (m, 1H), 2.40-2.31 (m, 1H), 2.29-2.20 (m, 1H), 2.18-2.00 (m, 5H), 1.98 (s, 3H), 1.89-1.67 (m, 4H), 1.63 (s, 3H), 1.62-1.45 (m, 4H), 1.54 (s, 3H), 1.35 (s, 3H), 1.28-1.23 (m, 1H), 1.16-1.01 (m, 2H), 0.97 (s, 3H), 0.94 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 170.7, 162.2 (d, *J* = 246.1 Hz), 141.9, 135.5, 133.8, 132.5, 129.8 (d, *J* = 8.1 Hz), 123.3, 115.5 (d, *J* = 21.5 Hz), 73.7, 71.4, 68.3, 49.3, 48.7, 43.3, 43.1, 39.5, 39.3, 37.1, 36.2 (2C), 35.6, 32.5, 30.3, 30.0, 29.4, 28.0, 25.6, 24.1, 22.7, 21.0, 20.7, 17.8 (2C) and 15.9; LC-MS (ESI): *m/z* 646 $[M+Na]^+$, 564 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.24 min.)

_N_-(4-sulfamoylbenzyl)fusidic acid amide (1.26)

White powder (0.007 g obtained from 0.050 g of **1.0**, 10%); *R*f 0.5 (EtOAc); Mp 182-184 ^{o}C; ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.3, 2H), 5.79 (d, *J* = 8.4 Hz, 1H), 5.11 (m, 1H), 4.53 (d, *J* = 15.0 Hz, 1H), 4.30 (m, 1H), 4.15 (d, *J* = 15.0 Hz, 1H), 3.64 (m, 1H), 3.04 (m, 1H), 2.65-2.52 (m, 2H), 2.30-2.19 (m, 1H), 2.19-2.01 (m, 5H), 1.91-1.69 (m, 4H), 1.90 (s, 3H), 1.64 (s, 3H), 1.63-1.43 (m, 4H), 1.55 (s, 3H), 1.38 (s, 3H), 1.24-1.18 (m, 1H), 1.17-1.07 (m, 2H),

0.99 (s, 3H), 0.94 (s, 3H), 0.89 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, MeOH-d_4) δ 174.3, 172.5, 144.6, 144.0, 143.7, 135.5, 133.3, 129.4 (2C), 127.4 (2C), 124.4, 75.3, 72.4, 68.6, 50.8, 49.9, 44.6, 43.9, 40.7, 40.3, 38.2, 37.9, 37.3, 36.9, 32.9, 31.0 (2C), 30.6, 28.8, 25.8, 23.8, 23.7, 22.3, 21.1, 17.9 (2C) and 16.4; LC-MS (ESI): *m/z* 625 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.01 min.)

***N*-(4-hydroxybenzyl)fusidic acid amide (1.27)**

Brown powder (0.011 g obtained from 0.050 g of **1.0**, 17%); *R*f 0.3 (60% EtOAc:DCM); Mp 182-184 ^{o}C; ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.70 (d, *J* = 8.5, 2H), 5.76 (d, *J* = 8.4 Hz, 1H), 5.09 (m, 1H), 4.37 (d, *J* = 14.3 Hz, 1H), 4.30 (m, 1H), 4.15 (d, *J* = 14.3 Hz, 1H), 3.65 (m, 1H), 3.02 (m, 1H), 2.61-2.51 (m, 2H), 2.28-2.19 (m, 1H), 2.19-2.00 (m, 5H), 1.91 (s, 3H), 1.89-1.70 (m, 4H), 1.64 (s, 3H), 1.61-1.43 (m, 4H), 1.54 (s, 3H), 1.37 (s, 3H), 1.24-1.16 (m, 1H), 1.17-1.07 (m, 2H), 0.99 (s, 3H), 0.94 (s, 3H), 0.88 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, MeOH-d_4) δ 174.0, 172.5, 158.0, 143.2, 135.7, 133.1, 130.5, 130.4 (2C), 124.5, 116.4 (2C), 75.3, 72.4, 68.6, 50.8, 49.9, 44.4, 44.0, 40.7, 40.3, 38.2, 37.8, 37.3, 36.9, 32.9, 31.0 (2C), 30.5, 28.7, 25.8, 23.9, 23.8, 22.4, 21.1, 17.9 (2C) and 16.4; LC-MS (ESI): *m/z* 644 $[M+Na]^+$, 562 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.09 min.)

***N*-(4-methylbenzyl)fusidic acid amide (1.28)**

White powder (0.035 g obtained from 0.050 g of **1.0**, 56%); *R*f 0.6 (60% EtOAc:DCM); Mp 182-184 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 5.72 (d, *J* = 8.4 Hz, 1H), 5.41 (m, 1H), 5.07 (m, 1H), 4.53 (dd, *J* = 4.1, 14.2 Hz, 1H), 4.32 (m, 1H), 4.07 (dd, *J* = 4.2, 14.2 Hz, 1H), 3.73 (m, 1H), 2.96 (m, 1H), 2.56-2.46 (m, 1H), 2.42-2.34 (m, 1H), 2.32 (s, 3H), 2.30-2.22 (m, 1H), 2.20-2.00 (m, 5H), 1.98 (s, 3H), 1.91-1.67 (m, 4H), 1.63 (s, 3H), 1.62-1.45 (m, 4H), 1.55 (s, 3H), 1.35 (s, 3H), 1.28-1.23 (m, 1H), 1.16-1.01 (m, 2H), 0.96 (s, 3H), 0.94 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 170.7, 141.7, 137.3, 135.6, 134.7, 132.4, 129.4 (2C), 128.1 (2C), 123.3, 73.7, 71.4, 68.3, 49.3, 48.7, 43.7, 43.2, 39.5, 39.3, 37.1, 36.2 (2C), 35.7, 32.4, 30.3, 30.0, 29.4, 28.0, 25.6, 24.0, 22.7, 21.0 (2C), 20.8, 17.8 (2C) and 15.9; LC-MS (ESI): *m/z* 642 $[M+Na]^+$, 560 $[M\text{-}OAc]^+$; purity (LC-MS): 98% (t_R = 3.31 min.)

2.0.2 General synthetic procedure for the synthesis of intermediate I

To a mixture of fusidic acid **1.0** (1 eq) in DCM (5 mL) at 30 ^{o}C was added the base DIPEA (3 eq) dropwise. The reaction was allowed to stir for while (10 min.) after which HATU (2 eq.) was added. The reaction was allowed to proceed until completion (TLC, 2 h). The reaction was diluted with DCM (20 mL) and extracted with water (2x15 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent removed *in vacuo*. Further purification to obtain **6.0** was accomplished by flash chromatography using a mixture of DCM and EtOAc as mobile phase.

***O*-(3*H*-[1,2,3]triazolo[4,5-b]pyridin-3-yl)fusidic acid ester (intermediate I)**

Yellow semi-solid (0.240 g obtained from 0.370 g of **1.0**, 53%); *R*f 0.6 (60% EtOAc:DCM); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (dd, *J* = 1.4, 4.4 Hz, 1H), 8.39 (dd, *J* = 1.4, 8.3 Hz, 1H), 7.40 (dd, *J* = 4.4, 8.3, 1H), 5.93 (d, *J* = 8.4 Hz, 1H), 5.23 (m, 1H), 4.40 (m, 1H), 3.77 (m, 1H), 3.19 (m, 1H), 2.82-2.75 (m, 1H), 2.72-2.65 (m, 1H), 2.45-2.39 (m, 3H), 2.33-2.26 (m, 1H), 2.22-2.13 (m, 2H), 2.12 (s, 3H), 1.99-1.92 (m, 1H), 1.92-1.72 (m, 3H), 1.71 (s, 3H), 1.67 (s, 3H), 1.66-1.52 (m, 4H),1.41 (s, 3H), 1.43-1.37 (m, 1H), 1.21-1.06 (m, 2H), 1.01 (s, 3H), 1.00 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.9, 164.9, 157.4, 151.5, 140.8, 135.0, 133.4, 129.2, 124.9, 122.5, 120.7, 74.3, 71.3, 68.2, 49.2, 49.0, 45.3, 39.5, 39.0, 37.1, 36.2 (2C), 35.6, 32.4, 30.3, 29.9, 29.0, 28.5, 25.7, 24.2, 22.8, 21.1, 20.7, 18.1, 17.8 and 15.9; LC-MS (ESI): *m/z* 635 $[M+H]^+$; purity (LC-MS): 98% (t_R = 3.23 min.)

2.0.3 General synthetic procedure for the synthesis of compound 1.23

To a mixture of intermediate I and the corresponding amine (4-hydroxy aniline) in *n*-BuOH at 25 ^{o}C was added the base KH_2PO_4 (5 eq). The reaction was then heated gently to 100^{o}C until reaction was complete (TLC, LCMS; 16 h). The solvent was removed completely by drying in the Genevac. Further purification to afford the target compounds was accomplished by preparative TLC using 10% MeOH:DCM as mobile phase.

***N*-(4-hydroxyphenyl)fusidic acid amide (1.23)**

Brown powder (0.015 g obtained from 0.050 g of **6.0**, 32%); *R*f 0.3 (60% EtOAc:DCM); Mp 332-334 ^{o}C; ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.37 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 8.6, 2H), 5.84 (d, *J* = 8.5 Hz, 1H), 5.19 (m, 1H), 4.35 (m, 1H), 3.68 (m, 1H), 3.12 (m, 1H), 2.74-2.63 (m, 2H), 2.39-2.29 (m, 1H), 2.29-2.15 (m, 5H), 1.94-1.65 (m, 4H), 1.73 (s, 3H), 1.68 (s, 3H), 1.63 (s, 3H), 1.60-1.45 (m, 4H), 1.43 (s, 3H), 1.24-1.18 (m, 1H), 1.20-1.11 (m, 2H), 1.03 (s, 3H), 0.98 (s, 3H), 0.92 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, MeOH-d_4) δ 172.6, 172.3, 155.3, 143.4, 135.8, 133.3, 131.8, 124.6, 123.1 (2C), 116.2 (2C), 75.5, 72.4, 68.6, 50.8, 49.9, 44.4, 40.7, 40.3, 38.3, 37.8, 37.4, 36.8, 32.9, 31.1, 31.0, 30.6, 28.8, 25.9, 23.9, 23.8, 22.4, 21.0, 17.9 (2C) and 16.4; LC-MS (ESI): *m/z* 631 $[M+Na]^+$, 548 $[M-OAc]^+$; purity (LC-MS): 98% (t_R = 2.92 min.)

3.0 Biological evaluation protocols

3.0.1 Antimycobacterial evaluation protocol

The minimum inhibitory concentration (MIC_{90}) that inhibits 90% of growth of the bacterial population was determined using the broth micro-dilution method against the *Mtb* H_{37}RvMa strain (ATCC 27294).[1,2] A 10 mL culture of the *Mtb* H_{37}RvMa strain was grown to an optical density (OD_{600}) of 0.6 – 0.7. Test compounds were reconstituted in DMSO to a concentration of 10 mM. Duplicate two-fold serial dilutions of the test compounds were prepared across 10 wells in a 96-well microtiter plate, in a volume of 50 µL, after which, 50 µL of the diluted *Mtb* culture (1:500) was added to each well in the plate. The final volume per well was 100 µL. The

plate layout was a modification of the method previously described.[3] A positive growth (DMSO =< 2.5%), a negative growth (Rifampicin at 2xMIC: 0.150 µM), and a Rifampicin dose response (range 0.15 – 0.0002 µM) controls were used to measure any contamination and/or plate-to-plate variations. The microtiter plate was sealed in a secondary container and incubated at 37^{o}C with 5% CO_2 and humidification.[4] The AlamarBlue (Bio-Rad) reagent was added to each well of the assay plate at day 7 and incubated further for 24 hours. The measurement of MIC values was done at day 8, either visually (the lowest concentration of compound displaying no visible growth was scored as the MIC_{90}, blue colour – no growth, pink/purple colour - growth) or by measuring relative fluorescence (excitation 540 nm; emission 590 nm) using a SpecraMax i3x Plate reader. The raw fluorescent data were used to calculate % inhibition using a 4-parameter curve fit protocol (Softmax® Pro 6 Version 6.5.1).

Media used:

7H9 GLU ADC TW: Middlebrook 7H9 media (Difco™) supplemented with 0.2% Glucose (Sigma), Middlebrook albumin-dextrose-catalase (ADC) enrichment (BD, BBL) and 0.05% Tween 80 (Sigma).[5]

7H9 GLU CAS TX: Middlebrook 7H9 media (Difco™) supplemented with 0.03% Casitone (Difco™), 0.4% Glucose and 0.05% Tyloxapol (Sigma).[6]

3.0.2 Cytotoxicity evaluation protocol

The *in vitro* cytotoxicity of the synthesized compounds was evaluated against the Chinese Hamster Ovarian (CHO) cancer cell line (CHO-K1) using the MTT [3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide] assay, which is a colorimetric assay based on assessing the cell metabolic activity. Cytotoxic activity was determined as per previously described protocols with minor modifications as described below.[7,8]

The synthesized compounds were assayed in triplicate. Stock solutions of 2 mg/mL of test samples in DMSO were prepared with poorly soluble samples being tested as suspensions. The compounds were kept at -20 ^{o}C until required.

Cells (American Type Culture Collection, Cat. No. CCL-61) are seeded at 10^5 cells/well 24h prior to exposure and allowed to attach to the wells. At the start of the exposure, the growth media is carefully removed from the plates, and replaced with fresh growth media containing the desired concentrations of the test compounds. Cells were incubated in the presence of the test compounds for 48h in 5% CO_2 at 37 ^{o}C. After 44h, the MTT (Sigma) dye was added to each well and allowed to incubate with the cells for 4h. The growth media was then removed and 25 µL DMSO added to the cells to dissolve the formazan crystals formed by surviving cells. Optical density at 540 nM was used to measure the amount of formazan produced, and this was plotted against drug concentration to determine the IC_{50} of the test compounds against the CHO cells.

In all experiments, emetine was used as a reference drug. Starting from an initial concentration of 100 µg/mL, ten-fold serial dilutions were made in complete medium to give 6 concentrations to the lowest concentration of 0.001 µg/mL. The cell viability was not affected by the highest concentration of the solvent to which the cells were exposed. The full dose-response curves were plotted using a non-linear dose-response curve fitting analysis via GraphPad Prism V4 software. By this, the minimum concentration required for 50% inhibition (IC_{50}) values were determined for each compound.

4.0 Molecular docking

The molecular docking experiments were carried out using the Glide software package implemented in Schrödinger Suite (2018-3, Schrödinger Inc., USA). Throughout the docking simulation, the ligands were allowed to be flexible while the protein was kept rigid.

Protein and Ligand Preparation

The Human Serum Albumin complexed with fusidic acid protein crystal structure was retrieved from the Protein Databank (PDB: 2VUF). The Protein Preparation wizard of Glide employing the Optimized Potentials for Liquid Simulation 3 (OPLS3e) forcefield was used to prepare the protein structure.[9]

During the pre-processing stage, missing hydrogens were added, and crystallographic water molecules were removed from the protein structure corresponding to pH 7.0. The side chains not close to the binding site were then neutralized.

The following stage entails the refinement of the crystal structure by initially optimizing the sample-water orientation then by restrained minimization of co-crystallized structure using the OPLS3e. This alleviates potential steric clashes by reorienting side chains.

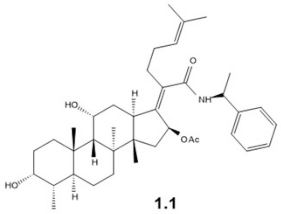
Any co-factors, water molecules and co-crystallized metals which may have crystallized during experimental crystallization of the structure were excluded using the default settings 'Receptor Grid Generation' protocol of Maestro to define the binding site for the docking simulation.

The 3D structures of the synthesized fusidic acid analogues were generated by using the LigPrep protocol.

Docking Simulation

For accuracy and precision of the applied docking protocol, the co-crystallized fusidic acid was extracted and re-docked using Glide docking algorithm in the extra precision mode without applying any constraints. A good agreement of the obtained pose of the co-crystallized and docked fusidic acid indicated the reliability of the selected docking parameters for the synthesized fusidic analogues. Therefore, molecular docking of the analogues against the generated grid was performed using Glide. Finally, analysis of the protein-ligand complexes to investigate various types of interactions was done by utilizing XP visualizer protocol.

5.0 Copies of NMR spectra



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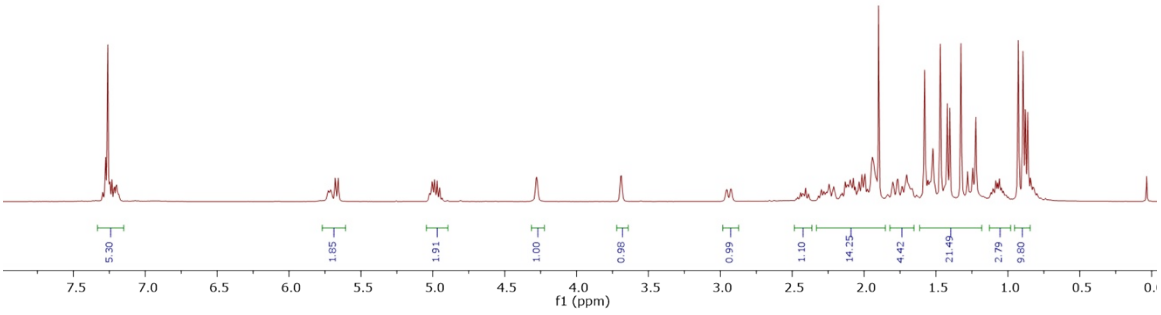

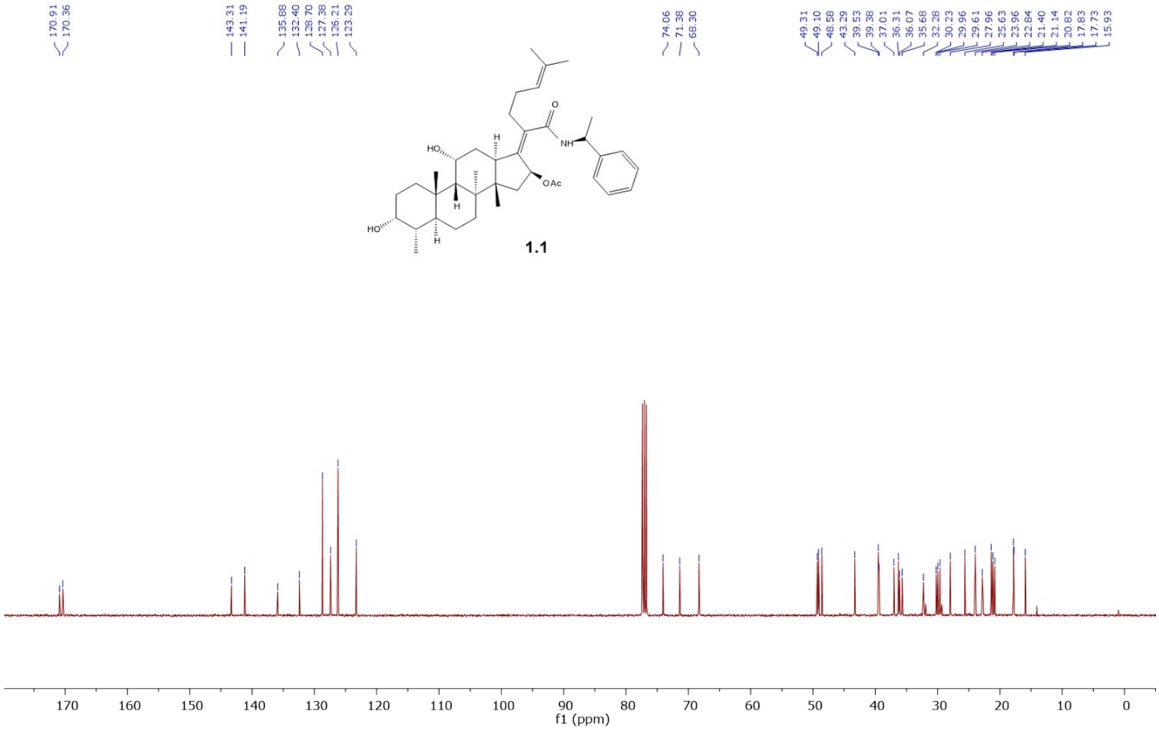
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15.93
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O
NH
OAc
H
HO
H
H
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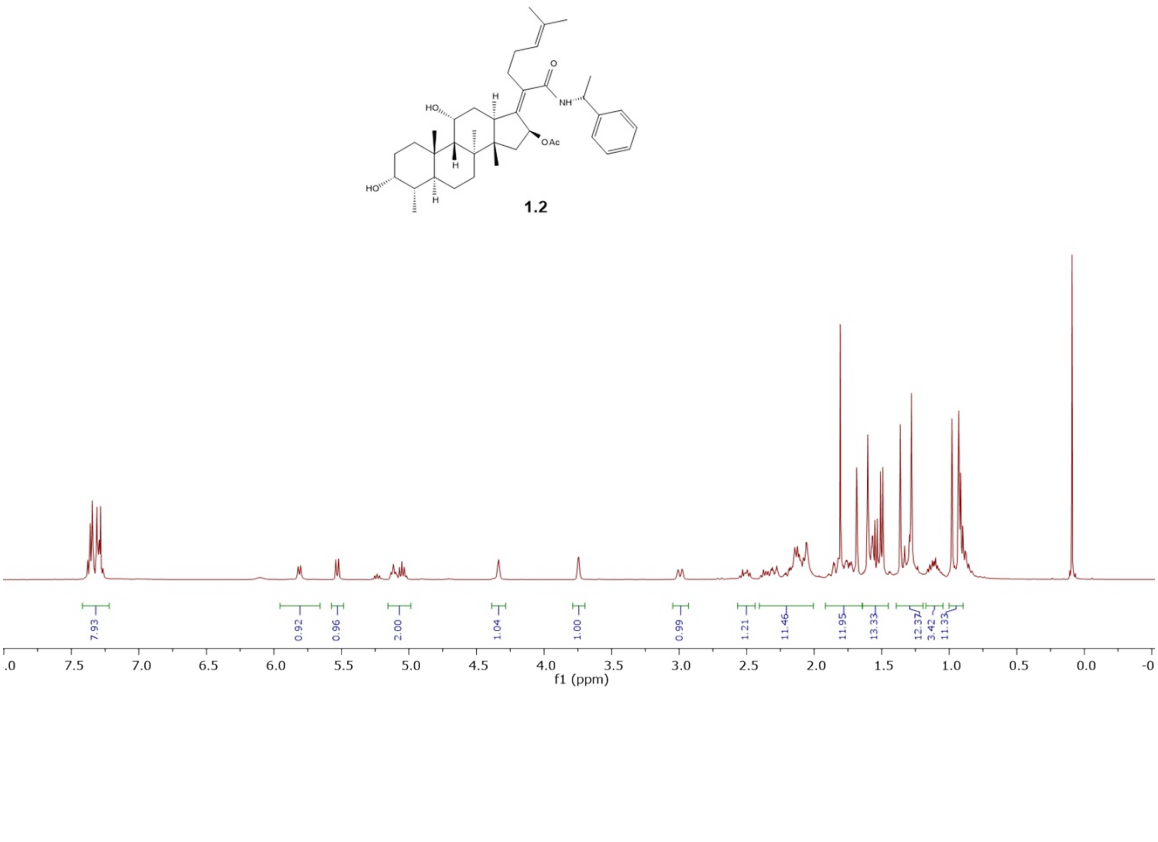
1.1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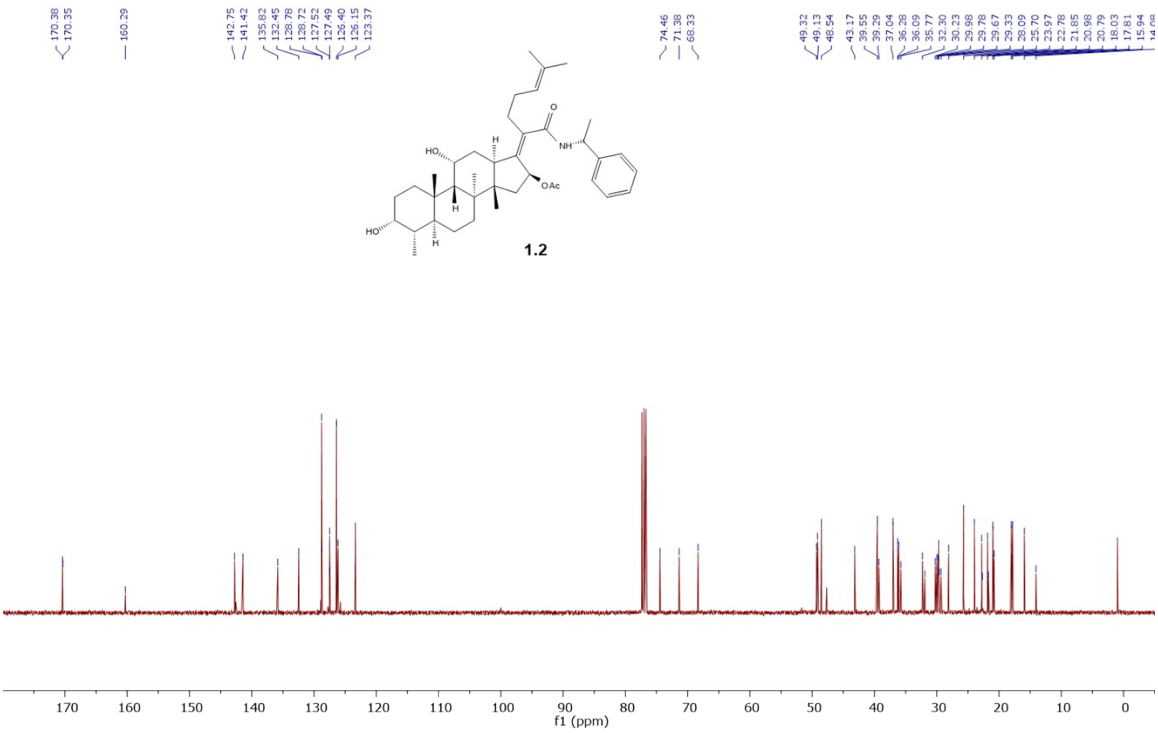
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H
H
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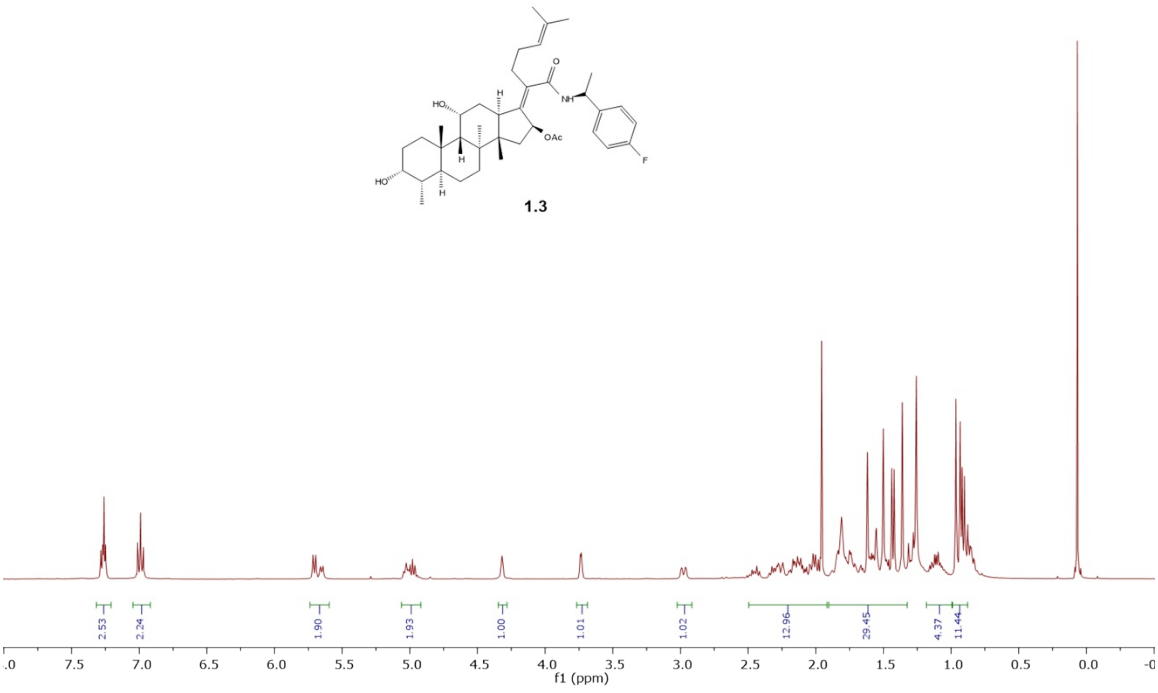
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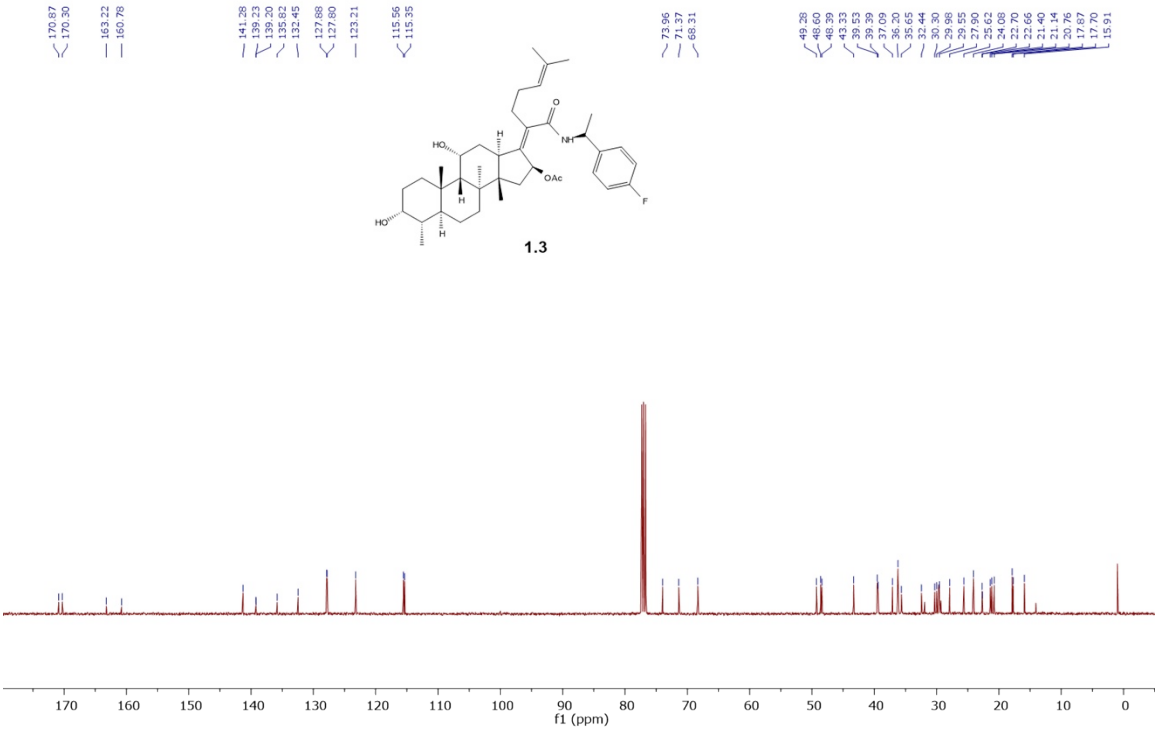
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F
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H
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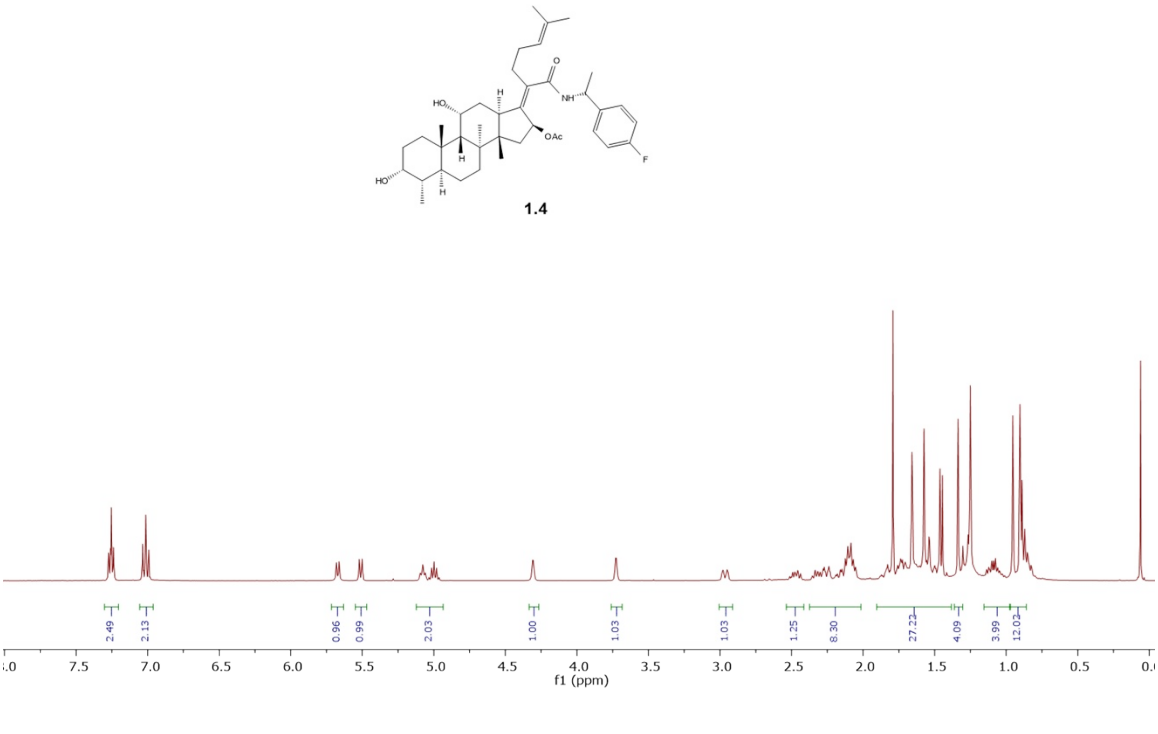
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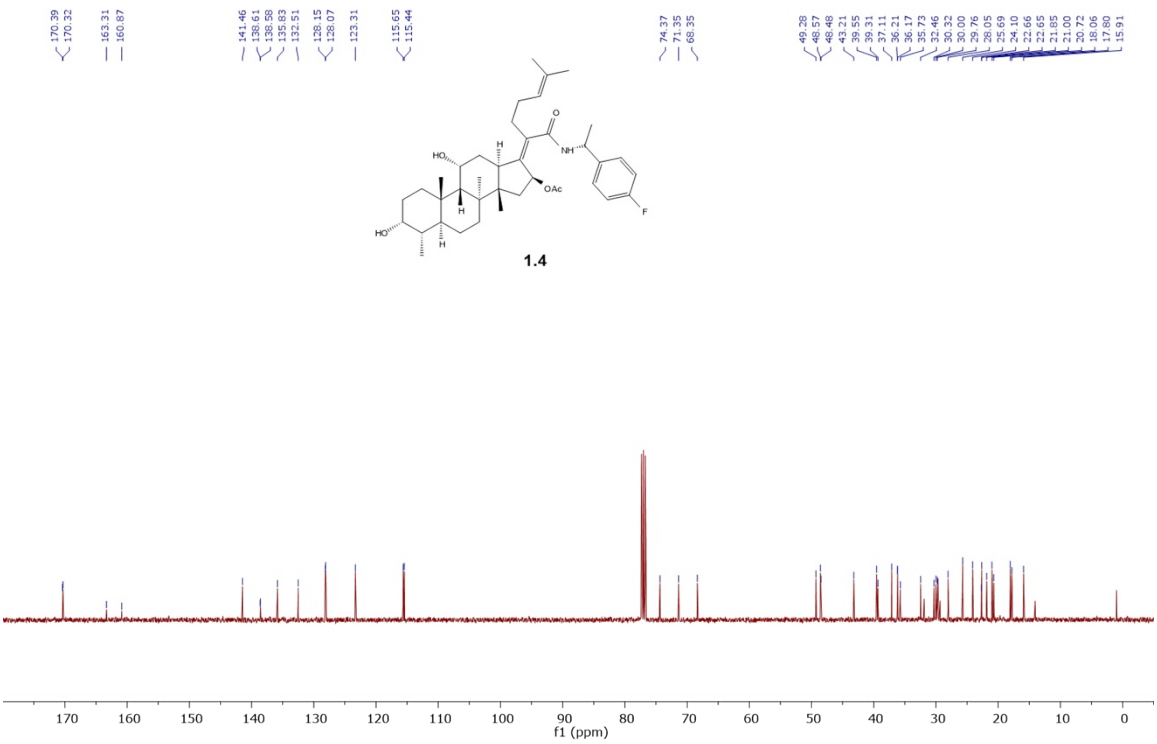
1.4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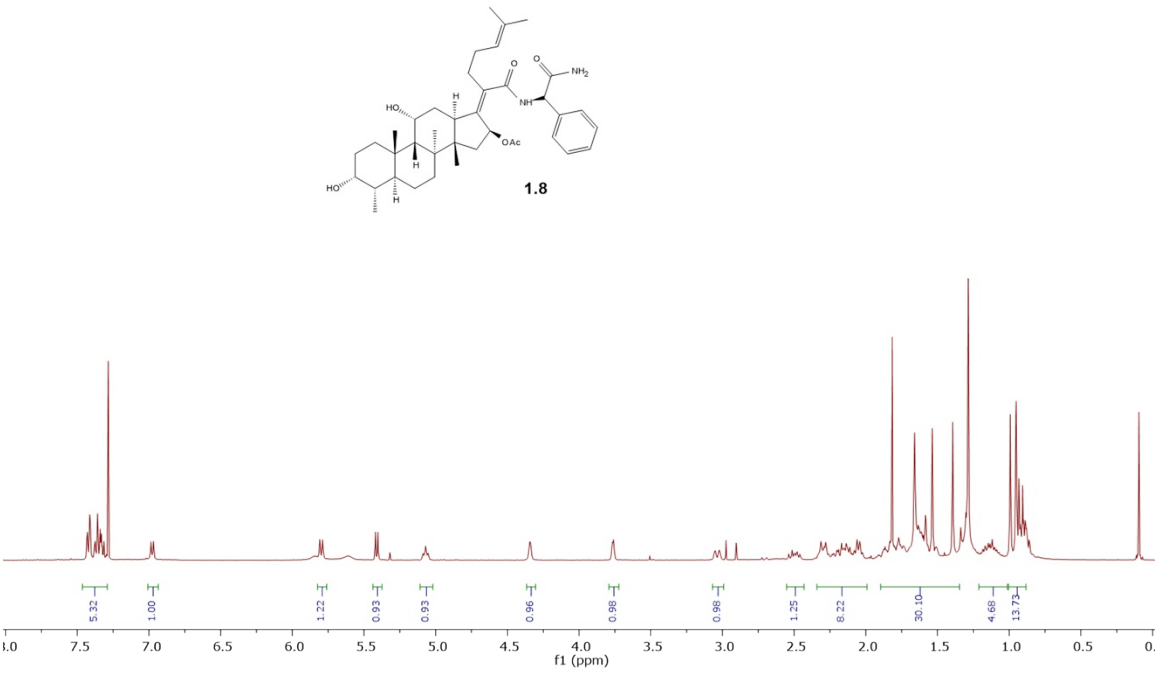
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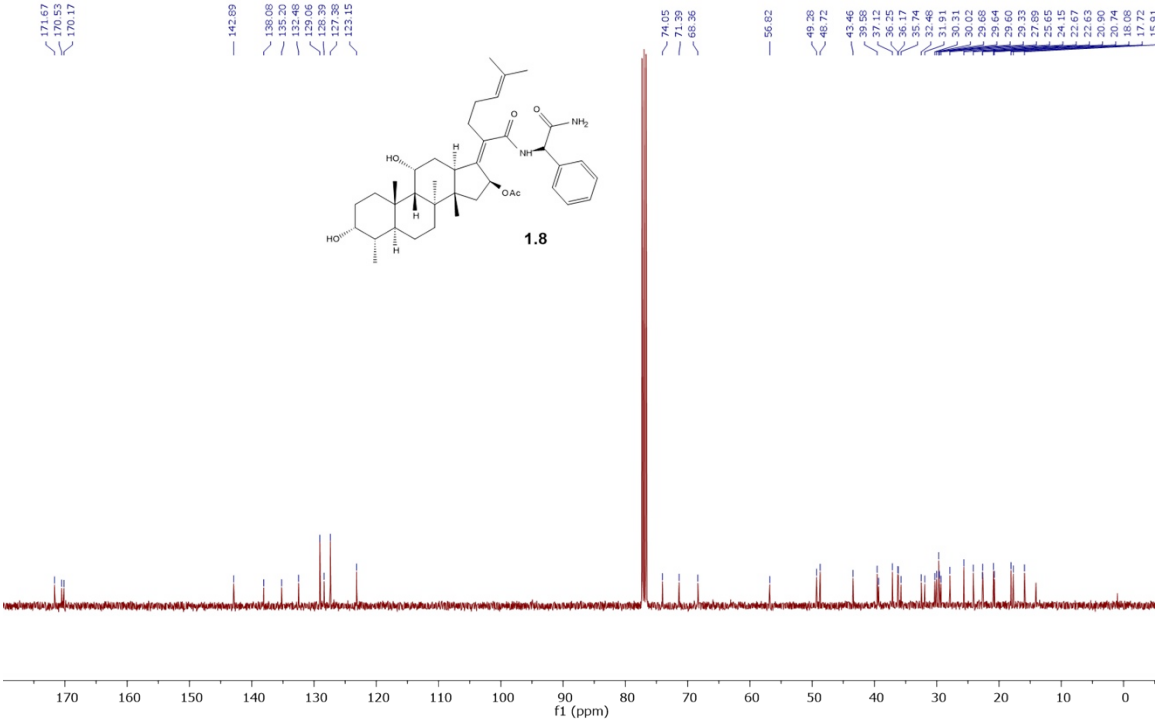
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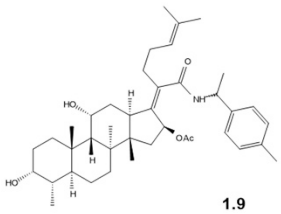
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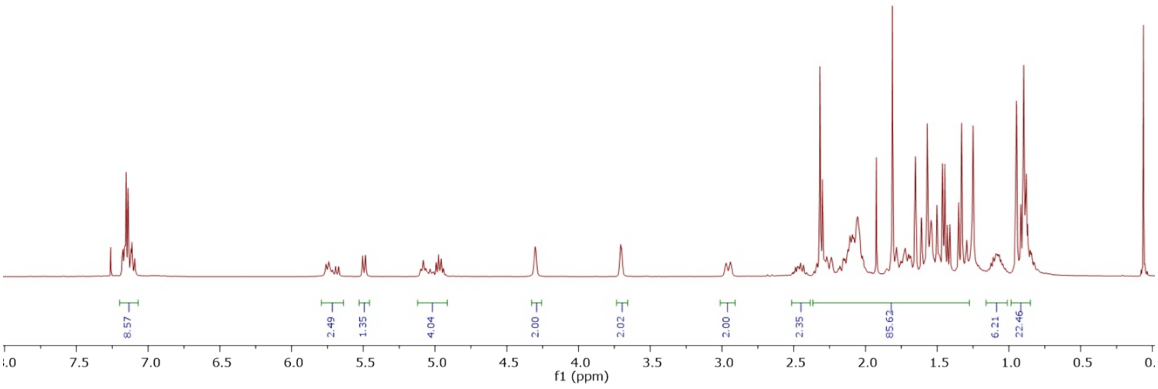
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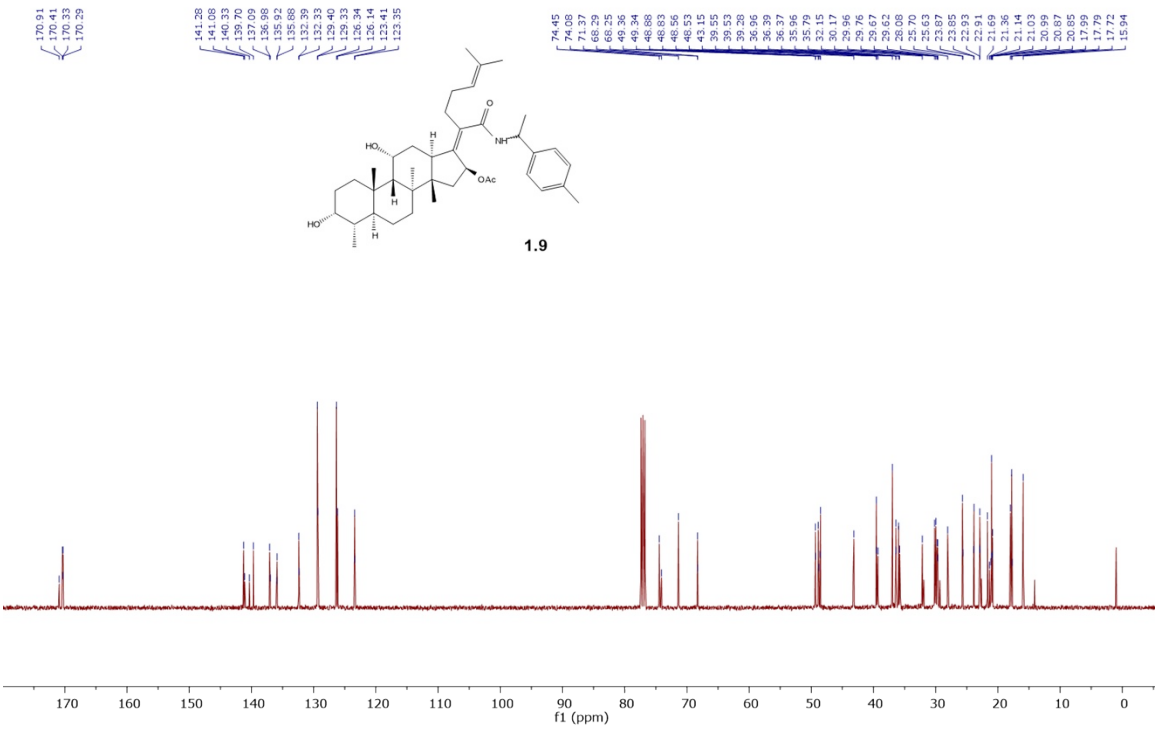
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OAc
H
HO
H
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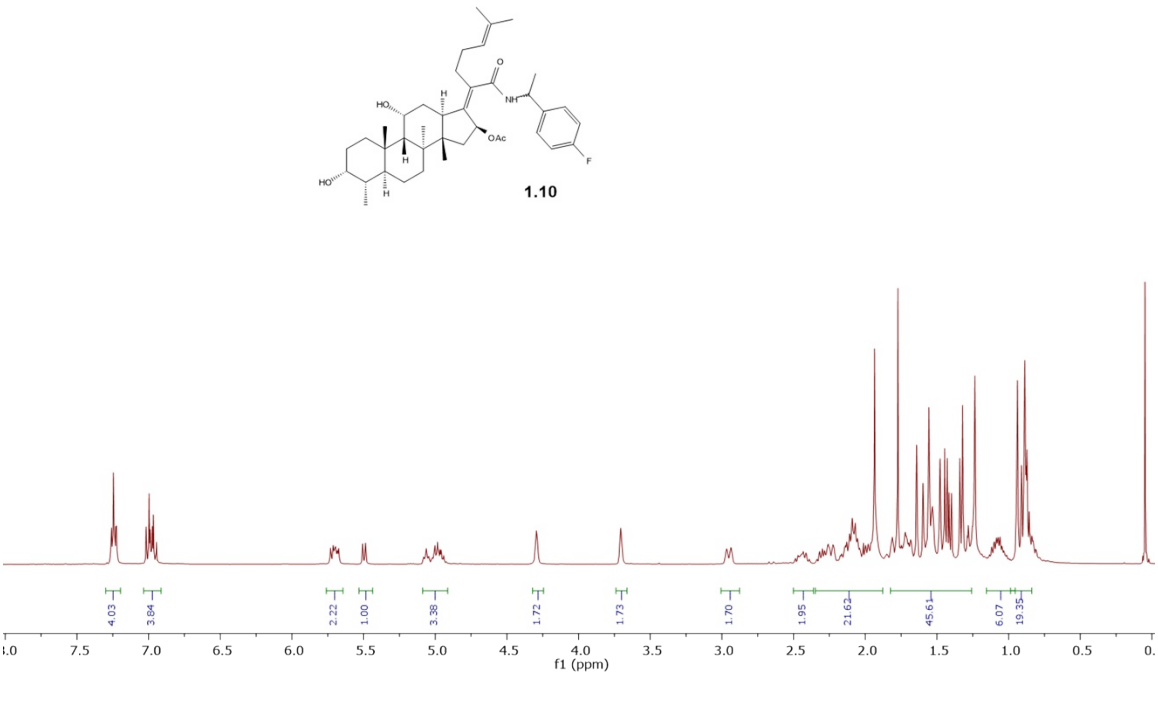
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HO
H
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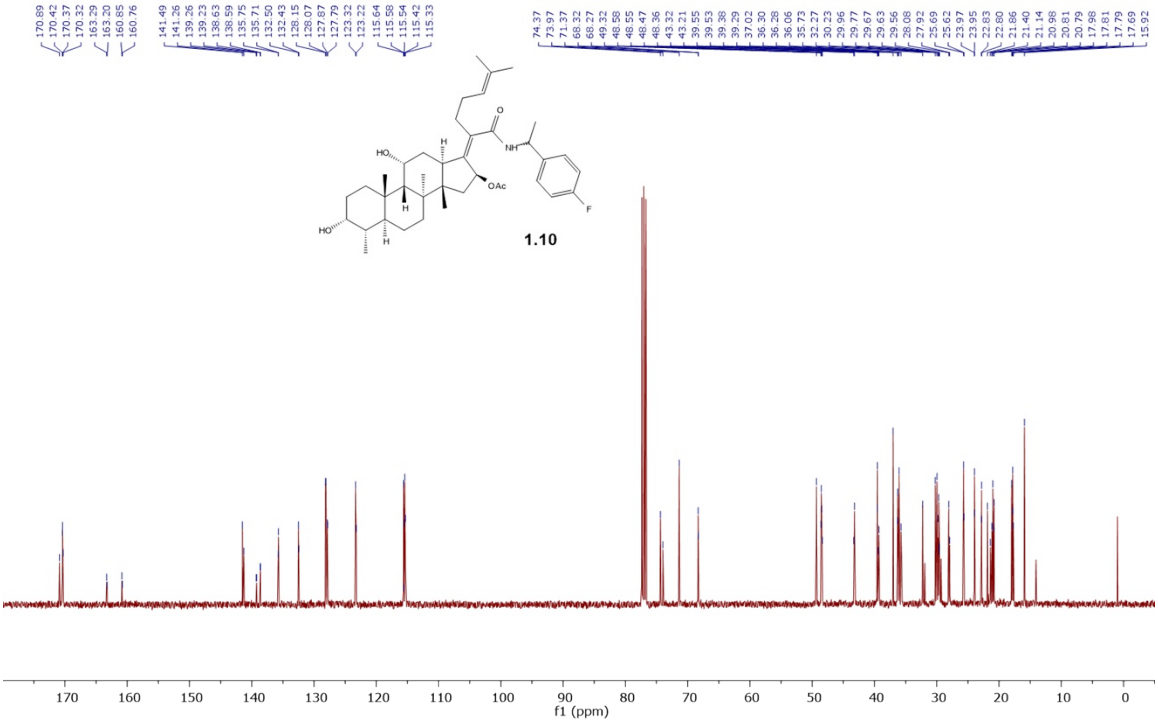
f1 (ppm)

1.10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F
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H
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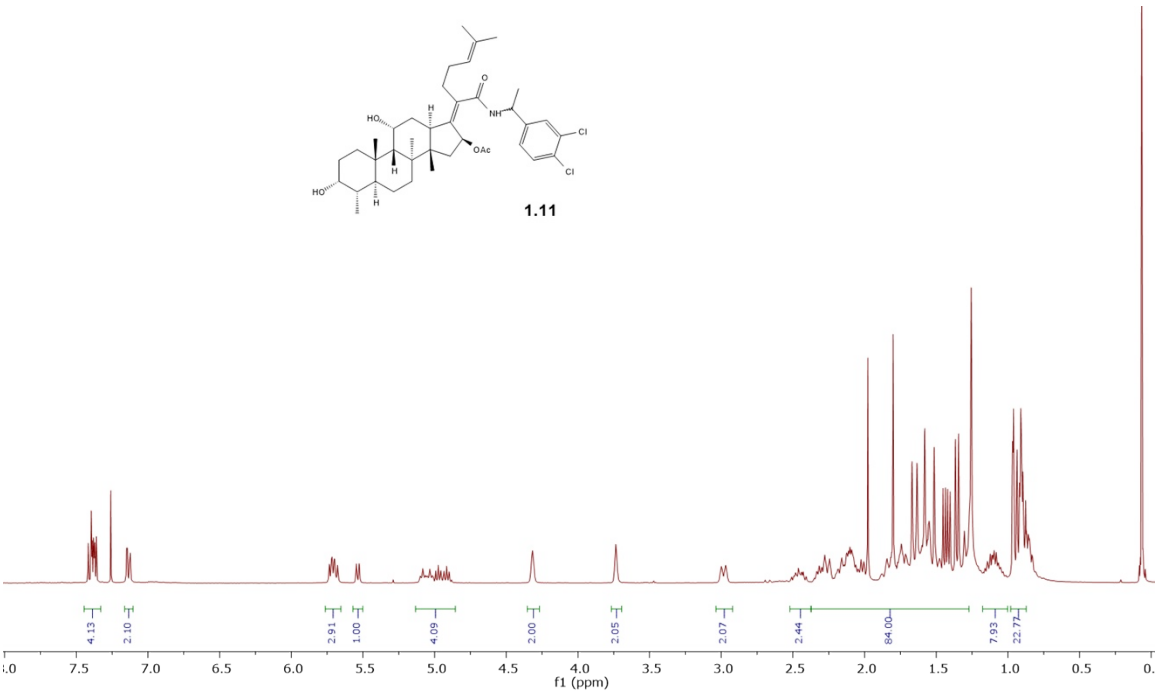
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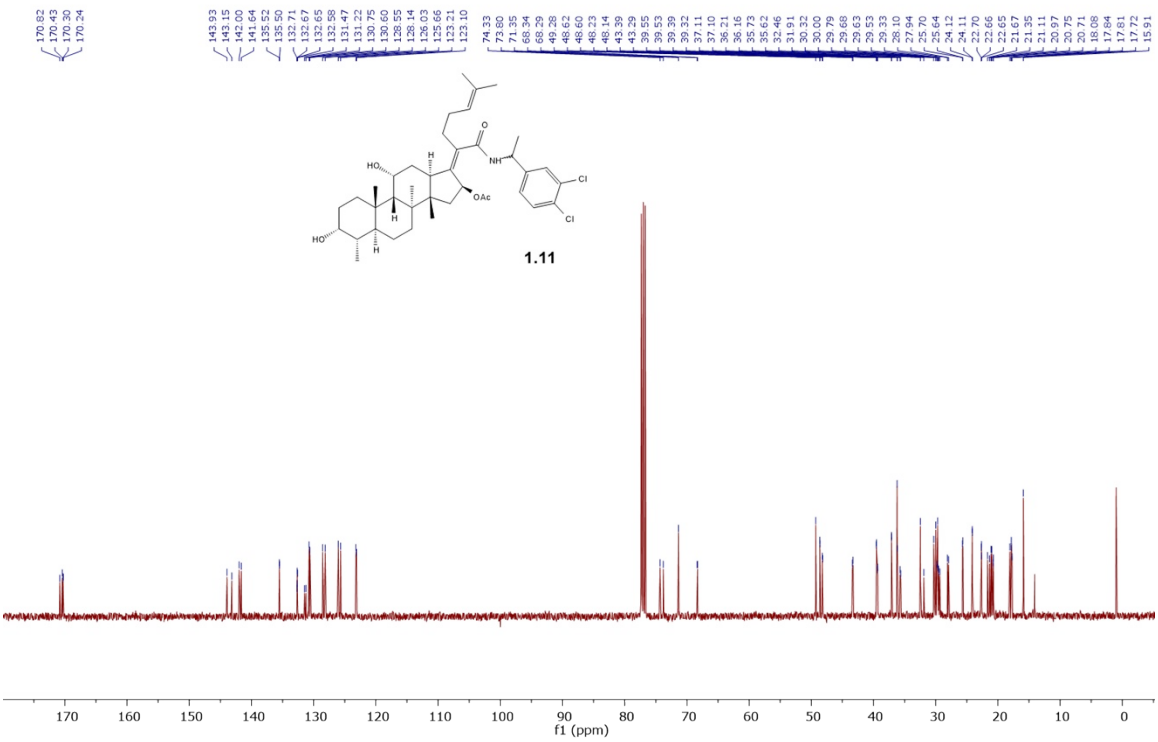
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HO
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NH
Cl
Cl
OAc
H
HO
1.11
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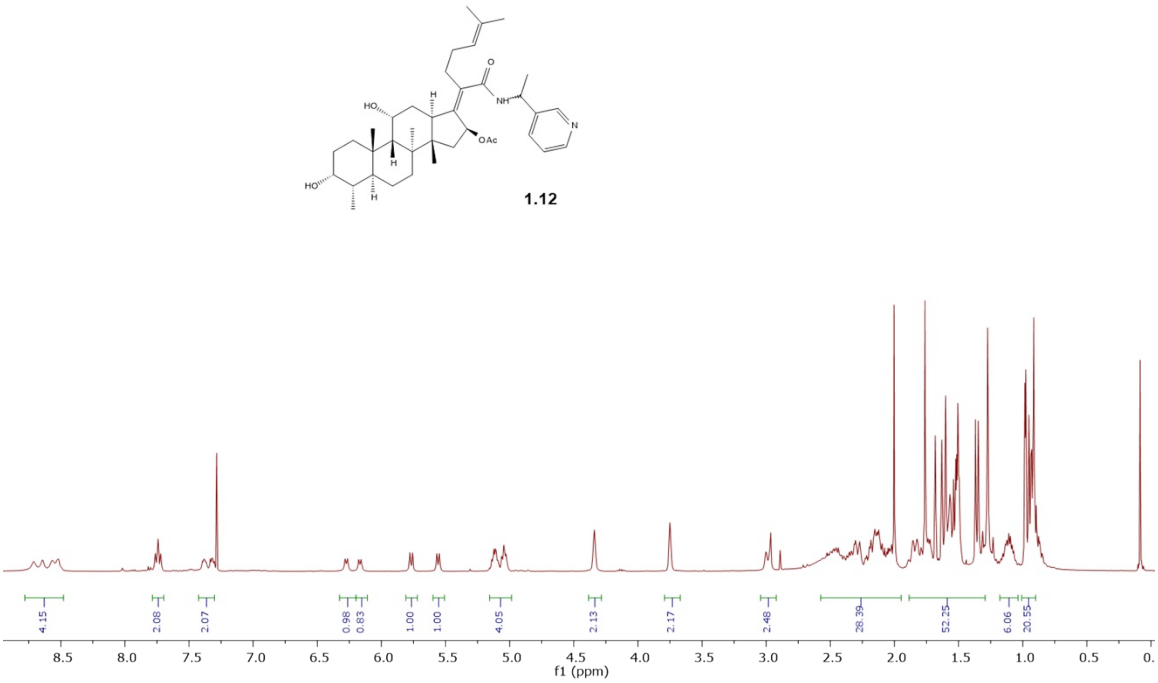
f1 (ppm)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2.17
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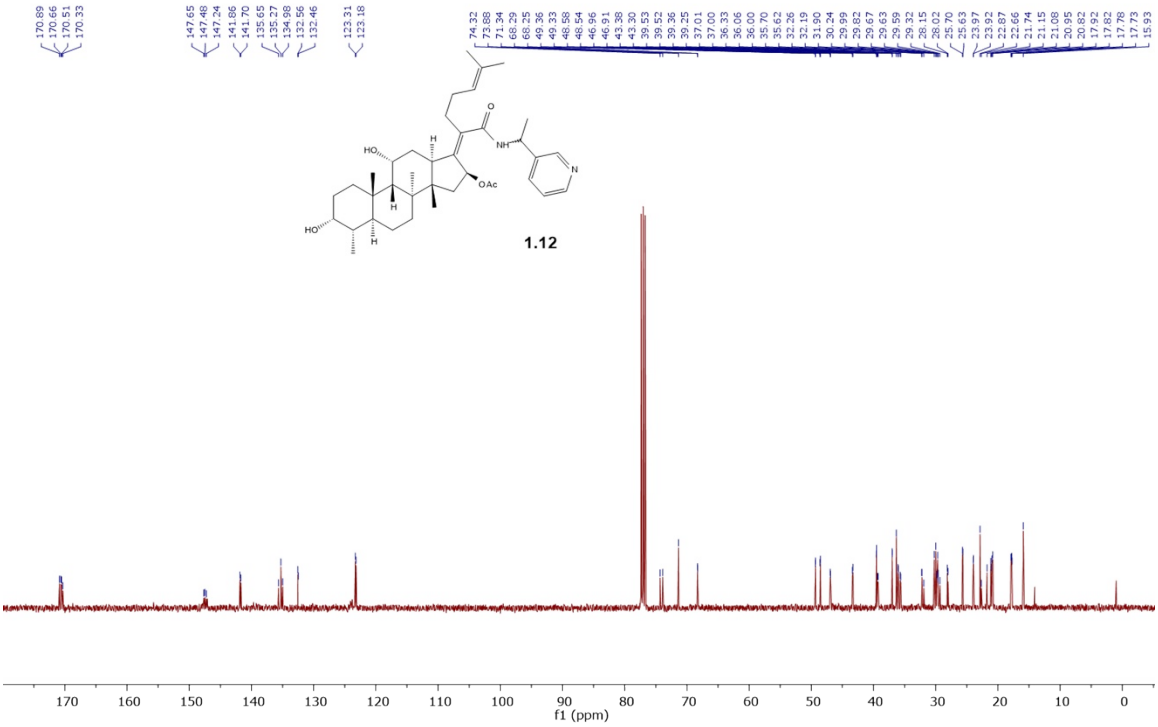
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46.91
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28.02
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23.92
22.87
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21.08
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17.78
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HO
H
1.12
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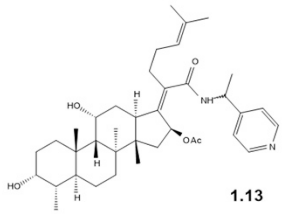
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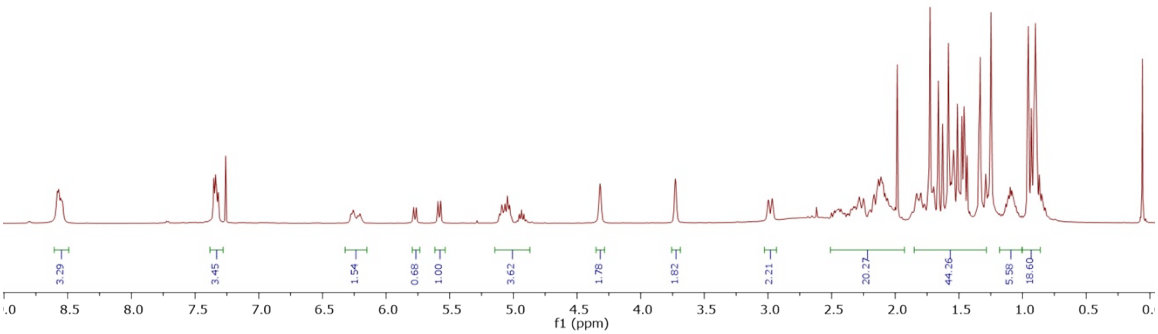
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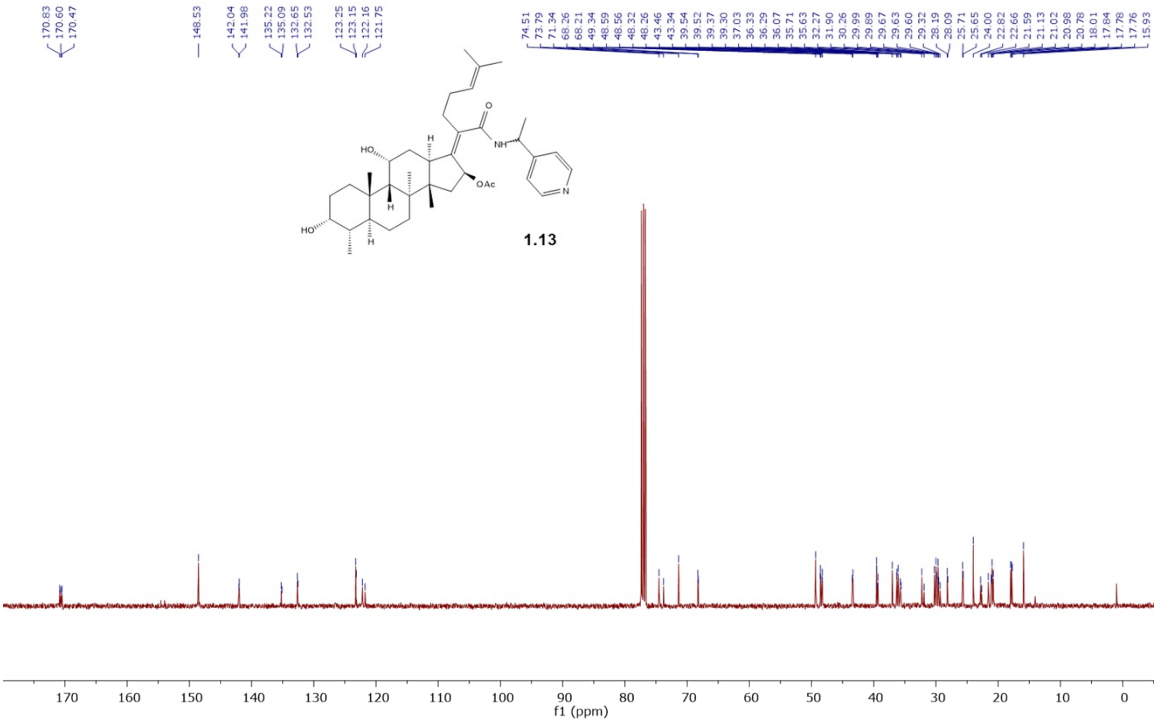
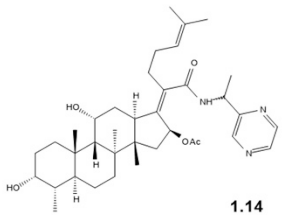
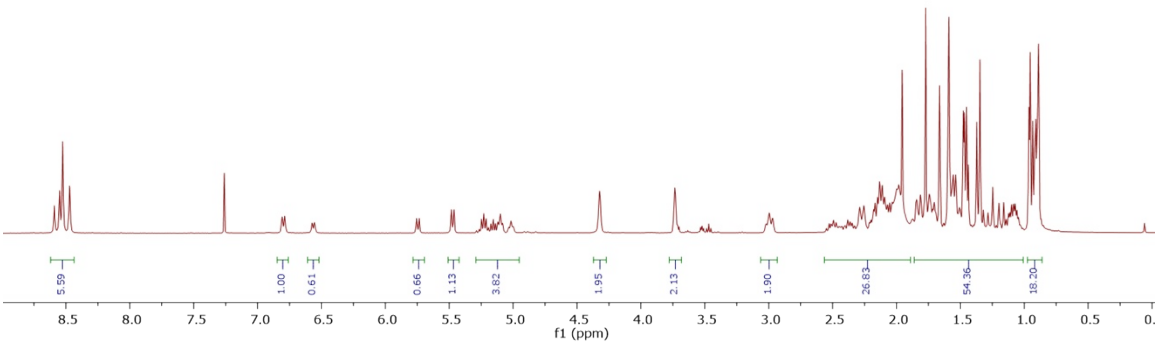
1.0
0.5
f1 (ppm)

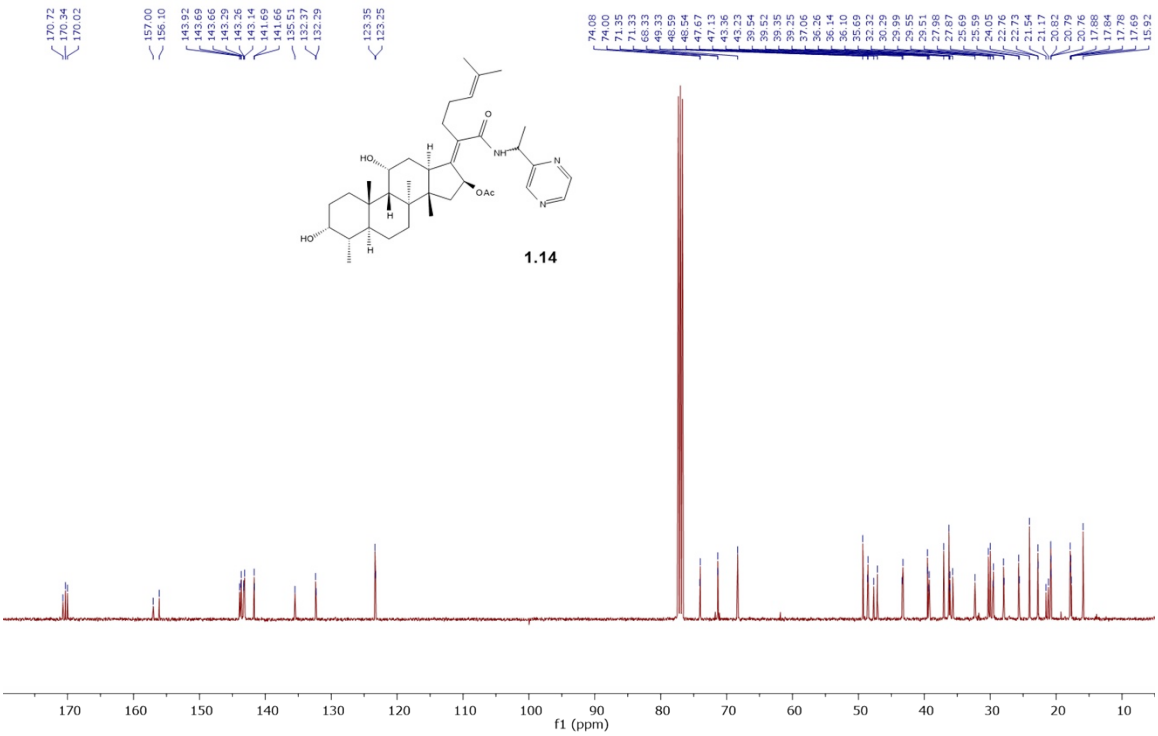

170.83
170.60
170.47
148.53
142.04
141.98
135.22
135.09
132.65
132.53
123.25
123.15
122.16
121.75
74.51
73.79
71.34
68.36
68.21
49.34
48.59
48.56
48.32
48.26
43.46
43.34
39.54
39.52
39.37
39.30
37.03
36.33
36.29
35.67
35.71
35.63
32.27
31.90
30.26
29.99
29.89
29.67
29.63
29.60
29.32
28.19
28.09
25.71
25.65
24.60
23.62
21.66
21.59
21.13
21.02
20.98
20.78
18.01
17.84
17.78
17.76
15.93
HO
O
NH
N
H
OAc
HO
H
H
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

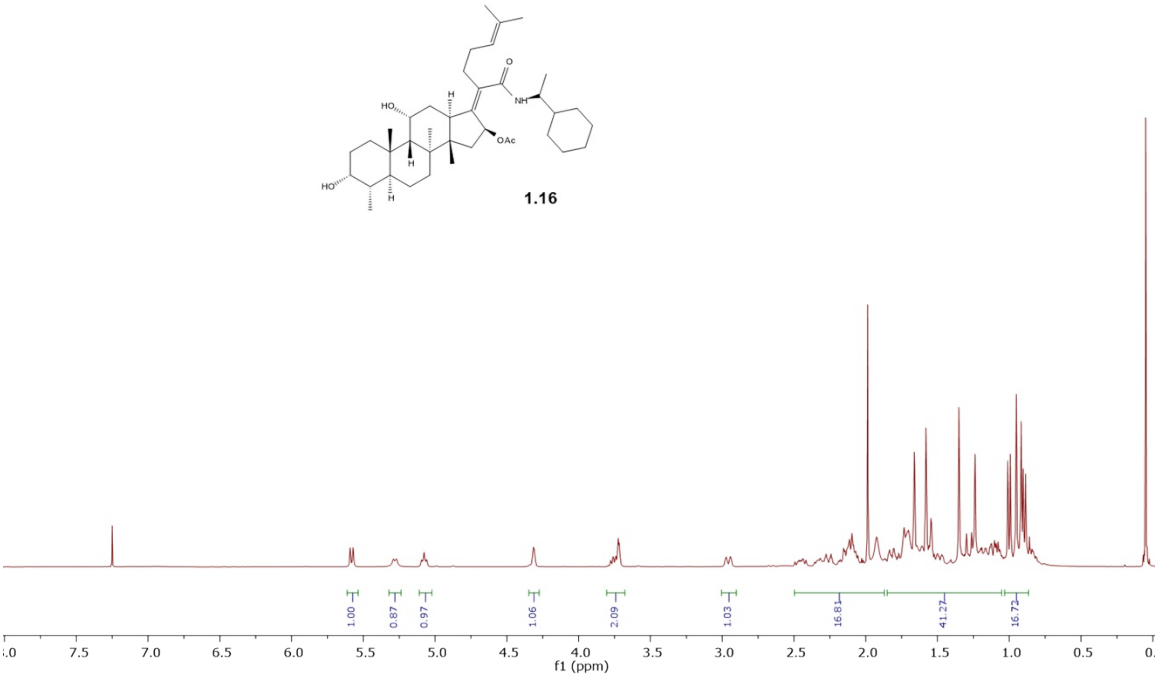
1.13

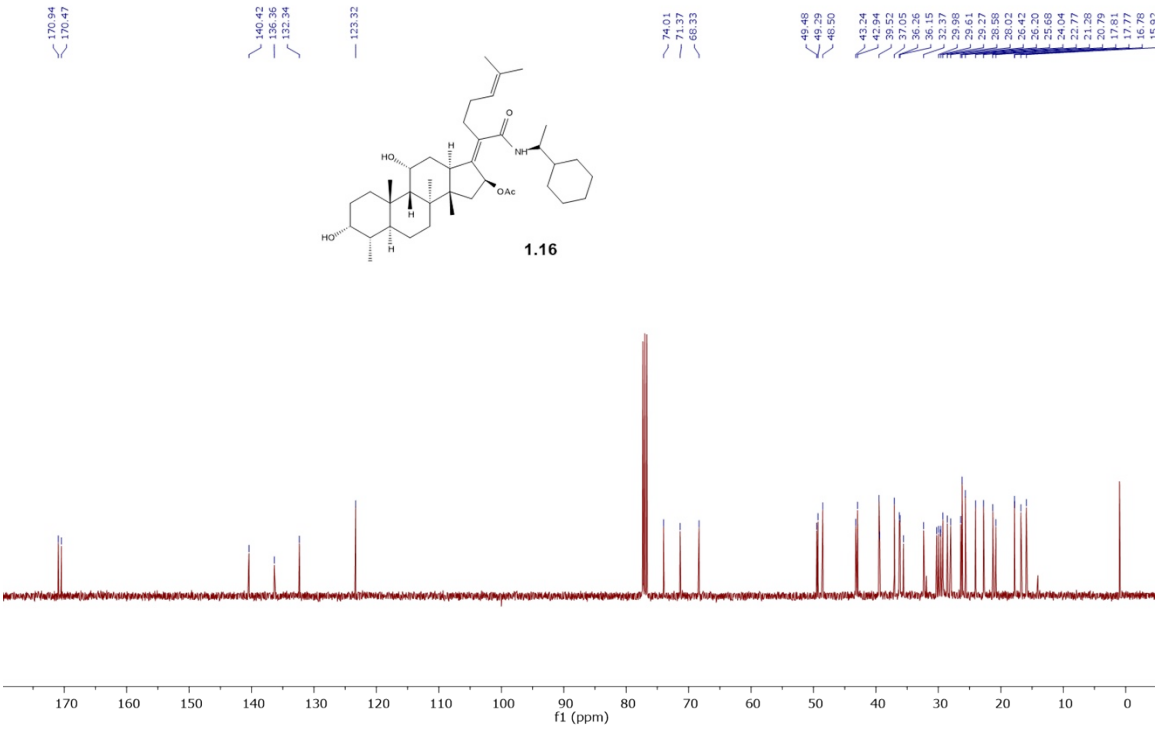

HO
O
NH
N
N
H
OAc
HO
H
H

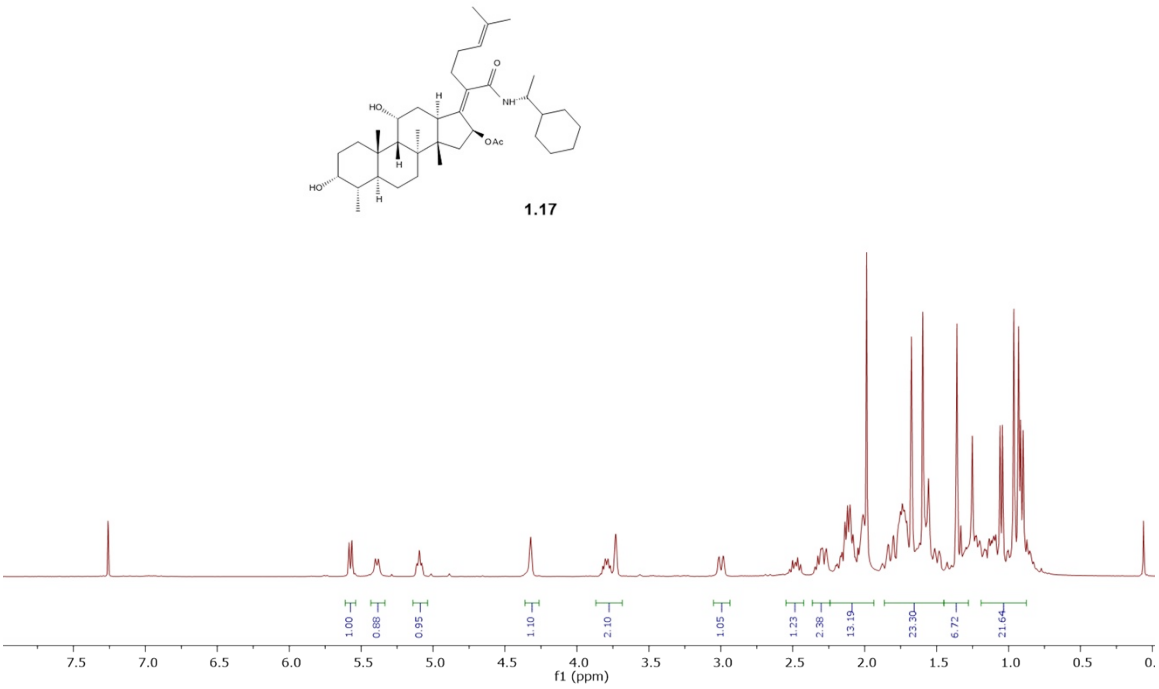
1.14

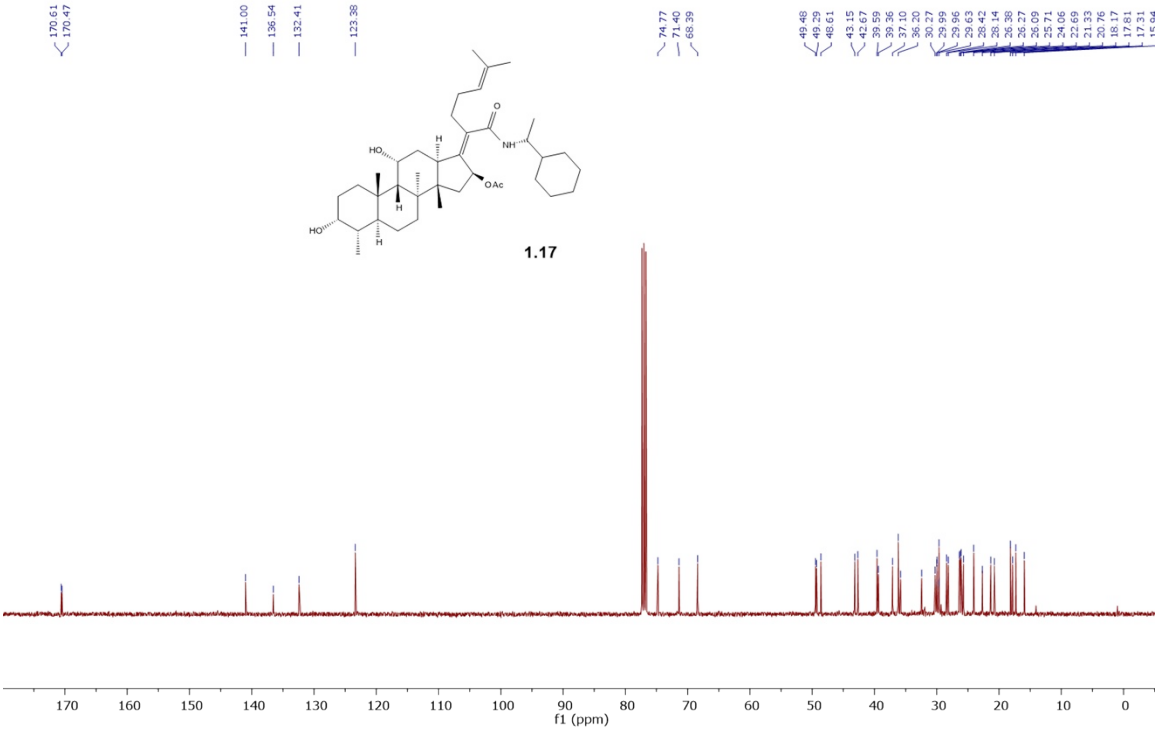

5.59
1.00
0.61
0.66
1.13
3.82
1.95
2.13
1.90
26.83
54.36
18.20
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


170.72
170.34
170.02
157.00
156.10
143.92
143.69
143.66
143.29
143.26
143.14
141.69
141.66
135.51
132.37
132.29
123.35
123.25
74.08
74.00
71.35
71.33
68.33
49.33
48.59
48.54
47.67
47.13
43.36
43.23
39.54
39.52
39.35
39.25
37.06
36.26
36.14
36.10
35.69
32.32
30.29
29.99
29.55
29.51
27.98
27.87
25.69
25.59
24.05
22.76
22.73
21.54
21.17
20.82
20.79
20.76
17.88
17.84
17.78
17.69
15.92
HO
HO
H
H
H
O
NH
N
N
OAc
1.14
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

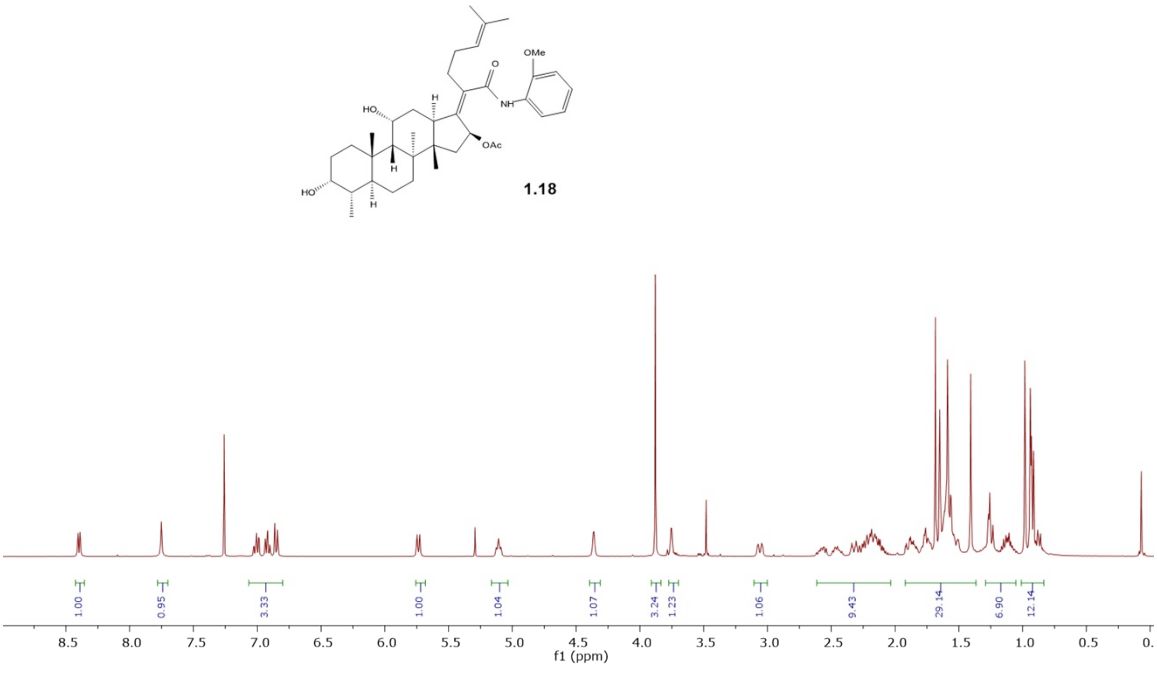

HO
HO
H
H
H
O
NH
OAc
1.16
1.00
0.87
0.97
1.06
2.09
1.03
16.81
41.27
16.72
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


170.94
170.47
140.42
136.36
132.94
123.32
74.01
71.37
68.33
49.48
49.29
46.50
43.24
42.94
39.52
37.55
36.26
36.15
32.37
29.98
29.61
29.27
28.58
28.02
26.42
26.20
25.68
24.04
22.77
21.28
20.79
17.81
17.77
16.78
HO
O
NH
OAc
H
HO
1.16
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

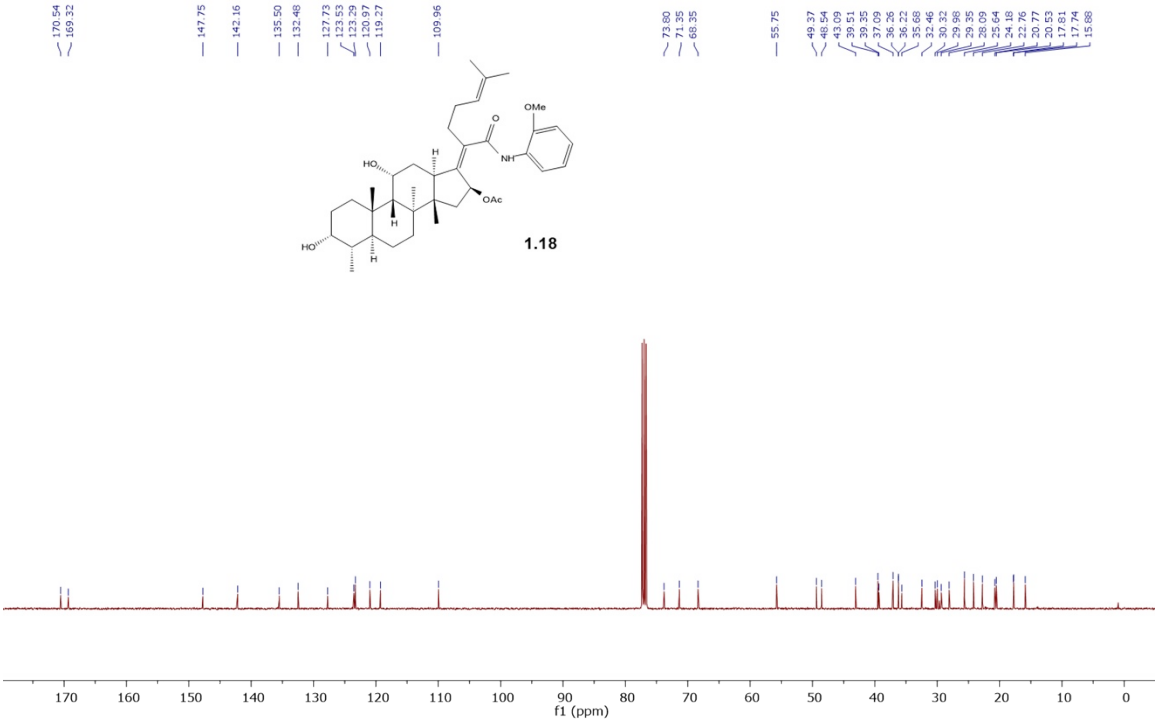

HO
O
NH
OAc
H
HO
1.17
1.00
0.88
0.95
1.10
2.10
1.05
1.23
2.38
13.19
23.30
6.72
21.64
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

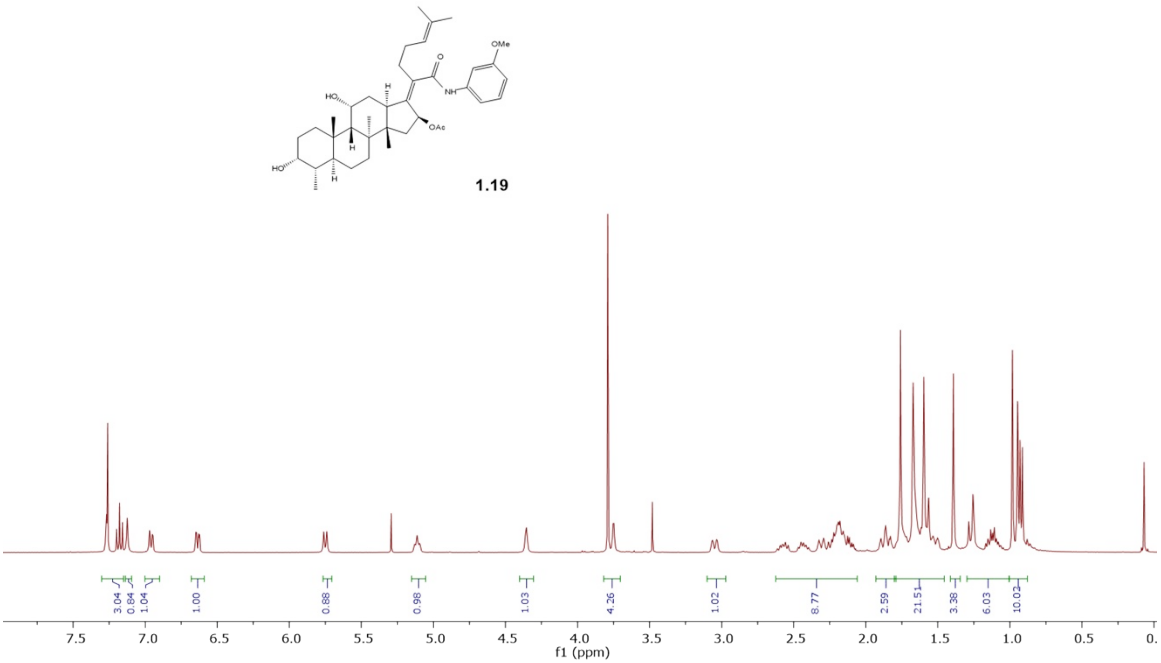

170.61
170.47
141.00
136.54
132.41
123.38
74.77
71.40
68.39
49.48
49.29
48.61
43.15
42.67
39.59
39.36
37.10
36.20
30.27
29.99
29.96
29.63
28.42
28.14
26.38
26.27
26.09
25.71
24.06
22.69
21.33
20.76
18.17
17.81
17.31
15.04
HO
H
O
NH
OAc
HO
H
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

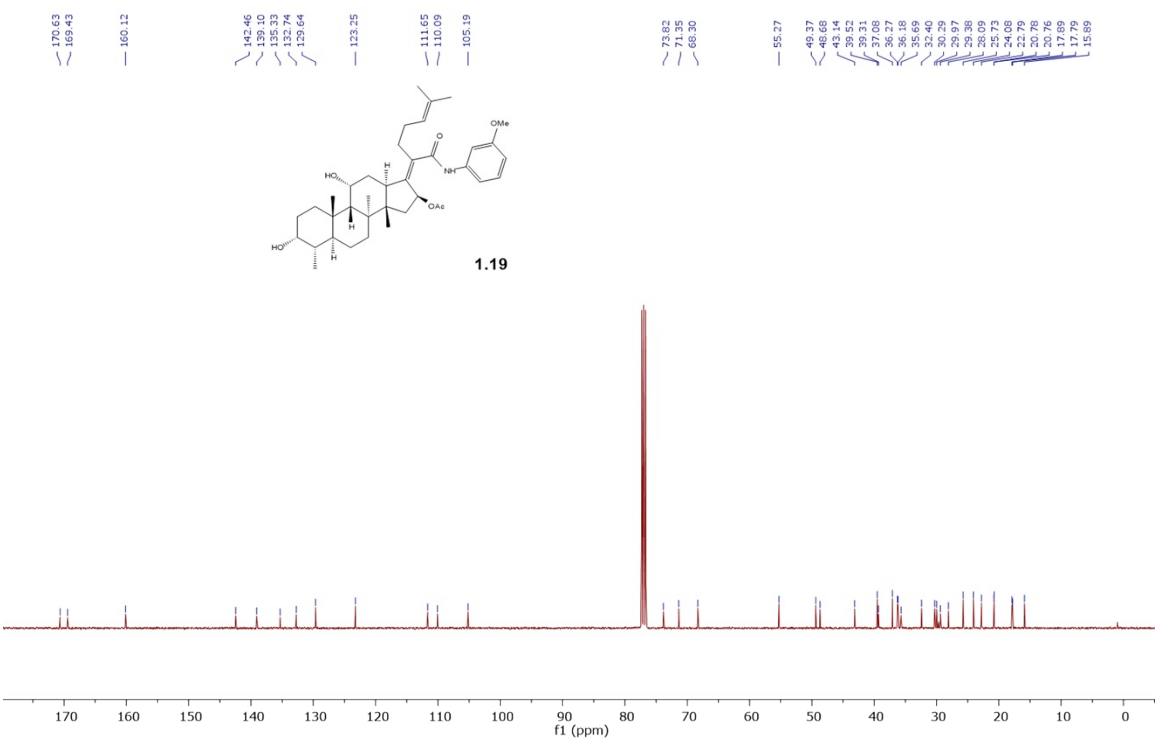
1.17

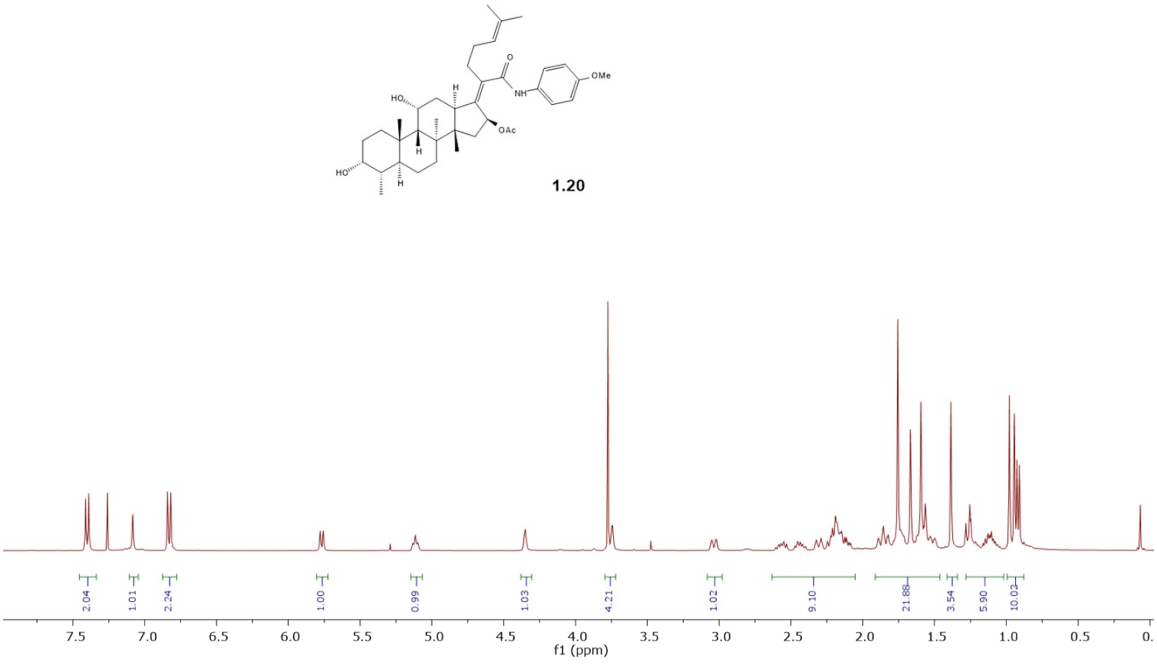

OMe
O
NH
HO
H
OAc
HO
H
1.00
0.95
3.33
1.00
1.04
1.07
3.24
1.23
1.06
9.43
29.14
6.90
12.14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

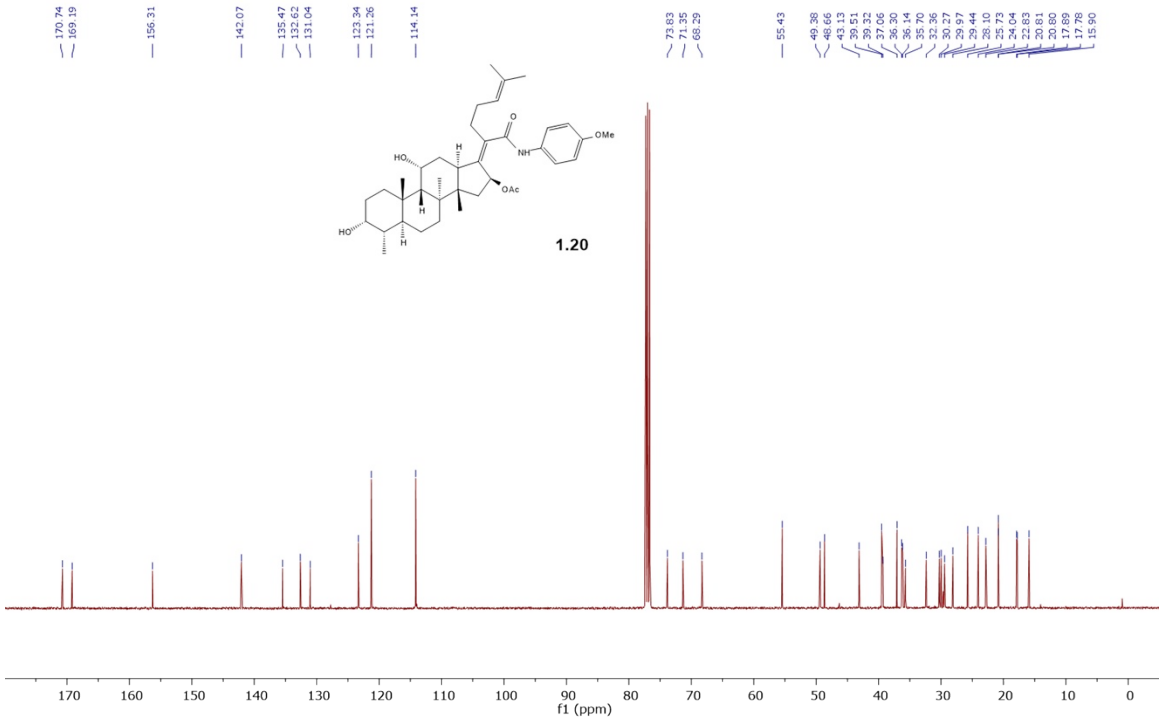
1.18

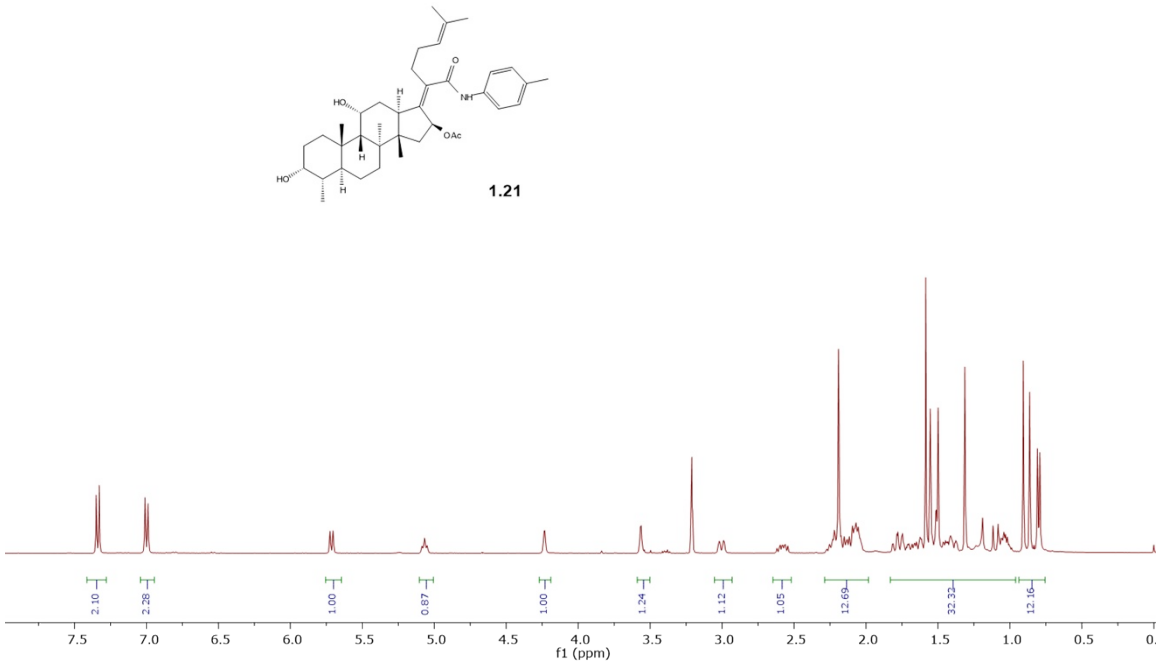

170.54
169.32
147.75
142.16
135.50
132.48
127.73
123.53
123.29
120.97
119.27
109.96
73.80
71.35
68.35
55.75
49.37
48.54
43.09
39.51
39.35
37.09
36.26
36.22
35.68
32.46
30.32
29.98
29.35
28.09
25.64
24.18
22.76
20.77
20.53
17.81
17.74
15.88
OMe
O
NH
HO
H
OAc
HO
H
1.18
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

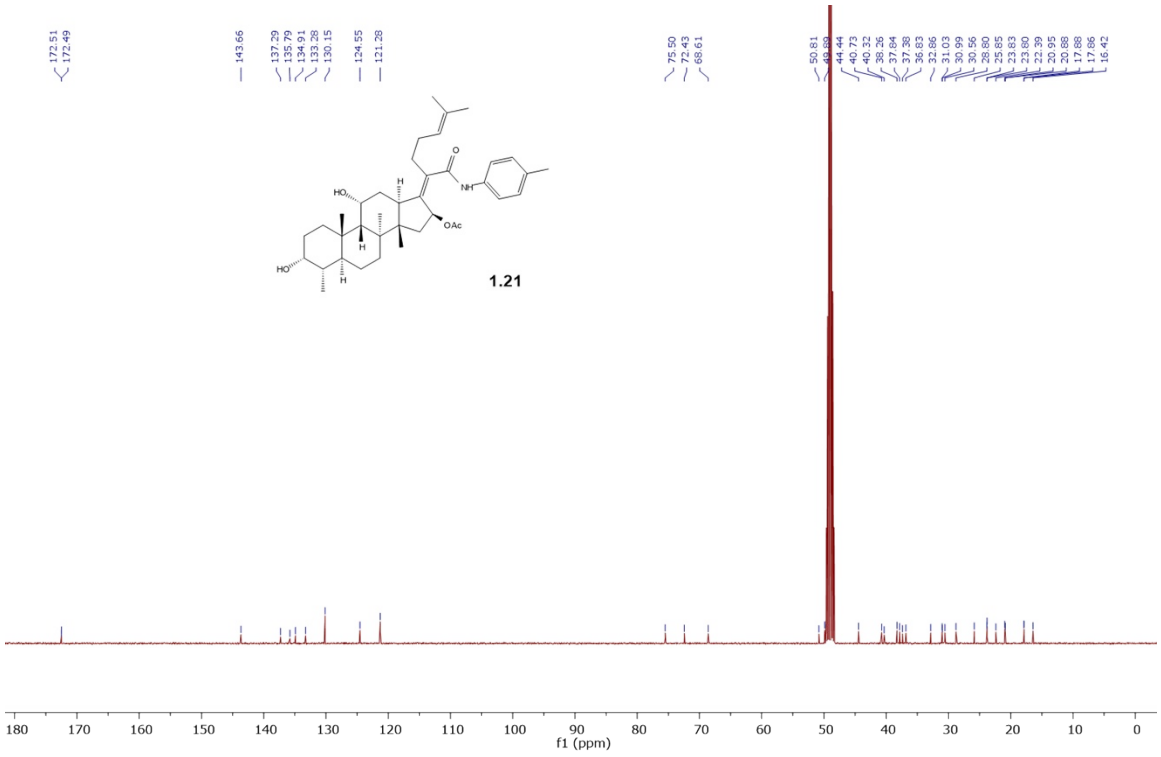

OMe
O
NH
HO
H
OAc
HO
H
1.19
3.04
0.84
1.04
1.00
0.88
0.98
1.03
4.26
1.02
8.77
2.59
21.51
3.38
6.03
10.03
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

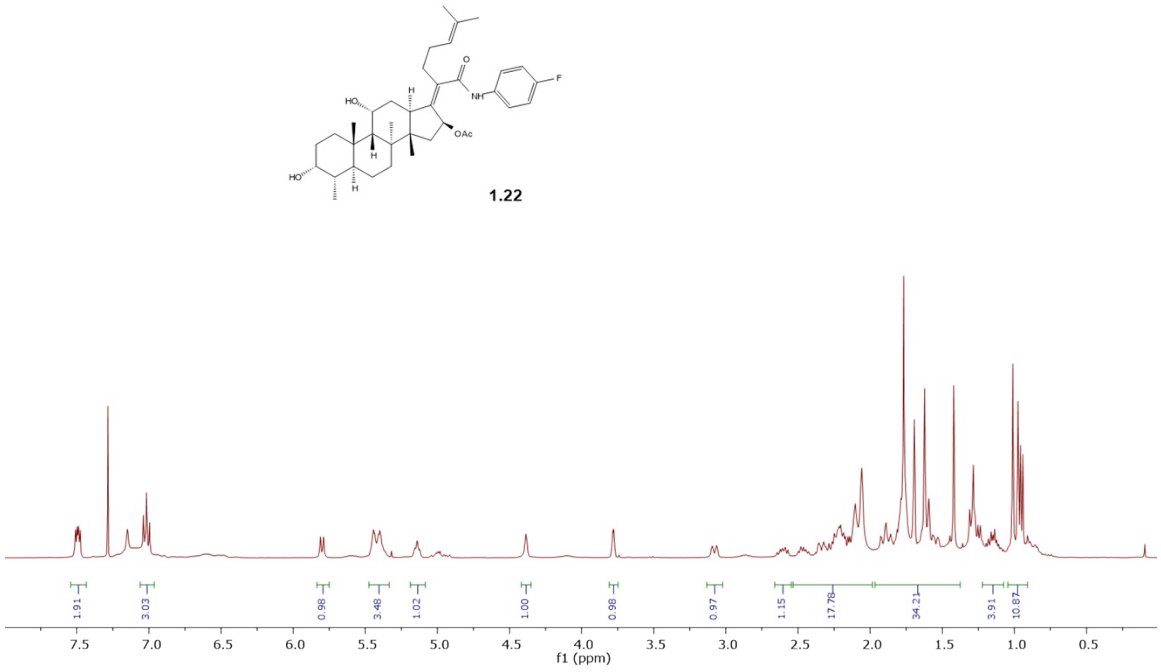

170.63
169.43
160.12
142.46
139.10
135.33
132.74
129.64
123.25
111.65
110.09
105.19
73.82
71.35
68.30
55.27
49.37
48.68
43.14
39.52
39.31
37.08
36.27
36.18
35.69
32.40
30.29
29.97
29.38
28.09
25.73
24.08
22.79
20.78
20.76
17.89
17.79
15.89
OMe
O
NH
HO
OAc
H
HO
H
1.19
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

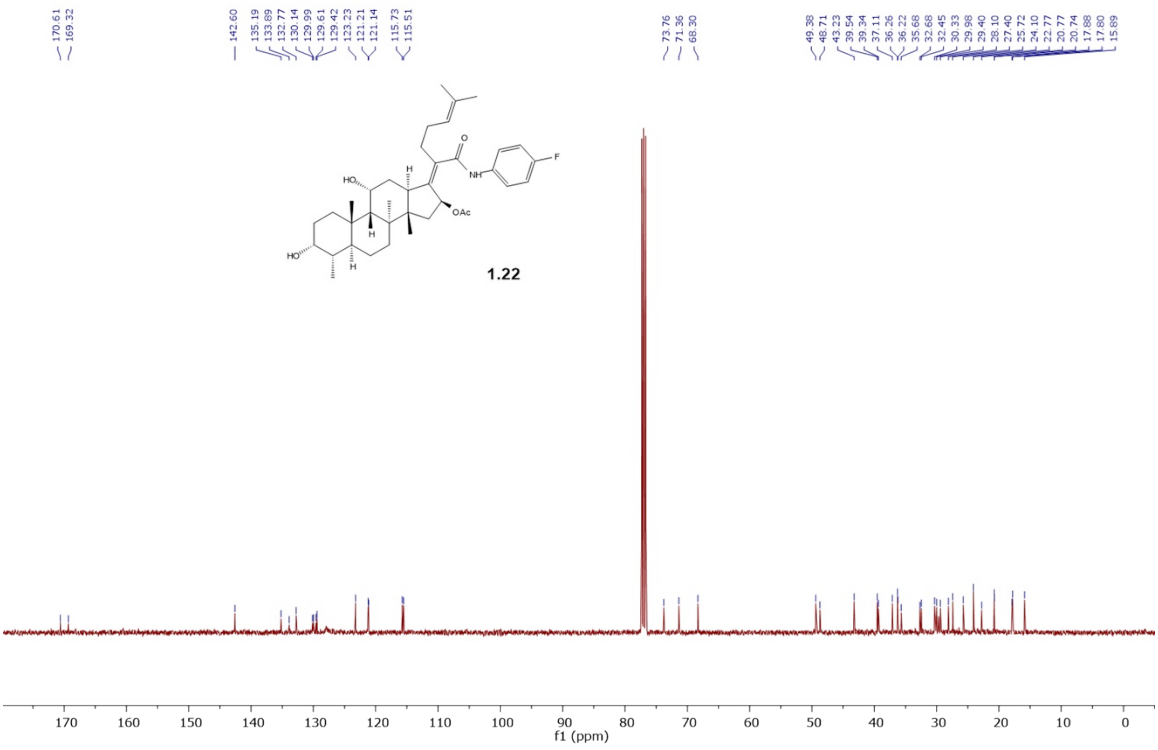

OMe
O
NH
H
HO
OAc
H
HO
H
1.20
2.04
1.01
2.24
1.00
0.99
1.03
4.21
1.02
9.10
21.88
3.54
5.90
10.03
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


170.74
169.19
156.31
142.07
135.47
132.62
131.04
123.34
121.26
114.14
73.83
71.35
68.29
55.43
49.38
48.66
43.13
39.51
39.32
37.06
36.30
36.14
35.70
32.36
30.27
30.07
29.44
28.10
25.73
24.04
22.83
20.81
20.80
17.89
17.78
15.90
HO
HO
H
H
H
O
NH
OMe
OAc
1.20
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

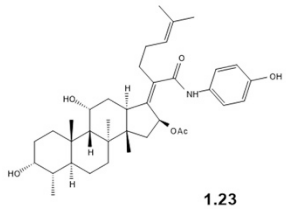

HO
HO
H
H
H
O
NH
OAc
1.21
2.10
2.28
1.00
0.87
1.00
1.24
1.12
1.05
12.69
32.33
12.16
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


172.51
172.49
143.66
137.29
135.79
134.91
133.28
130.15
124.55
121.28
75.50
72.43
68.61
50.81
48.83
44.44
40.73
40.32
38.26
37.84
37.38
36.83
35.86
31.03
30.99
30.56
28.80
25.85
23.83
23.80
22.39
20.95
20.88
17.88
17.86
16.42
HO
H
NH
O
OAc
HO
H
H
1.21
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

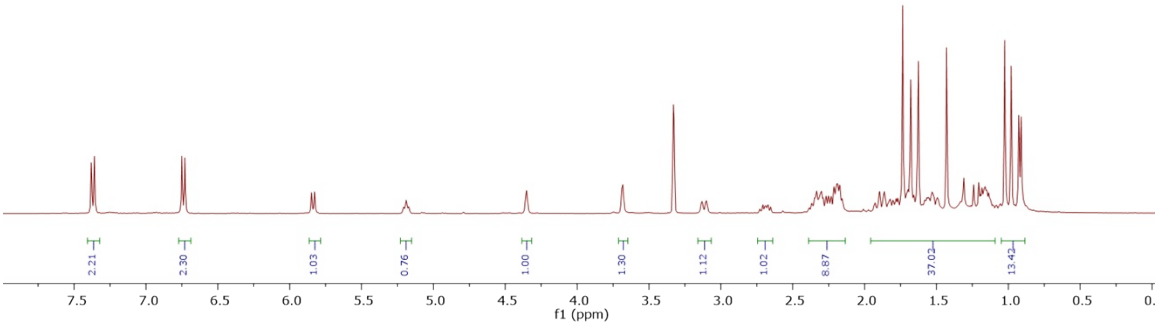

HO
H
NH
O
F
OAc
HO
H
H
1.22
1.91
3.03
0.98
3.48
1.02
1.00
0.98
0.97
1.15
17.78
34.21
3.91
10.87
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

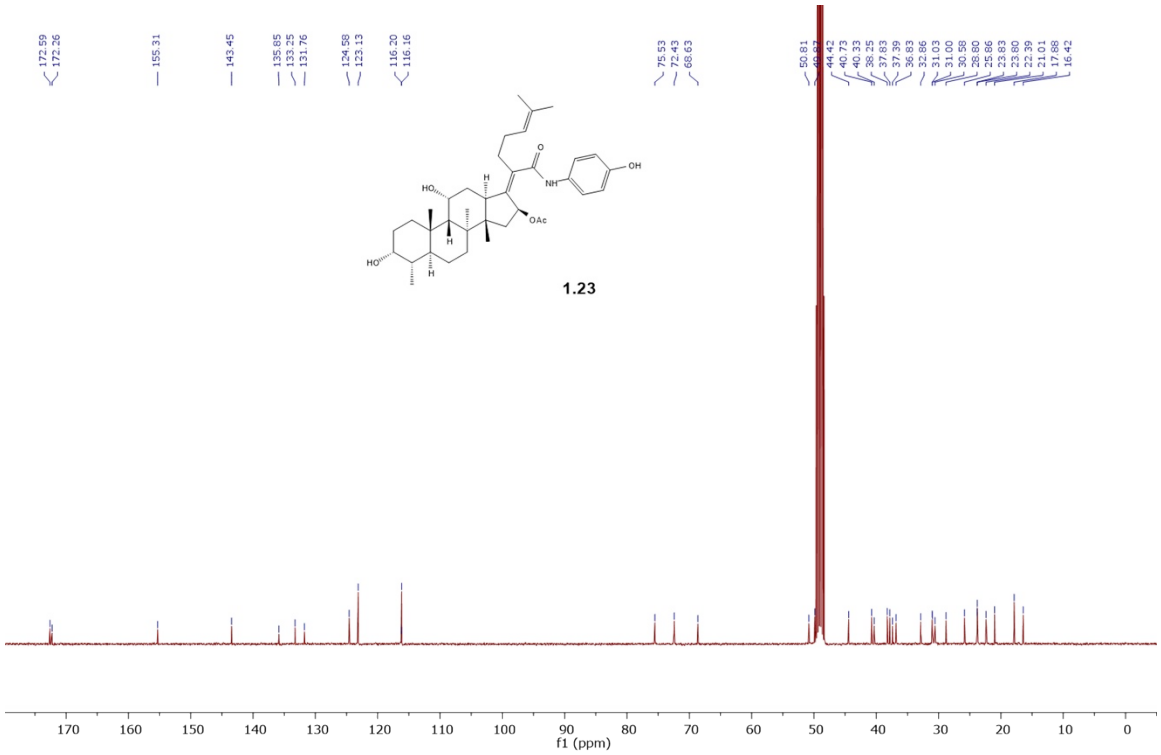

170.61
169.32
142.60
135.19
133.89
132.77
130.14
129.99
129.61
129.42
123.23
121.21
121.14
115.73
115.51
73.76
71.36
68.30
49.38
48.71
43.23
39.54
39.34
37.11
36.25
36.22
35.68
32.68
32.45
30.33
29.98
29.40
28.10
27.40
25.72
24.10
22.77
20.77
20.74
17.88
17.80
15.89
HO
H
NH
F
OAc
HO
H
H
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1.22

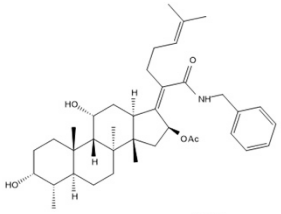

HO
H
NH
OH
OAc
HO
H
H

1.23

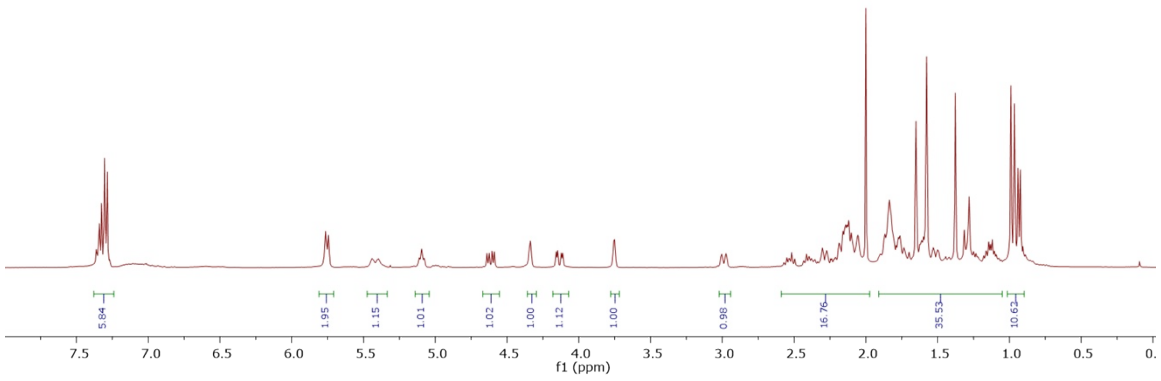

2.21
2.30
1.03
0.76
1.00
1.30
1.12
1.02
8.87
37.02
13.42
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

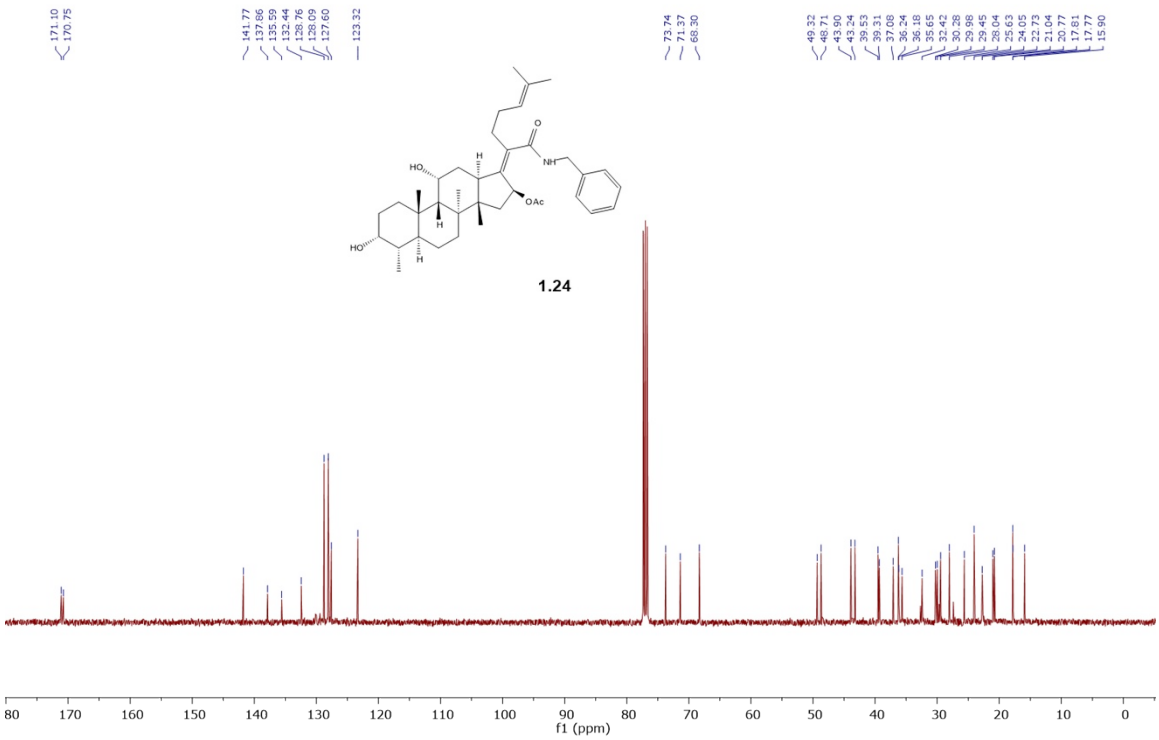

172.59
172.26
155.31
143.45
135.85
133.25
131.76
124.58
123.13
116.20
116.16
75.53
72.43
68.63
50.81
44.42
40.73
40.33
38.25
37.83
37.39
36.83
32.86
31.03
31.00
30.98
28.80
25.86
23.83
23.80
22.39
21.01
17.88
16.42
HO
H
O
NH
OH
OAc
HO
H
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1.23

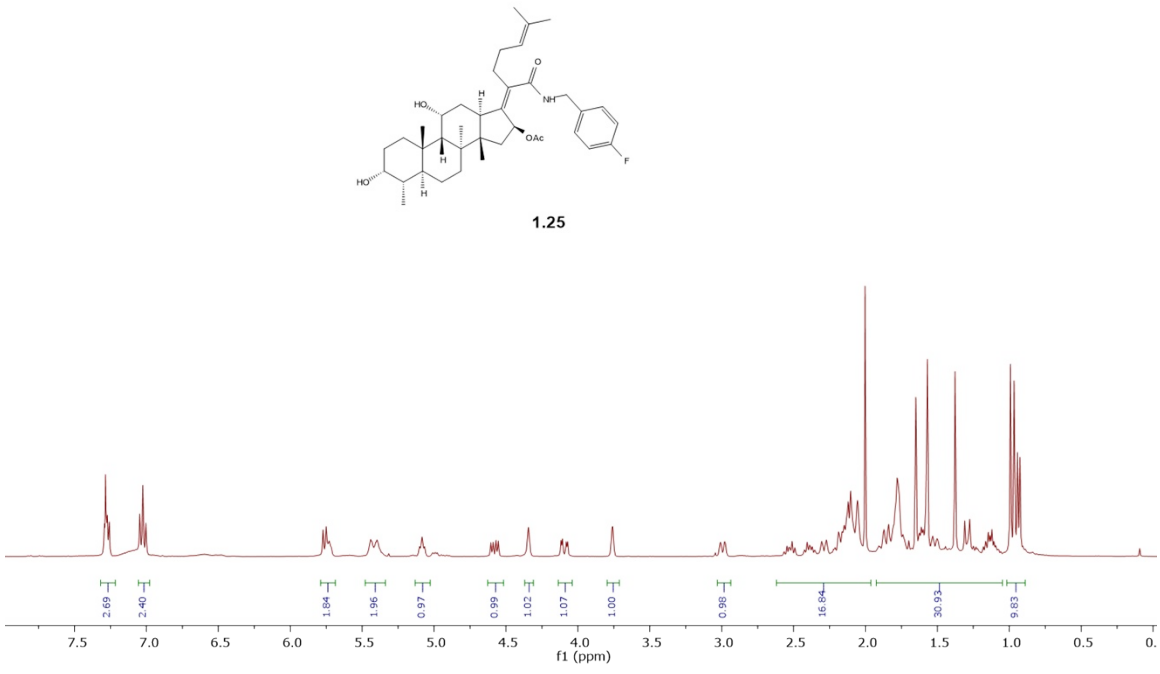

HO
H
O
NH
OAc
HO
H

1.24

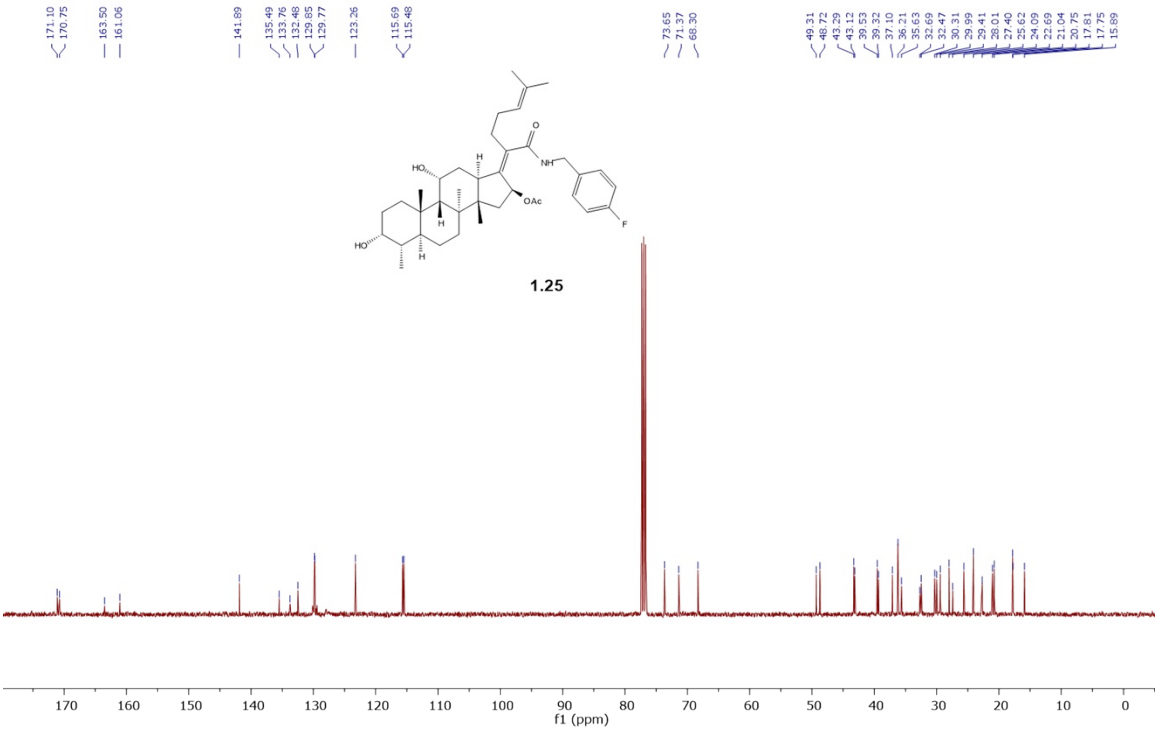

5.84
1.95
1.15
1.01
1.02
1.00
1.12
1.00
0.98
16.76
35.53
10.62
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


171.10
170.75
141.77
137.86
135.59
132.44
128.76
128.09
127.60
123.32
73.74
71.37
68.30
49.32
48.71
43.90
43.24
39.53
39.31
37.88
36.24
36.18
35.65
32.42
30.28
29.98
29.45
28.04
25.63
24.05
22.73
21.04
20.77
17.81
17.77
15.90
HO
H
O
NH
OAc
HO
H
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

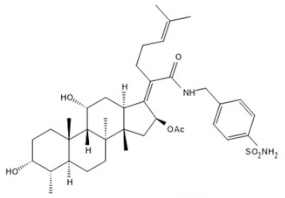
1.24


HO
H
O
NH
OAc
F
HO
H
2.69
2.40
1.84
1.96
0.97
0.99
1.02
1.07
1.00
0.98
16.84
30.93
9.83
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

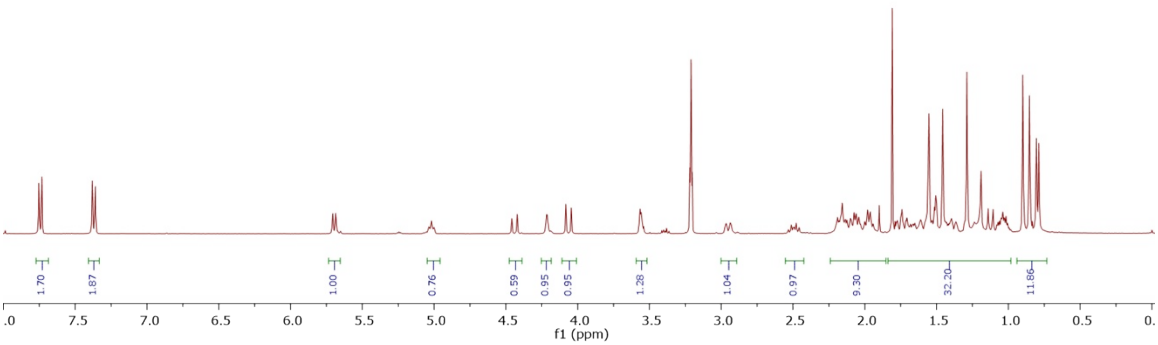
1.25

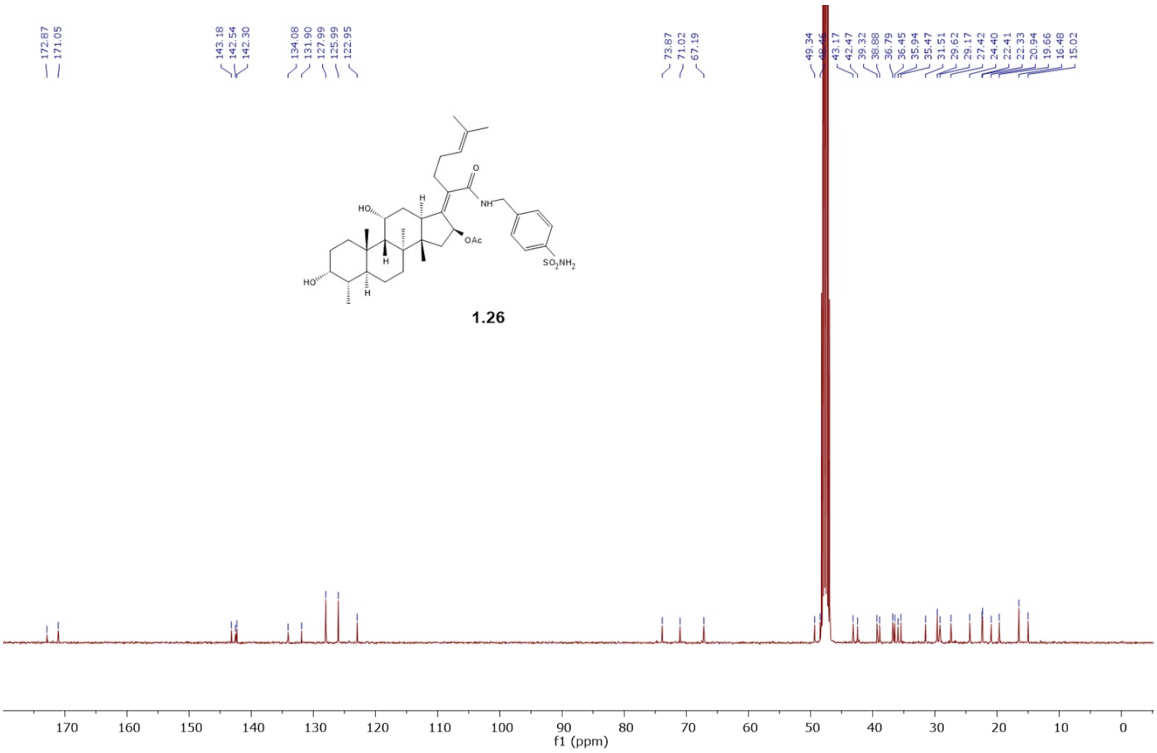

171.10
170.75
163.50
161.06
141.89
135.49
133.76
132.48
129.85
129.77
123.26
115.69
115.48
73.65
71.37
68.30
49.31
48.72
43.29
43.12
39.53
39.32
37.10
36.21
35.63
32.69
32.47
30.31
29.99
29.41
28.01
27.40
25.62
24.09
22.69
21.04
20.75
17.81
17.75
15.89
HO
H
O
NH
OAc
F
HO
H
H
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1.25

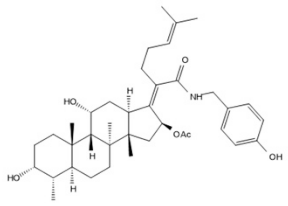

HO
H
O
NH
OAc
SO2NH2
HO
H
H

1.26

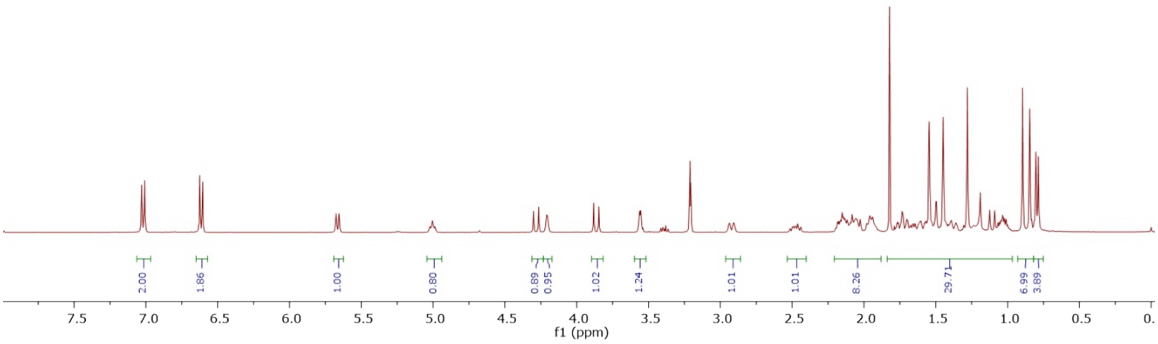

1.70
1.87
1.00
0.76
0.59
0.95
0.95
1.28
1.04
0.97
9.30
32.20
11.86
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

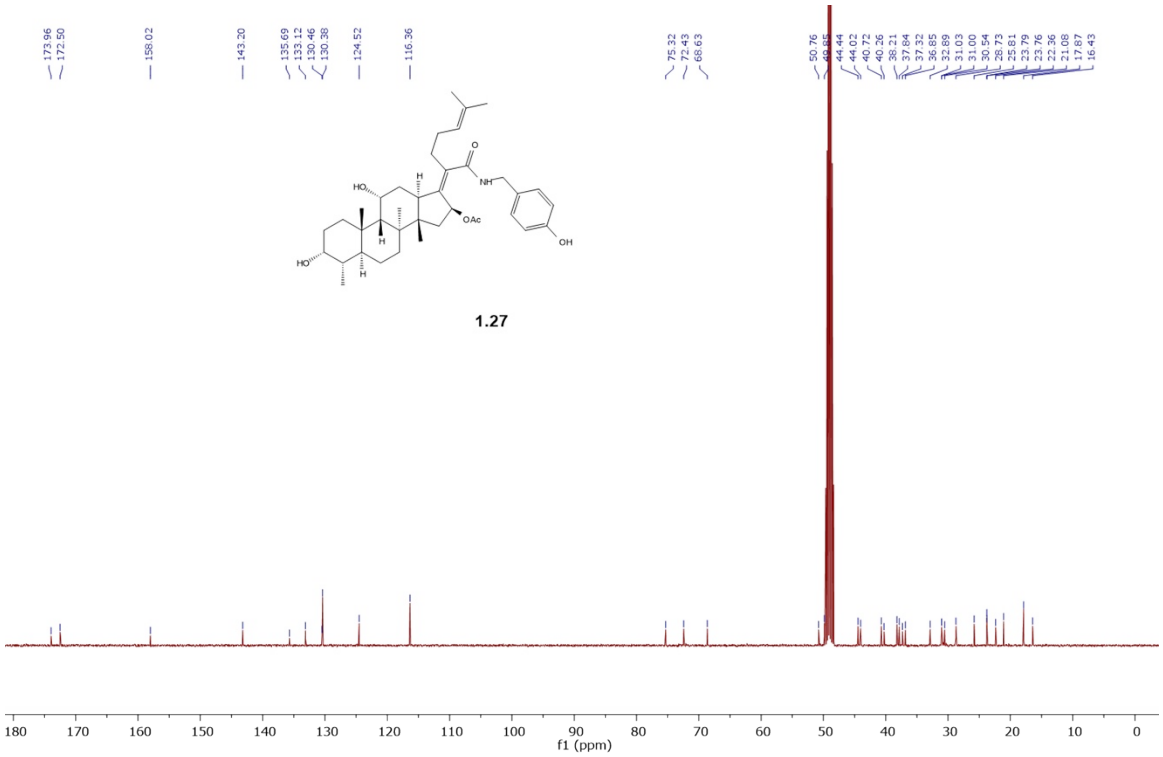

172.87
171.05
143.18
142.54
142.30
134.08
131.90
127.99
125.99
122.95
73.87
71.02
67.19
49.34
43.17
42.47
39.32
38.68
38.29
36.45
35.94
35.47
31.51
29.62
29.17
27.42
24.40
22.41
22.33
20.94
19.66
16.48
15.02
HO
H
O
NH
OAc
HO
H
SO2NH2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1.26

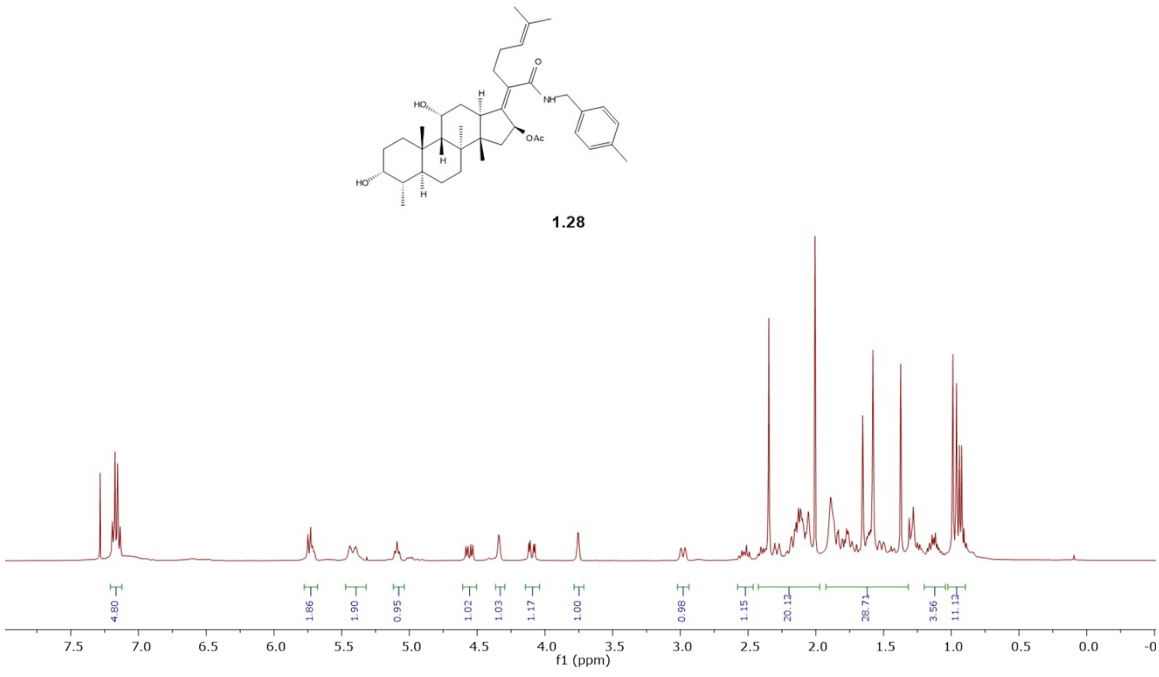

HO
H
O
NH
OAc
HO
H
OH

1.27

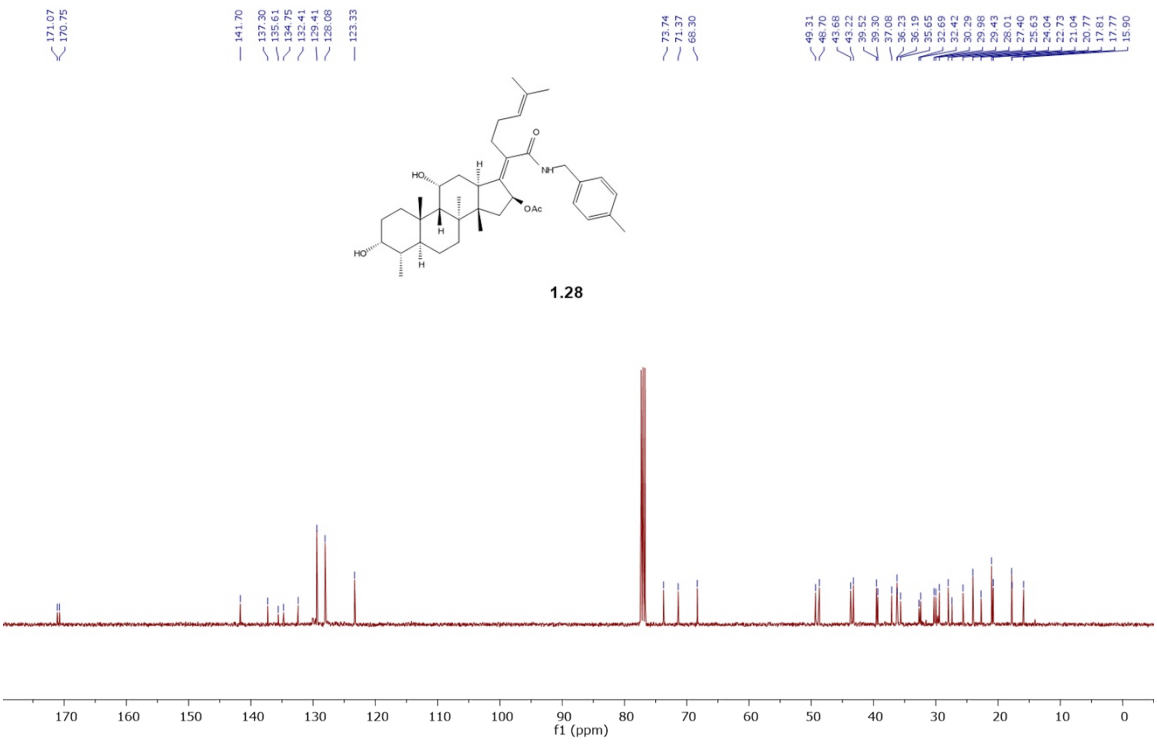

2.00
1.86
1.00
0.80
0.89
0.95
1.02
1.24
1.01
1.01
8.26
29.71
6.99
3.89
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


173.96
172.50
158.02
143.20
135.69
133.12
130.46
130.38
124.52
116.36
75.32
72.43
68.63
50.76
49.85
44.44
44.02
40.72
40.26
38.21
37.64
37.32
36.85
32.89
31.03
31.00
30.54
28.73
25.81
23.79
23.76
22.36
21.08
17.87
16.43
HO
H
O
NH
OAc
OH
HO
H
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

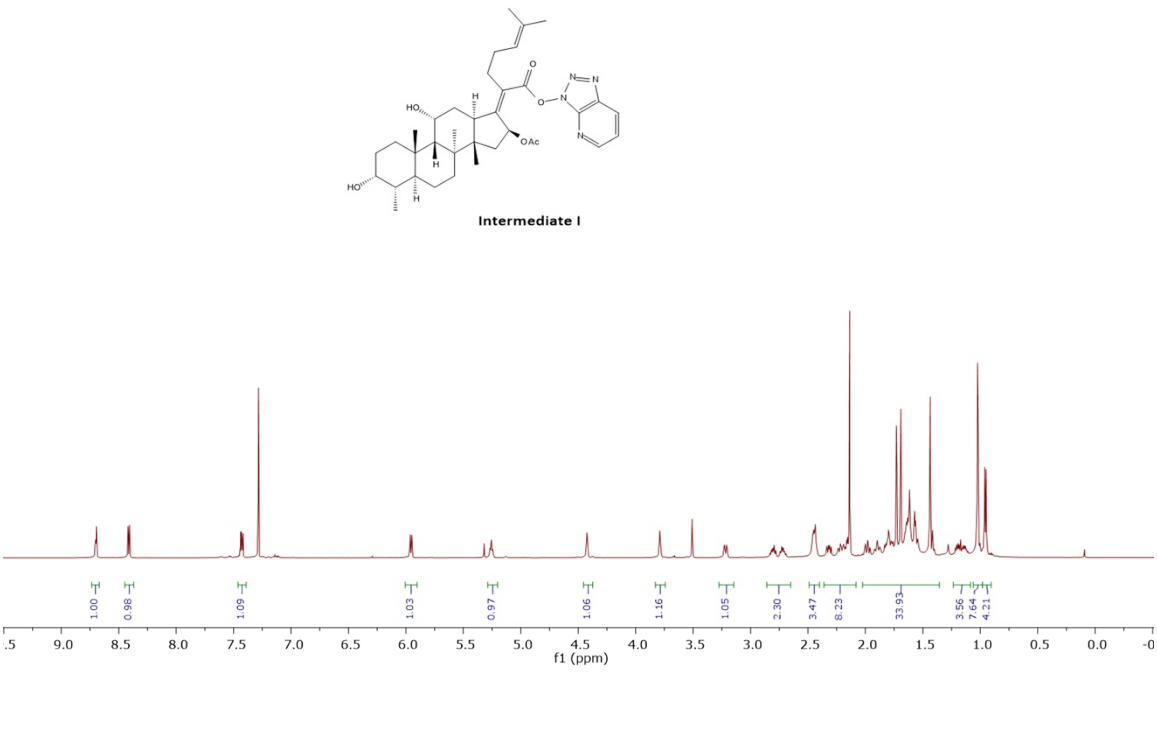
1.27


HO
H
O
NH
OAc
HO
H
4.80
1.86
1.90
0.95
1.02
1.03
1.17
1.00
0.98
1.15
20.12
28.71
3.56
11.12
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

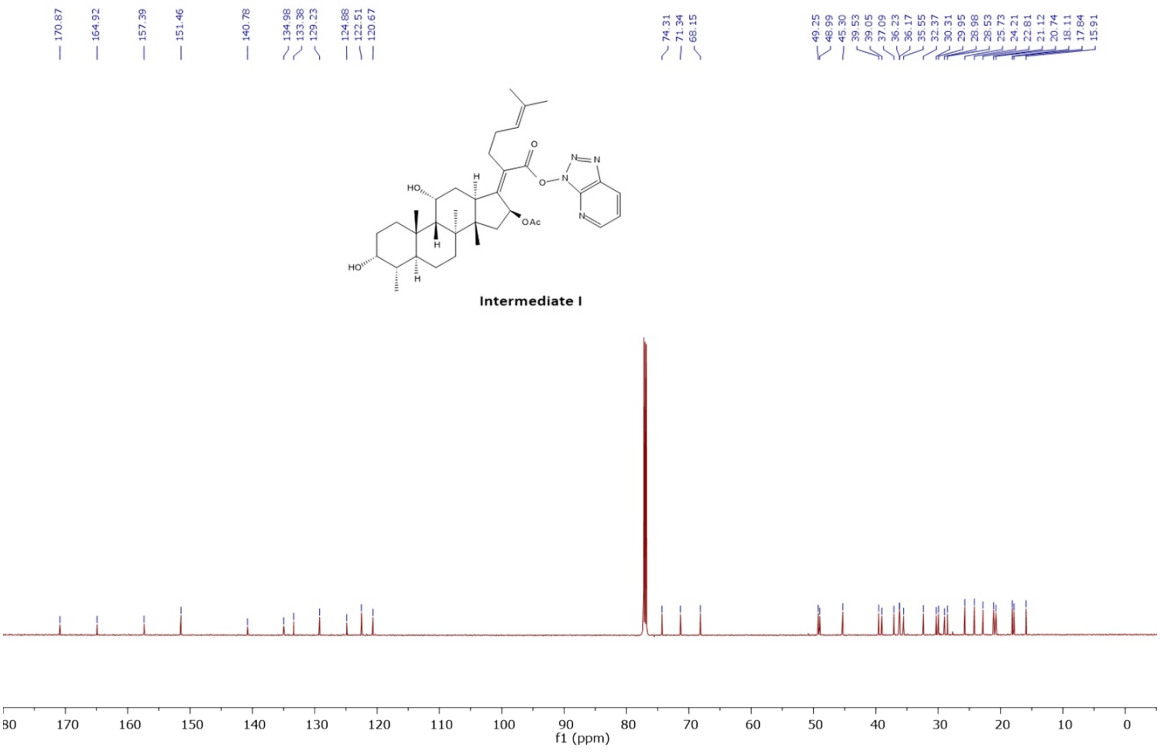
1.28



1.28



Intermediate I



6.0 References

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