Anti-cancer activity of heteroaromatic acetals of andrographolide and its isomers

Supplementary Section

Synthesis of heteroaromatic (3,19) acetals of andrographolide

3,19-Benzylidene-andrographolide (**2a**)

Andrographolide (**1**) (5g) was dissolved in a mixture of toluene (100ml) and DMSO (10ml), to this benzaldehyde (6.05g) and a catalytic amount of PPTs was added (Molar ratio; Andrographolide: benzaldehyde=1:4). The reaction was allowed to stir at 70 ^{0}C till the completion of the reaction as checked by TLC. The reaction mixture was then allowed to cool to room temperature and quenched using the cold saturated bicarbonate solution and extracted with Dichloromethane (DCM). The organic layer was then washed with brine, water and dried with anhydrous sodium sulphate after which the crude product was obtained upon evaporation of the solvent. The product was purified using column chromatography (petroleum ether/acetone) 80:20 to obtain the desired compound. Yield 80%, m.p. -141-142 ^{0}C.

IR (KBr) cm^{-1}: 3400 (**O-H stretch**), 3081 (aromatic C-H stretch), 2944 (sp^3 C-H stretch), 1751 (C=O stretch), 1675 (exocyclic C=C stretch), 1199 (C-O stretch), 988, 906, 800 & 761 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, CDCl3)**: δ 7.49 (2H, d, J=7.6 Hz, H-23, H-27), 7.36 (3H, m, H-24, H-25, H-26), 6.95 (1H, dt, J=7.04 Hz, 1.48Hz, H-12), 5.76 (1H, s, H-21), 4.99 (1H, brs, H-14), 4.91 (1H, brs, H_a-17), 4.63 (1H, brs, H_b-17), 4.43 (1H, dd, J=10.44 Hz, 6.12 Hz, H_a-15), 4.28-4.21 (2H, m, H_b-15, H_a-19), 3.67 (1H, dd, J=12.64 Hz, 4.48 Hz, H-3), 3.59 (1H, d, J=11.32, H_b-19), 2.63-2.62 (1H, m, -OH), 2.59-2.54 (2H, m), 2.47-2.43 (2H, m), 2.05-1.99 (1H,m), 1.92-1.83 (4H, m), 1.49 (3H, s), 1.31-1.25 (3H, m), 0.87 (3H, m). **^{13}C NMR(100 MHz, CDCl3)**: δ 170.11 (C-16), 148.88 (C-8), 146.51 (C-12), 138.79 (C-22), 128.91 (C-13), 128.36 (C-24, C-26), 128.01 (C-25), 126.20 (C-23, C-27) 109.23 (C-17), 95.24 (C-21), 80.67 (C-3), 74.35 (C-15), 69.48 (C-19), 66.14 (C-14), 55.75 (C-9), 54.81

(C-5), 38.88 (C-4), 37.58 (C-7), 36.93 (C-10), 36.08 (C-1), 26.05 (C-2), 24.75 (C-6), 22.78 (C-11), 21.70 (C-20,) 15.35 (C-18), **Mass (*m/z*)**: $[M+H]^+$ 439.2459, $[M+Na]^+$ 461.2277, $[2M+Na]^+$ 899.4669

3,19-(2-Furfurylidene)-andrographolide (**2b**)

Compound **2b** was synthesized from **1** following the same method described for the synthesis of **2a**. Yield 74%, m.p. - 193-196 ^{0}C. **IR (KBr) cm^{-1}**: 3405 (**O-H stretch**), 3133 (aromatic C-H stretch), 2942 (sp^3 C-H stretch), 1726 (C=O stretch), 1675 (exocyclic C=C stretch), 1222 (C-O stretch), 983, 810 & 745 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, CDCl3)**: δ 7.40 (1H, brs, H-25), 6.95 (1H, brs, H-12), 6.44 (1H, s, H-24), 6.36 (1H, s, H-23), 5.85 (1H, s, H-21), 5.01 (1H, brs, H-14), 4.91 (1H, brs, H_a-17), 4.62 (1H, brs, H_b-17), 4.47-4.43 (1H, m, H_a-15), 4.26-4.22 (2H, m, H_b-15, H_a-19), 3.67 (1H, d, J=12Hz, H-3), 3.57 (1H, d, J=11.24Hz, H_b-19), 2.58-2.57 (2H, m), 2.46-2.35 (2H, m), 2.04-1.98 (1H, m), 1.88-1.85 (4H, m), 1.71.1.68 (1H, m), 1.47 (3H, s, H-18), 1.29-1.25 (3H, m), 0.85 (3H, s, H-20); **^{13}C NMR (100 MHz, CDCl3)**: δ 170.13 (C-16), 151.39 (C-22), 148.84 (C-8), 146.39 (C-12), 142.50 (C-25), 128.03 (C-13), 110.2 (C-24), 109.29 (C-22), 107.42 (C-17), 89.72 (C-21), 80.96 (C-3), 74.41 (C-15), 69.38 (C-19), 66.15 (C-14), 55.69 (C-9), 54.75 (C-5), 38.82 (C-4), 37.52 (C-7), 37.02 (C-10), 35.96 (C-1), 25.88 (C-2), 24.72 (C-6), 22.73 (C-11), 21.51 (C-20), 15.30 (C-18), **Mass (*m/z*)**: $[M+H]^+$ 429.2259, $[M+Na]^+$ 451.2080, $[2M+Na]^+$ 879.4245

3,19-(2-Pyrilidene)-andrographolide (**2c**)

Compound **2c** was synthesized from **1** following the same method described for the synthesis of **2a**. Yield 60%, m.p. - 193-196 ^{0}C. **IR (KBr) cm^{-1}**: 3409 (**O-H stretch**), 3082 (aromatic C-H stretch), 2941 (sp^3 C-H stretch), 1756 (C=O stretch), 1675 (exocyclic C=C stretch), 1222 (C-O stretch), 981, 906 & 708 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.5 (1H, brs, H-26), 7.77 (1H, t, J=7.5, 7.4 Hz, H-24), 7.6 (1H, d, J=7.6 Hz, H-23),

7.29-7.27 (1H, m, H-25), 6.94 (1H, brs, H-12), 5.84 (1H, s, H-21), 5.05 (1H, brs, H-14), 4.91(1H, brs, H_a-17), 4.65 (1H, brs, H_a-17), 4.45-4.42 (1H, m, H_a-15), 4.31 (1H, d, J=11.32, H_a-19), 4.24 (1H, d, J=10.24, H_b-15), 3.71 (1H, d, J=12.12Hz, H-3), 3.62 (1H, d, J=11.20 Hz, H_b-19), 2.59 (2H, brs), 2.46 (2H, d, J=13.00 Hz), 2.02-1.99 (1H, m), 1.86 (5H, brs), 1.48 (3H, s, H-18), 1.31-1.25 (3H, m), 0.86 (3H, s, H-20); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 170.19 (C-16), 157.29 (C-22), 148.65 (C-26), 148.49 (C-8), 146.32 (C-12), 137.23 (C-24), 128.13 (C-13), 124.00 (C-23), 120.59 (C-25), 109.43 (C-17), 95.31 (C-21), 80.83 (C-3), 74.45 (C-15), 69.53 (C-19), 66.00 (C-14), 55.76 (C-9), 54.79 (C-5), 38.84 (C-4), 37.55 (C-7), 37.01 (C-10), 36.00 (C-1), 26.00 (C-2), 24.66 (C-6), 22.75 (C-11), 21.70 (C-20,) 15.31 (C-18), **Mass (*m/z*)**: $[M+H]^+$ 440.2426, $[2M+Na]^+$ 901.4589

3,19-(2-Thiophenylidene)-andrographolide (**2d**)

Compound **2d** was synthesized from **1** following the same method described for the synthesis of **2a**. Yield 66%, m.p. - 193-196 ^{0}C. **IR (KBr) cm^{-1}**: 3389 (**O-H stretch**), 3113 (aromatic C-H stretch), 2939 (sp^3 C-H stretch), 1726 (C=O stretch), 1675 (exocyclic C=C stretch), 1187 (C-O stretch), 978, 904 & 705 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.29 (1H, brs, H-25), 7.12 (1H, brs, H-24), 6.98-6.93 (2H, m, H-23, H-12), 6.03 (1H, s, H-21), 4.99 (1H, brs, H-14), 4.91 (1H, s, Ha-17), 4.62 (1H, s, H_b-17), 4.46-4.42 (1H, m, Ha-15), 4.27-4.22 (2H, m, H_b-15, H_a-19), 3.67 (1H, d, J=11.76 Hz, H-3), 3.57 (1H, d, J=11.32 Hz, H-19$_b$), 2.67-2.66 (1H, m, H_a-2), 2.58-2.54(2H, m, H_b-2, -OH), 2.46-2.33 (2H, m, H_a-7, H_a-11), 2.04-1.99 (1H, m, H_b-7), 1.91-1.80 (4H, m, H-9, H_a-1, H_a-6, H_b-11), 1.47 (3H, s, H-18), 1.32-1.21 (3H, m, H_b-6, H_b-1, H-5), 0.85(3H, s, H-20); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 170.14 (C-16), 148.86 (C-12), 146.42 (C-22), 141.96 (C-8), 128.02 (C-13), 126.39 (C-25), 125.16 (C-24), 125.08 (C-23), 109.4 (C-17), 91.9 (C-21), 80.87 (C-3), 74.41 (C-15), 69.39 (C-19), 66.14 (C-14), 55.68 (C-9), 54.72 (C-5), 38.83 (C-4), 37.54 (C-7), 36.86 (C-

10), 36.01 (C-1), 25.92 (C-2), 24.73 (C-6), 22.74 (C-11), 21.71 (C-20), 15.32 (C-18), **Mass (*m/z*)**: $[M+H]^+$ 445.2033

12-Hydroxy-3,19-benzylidene-andrographolide (**3a**)

3,19-Benzylidene-andrographolide (200mg) was dissolved in DCM (2ml) and to it catalytic amount of PDC (8mg) was added and stirred at room temperature till the completion of the reaction as confirmed by TLC (4days). The reaction contents were impregnated on silica gel (60-120 mesh) and column chromatography (petroleum ether/acetone:70/30) was carried out to obtain the desired compound (3a). Yield 80%, m.p. - 198-200 ^{0}C. **IR (KBr) cm^{-1}**: 3469 (**O-H stretch**), 3078 (aromatic C-H stretch), 2947 (sp^3 C-H stretch), 1734 (C=O stretch), 1638 (exocyclic C=C stretch), 1194 (C-O stretch), 995, 887, 832 & 762 (aromatic C-H out of plane bending).**^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.48 (2H, brs, H-23, H-27), 7.34 (3H, m, H-24, H-25, H-26), 7.28 (1H, m, H-14), 5.75 (1H, s, H-21), 4.93 (1H, s, H_a-17), 4.84 (2H, brs, H-15), 4.77 (1H, s, H_b-17), 4.54 (1H, brs, H-12), 4.25 (1H, d, J=10.44 Hz, H_a-19), 3.65 (1H, m, H-3), 3.57 (1H, d, J=10.56 Hz, H_b-19), 2.67 (12-OH), 2.43 (2H, m, H-7), 2.06-1.82 (6H, m), 1.62 (1H, m), 1.47 (3H, m), 1.25 (3H, s, H-20), 1.13(1H, m), 0.81(3H, s, H-18); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 173.01 (C-16), 147.98 (C-8), 145.39 (C-14), 138.89 (C-22), 136.02 (C-13), 128.90 (C-25), 128.36 (C-24, C-26), 126.23 (C-23, C-27), 108.22 (C-17), 95.22 (C-21), 80.73 (C-3), 70.52 (C-15), 69.50 (C-19), 67.40 (C-12), 54.98 (C-5), 52.91 (C-9), 39.19 (C-4), 38.06 (C-10), 36.98 (C-7), 35.81 (C-1), 30.24 (C-11), 26.04 (C-2), 23.02 (C-6), 21.70 (C-20), 15.43 (C-18), **Mass (*m/z*)**: $[M+Na]^+$ 461.2292, $[2M+Na]^+$ 899.4672

12-Hydroxy-3,19-(2-furfurylidene)-andrographolide (**3b**)

Compound **3b** was synthesized from **2b** following the same method described for the synthesis of **3a**. Yield 91%, m.p. - 154-157 ^{0}C. **IR(KBr) cm^{-1}**: 3473 (**O-H stretch**), 3126 (aromatic C-H stretch), 2955 (sp^3 C-H stretch), 1754 (C=O stretch), 1642 (exocyclic C=C stretch), 1505 &

1445 (aromatic C=C), 1206 (C-O stretch), 956, 899 & 840 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.39 (1H, m, H-25), 7.28 (1H, m, H-14), 6.44 (1H, d, J=3.24 Hz, H-23), 6.36 (1H, dd, J=3.24, 1.8 Hz, H-24), 5.83 (1H, s, H-21), 4.93 (1H, s, H_a-17), 4.85 (2H, s, H-15), 4.77 (1H, s, H_b-17), 4.54 (1H, brs, H-12), 4.21 (1H, d, J=11.4 Hz, H_a-19), 3.64 (1H, dd, J=12.72, 4.88 Hz, H-3), 3.55 (1H, d, J=11.4 Hz, H_b-19), 2.63 (12-OH), 2.46-2.28 (2H, m), 2.10-2.05 (1H, m), 1.95-1.77 (6H, m), 1.62-1.59 (1H, m), 1.45 (3H, s, H-20), 1.25 (2H, s), 1.16-1.09 (1H, m), 0.79 (3H, s, H-18); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 172.98 (C-16), 147.88 (C-8), 145.35 (C-14), 151.47 (C-22), 136.00 (C-13), 142.50 (C-25), 110.19 (C-24), 108.29 (C-23), 107.41 (C-17), 89.71 (C-21), 80.77 (C-3), 70.51 (C-15), 69.40 (C-19), 67.45 (C-12), 54.94 (C-5), 52.90 (C-9), 39.13 (C-4), 38.01 (C-10), 37.05 (C-7), 35.71 (C-1), 30.21 (C-11), 25.87 (C-2), 22.97 (C-6), 21.48 (C-20), 15.40 (C-18); **Mass (*m/z*)**: $[M+H]^+$ 429.2253, $[M+Na]^+$ 451.2076, $[2M+Na]^+$ 879.4256

12-Hydroxy-3,19-(2-pyrilidene)-andrographolide (**3c**)

Compound **3c** was synthesized from **2c** following the same method described for the synthesis of **3a**. Yield 60 %, m.p. - 192-195 ^{0}C. **IR (KBr) cm^{-1}**: 3454 (**O-H stretch**), 3096 (aromatic C-H stretch), 2949 (sp^3 C-H stretch), 1758 (C=O stretch), 1644 (exocyclic C=C stretch), 1598 & 1444 (aromatic C=C), 1194 (C-O stretch), 990, 879 & 784 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.57 (1H, brs, H-26), 7.74 (1H, brs, H-24), 7.64 (1H, brs, H-23), 7.29 (2H, m, H-25, H-14), 5.83 (1H, s, H-21), 4.93 (1H, s, H_a-17), 4.84 (2H, s, H-15), 4.77 (1H, s, H_b-17), 4.55 (1H, brs, H-12), 4.30 (1H, d, J=10.8 Hz, H_a-19), 3.70 (1H, m, H-3), 3.60 (1H, d, J=10.48 Hz, H_b-19), 2.70 (12-OH), 2.44 (2H, m), 2.07-2.06 (1H, m), 1.96-1.73 (6H, m), 1.64-1.62 (1H, m), 1.46 (3H, s, H-20), 1.26 (2H, s), 1.18-1.11 (1H, m), 0.81 (3H, s, H-18); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 173.00 (C-16), 148.96 (C-8), 145.33 (C-14), 157.40 (C-22), 136.09 (C-13), 120.86 (C-25), 136.97 (C-24), 148.96 (C-26), 123.83 (C-23), 108.24 (C-17), 95.44 (C-21), 80.86 (C-3), 70.50 (C-15), 69.59 (C-19), 67.40 (C-12), 54.98 (C-5), 52.92 (C-9),

39.18 (C-4), 38.04 (C-10), 37.04 (C-7), 35.76 (C-1), 30.26 (C-11), 26.02 (C-2), 22.99 (C-6), 21.63 (C-20), 15.36 (C-18); **Mass (*m/z*)**: $M+H]^+$ 440.2460, $[2M+Na]^+$ 901.4667

12-Hydroxy-3,19-(2-thiophenylidene)-andrographolide (**3d**)

Compound **3d** was synthesized from **2d** following the same method described for the synthesis of **3a**. Yield 91%, m.p. - 195-197 ^{0}C. **IR (KBr) cm^{-1}**: 3480 (**O-H stretch**), 3080 (aromatic C-H stretch), 2968 (sp^3 C-H stretch), 1733 (C=O stretch), 1640 (exocyclic C=C stretch), 1190 (C-O stretch), 996, 888 & 831 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.28 (2H, brs, H-25, H-14), 7.11 (1H, brs, H-23), 6.97 (1H, brs, H-24), 6.02 (1H, s, H-21), 4.93 (1H, s, H_a-17), 4.84 (2H, s, H-15), 4.77 (1H, s, H_b-17), 4.54 (1H, brs, H-12), 4.23 (1H, d, J=10.32 Hz, H_a-19), 3.65 (1H, m, H-3), 3.55 (1H, d, J=10.68 Hz, H_b-19), 2.64 (12-OH), 2.46-2.34 (2H, m), 2.07-1.82 (7H, m), 1.62-1.61 (1H, m), 1.45 (3H, s, H-20), 1.25 (2H, s), 1.12 (1H, m), 0.79 (3H, s, H-18); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 173.00 (C-16), 147.92 (C-8), 145.38 (C-14), 142.07 (C-22), 136.01 (C-13), 126.38 (C-25), 125.72 (C-24), 125.09 (C-23), 108.27 (C-17), 91.84 (C-21), 80.94 (C-3), 70.52 (C-15), 69.42 (C-19), 67.42 (C-12), 54.91 (C-5), 52.89 (C-9), 39.15 (C-4), 38.04 (C-10), 36.89 (C-7), 35.75 (C-1), 30.22 (C-11), 25.92 (C-2), 22.99 (C-6), 21.67 (C-20), 15.42 (C-18); **Mass (*m/z*)**: $[M+H]^+$ 445.2020, $[M+Na]^+$ 467.1846

14-Deoxy-12-hydroxy-andrographolide (**4**)

Compound **3a** was dissolved in 15ml of MeOH. To the solution catalytic amount of TsOH was added and sonicated for 30 min. The reaction mixture was then diluted with EtOAc and washed with saturated bicarbonate solution and the organic layer was separated and left for drying to obtain the desired product (**4**). Yield 54%, m.p. - 152-155 ^{0}C. **IR (KBr) cm^{-1}**: 3379 (**O-H stretch**), 3080 (sp^2 C-H stretch) 2944 (sp^3 C-H stretch), 1745 (C=O stretch), 1639 (exocyclic C=C stretch), 1210 (C-O stretch). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.28 (1H, m, H-14), 4.91 (1H, s, H_a-17), 4.84 (2H, s, H-15), 4.73 (1H, s, H_b-17), 4.52 (1H, brs, H-12), 4.16 (1H, d,

J=11.12 Hz, H_a-19), 3.45 (1H, brd, H-3), 3.29 (1H, d, J=11.08 Hz, H_b-19), 2.96-2.69 (2OH, 1H, m), 2.46-2.88 (2H, m), 2.41(1H, m, H_a-7), 2.04 (1H, m, H_b-7), 1.89-1.71 (-OH, 3H, m), 1.29-1.05 (7H, m), 0.63 (3H, s, H-18); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 172.94 (C-16), 148.20 (C-8), 145.29 (C-14), 136.02 (C-13), 107.91 (C-17), 80.51 (C-3), 70.48 (C-15), 67.66 (C-12), 64.08 (C-19), 55.29 (C-5), 53.27 (C-9), 42.94 (C-4), 39.20 (C-10), 38.21 (C-7), 36.70 (C-1), 30.24 (C-11), 28.21 (C-2), 23.96 (C-6), 22.67 (C-20), 15.25 (C-18); Mass (*m/z*): $[M+Na]^+$ 373.1779, $[2M+Na]^+$ 723.3678

Isoandrographolide (**5**)

Andrographolide 10g was dissolved in cold concentrated HCl (180ml) and stirred at room temperature for 24 hours till the completion of the reaction. It was then extracted using DCM and washed with bi-carbonate solution and brine. The organic layer was dried over anhydrous sodium sulphate and concentrated. It was further purified using recrystallization with EtOAc as solvent of choice. Yield 55%, m.p. -199.8-202.1^{0}C. **IR (KBr) cm^{-1}**: 3314 (**O-H stretch**),3015 (sp^2 C-H stretch) 2932 (sp^3 C-H stretch), 1761 (conj. C=O stretch), 1645 (conj. C=C stretch), 1210 (C-O stretch). **^{1}H NMR (400 MHz, $CDCl_3$, TMS):** δ 7.28 (1H, s, H-14), 4.81 (2H, s, H-15), 4.69 (1H, t, J=9.6 Hz, H-12), 4.26 (1H, d, J=10.96 Hz, H_a-19), 3.45 (1H, brd, H-3), 3.36 (1H, d, J=10.96 Hz, H_b-19), 2.43 (1H, m, H_a-11), 2.17 (1H, m, H_b-11), 2.04 (1H, m, H_a-1), 1.73 (3H, m, H_a-7, H-2), 1.53(3H, m, H_b-1, H_a-6, H-9), 1.44 (1H, m, H_b-6), 1.25 (3H, s, H-18), 1.10 (3H, s, H-17), 1.04(1H, m, H_b-7), 0.98(1H, m, H-5), 0.95 (3H, s, H-20), δ 3.12 & 3.04 (3 and 19 –OH). **13C NMR (100 MHz, $CDCl_3$, TMS):** δ 172.67 (C16), 143.28 (C14), 138.41 (C13), 82.73 (C8), 80.86 (C3), 73.13 (C12), 70.58 (C15), 64.21 (C19), 57.94 (C9), 52.70 (C5), 42.51 (C4), 39.00 (C7), 36.23 (C10), 35.64 (C1), 32.88 (C11), 31.56 (C17), 27.44 (C2), 22.77 (C18), 18.17 (C6), 16.45 (C20); Mass (*m/z*): $[M+H]^+$ 351.2134, $[M+Na]^+$ 373.1958, $[2M+Na]^+$ 723.4024

The synthesized isoandrographolide was further treated with different aldehydes to obtain the required acetals of isoandrographilde **6a-d**.

Synthesis of heteroaromatic (3,19) acetals of isoandrographolide

3,19-Benzylidene-isoandrographolide (**6a**)

Isoandrographolide (**5**) (200mg) was dissolved in DMSO (2ml), to it benzaldehyde (232µl) and catalytic amount of PPTs was added (Molar ratio; Isoandrographolide: benzaldehyde=1:4). The reaction was allowed to stir at 70 ^{0}C till completion of the reaction (checked by TLC). Reaction mixture was then allowed to cool to room temperature and quenched using cold saturated sodium bi-carbonate solution and extracted with DCM. The organic layer was washed with brine, water and dried with anhydrous sodium sulphate. The product was purified using column chromatography (petroleum ether/acetone) to give the desired compound. Yield 85 %, m.p. 203.5-205.3 ^{0}C. **IR (KBr) cm^{-1}**: 3110 (aromatic C-H stretch), 2946 (sp^3 C-H stretch), 1757 (conj. C=O stretch), 1648 (conj. C=C stretch), 1204 (C-O stretch), 801 (aromatic C-H out of plane bending).**^{1}H NMR (400 MHz, CDCl$_3$, TMS):** δ 7.49 (2H, brs, H-14, H-25), 7.35 (2H, brs, H-23, H-27), 7.29 (2H, m, H-24, H-26), 5.72 (1H, s, H-21), 4.81 (2H, s, H-15), 4.71 (1H, brs, H-12), 4.36 (1H, brs, H$_a$-19), 3.64 (2H, brs, H-3, H$_b$-19), 2.44(1H, m, H$_a$-11), 2.22 (1H, m, H$_b$-11), 2.03 (1H, brs, H$_a$-1), 1.86 (3H, m, H$_a$-7, H-2), 1.60 (3H, m, H$_b$-1, H$_a$-6, H-9), 1.42 (1H, m, H$_b$-6), 1.48 (3H, s, H-18), 1.13 (6H, s, H-17, H-20), 1.04 (2H, m, H-5, H$_b$-7). **^{13}C NMR (100 MHz, CDCl$_3$, TMS):** δ 172.60 (C-16), 143.21 (C-14), 138.90 (C-13), 138.34 (C-22), 128.84 (C-25), 128.32 (C-24, C-26), 126.18 (C-23, C-27), 95.35 (C-21), 82.73 (C-8), 81.36 (C-3), 73.05 (C-12), 70.55 (C-15), 69.71 (C-19), 57.94 (C-9), 51.65 (C-5), 38.18 (C-4), 36.45 (C-7), 35.91 (C-10), 35.63 (C-1), 32.77 (C-11), 31.77 (C-17), 25.96 (C-18), 21.04 (C-2), 17.29 (C-6), 16.37 (C-20); Mass (*m/z*): $[M+H]^+$ 439.2488, $[M+Na]^+$ 461.2313, $[2M+Na]^+$ 899.4732

3,19-(2-Furfurylidene)-isoandrographolide (**6b**)

Compound **6b** was synthesized from **5** following the same method described for the synthesis of **6a**. Yield 65%, m.p.-199.5-199.8 ^{0}C. **IR (KBr) cm^{-1}:** 3160 (aromatic C-H stretch), 2940 (sp^3 C-H stretch), 1736 (conj. C=O stretch), 1602 (conj. C=C stretch), 1581-1421 skeletal bands, 1206, 1092 & 1020 (C-O stretch), 925 out of plane (C-H bending), 710 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, CDCl$_3$, TMS):** δ 7.29 (1H, m, H-14), 7.25 (1H, d, J=1.72 Hz, H-25), 6.45 (1H, d, J=3.2 Hz, H-23), 6.36 (1H, dd, J=3.2, 1.8 H-24), J= 5.84 (1H, s, H-21), 4.81 (2H, s, H-15), 4.70 (1H, t, J=7.56 Hz, H-12), δ 4.33 (1H, d, J=11.44 Hz, H_a-19), 3.62 (2H, m, H-3, H_b-19), 2.46 (1H, dd, J=13.88, 7.96 Hz, H-11a), 2.33 (1H, dd, J=13.88, 2.88 Hz, H_b-11), 2.03(1H, m, H_a-1), 1.86 (3H, m, H_a-7, H-2), 1.56 (3H, m, H_b-1, H_a-6, H-9), 1.40 (1H, m, H_b-6), 1.47 (3H, s, H-18), 1.11 (6H, s, H-17, H-20), 1.03(1H, m, H_b-7), 0.99 (1H, m, H-5). **^{13}C NMR (100 MHz, CDCl$_3$, TMS):** δ 172.60 (C-16), 151.47 (C-22), 143.23 (C-14), 142.51 (C-25), 138.34 (C-13), 110.18 (C-23), 107.41 (C-24), 89.91 (C-21), 82.72 (C-8), 81.44 (C-3), 73.07 (C-12), 70.56 (C-15), 69.65 (C-19), 57.94 (C-9), 51.65 (C-5), 38.11 (C-4), 36.58 (C-7), 35.88 (C-10), 35.61 (C-1), 32.78 (C-11), 31.77 (C-17), 25.84 (C-2), 20.84 (C-18), 17.28 (C-6), 16.36 (C-20); Mass (*m/z*): $[M+H]^+$ 429.2266, $[M+Na]^+$ 451.2072, $[2M+Na]^+$ 879.4258

3,19-(2-Pyrilidene)-isoandrographolide (**6c**)

Compound **6c** was synthesized from **5** following the same method described for the synthesis of **6a**. Yield 80%, m.p. - 206-209 ^{0}C. **IR (KBr) cm^{-1}**: 3095 (aromatic C-H stretch), 2931 (sp3 C-H stretch), 1745 (conj. C=O stretch), 1653 (conj. C=C stretch), 1207 (C-O stretch), 927, 778, 743 (aromatic C-H out of plane bending). **^{1}H NMR (400 MHz, CDCl$_3$, TMS):** δ 8.58 (1H, d, J=4.08 Hz, H-26), 7.74 (1H, dt, J=7.72, 1.72 Hz, H-24), 7.64 (1H, d, J=7.88 Hz, H-23), 7.29-7.28 (1H, m, H-25), 7.27-7.24 (1H, dd, J=4.88, 1.28 Hz, H-14), 5.84 (1H, s, H-21), 4.82-4.81

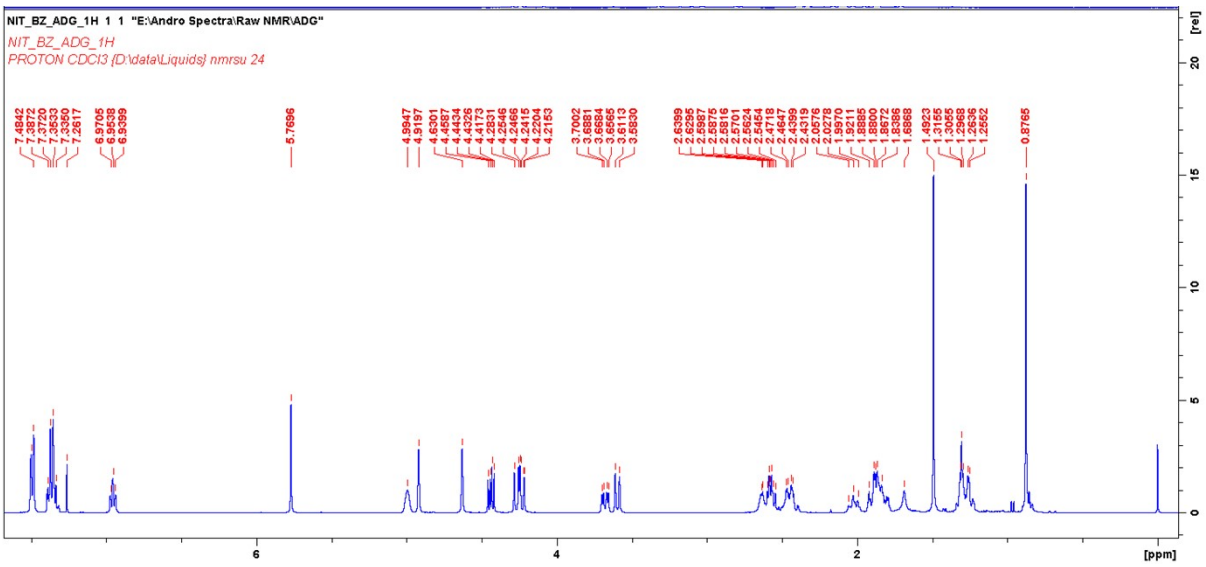
(2H, m, H-15), 4.71 (1H, t, J=9.52 Hz, H-12), 4.42 (1H, d, J=11.48 Hz, H_a-19), 3.72-3.65 (2H, m, H-3, H_b-19), 2.50-2.37 (2H, m, H-11), 2.24-2.17 (1H, m, H_a-1), 2.07-1.99 (1H, m, H_a-7), 1.89-1.86 (1H, m), 1.78-1.73 (2H, m), 1.58-1.56 (3H, m), 1.48 (3H, s, H-18), 1.34 (6H, s, H-17, H-20), 1.05-1.01 (2H, m). **^{13}C NMR (100 MHz, $CDCl_3$, TMS):** δ 172.56 (C-16), 143.21 (C-14), 157.40(C-22), 138.35 (C-13), 123.80 (C-23), 136.93 (C-24), 120.86 (C-25), 148.65 (C-26), 95.63 (C-21), 82.72 (C-8), 81.53 (C-3), 73.07 (C-12), 70.53 (C-15), 69.84 (C-19), 57.99 (C-9), 51.68 (C-5), 38.19 (C-4), 36.57 (C-7), 35.65 (C-10), 35.89 (C-1), 32.78 (C-11), 31.73 (C-17), 25.98 (C-2), 20.99 (C-18), 17.30 (C-6), 16.32 (C-20); Mass (*m/z*): $M+H]^+$ 440.2426, $[2M+Na]^+$ 901.4596

3,19-(2-Thiophenylidene)-isoandrographolide (**6d**)

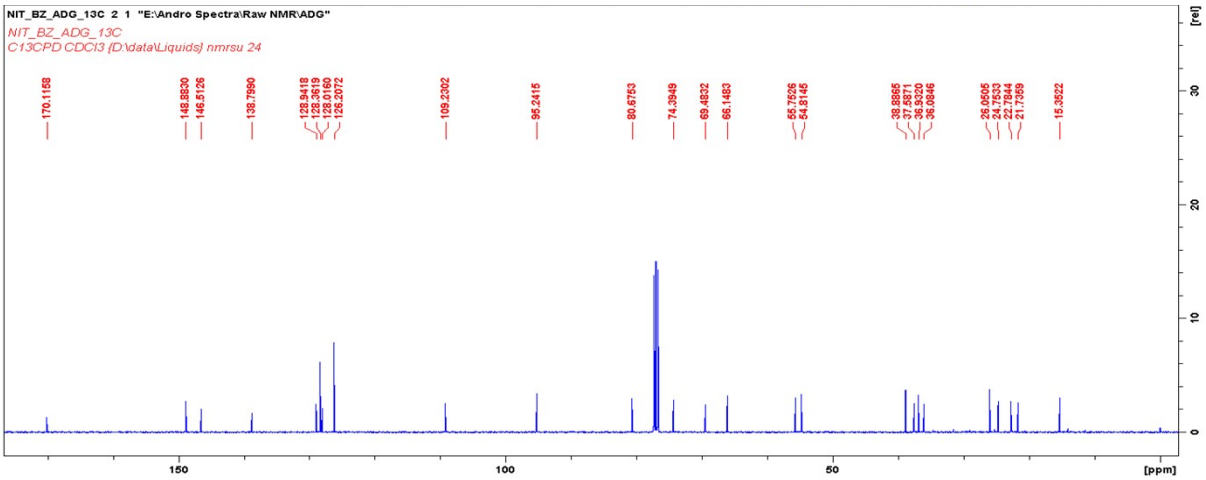
Compound **6d** was synthesized from **5** following the same method described for the synthesis of **6a**. Yield 77%, m.p.- 230.1-232.6^oC ^0C. **IR (KBr) cm^{-1}**: 3111 (aromatic C-H stretch), 2945 sp^3 (C-H stretch), 1740 (conj. C=O stretch) , 1244,1094 & 1025 (C-O stretch), 929 & 850 (aromatic C-H out of plane bending).**^{1}H NMR (400 MHz, $CDCl_3$, TMS):** δ 7.29 (1H, s, H-14), 7.27 (1H, s, H-25), 7.12 (1H, brs, H-23), 6.98 (1H, brs, H-24), 6.03 (1H, s, H-21), 4.82 (2H, s, H-15), 4.71 (1H, brs, H-12), 4.35 (1H, brs, H_a-19), 3.64 (2H, m, H-3, H_b-19), 2.46 (1H, m, H_a-11), 2.20 (1H, m, H_b-11), 2.03 (1H, m, H_a-1), 1.74 (3H, m, H_a-7, H-2), 1.57(3H, m, H_b-1, H_a-6, H-9), 1.44 (1H, m, H_b-6), 1.46 (3H, s, H-18), 1.12 (6H, s, H-17, H-20), 1.03 (2H, m, H-5, H_b-7). **^{13}C NMR (100 MHz, $CDCl_3$, TMS):** δ 172.63 (C-16), 143.24 (C-14), 142.10 (C-22), 138.53 (C-13), 126.41 (C-25), 125.69 (C-23), 125.07 (C-24), 92.05 (C-21), 82.74 (C-8), 81.59 (C-3), 73.07 (C-12), 70.58 (C-15), 69.66 (C-19), 57.94 (C-9), 51.62 (C-5), 38.15 (C-4), 36.42 (C-7), 35.90 (C-10), 35.63 (C-1), 32.79 (C-11), 31.78 (C-17), 25.89 (C-2), 21.04 (C-18), 17.30 (C-6), 16.38 (C-20); Mass (*m/z*): $[M+H]^+$ 445.2030, $[M+Na]^+$ 467.1856

3,19-Benzylidene-andrographolide (**2a**)

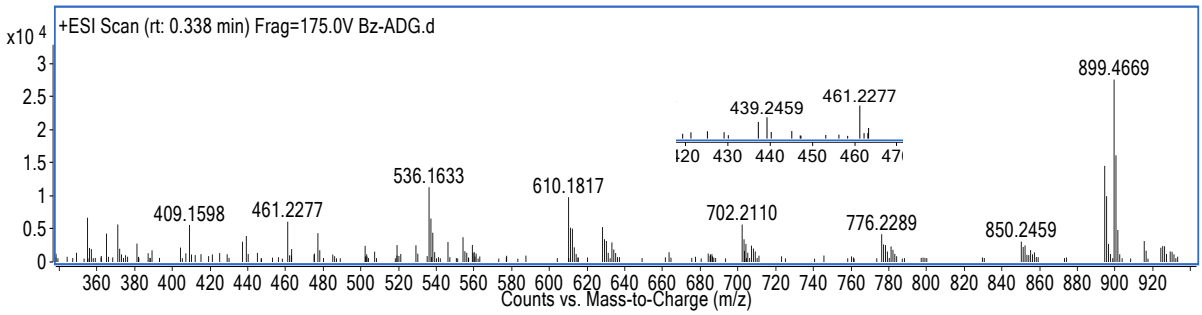
^{1}H NMR Spectrum



^{13}C NMR Spectrum

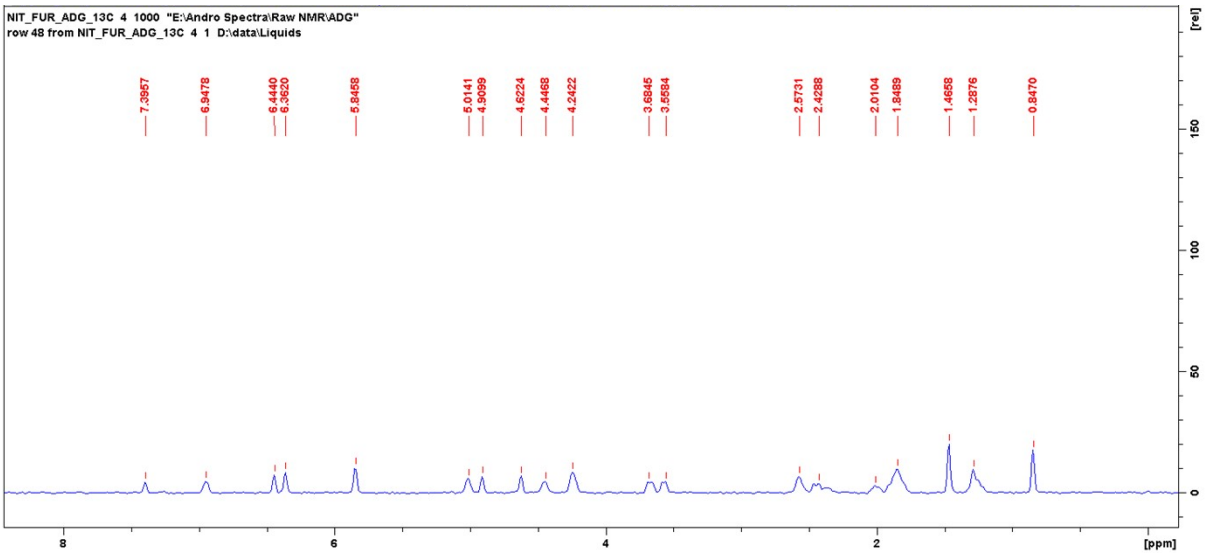


Mass Spectrum

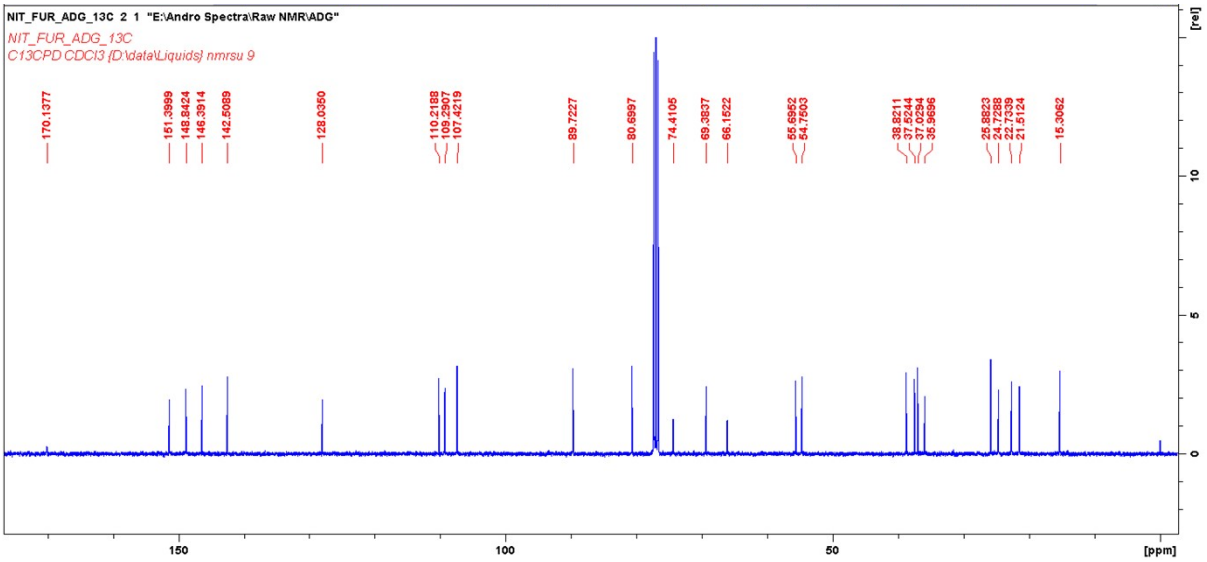


3,19-(2-Furfurylidene)-andrographolide (**2b**)

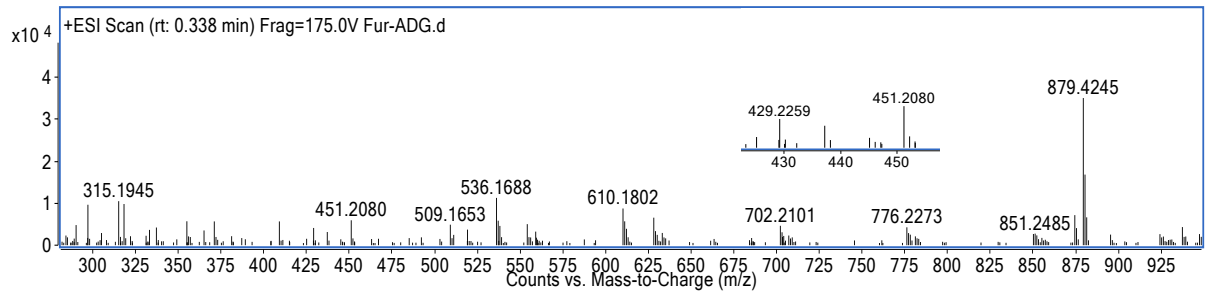
^{1}H NMR Spectrum



^{13}C NMR Spectrum

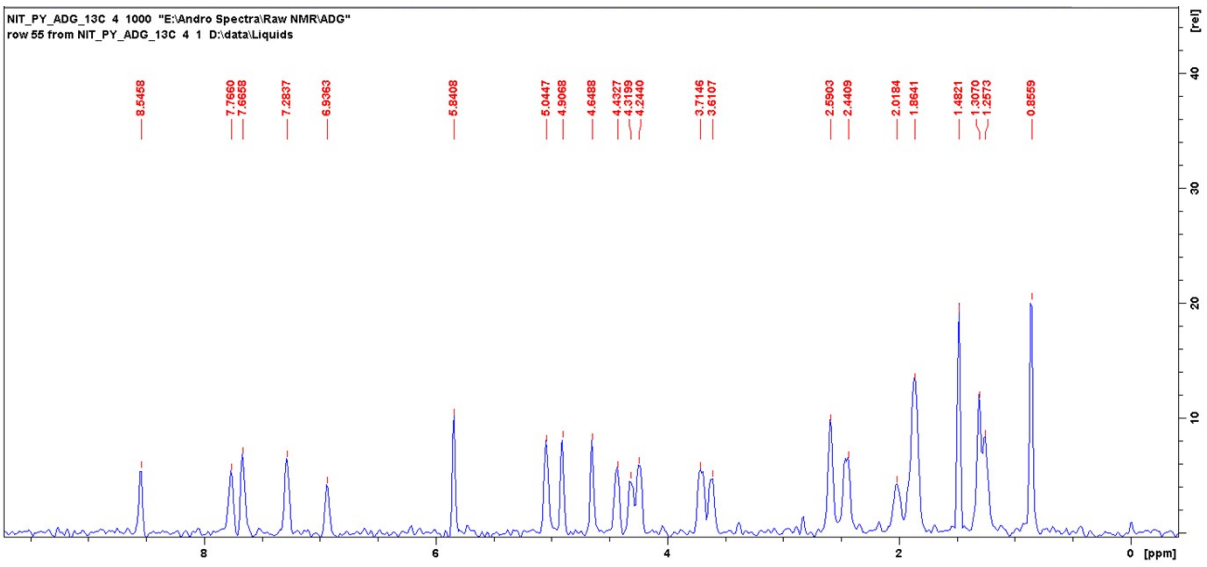


Mass Spectrum

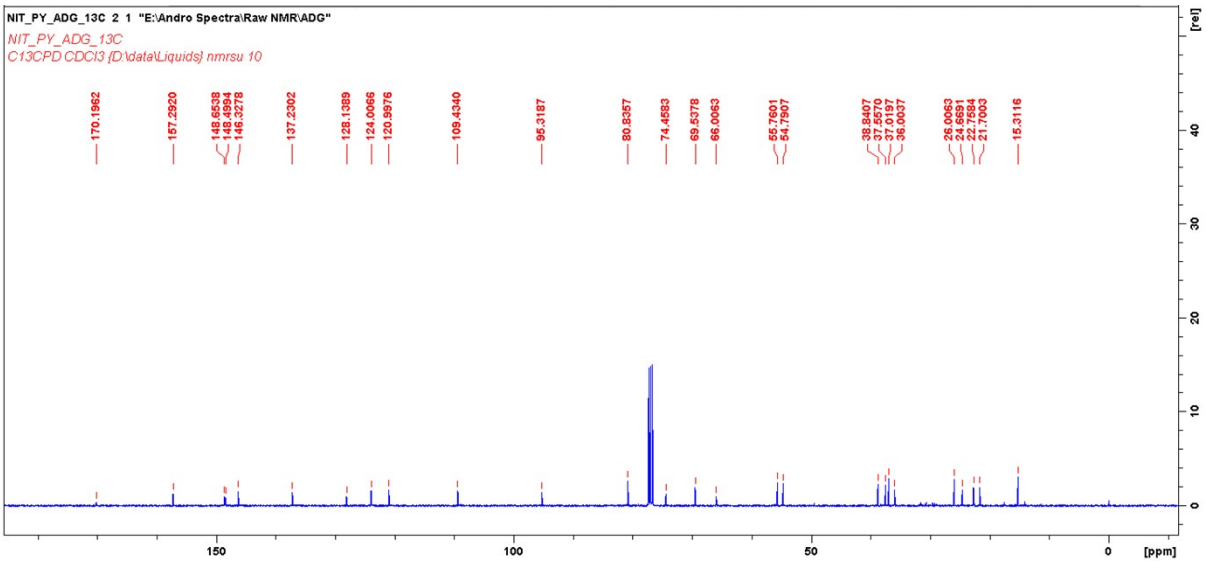


3,19-(2-Pyrilidene)-andrographolide (**2c**)

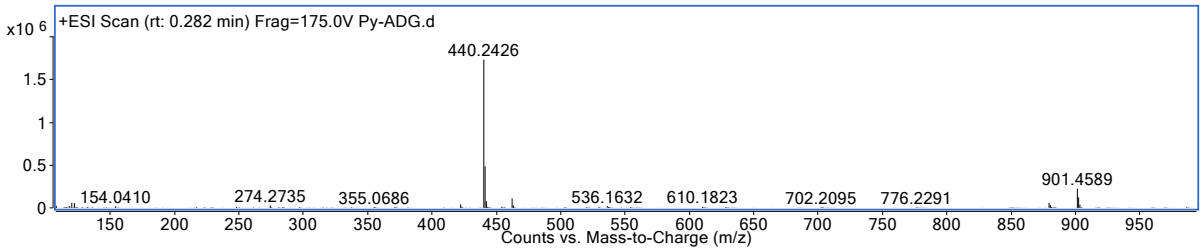
^{1}H NMR Spectrum



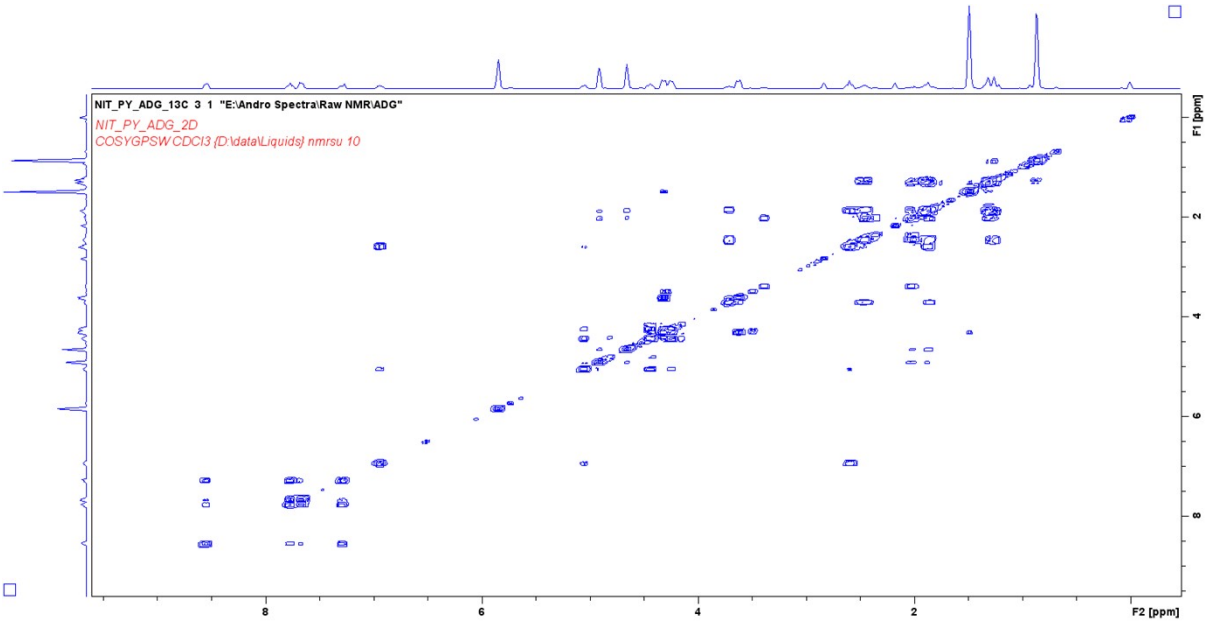
^{13}C NMR Spectrum



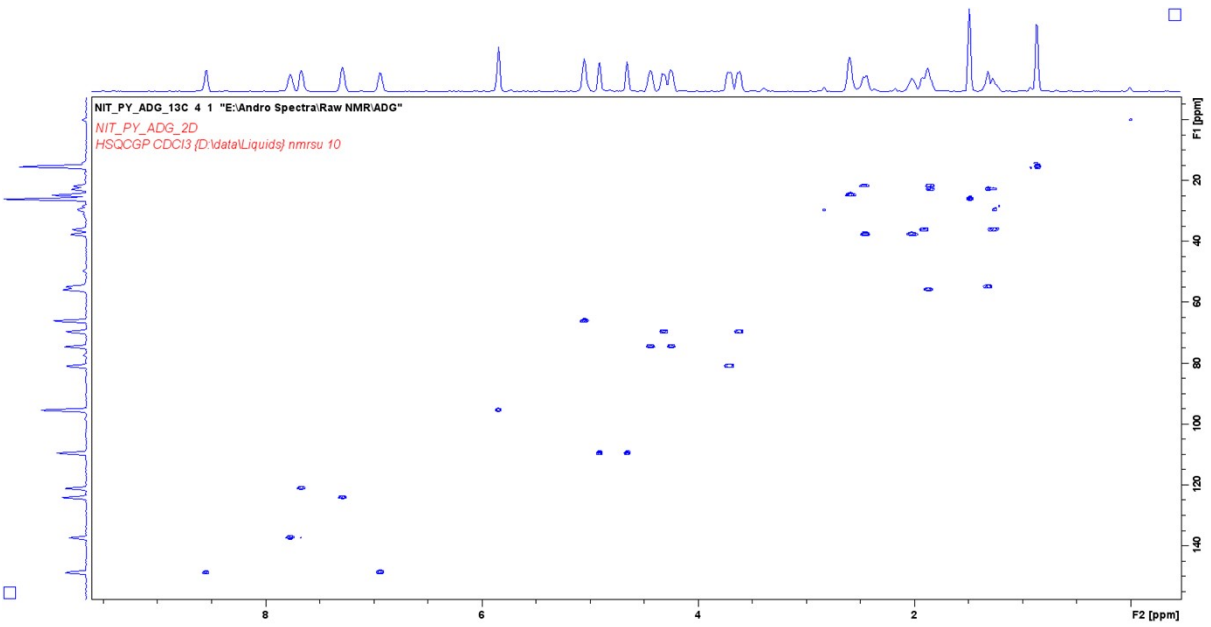
Mass Spectrum



HOMO-COSY

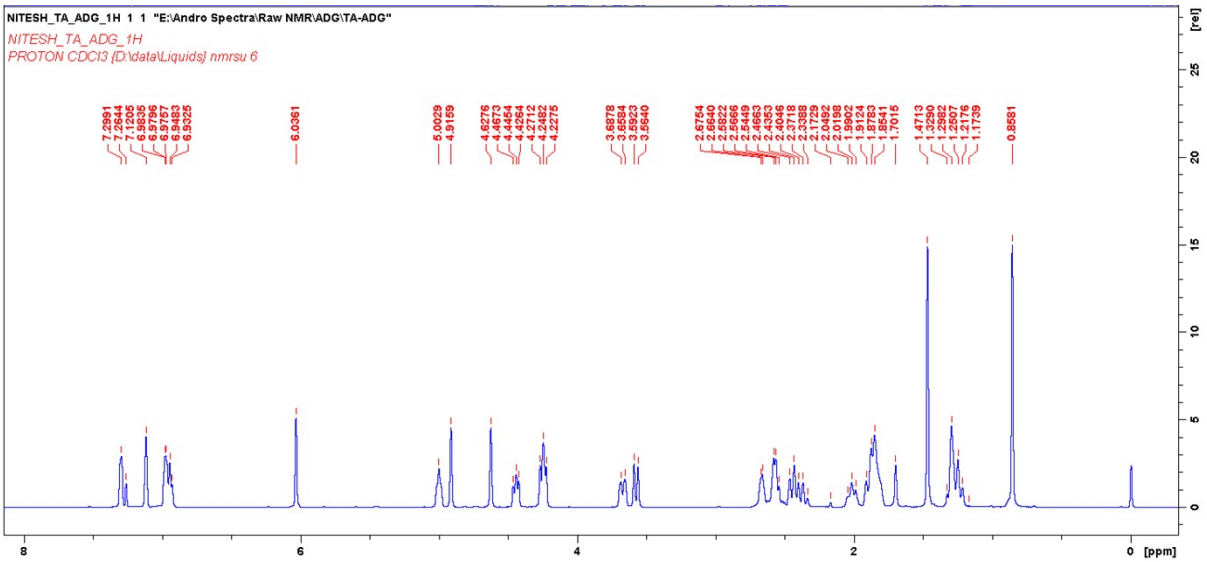


HSQC

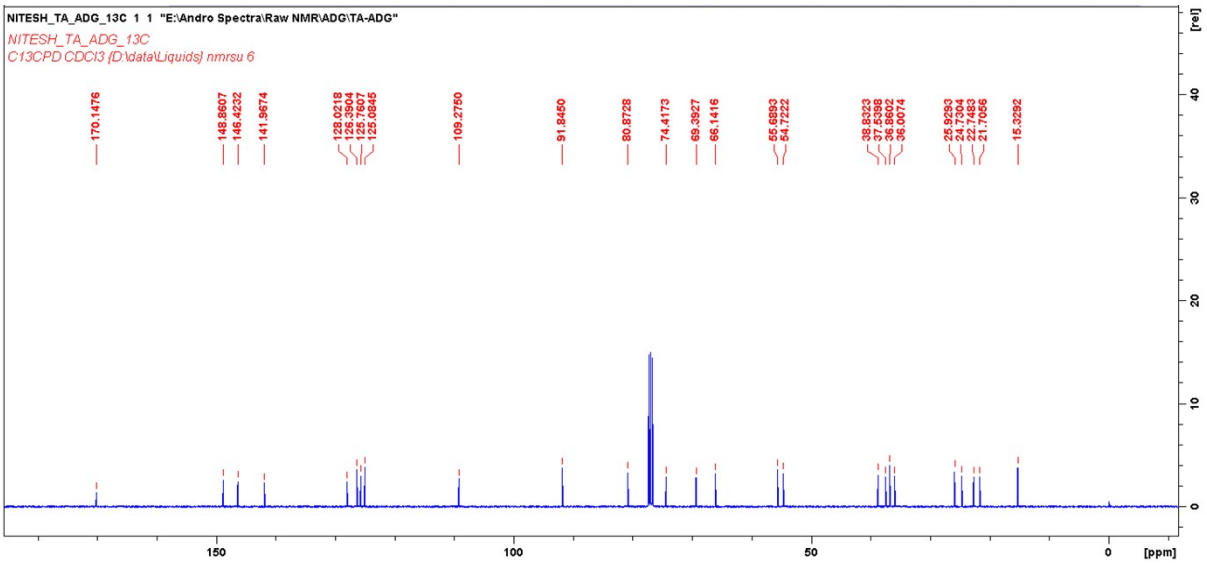


3,19-(2-Thiophenylidene)-andrographolide (**2d**)

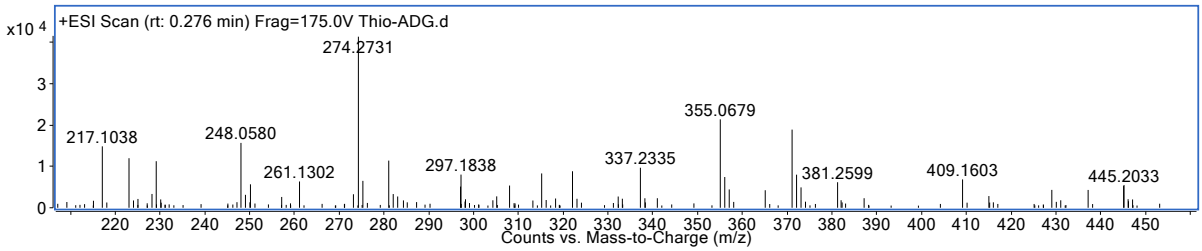
^{1}H NMR Spectrum



^{13}C NMR Spectrum

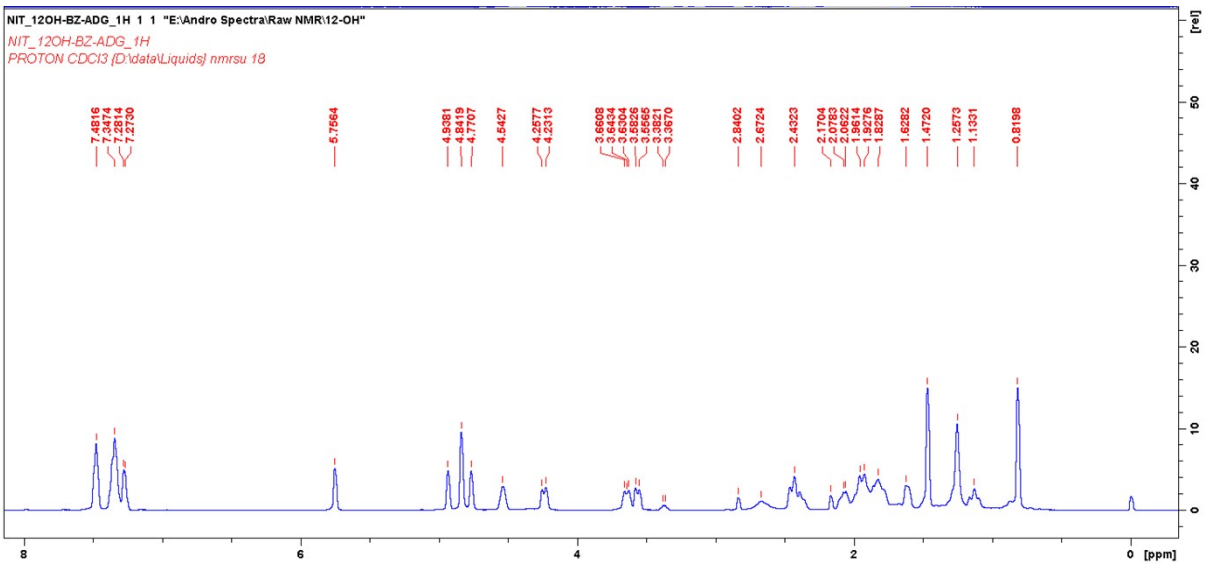


Mass Spectrum

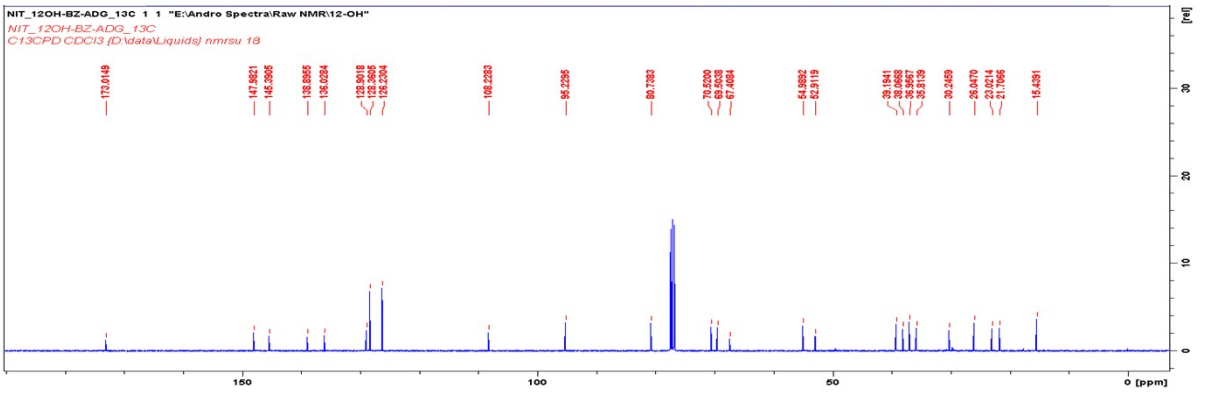


12-Hydroxy-3,19-benzylidene-andrographolide (**3a**)

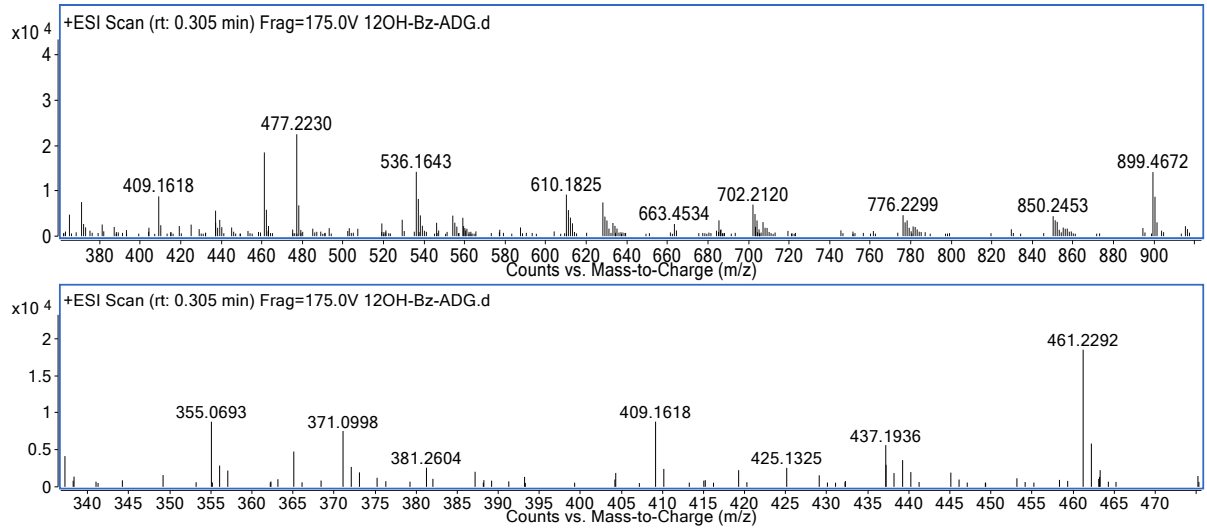
^{1}H NMR Spectrum



^{13}C NMR Spectrum

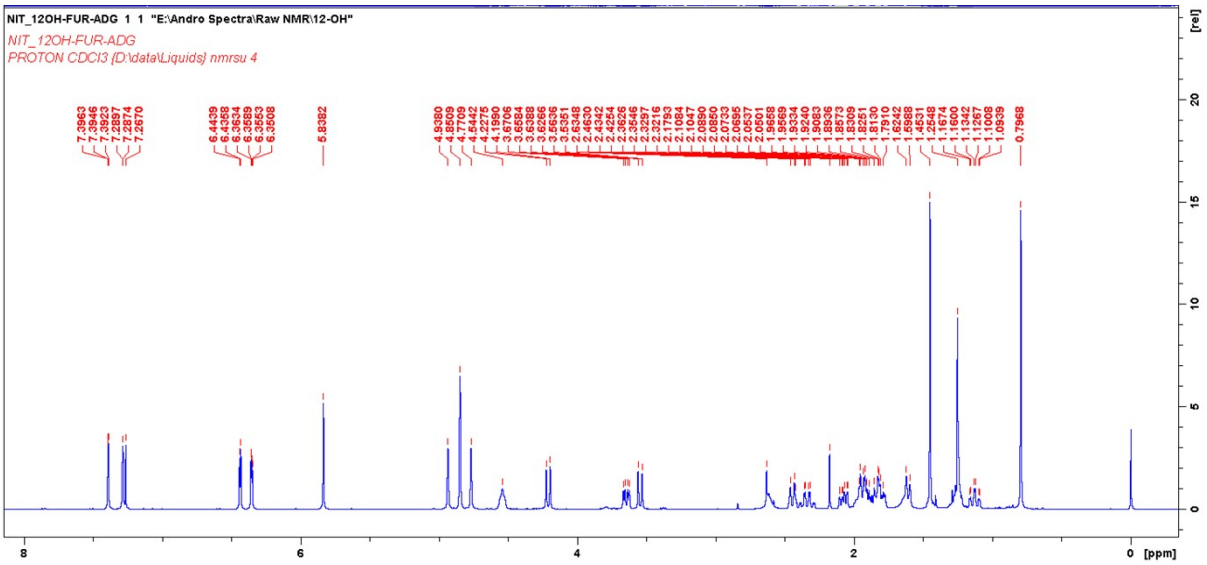


Mass Spectrum

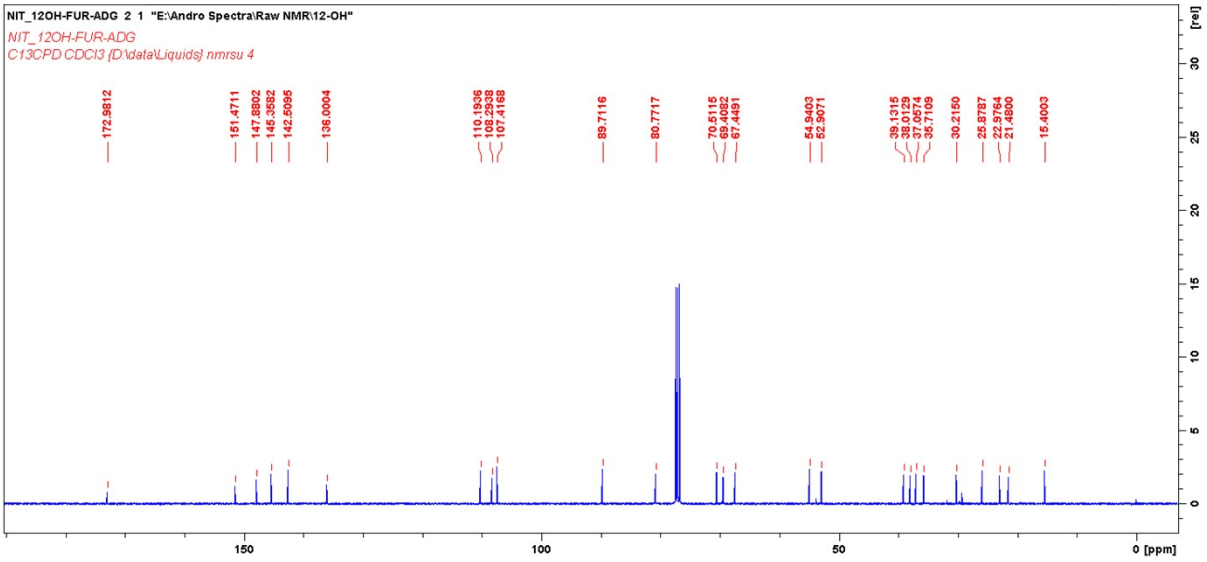


12-Hydroxy-3,19-(2-furfurylidene)-andrographolide (**3b**)

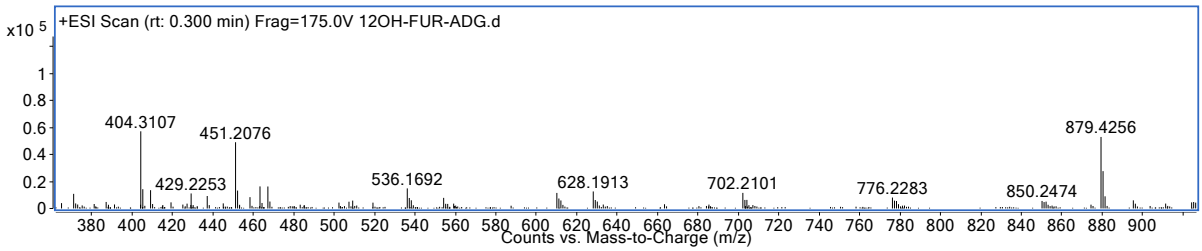
^{1}H NMR Spectrum



^{13}C NMR Spectrum

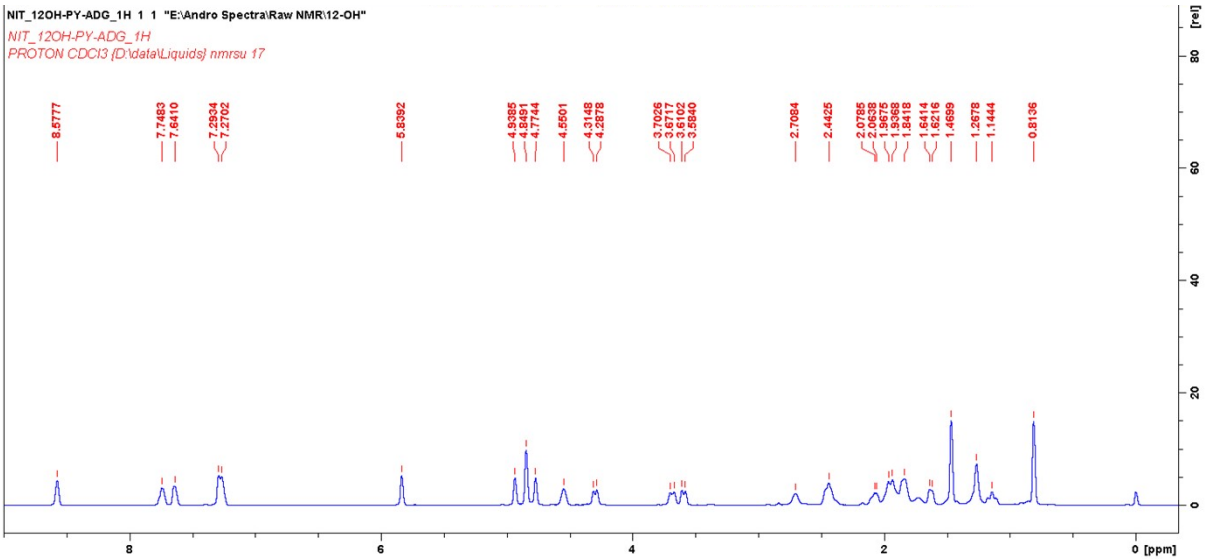


Mass Spectrum

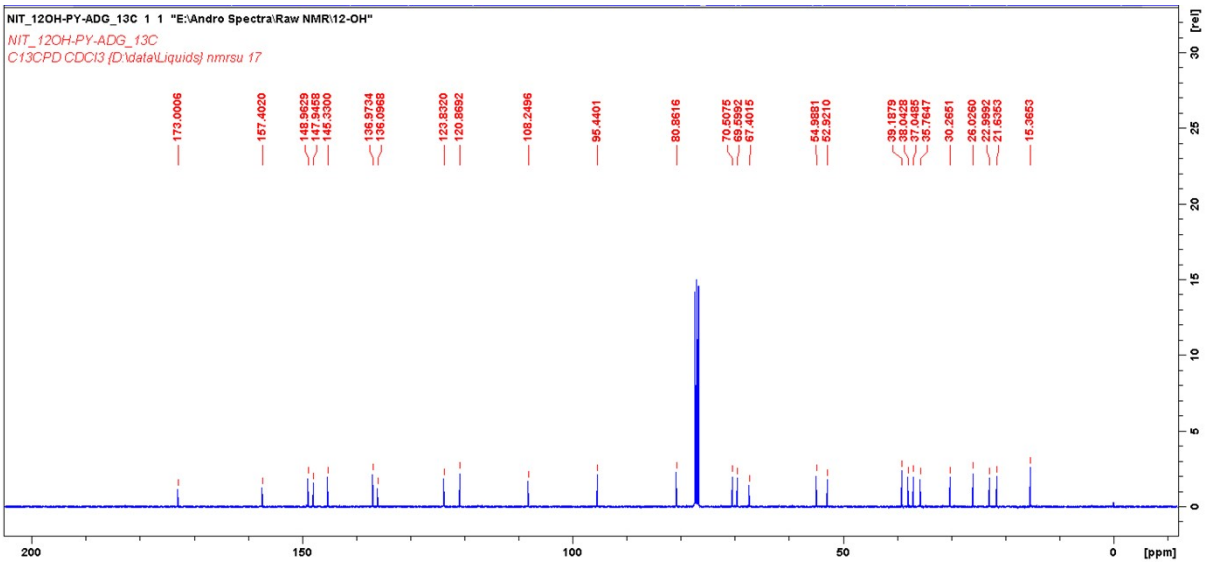


12-Hydroxy-3,19-(2-pyrilidene)-andrographolide (**3c**)

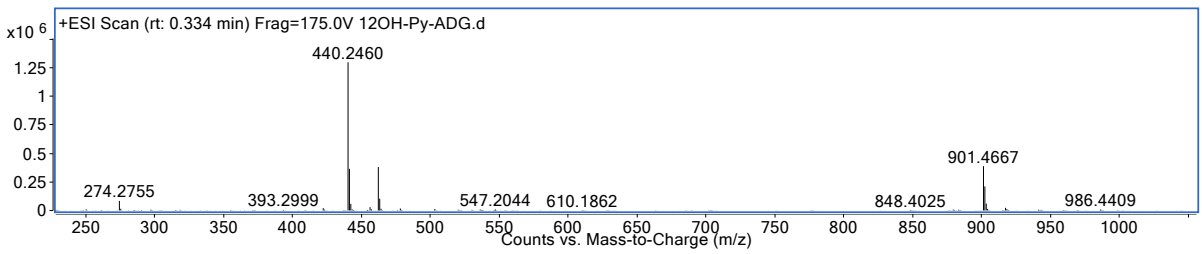
^{1}H NMR Spectrum



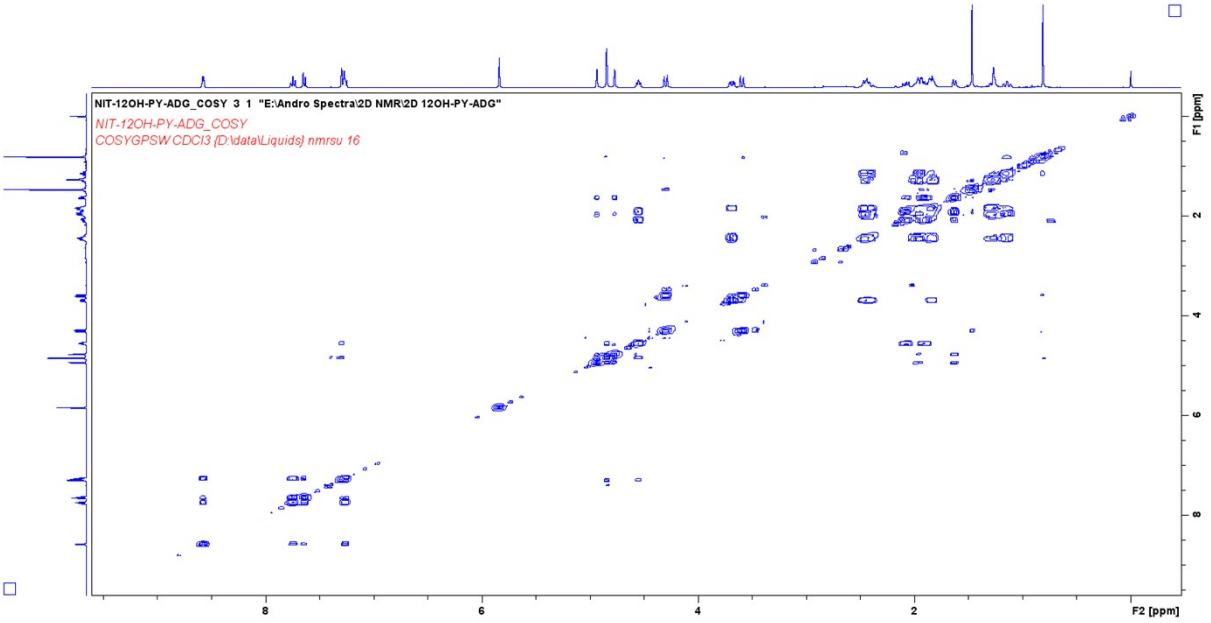
^{13}C NMR Spectrum



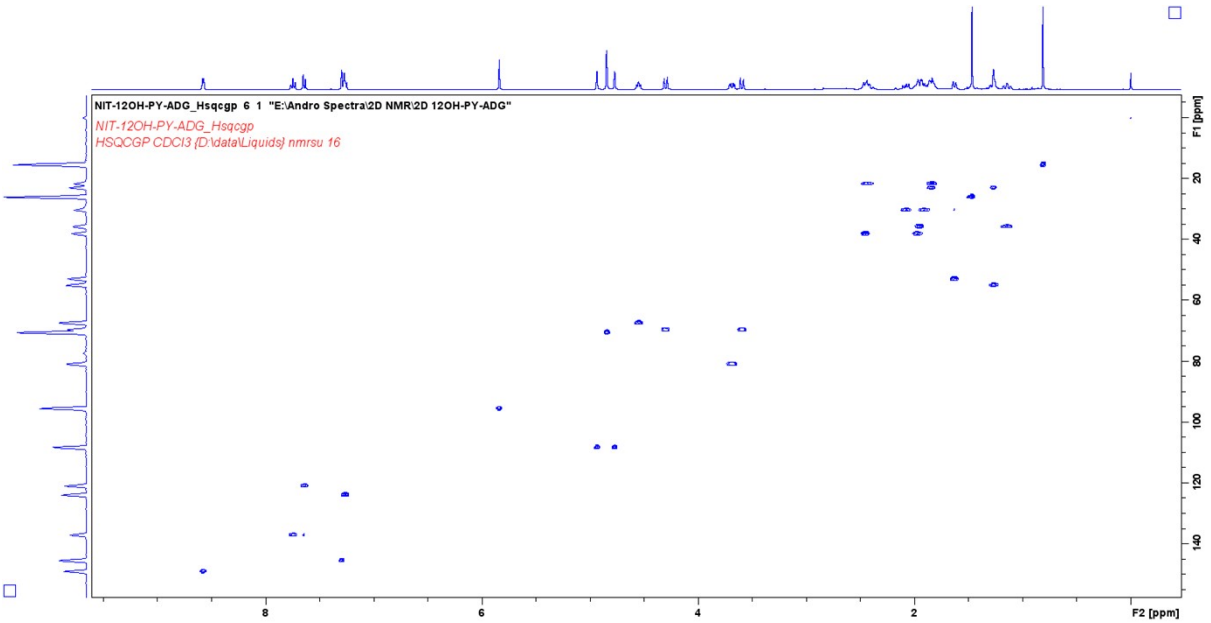
Mass Spectrum



HOMO-COSY

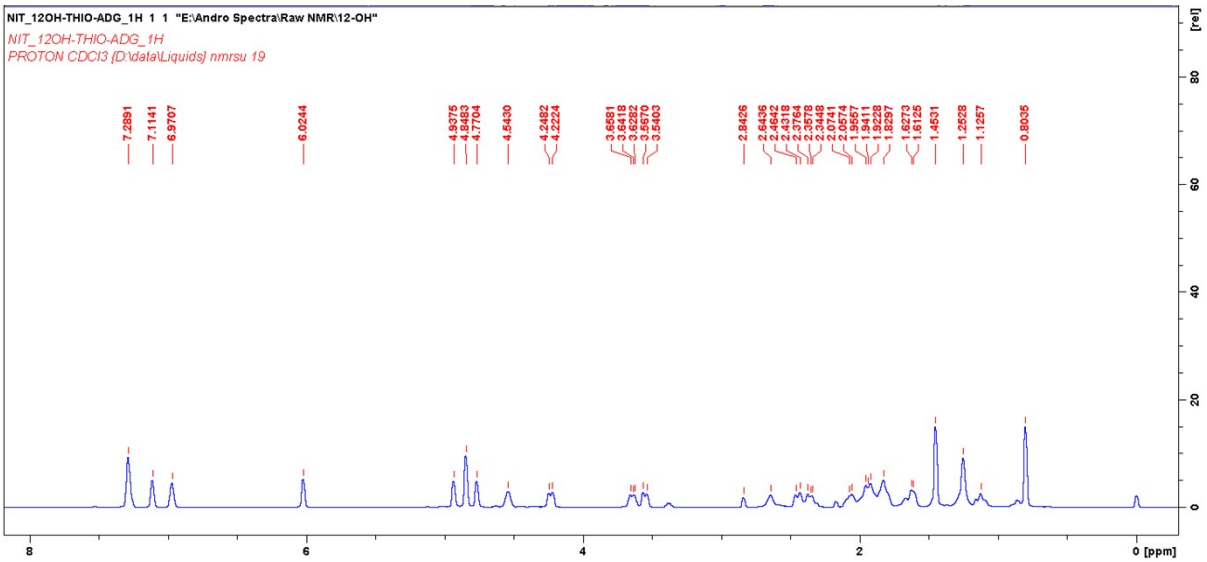


HSQC

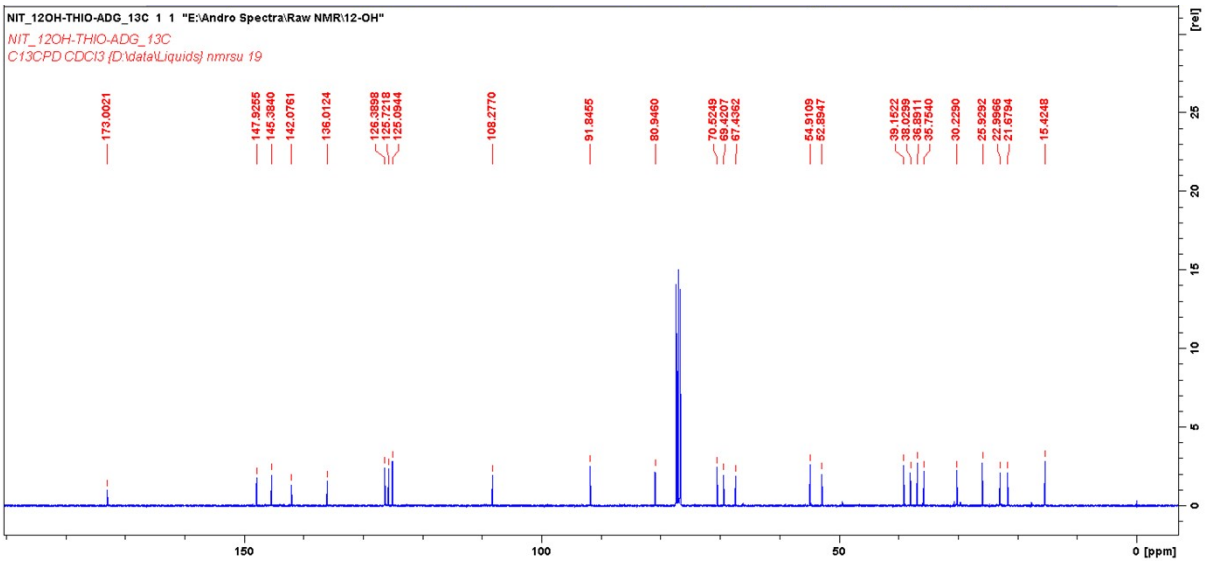


12-Hydroxy-3,19-(2-thiophenylidene)-andrographolide (**3d**)

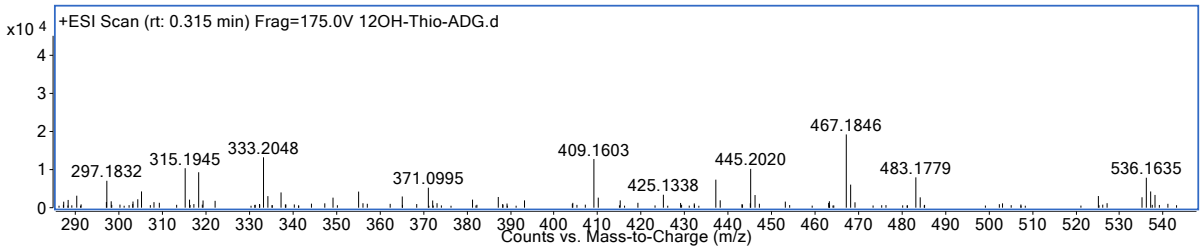
^{1}H NMR Spectrum



^{13}C NMR Spectrum

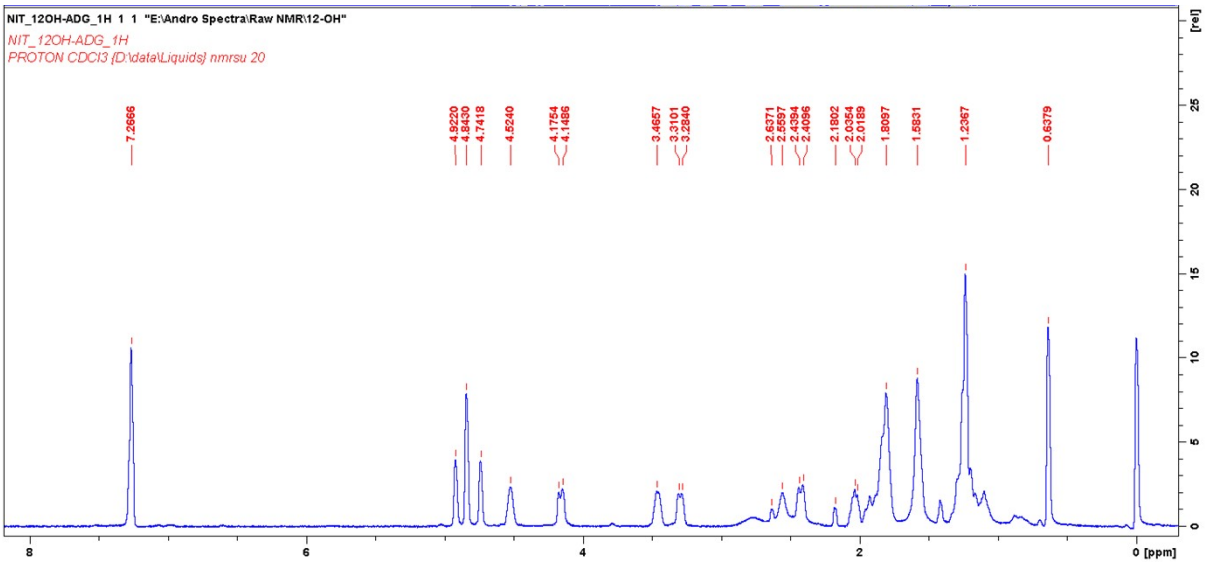


Mass Spectrum

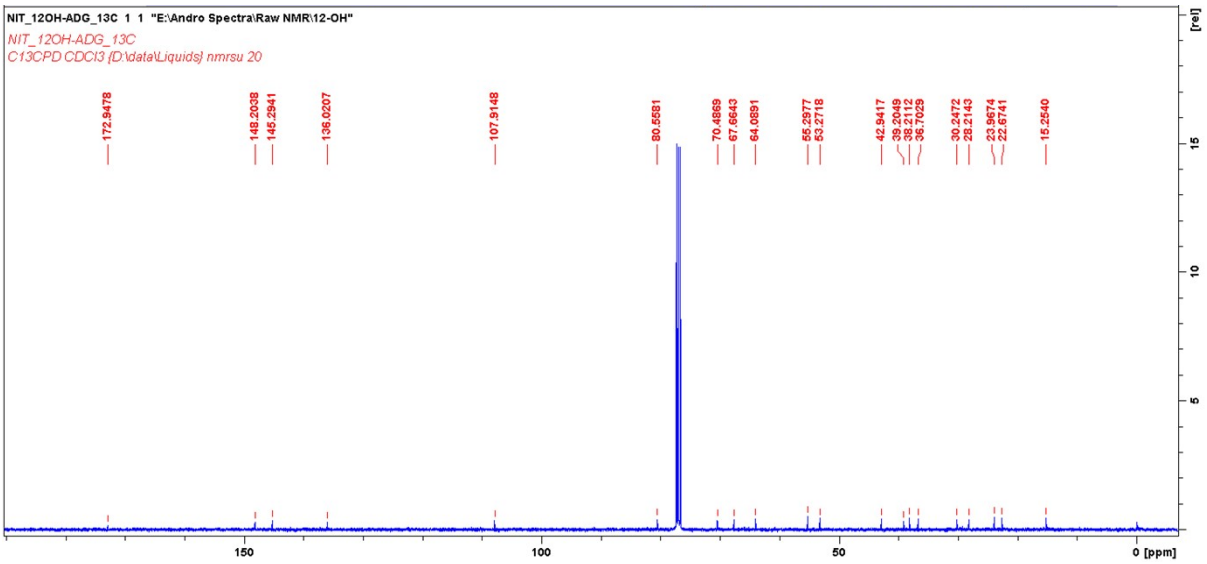


14-Deoxy-12-hydroxy-andrographolide (**4**)

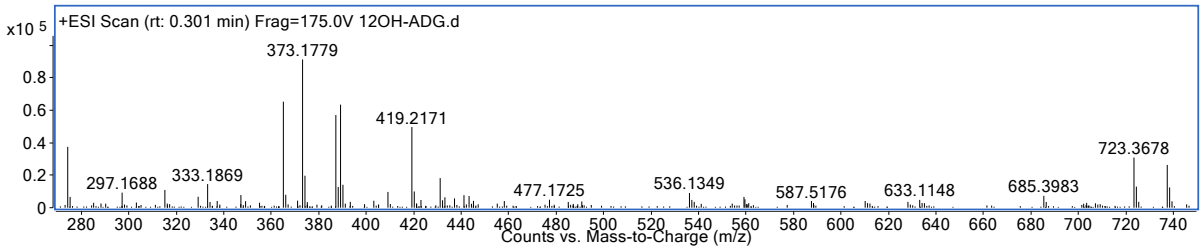
^{1}H NMR Spectrum



^{13}C NMR Spectrum

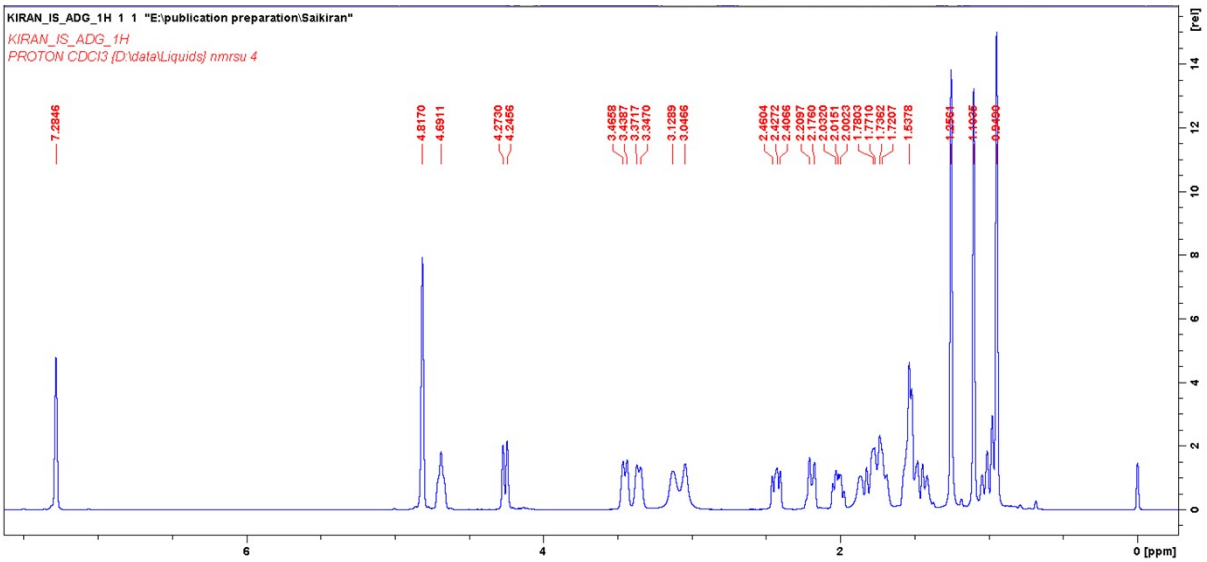


Mass Spectrum

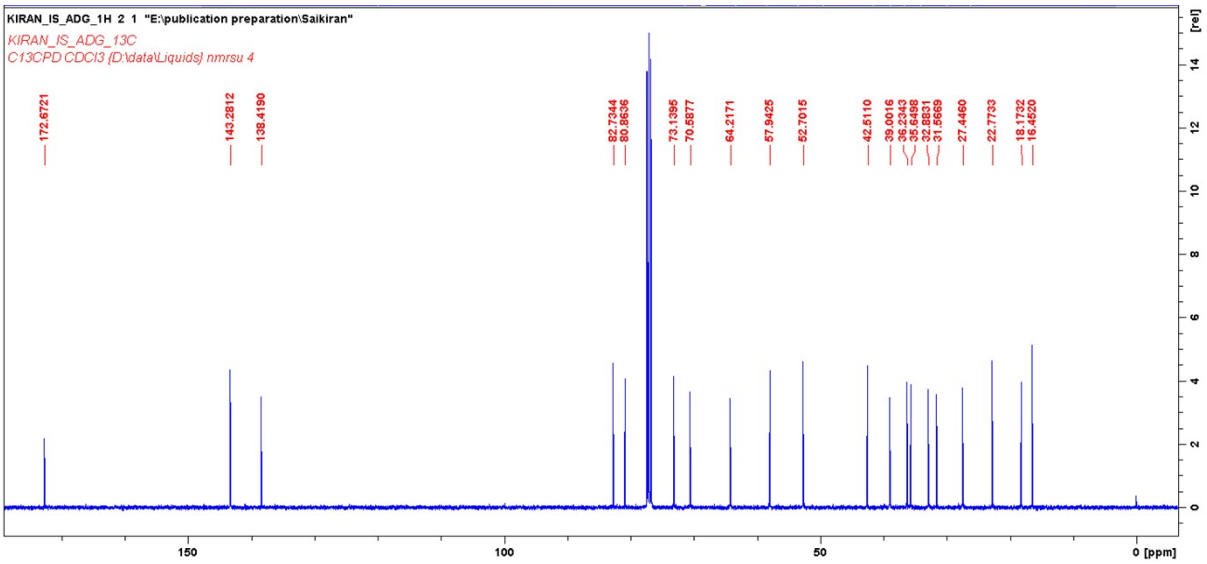


Isoandrographolide (**5**)

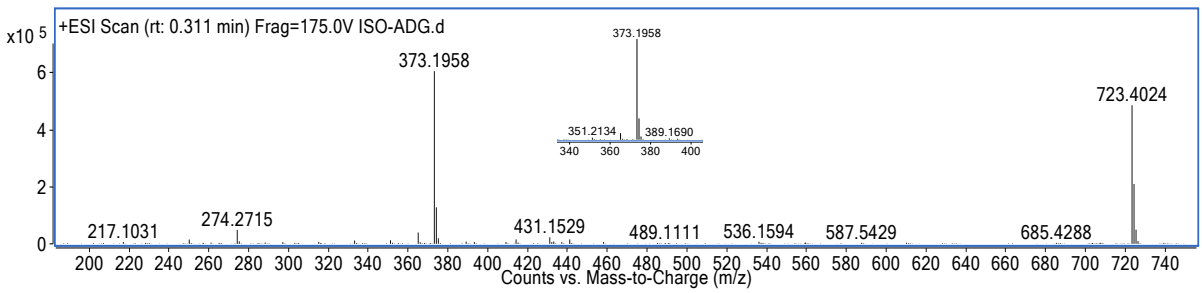
^{1}H NMR Spectrum



^{13}C NMR Spectrum

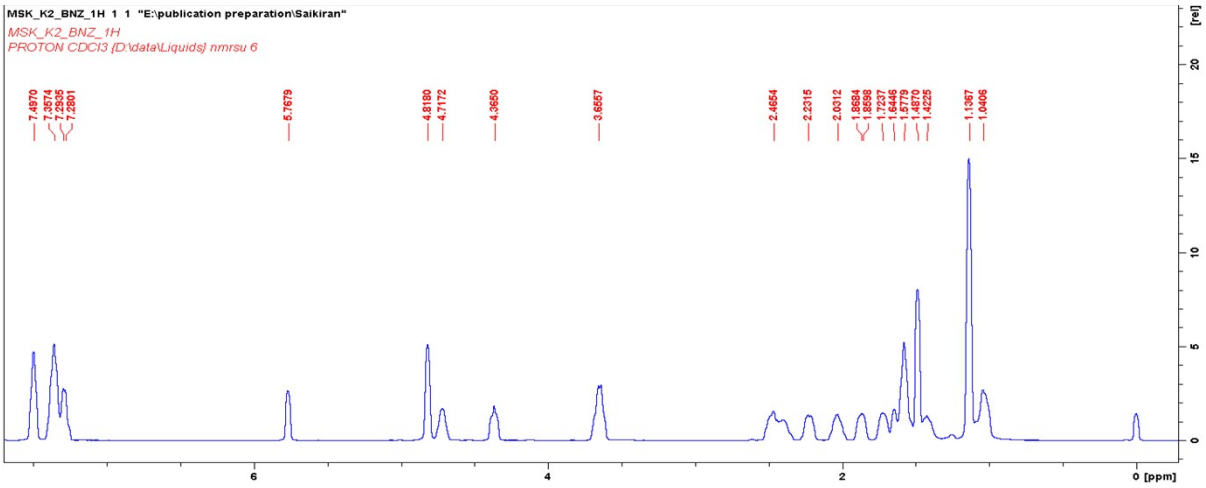


Mass Spectrum

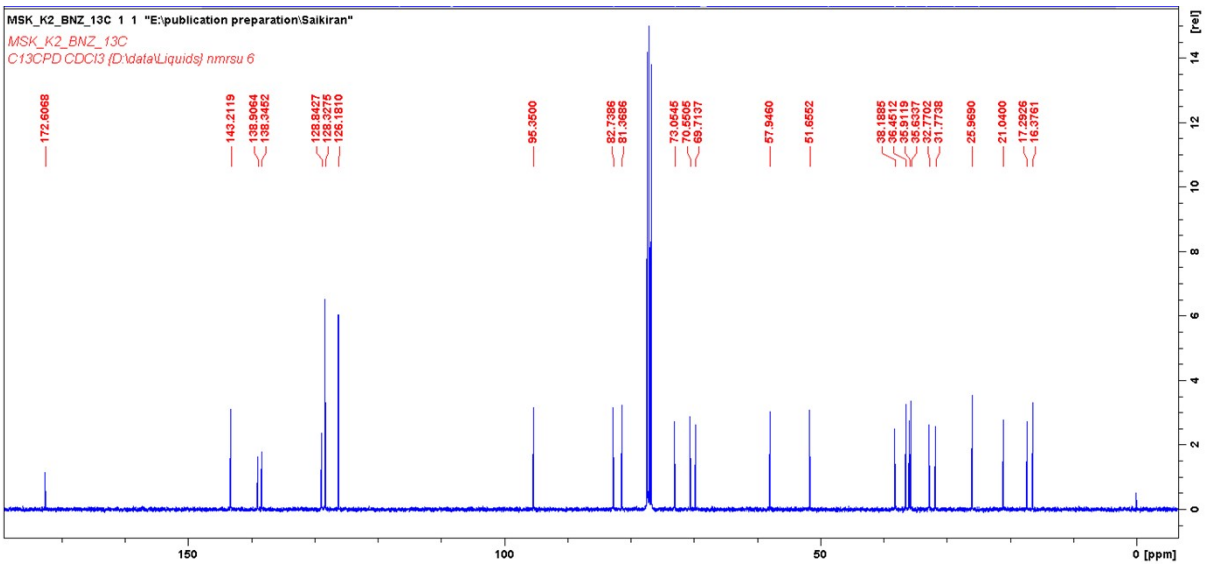


3,19-benzylidene-isoandrographolide (**6a**)

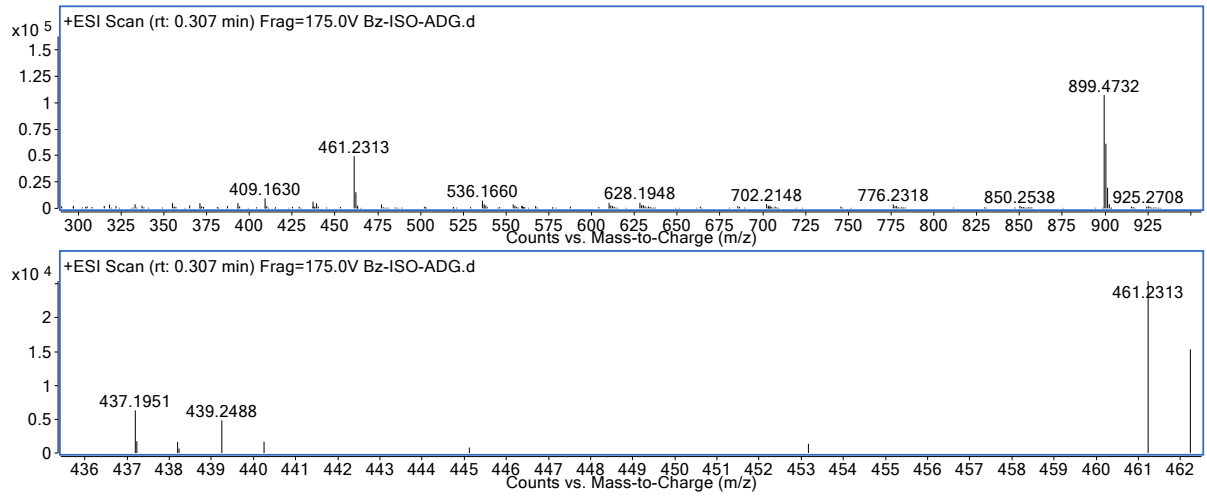
^{1}H NMR Spectrum



^{13}C NMR Spectrum

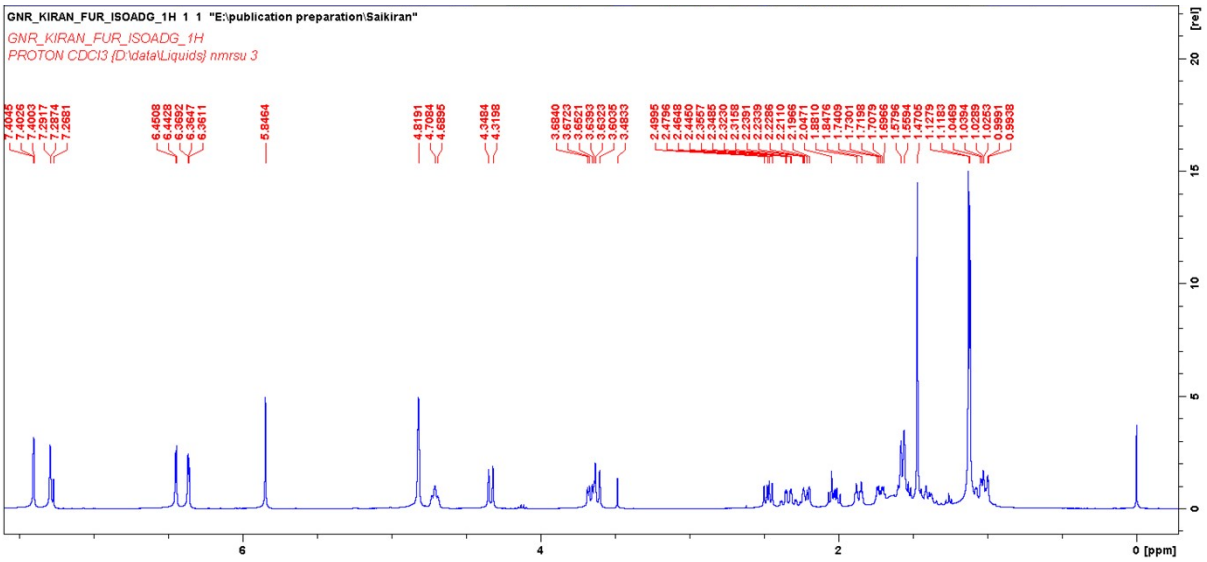


Mass Spectrum

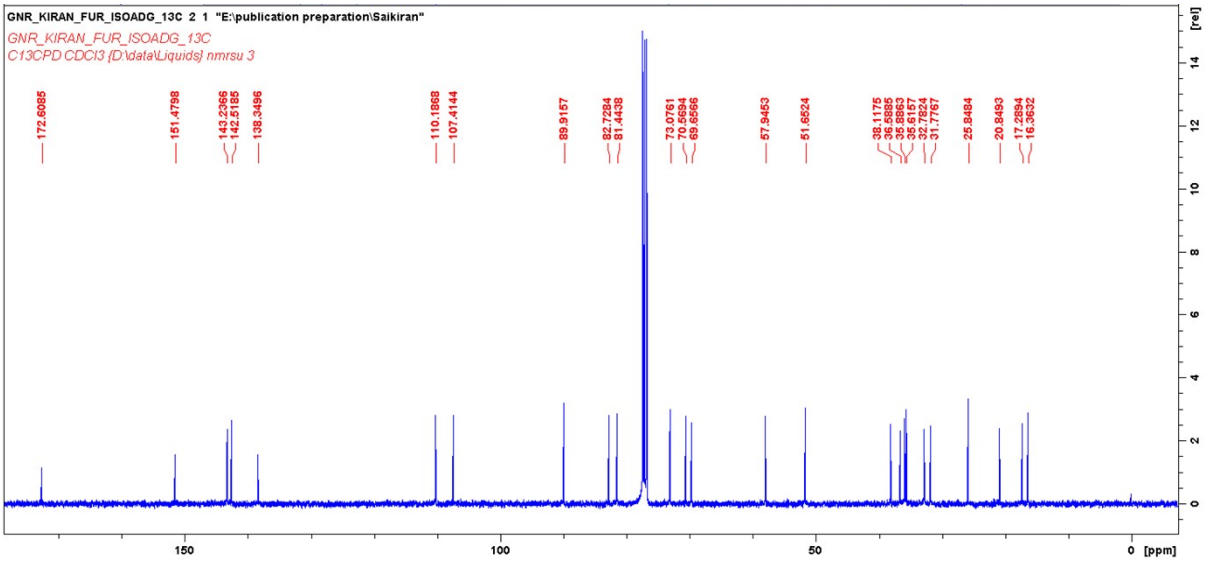


3,19-(2-Furfurylidene)-isoandrographolide (**6b**)

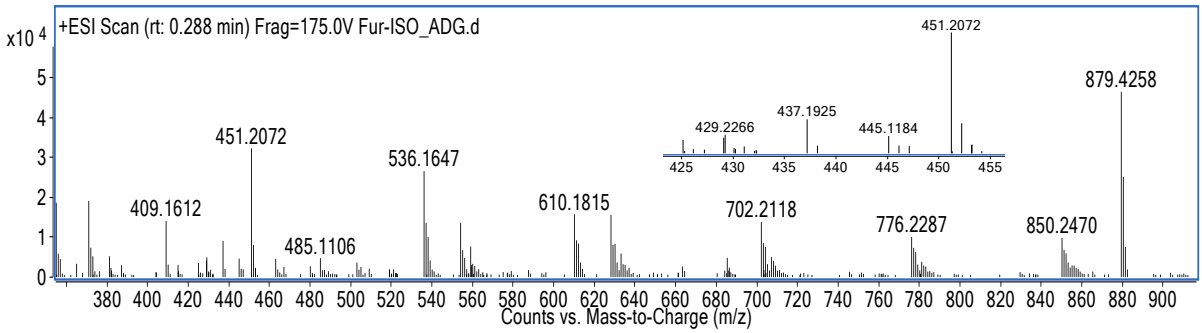
^{1}H NMR Spectrum



^{13}C NMR Spectrum

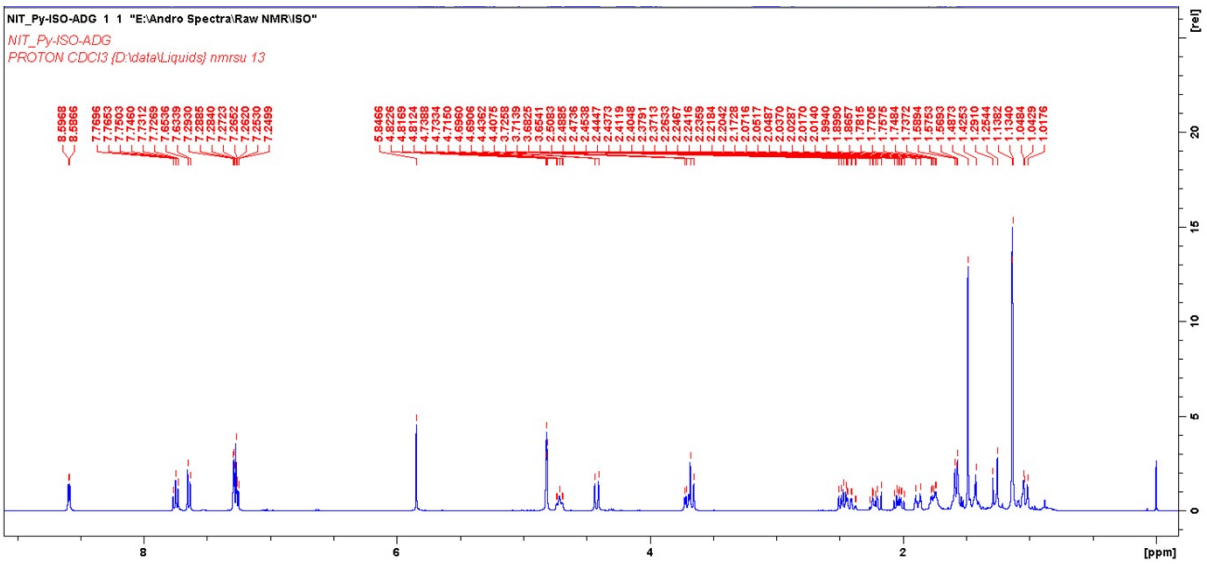


Mass Spectrum

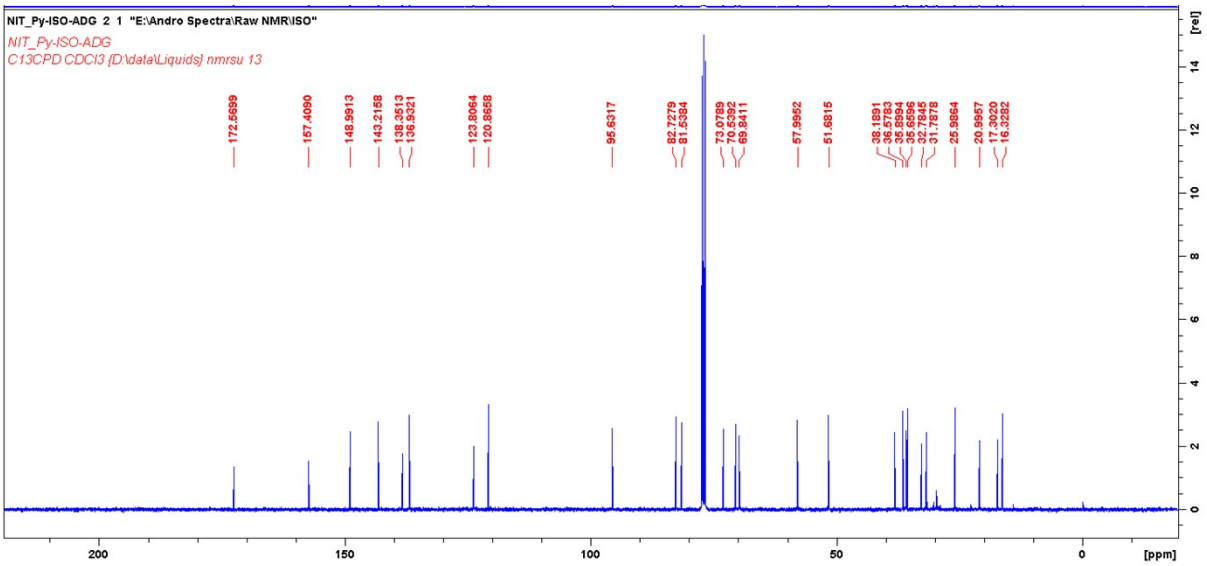


3,19-(2-Pyrilidene)-isoandrographolide (**6c**)

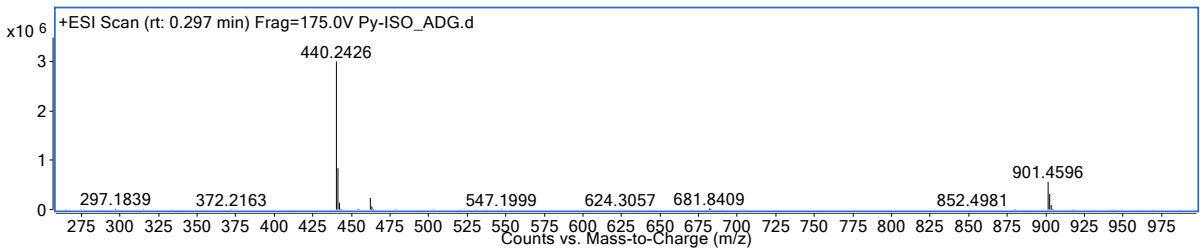
^{1}H NMR Spectrum



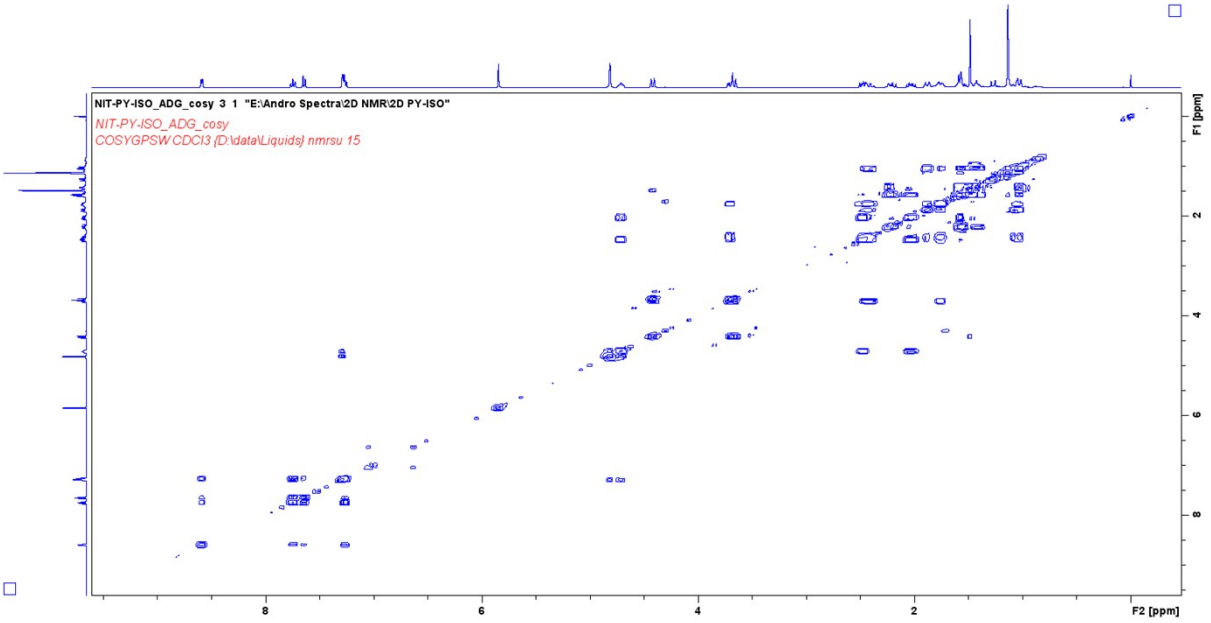
^{13}C NMR Spectrum



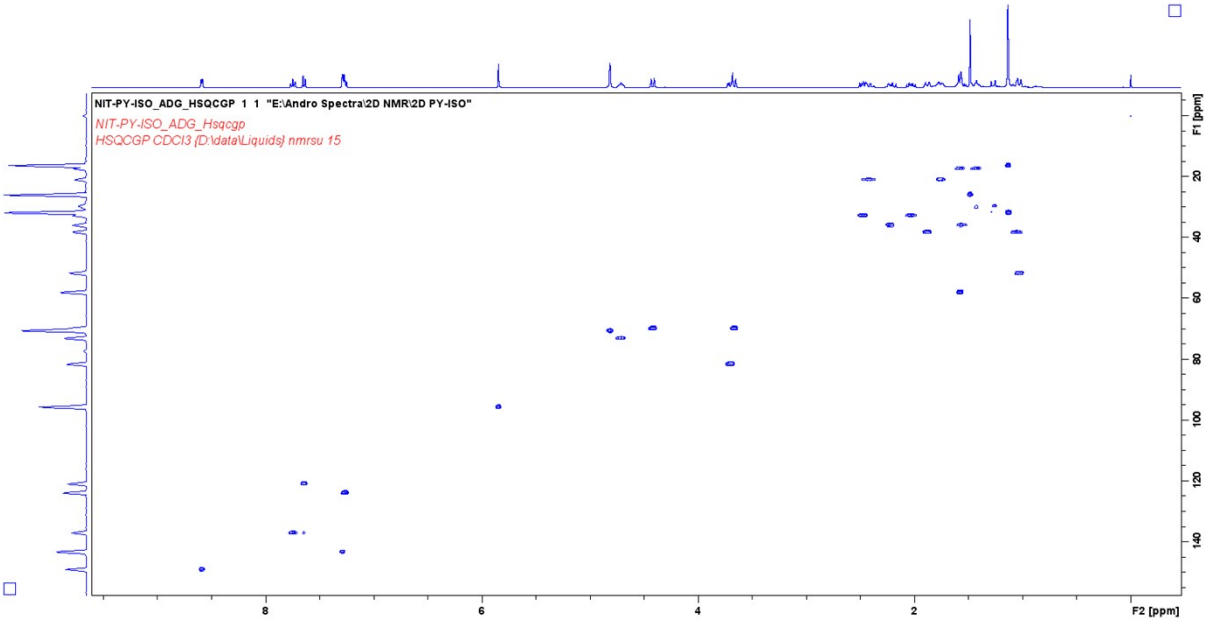
Mass Spectrum



HOMO-COSY

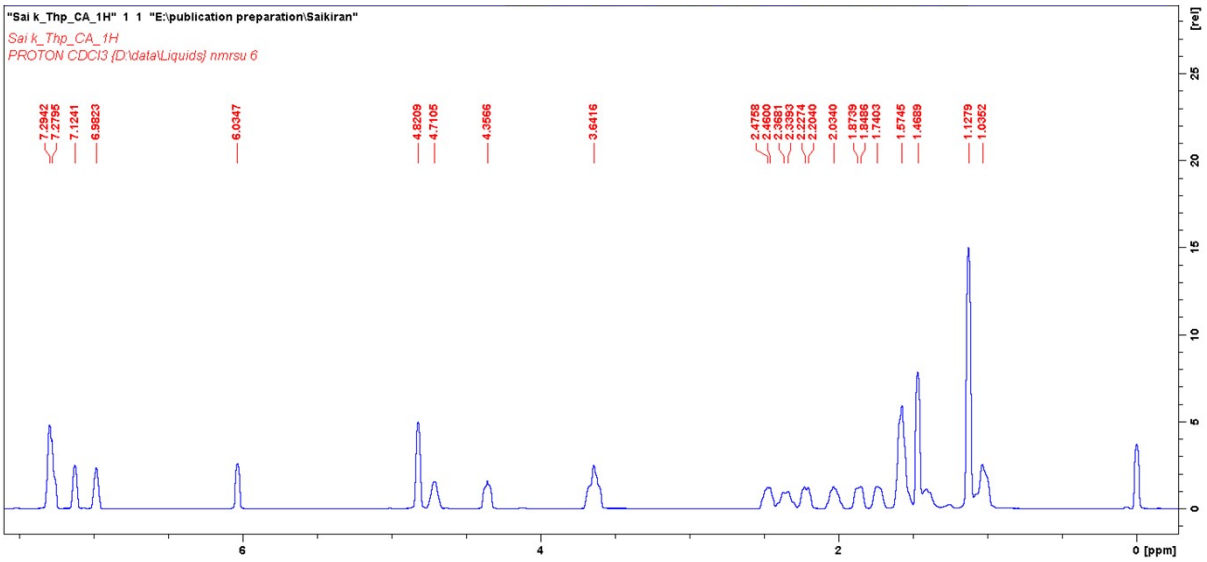


HSQC

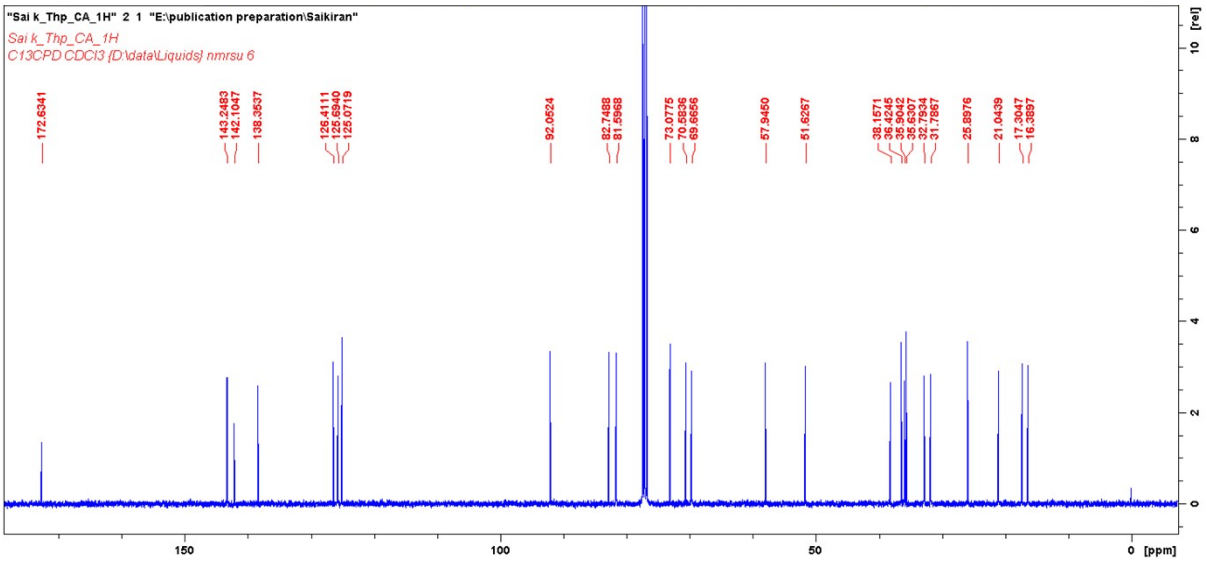


3,19-(2-Thiophenylidene)-isoandrographolide (**6d**)

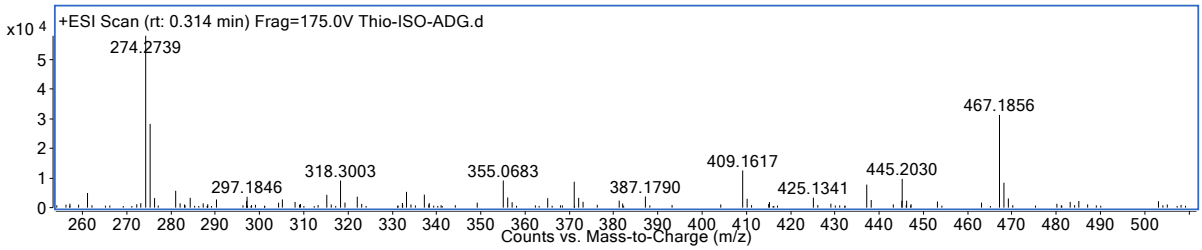
^{1}H NMR Spectrum



^{13}C NMR Spectrum



Mass Spectrum



Sulphorhodamine B Assay:

The human tumor cell lines of the cancer screening panel were grown in RPMI 1640 medium containing 5% fetal bovine serum and 2 mM L-glutamine. For a typical screening experiment, cells were inoculated into 96 well microtiter plates in 100 µL at plating densities ranging from 5,000 to 40,000 cells/well depending on the doubling time of individual cell lines. After cell inoculation, the microtiter plates were incubated at 37° C, 5 % CO2, 95 % air and 100 % relative humidity for 24 h prior to addition of experimental drugs. After 24 h, two plates of each cell line were fixed *in situ* with TCA, to represent a measurement of the cell population for each cell line at the time of drug addition (Tz). Experimental drugs were solubilized in dimethyl sulfoxide at 400-fold the desired final maximum test concentration and stored frozen prior to use. At the time of drug addition, an aliquot of frozen concentrate was thawed and diluted to twice the desired final maximum test concentration with complete medium containing 50 µg/ml gentamicin. Additional four, 10-fold or ½ log serial dilutions were made to provide a total of five drug concentrations plus control. Aliquots of 100 µl of these different drug dilutions were added to the appropriate microtiter wells already containing 100 µl of medium, resulting in the required final drug concentrations. Following drug addition, the plates were incubated for an additional 48 h at 37°C, 5 % CO2, 95 % air, and 100 % relative humidity. For adherent cells, the assay was terminated by the addition of cold TCA. Cells were fixed *in situ* by the gentle addition of 50 µl of cold 50 % (w/v) TCA (final concentration, 10 % TCA) and incubated for 60 minutes at 4°C. The supernatant was discarded, and the plates were washed five times with tap water and air dried. Sulforhodamine B (SRB) solution (100 µl) at 0.4 % (w/v) in 1 % acetic acid was added to each well, and plates were incubated for 10 minutes at room temperature. After staining,unbound dye was removed by washing five times with 1 % acetic acid and the plates were air dried. Bound stain was subsequently solubilized with 10 mM trizma base, and the absorbance was read on an automated plate reader at a wavelength of 515 nm. For suspension cells, the methodology was the same except that the assay was terminated by fixing settled cells at the bottom of the wells by gently adding 50 µl of 80 % TCA (final concentration, 16 % TCA). Using the seven absorbance measurements [time zero, (Tz), control growth, (C), and test growth in the presence of drug at the five concentration levels (Ti)], the percentage growth was calculated at each of the drug concentrations levels[1,2].

Percentage growth inhibition was calculated as:

[(Ti-Tz)/(C-Tz)] x 100 for concentrations for which Ti>/=Tz

[(Ti-Tz)/Tz] x 100 for concentrations for which Ti<Tz.

Results for each compound (One dose data) were reported as percent growth inhibition of the treated cells when compared with untreated control cells. The number reported for the One-dose assay is growth inhibition relative to the no-drug control, and relative to the time zero number of cells.

Table 1: Growth Inhibition % of the tested compounds against Leukaemia Cancer cell lines

Compound	Leukaemia Cancer					
	CCRF-CEM	**HL-60(TB)**	**K-562**	**MOLT-4**	**RPMI-8226**	**SR**
1	76.518	-0.043	34.473	1.891	16.718	20.467
2a	90.972	51.122	56.312	16.038	71.779	63.124
2b	89.842	1.865	55.449	9.0511	82.883	70.994
2c	86.211	13.790	47.295	9.230	58.085	83.823
2d	66.7832	-0.81538	23.5485	0.611945	29.46503	23.59896
3a	57.44093	15.43972	17.21649	-1.6304	12.17347	8.928399
3b	55.42852	11.98941	26.27193	-0.09145	20.47574	18.52426
3c	49.85908	10	20.96628	2.179335	23.0421	28.37051
3d	29.277	7.360911	8.091908	0.105795	6.834309	7.56749
4	39.76075	4.677132	26.86882	-4.44939	16.22877	16.37696
5	1.140075	-3.75882	-6.69841	-2.53097	-2.3327	-6.55106
6a	15.93967	0.531571	33.75518	7.028479	40.67797	12.6464
6b	-1.3227	1.702208	7.42955	2.467475	nd	4.279182
6c	-3.89242	2.852529	4.735854	-2.4127	-4.69679	-3.37448
6d	0.752415	-5.42649	0.036744	-2.38772	0.134973	-8.46255

Table 2: Growth Inhibition % of the tested compounds against Non- Small cell Lung Cancer cell lines

Compound	Non- Small cell Lung Cancer									
	A549/ATCC	**EKVX**	**HOP-62**	**HOP-92**	**NCI-H226**	**NCI-H23**	**NCI-H322M**	**NCI-H460**	**NCI-H522**	**A549/ATCC**
1	12.17981	-4.74849	3.729777	-7.70035	8.264506	2.107728	7.257867	2.023605	82.86785	12.17981
2a	7.436133	-0.15243	-9.66659	-4.56576	3.943978	3.155962	2.900184	0.219194	36.48218	7.436133
2b	4.33074	-1.7339	-6.68933	-12.4029	nd	1.379746	-2.98648	6.921003	36.90639	4.33074
2c	2.364054	-13.3594	-2.53928	-22.2169	nd	0.368318	0.779082	-0.31269	34.87133	2.364054
2d	-1.66653	-2.89368	-5.67142	-7.61947	nd	-7.18257	-3.62387	1.17133	15.89719	-1.66653
3a	-1.51921	-4.53137	-9.00478	-16.9301	-2.36791	-5.35575	2.601124	-5.94628	14.67685	-1.51921
3b	-1.90328	-2.57178	-15.0982	-21.8673	-5.64679	-1.93935	-2.71751	-4.15312	12.73209	-1.90328
3c	-7.81194	-3.86797	-11.1813	-23.9685	-1.25635	-0.29916	-6.20506	-5.89712	19.38366	-7.81194
3d	1.157776	-5.53405	-13.2733	-19.8139	-2.8876	-4.13325	0.15818	-6.57442	10.2898	1.157776
4	4.04036	-1.66456	-2.43024	-0.61129	-7.68403	-3.94361	-2.99678	-3.46162	17.47577	4.04036
5	-1.38674	4.737894	-1.48228	-11.1634	nd	-7.83063	-1.68244	-12.0105	4.167624	-1.38674
6a	2.765844	22.98103	1.835665	19.52053	nd	16.21347	8.125522	-1.38325	17.37486	2.765844
6b	-7.3602	8.371837	-5.19227	-0.03348	-1.03579	-2.76495	1.093307	-2.19269	-8.85738	-7.3602
6c	-4.89042	-0.31194	-3.15651	-3.26976	-6.56821	-1.14408	-6.03328	-3.86686	3.167088	-4.89042
6d	0.521607	4.268997	1.317952	-3.17493	nd	-1.14524	3.4673	-7.11625	6.119009	0.521607

Table 3: Growth Inhibition % of the tested compounds against Colon Cancer cell lines

Compound	Colon Cancer						
	COLO 205	**HCC-2998**	**HCT-116**	**HCT-15**	**HT29**	**KM12**	**SW-620**
1	5.097646	-14.3897	39.98749	38.11131	72.99512	19.75982	55.71462
2a	-7.70086	-8.21094	61.62855	34.48492	45.20326	13.94366	50.33401
2b	-18.4298	-10.7528	48.53267	40.8254	36.91639	7.577149	54.62084
2c	-22.0892	-12.8871	38.35728	28.68756	30.12295	-1.46775	51.49171
2d	-16.683	-12.5799	15.56572	13.59204	15.95049	-1.11809	8.400032
3a	-16.2004	-6.64234	17.33525	10.79678	3.750146	-2.51952	-5.00389
3b	-16.911	-5.18023	14.22497	11.54679	-1.93201	-2.52974	2.338001
3c	-27.3344	-14.0253	16.11826	13.13765	-3.01286	2.286736	9.539144
3d	-13.0703	-4.85242	9.143477	6.459341	-1.99997	-0.62805	-12.489
4	-30.0445	-4.41568	4.595258	9.090909	3.493163	-10.5681	5.086791
5	-15.8258	-2.56102	-3.15721	-1.77933	-1.89252	-9.36922	-7.10549
6a	-1.75914	6.088575	11.91993	9.140509	9.870989	3.271698	-1.26404
6b	-10.1189	-5.13963	-3.56709	2.349979	-4.94404	-3.39016	-6.56877
6c	-14.7909	-9.44081	-9.14597	-5.70147	-14.3573	-10.5154	-7.95751
6d	-14.0819	-0.9288	-1.56262	-0.86341	1.884867	-3.5976	-4.55443

Table 4: Growth Inhibition % of the tested compounds against CNS Cancer cell lines

Compound	CNS Cancer									
	SF-268	**SF-295**	**SF-539**	**SNB-19**	**SNB-75**	**U251**	**SF-268**	**SF-295**	**SF-539**	**SNB-19**
1	2.342445	-13.8934	16.58965	11.96799	38.04721	24.20832	2.342445	-13.8934	16.58965	11.96799
2a	2.52919	-2.41272	7.943713	2.968575	-0.04726	35.75192	2.52919	-2.41272	7.943713	2.968575
2b	-1.248	-4.60775	-6.71624	3.429213	-13.931	35.83239	-1.248	-4.60775	-6.71624	3.429213
2c	1.676046	-10.6696	-2.90218	3.234801	1.079393	26.98123	1.676046	-10.6696	-2.90218	3.234801
2d	-0.92889	-3.97328	-4.62695	-2.36024	-1.20229	7.296883	-0.92889	-3.97328	-4.62695	-2.36024
3a	1.001441	-7.18298	3.69639	2.914272	0.560867	0.436273	1.001441	-7.18298	3.69639	2.914272
3b	-0.02794	-9.56201	-0.43917	-1.34735	9.27866	5.685859	-0.02794	-9.56201	-0.43917	-1.34735
3c	0.067659	-8.72207	2.542648	-3.444	6.979465	6.390977	0.067659	-8.72207	2.542648	-3.444
3d	-1.57393	-4.8884	-0.34624	-2.66833	4.597146	-1.08475	-1.57393	-4.8884	-0.34624	-2.66833
4	1.208589	-3.36158	-7.83748	2.129426	3.619588	11.77299	1.208589	-3.36158	-7.83748	2.129426
5	1.271145	-1.04743	-2.45255	-1.31035	3.532483	-6.14965	1.271145	-1.04743	-2.45255	-1.31035
6a	-0.34731	7.205885	1.799286	8.562396	7.919101	2.798619	-0.34731	7.205885	1.799286	8.562396
6b	1.460968	2.050555	-6.64267	2.660183	nd	-9.70436	1.460968	2.050555	-6.64267	2.660183
6c	-0.90348	-8.98585	2.448624	-1.32439	12.15794	-4.476	-0.90348	-8.98585	2.448624	-1.32439
6d	-0.69703	0.970115	4.473282	4.950583	6.70733	-0.05143	-0.69703	0.970115	4.473282	4.950583

Table 5: Growth Inhibition % of the tested compounds against Melanoma Cancer cell lines

Compound	Melanoma Cancer								
	LOX IMVI	**MALME-3M**	**M14**	**MDA-MB-435**	**SK-MEL-2**	**SK-MEL-28**	**SK-MEL-5**	**UACC-257**	**UACC-62**
1	78.16154	0.218196	15.12195	27.37977	nd	4.539677	22.73368	23.48627	30.07967
2a	66.1861	-10.4165	nd	18.60171	6.650645	-7.43907	5.322558	15.01493	14.25062
2b	77.96371	-3.05899	8.019613	13.0865	-2.73307	-12.7638	6.683541	1.695226	8.89902
2c	77.02182	-1.0191	10.00439	16.7776	-2.09028	-5.77773	0.851203	2.451067	5.155385
2d	27.00125	-3.00992	3.221985	1.74135	-9.3376	-15.1647	-0.01183	-0.22851	3.722504
3a	19.99031	-8.56206	nd	5.07403	-8.60063	-6.00623	-3.37004	1.477887	10.59767
3b	31.32191	-2.19278	nd	7.448958	-7.50768	-7.5937	-3.52539	-1.48202	8.341647
3c	34.63518	-6.97634	nd	4.643198	-3.66304	-0.67743	-2.80027	0.169683	7.720058
3d	9.522512	-3.987	nd	2.55658	-6.31825	-8.05098	-1.72603	2.118111	7.470734
4	27.13617	-4.86654	nd	5.352311	-2.9893	-8.23296	-1.26076	6.911724	11.07706
5	-0.47063	-1.13163	3.056935	-6.85379	-3.27373	-13.033	2.144214	-3.5308	3.315564
6a	7.503063	8.36235	7.994866	1.954539	-3.31887	-5.03408	32.13259	-1.05914	24.25126
6b	-6.18904	1.461066	1.397853	-2.81738	-31.3758	-5.63	-0.52232	-10.4703	12.15696
6c	-2.72863	-12.0334	nd	-3.32761	-15.8592	-10.0567	-4.37129	-7.03767	7.421066
6d	1.119416	3.63739	2.06889	-3.17793	-0.11819	-3.46193	0.641514	-0.9581	5.135694

Table 6: Growth Inhibition % of the tested compounds against Ovarian Cancer cell lines

Compound	Ovarian Cancer						
	IGROV1	**OVCAR-3**	**OVCAR-4**	**OVCAR-5**	**OVCAR-8**	**NCI/ADR-RES**	**SK-OV-3**
1	-3.71225	40.82735	17.12707	-4.2449	15.52401	16.25265	-3.76095
2a	10.65958	36.22771	16.61592	-5.46211	43.42864	42.98087	-19.4454
2b	-3.54913	25.53807	16.16274	-22.2076	42.62078	23.2814	nd
2c	-4.59588	15.85242	19.48269	-23.8692	26.3734	12.0729	nd
2d	-8.12495	-3.07692	8.386053	-24.0803	21.32794	6.237558	nd
3a	5.633267	1.173862	6.580458	-11.9063	21.00358	6.427082	-17.4886
3b	-0.05686	-1.59773	0.018262	-12.375	11.21848	10.98565	-15.6418
3c	-7.75531	3.229344	1.542636	-18.2733	7.621071	10.40566	-11.7911
3d	-2.03711	-5.32913	-3.16639	-10.1415	6.233056	0.658246	-10.3236
4	-6.80717	6.75526	5.31261	-19.6476	1.458116	2.005152	-13.1397
5	-3.289	-13.5144	0.920197	-5.675	-4.17616	-7.27906	nd
6a	13.78575	2.456371	22.89379	5.286986	0.474368	9.687814	nd
6b	6.214865	-5.49876	-2.66172	0.205039	-7.94036	1.476462	-20.5756
6c	-4.10212	-5.04591	-3.24759	-5.77868	-1.37489	-2.0656	-1.47416
6d	-3.36385	-9.23737	-4.11369	1.443825	-3.00923	-4.43436	nd

Table 7: Growth Inhibition % of the tested compounds against Renal Cancer cell lines

Compound	Renal Cancer								
	786-0	**A498**	**ACHN**	**CAKI-1**	**RXF 393**	**SN12C**	**TK-10**	**UO-31**	**786-0**
1	15.29208	12.20705	10.24531	3.296389	-25.2361	18.27	2.51443	10.40465	15.29208
2a	-10.7473	-8.62841	-0.20235	16.29632	-26.5488	20.06998	-9.00035	24.3178	-10.7473
2b	1.365011	-19.9553	1.265066	-7.85137	-8.04901	14.75034	-24.7327	8.409321	1.365011
2c	0.161687	-25.1424	-1.35471	-8.05508	-14.3982	11.64314	-20.7023	1.701089	0.161687
2d	-7.44642	-13.8553	-4.14588	-2.23003	-19.5717	6.788896	-9.88623	13.1346	-7.44642
3a	-15.8143	-2.64448	1.584158	6.941495	-19.8211	9.981548	-10.9972	14.72382	-15.8143
3b	-15.8147	-5.50512	-9.3836	4.257348	-16.7287	5.560834	-14.8161	9.881319	-15.8147
3c	-13.9463	-2.13864	-12.5827	0.982598	-10.0608	2.239986	-14.2188	0.746018	-13.9463
3d	-13.4615	13.29368	-6.90137	3.066767	-26.7037	5.098487	-10.8115	6.134491	-13.4615
4	-11.0738	5.558554	-0.89538	-1.45011	-22.9985	13.21139	-14.0514	0.622311	-11.0738
5	2.032269	-10.6764	-6.62127	2.220923	-25.1127	-2.37082	-4.78448	11.88076	2.032269
6a	8.841477	9.66937	12.82063	18.15403	-10.966	10.20994	10.20661	36.14554	8.841477
6b	6.562337	-2.81594	-2.36473	7.604927	0.713596	3.551148	-4.94442	18.48387	6.562337
6c	-0.00455	-5.47238	-5.67206	4.1957	-10.1231	1.6191	-7.71039	9.857435	-0.00455
6d	7.186504	-5.22597	-0.51635	3.251603	-22.8222	0.186279	4.682111	18.93457	7.186504

Table 8: Growth Inhibition % of the tested compounds against Prostate and Breast Cancer cell lines

Compound	Prostate Cancer		Breast Cancer					
	PC-3	**DU-145**	**MCF7**	**MDA-MB-231/ATCC**	**HS 578T**	**BT-549**	**T-47D**	**MDA-MB-468**
1	6.601658	19.94372	42.44727	-6.74523	-10.3345	12.88968	12.23692	58.00483
2a	17.64745	7.873114	53.91392	0.653746	-0.69875	36.15292	29.35306	8.585889
2b	15.2328	6.356672	51.30576	-14.7872	-7.98918	-9.90585	14.22202	18.63407
2c	5.167519	10.11836	36.01204	-15.1366	-6.87678	-2.18949	6.839594	17.86614
2d	5.544554	-3.30896	27.86736	-11.8672	-4.31048	-13.7768	5.781722	-1.86002
3a	5.132461	-0.10069	17.60966	-3.89002	-2.56237	2.504883	7.979027	-2.0113
3b	4.145475	-5.09818	25.37701	-5.06754	-5.12832	-9.61316	1.200512	9.708329
3c	2.926291	-1.20275	22.46522	-5.86651	-0.96261	-0.47808	-4.71578	12.90283
3d	-4.89874	-6.98849	17.78289	-11.3157	-1.86687	-3.24041	-1.24244	3.78498
4	0.327753	-2.2685	23.04531	-10.1357	7.730078	-8.50448	3.440516	9.231381
5	-5.33407	-12.0189	3.657464	-5.08589	-6.7395	-11.2866	-4.86008	-6.04553
6a	13.84161	-1.43348	24.42675	12.86242	-5.34263	6.592913	39.78549	28.09138
6b	9.453757	-6.80928	1.149466	9.756184	-7.14238	nd	-0.80355	8.176459
6c	-1.34037	-10.1304	-2.57475	1.286377	3.728219	-15.4621	-4.03887	2.014309
6d	-0.06416	-9.52929	9.51125	-1.53234	-3.12795	-4.64591	1.690624	-0.28966

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