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$SiCl_4$ mediated one-pot synthesis of novel spirobibenzopyrans as potent anticancer agents

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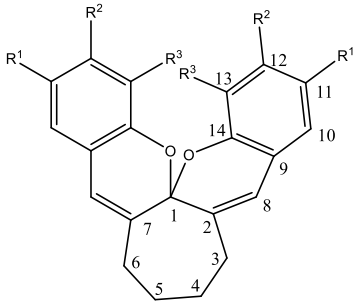
Supporting information:

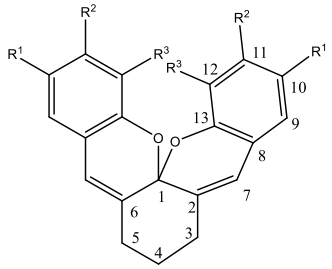
1. Synthesis

The spirobibenzopyrans were synthesized by stirring a mixture of the ketone (0.01 mol), the required substituted salicylaldehyde (0.02 mol), and $SiCl_4$ (silicon tetrachloride, 0.03 mol) in absolute ethanol (20ml) under nitrogen atmosphere. The above reaction mixture was stirred till the completion of the reaction indicated by formation of solid (generally white in color) in the reaction vessel. After completion the contents were poured into ice to quench the catalyst and stirred for 15 minutes. The solid was filtered, washed with water, dried and recrystallized from distilled chloroform. If there was formation of a colored solid in the reaction vessel, the reaction was worked up in the similar manner as mentioned before. The coloured solid obtained was then suspended in diethyl ether (20 mL) and to it 20 mL of aqueous ammonia was added. The suspension was shaken vigorously and the ether layer was separated, dried over anhydrous Na_2SO_4. Then the ether layer was evaporated to obtain a crude solid which was recrystallized from distilled acetone or chloroform. The compounds synthesized along with their sample code and yield shown in **SD table I** below.

SD Table I: Structure, IUPAC names, % yield and melting points of the synthesized spirobibenzopyrans.



CODE	IUPAC NAME	SUBSTITUENT	YIELD (%)
CHP-SAL	6,7,8,9-tetrahydrocyclohepta[1,2-b:1,7-b']dichromene	R^1 = -H R^2 = -H	90

CHP-4MO-SAL	2,13-dimethoxy-6,7,8,9-tetrahydrocyclohepta[1,2-b:1,7-b']dichromene	R^1 = -H R^2 = -OCH_3	64
CHP-5MO-SAL	3,12-dimethoxy-6,7,8,9-tetrahydrocyclohepta[1,2-b:1,7-b']dichromene	R^1 = -OCH_3 R^2 = -H	84
CHP-5Cl-SAL	3,12-dichloro-6,7,8,9-tetrahydrocyclohepta[1,2-b:1,7-b']dichromene	R^1 = -Cl R^2 = -H	88
CHP-5Br-SAL	3,12-dibromo-6,7,8,9-tetrahydrocyclohepta[1,2-b:1,7-b']dichromene	R^1 = -Br R^2 = -H	86
CHP-DiCl-SAL	1,3,12,14-tetrachloro-6,7,8,9-tetrahydrocyclohepta[1,2-b:1,7-b']dichromene	R^1 = -Cl R^2 = -H R^3 = -Cl	69
			
CHX-SAL	7,8-dihydro-6H-chromeno[3,2-d]xanthene	R^1 = -H R^2 = -H	40
CHX-4MO-SAL	2,12-dimethoxy-7,8-dihydro-6H-chromeno[3,2-d]xanthene	R^1 = -H R^2 = -OCH_3	33
CHX-5MO-SAL	3,11-dimethoxy-7,8-dihydro-6H-chromeno[3,2-d]xanthene	R^1 = -OCH_3 R^2 = -H	81
CHX-5Cl-SAL	3,11-dichloro-7,8-dihydro-6H-chromeno[3,2-d]xanthene	R^1 = -Cl R^2 = -H	86
CHX-5Br-SAL	3,11-dibromo-7,8-dihydro-6H-chromeno[3,2-d]xanthene	R^1 = -Br R^2 = -H	78
CHX-DiCl-SAL	1,3,11,13-tetrachloro-7,8-dihydro-6H-chromeno[3,2-d]xanthene	R^1 = -Cl R^2 = -H R^3 = -Cl	75

2. *Instrumentation*

The ^{1}HNMR spectra were obtained on VARIAN 200 MHz, ^{13}CNMR on VARIAN 50 MHz for CHP-SAL, CHP-4MO-SAL, CHP-5Cl-SAL, and CHP-5Br-SAL, for CHP-5MO-SAL and CHX-4MO-SAL the ^{1}HNMR spectra were obtained on VARIAN 500 MHz, and ^{13}CNMR on VARIAN 125 MHz and finally the ^{1}HNMR spectra were obtained on VARIAN 400 MHz, and ^{13}CNMR on VARIAN 100 MHz for CHP-DiCl-SAL and all the remaining CHX derivatives. TMS was used as the internal standard and $CDCl_3$ as the solvent. For mass spectra AGILENT 6430 Triple Quad LC/MS was employed. The FT-IR spectra were recorded between 400 and 4000cm^{-1} using KBr

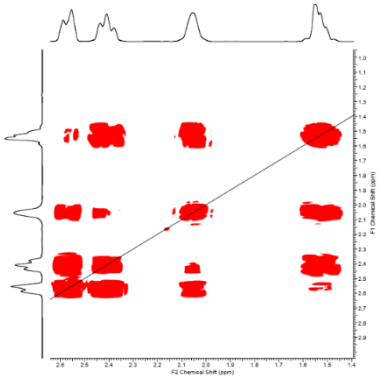
pellets employing Thermo-Nicolet Avatar 370 spectrophotometer. UV-Vis spectra in methanol were recorded in the wavelength range 200-600 nm using Shimadzu 2450 spectrophotometer.

For HPLC Agilent 1260 Infinity high performance liquid chromatography system, equipped with a quaternary solvent deliver system, inline degasser, autosampler and photo diode array detector, was used. A Waters Nova - Pak C18 (3.9mm X 150mm) connected with a Zorbax C18 guard column (20 mm × 4 mm, 5 µm) was applied for all analyses. Detection wavelengths were set at the respective λ_{max} for each compound (characterization data). The mobile phase A consisted of water and mobile phase B was acetonitrile. A flow rate of 1 ml/min was maintained and the elution was conducted using a linear gradient mode as shown in supplementary (SD table 1 and 2). The separation was carried out at 25 °C with an injection volume of 20µl and samples were analyzed in triplicate. Spectral characteristics of eluted peaks were recorded using diode array detector from 200 to 700 nm.

Single crystals of suitable dimensions were chosen carefully for X-ray diffraction studies. The X-ray intensity data were collected at a temperature of 293(2) K on a Bruker Proteum2 CCD diffractometer equipped with an X-ray generator operating at 45 kV and 10 mA, using CuK_{α} radiation of wavelength 1.54178 Å. Data were collected for 24 frames per set with different settings of φ (0° and 90°), keeping the scan width of 0.5°, exposure time of 2 s, the sample to detector distance of 45.10 mm and 2θ value at 46.6°. The complete data sets were processed using *SAINT PLUS* [1]. The structures were solved by direct methods and refined by full-matrix least squares method on F^2 using *SHELXS* and *SHELXL* programs [2]. The geometrical calculations were carried out using the program *PLATON* [3]. The molecular and packing diagrams were generated using the software *MERCURY* [4].

3. Characterization

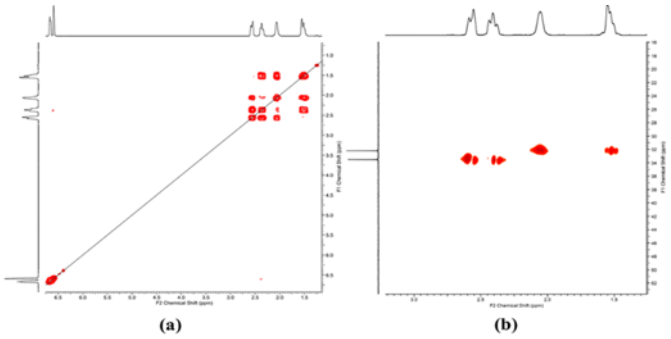
The ^{1}H-COSY for the $-CH_2-$ protons is shown in figure I.



SD Figure I. 2D-COSY of CHP-SAL zoomed to view the $-CH_2-$ protons

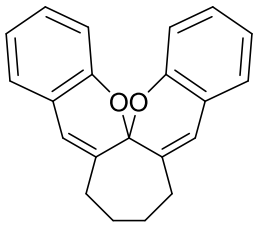
From the contour of the signal it is evident that the signals at δ2.56 and δ2.41 are the geminal hydrogens H-3a, H-3b / H-6a, H-6b. Also the fact that both the signals couple with the other signals appearing at δ2.05 and δ1.53 which are H-4 and H-5 respectively indicate that they are indeed geminal hydrogens. It is further confirmed by two more facts: one, there is a small amount of

allylic coupling observed with the signal at δ2.41 with the H-7 at δ6.70 which is absent for the signal at δ2.56 (shown in figure IIa). This tells us that one of the hydrogens is projecting outward the cycloheptanone ring with the allylic coupling (Ha) and the other hydrogen is inwards having no allylic coupling (Hb). Fact two, from the HMQC spectra shown in figure IIb it is clear that the signals at δ2.56 and δ2.41 are for 2 hydrogens each H-3a, H-6a and H-3b, H-6b corresponding to C3 and C6 which appear at the same value of δ32 in the ^{13}C-NMR spectrum. Additionally, from the Gaussian studies we obtained the theoretical NMR values which upon analysis showed that indeed the protons H-3a and H-3b, H-6a and H-6b to have different chemical shift values. The calculation table is given in supplementary section as SD table 4. Our theory of the difference in chemical environment of H-3a and H-3b is finally confirmed by the single crystal XRD structure shown in **figure III** for **CHP-5Cl-SAL** where the H-3a and H-6a protons are outward and the H3b and H6b protons are inwards. Similar observation can be made from the single crystal XRD structure of **CHP-5MO-SAL** shown in figure IV. We thus understand the non-equivalence of the protons at H3/H6 in the **CHP** system using the spectroscopic techniques.

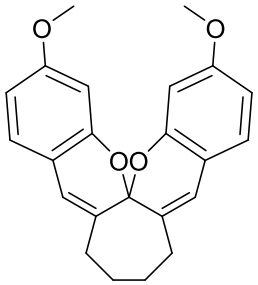


SD Figure II. (a) 2D-COSY of CHP-SAL zoomed to view the allylic coupling. (b) 2D-HMQC of CHP-SAL zoomed to view the –CH$_2$- region

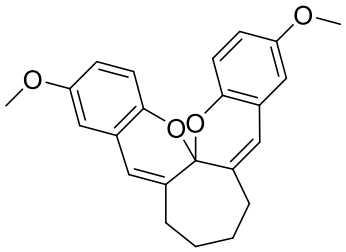
Characterization data of the synthesized spirobibenzopyrans:



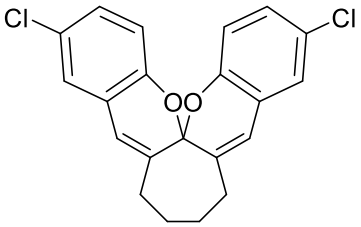
CHP-SAL: Colorless solid. M.P.: 215-216 °C; 1H-NMR(200 MHz, CDCl3) δ, ppm = 7.20 (t, H-12, J=7.0 Hz), 7.10 (d, H-10, J=7.0 Hz), 6.95 (t, H-11, J=7.0 Hz), 6.8(d, H-13, J=7.0 Hz), 6.70 (s, H-8), 2.60 (m, H-3b and H-6b, J=6.4 Hz), 2.40 (m, H-3a and H-6a), 2.10 (m, H-4), and 1.55 (m, H-5); 13C-NMR(150 MHz, CDCl3) δ, ppm = 150(C14), 136 (C2, C7), 130(C12), 126 (C10), 124 (C11), 122 (C8), 121 (C9), 116(C13), 107 (C1), 34(C4, C5), and 32 (C3, C6); IR (KBr disc): 3061-w (alkene C-H stretch), 2920-m (aliphatic C-H stretch), 1604-s (C=C stretch), 1575, 1557-m (aromatic skeletal bands), 1437 (aromatic C-H bend),1374-m,1247-s, 1141-s (C—O stretch), 795-s, 753-s (C-H oop bend); UV-vis (CHCl3) λmax nm: 241, 298; Mass: m/z [M]+= 302.0



CHP-4MO-SAL: Pale colored solid. M.P.: 168.2-169.1 °C; 1H-NMR(200 MHz, CDCl3) δ, ppm = 7.25 (s, H-8), 7.06 (d, H-10), 6.61 (m, H-11), 6.40 (d, H-13), 2.52-2.39 (m, H-3 and H-6), 2.04 (m, H-4), 1.50 (m, H-5), and 3.71 (s, -OCH3); 13C-NMR(50 MHz, CDCl3) δ, ppm = 160(C12), 151 (C14), 132(C2, C7), 126 (C8), 123 (C1), 114 (C9), 108 (C11), 102 (C13), 101 (C9), 33 (C4, C5), and 32 (C3, C6); IR (KBr disc): 3065-w (alkene C-H stretch), 2919-m (aliphatic C-H stretch), 1614-s (C=C stretch), 1572-m, 1463-s (aromatic skeletal bands), 1438-s, 1372-s (aromatic C-H bend), 1325-s, 1272-s, 1117-s (C—O stretch), 908-s, 864-s, 768s (C-H oop bend); UV-vis (CHCl3) λmax nm: 240, 278; Mass: m/z [M]+= 362.0

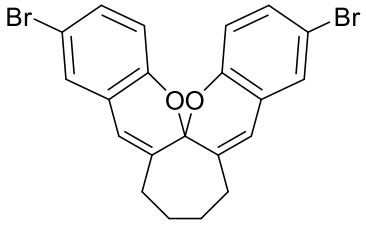


CHP-5MO-SAL: Pale yellow solid. M.P.: 180.2-180.9 °C; 1H-NMR(500 MHz, CDCl3) δ, ppm = 7.20 (s, H-8), 6.71 (d, H-13, J=7.8 Hz), 6.69 (d, H-12, J=7.8 Hz), 6.61 (s, H-10), 2.55 (m, H-3b and H-6b), 2.40 (m, H-3a and H-6a), 2.05 (m, H-4), 1.52 (m, H-5), and 3.77 (s, -OCH3); 13C-NMR(101 MHz, CDCl3) δ, ppm = 154 (C11), 144 (C14), 136 (C2, C7), 122 (C8), 121 (C9), 119 (C12), 117 (C13), 111 (C10), 102 (C1), 34 (C4, C5), 32 (C3, C6), and 56 (-OCH3); IR (KBr disc): 3051-w (alkene C-H stretch), 2927-m (aliphatic C-H stretch), 1616-m (C=C stretch) 1581-m, 1487-s (aromatic skeletal bands), 1451-s 1433-s (aromatic C-H bend), 1311-s, 1200-s, 1141-s (C—O stretch), 955-s, 880-s, 750-s (C-H oop bend); UV-vis (CHCl3) λmax nm: 243, 321; Mass: m/z [M+H]+ = 363.1592

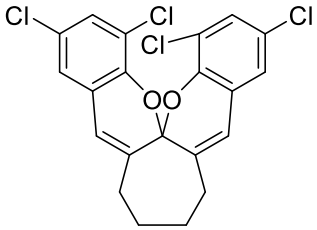


CHP-5Cl-SAL: White solid. M.P.: 127-128 °C; 1H-NMR (200 MHz, CDCl3) δ, ppm = 7.13 (s, H-10), 7.09 (d, H-12, J=8 Hz), 6.71 (d, H-13, , J=8 Hz), 6.60(s, H-8), 2.55 (m, H-3b and H-6b), 2.37 (m, H-3a and H-6a), 2.06 (m, H-4), and 1.55 (m, H-5); 13C-NMR(50 MHz, CDCl3) δ, ppm = 148 (C14), 137 (C2, C7), 129 (C12), 127 (C11), 126 (C10), 123 (C9), 118 (C13), 114 (C8), 101

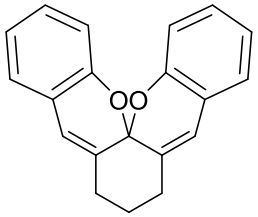
(C1), 34 (C4, C5), and 32 (C3, C6); IR (KBr disc): 3060-w (alkene C-H stretch), 2926-m (aliphatic C-H stretch), 1634-m (C=C stretch), 1560-m (aromatic skeletal bands), 1479-s, 1445-s (aromatic C-H bend), 1362-s, 1229-s, 1181-s (C—O stretch), 1077-m, 1052-s (Aromatic -Cl stretch), 875-s, 749-s, 716-s (C-H oop bend); UV-vis (CHCl3) λmax nm: 242, 308; Mass: m/z [M-H]+= 370.0, [M-H+2]+= 372.0



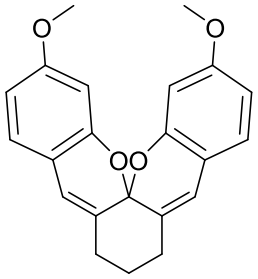
CHP-5Br-SAL: White solid. M.P.: 120-122 °C; 1H-NMR (200 MHz, CDCl3) δ, ppm = 7.40 (s, H-10), 7.30 (d, H-12, J=7.7 Hz), 6.70 (d, H-13, , J=7.7 Hz), 6.60(s, H-8), 2.60 (m, H-3b and H-6b), 2.40 (m, H-3a and H-6a), 2.00 (m, H-4), and 1.60 (m, H-5); 13C-NMR(50 MHz, CDCl3) δ, ppm = 148 (C14), 136 (C2, C7), 132 (C12), 128 (C10), 125 (C1), 123 (C11), 119 (C13), 117 (C8), 114 (C9), 34 (C4, C5), and 32 (C3, C6); IR (KBr disc): 3059-w (aromatic C-H stretch); 2927-s (aliphatic C-H), 1633-m (C=C stretch); 1476 – s, 1419 -m (aromatic C-H bend), 1339-m (CH3 bend); 1286-m, 1228-m, 1179-m, 1126-m (C—O stretch); 1067-m, 1054-m (Ar-Br stretch); 852-s, 682-s (C-H oop). UV-vis (CHCl3) λmax nm: 242, 309; Mass: m/z [M]+ = 460.0 and [M+2]+ = 462.0



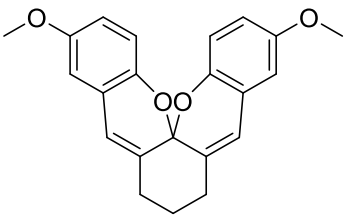
CHP-DiCl-SAL: Pale white solid. 1H-NMR(400 MHz, CDCl3) δ, ppm = 7.20 (d, H-10, J=2.8Hz), 7.06 (d, H-12, J=2.8Hz), 6.63 (s, H-8), 2.63 (m, H-3b and H-6b), 2.39 (m, H-3a and H-6a), 2.09 (m, H-4), and 1.54 (m, H-5); 13C-NMR(100 MHz, CDCl3) δ, ppm = 144 (C14), 137 (C2, C7), 129 (C12), 128 (C11), 125 (C13), 124 (C9), 123 (C10), 122 (C8), 101 (C1), 33 (C4, C5), and 31 (C3, C6); IR (KBr disc): 3040-w (alkene C-H stretch), 2920-m (aliphatic C-H stretch), 1610-s (C=C stretch), 1577-m, 1465-s (aromatic skeletal bands), 1440-s, 1373-s (aromatic C-H bend), 1320-s, 1275-s, 1110-s (C—O stretch), 910-s, 866-s, 770s (C-H oop bend); UV-vis (CHCl3) λmax nm: 240, 278; Mass: m/z [M - H]+= 439, [M – H + 2]+= 441



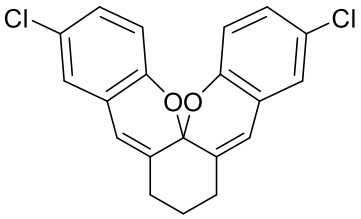
CHX-SAL: White solid. M.P.: 160-161 °C; 1H-NMR (400 MHz, CDCl3) δ, ppm = 7.22 (2H, d, H-9, J=7.4 Hz), 7.16 (2H, t, H-11, J=7.4 Hz), 7.02 (2H, t, H-10, J=7.4 Hz), 6.92 (2H, d, H-12, J=7.4 Hz), 6.69(2H, s, H-7), 2.53 (4H, t, H-3 and H-5, J=6.5 Hz), and 1.82 (2H, m, H-4, J=6.5 Hz); 13C-NMR (100 MHz, CDCl3) δ, ppm = 150.0 (C13), 132.0 (C2, C6), 129.0 (C11), 126.0 (C9), 122.0 (C10), 121.8 (C8), 121.3 (C7), 117.0 (C12), 96.0 (C1), 26.0 (C3, C5), and 20.0 (C4); IR (KBr disc): 3150 cm-1 -w (sp2 C-H stretch); 2920-m (aliphatic C-H), 1606-m, (C=C stretch); 1572 – s, 1481 –m, 1455 -m (aromatic C-H bend), 1219-m, 1124-m, (C—O stretch); 751-s (C-H oop). UV-vis (CHCl3) λmax nm: 259, 296; Mass: m/z [M]+ = 288.0



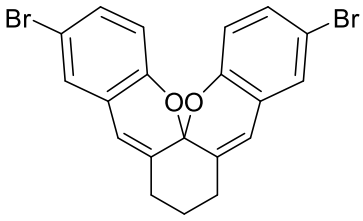
CHX-4MO-SAL: White solid. M.P.: 168.2-169.1 °C; 1H-NMR(500 MHz, CDCl3) δ, ppm = 7.20 (s, H-7), 6.71 (d, H-9, J=7.8 Hz), 6.69 (d, H-10, J=7.8 Hz), 6.61 (s, H-12), 2.49 (t, H-3 and H-5), 1.78 (quintet, H-4), and 3.72 (s, -OCH3); 13C-NMR (125 MHz, CDCl3) δ, ppm = 160.0 (C13), 151.0 (C11), 129.0 (C10), 126.2 (C2, C6), 121.4 (C9), 115.8 (C8), 108.3 (C7), 102.0 (C12), 96.0 (C1), 55.4 (-OCH3), 26.0 (C3, C5), and 20.0 (C4); IR (KBr disc): 3065-w (alkene C-H stretch), 2919-m (aliphatic C-H stretch), 1614-s (C=C stretch), 1572-m, 1463-s (aromatic skeletal bands), 1438-s, 1372-s (aromatic C-H bend), 1325-s, 1272-s, 1117-s (C—O stretch), 908-s, 864-s, 768s (C-H oop bend); UV-vis (CHCl3) λmax nm: 240, 278; Mass: m/z [M + H]+= 349.1



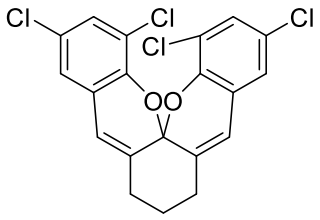
CHX-5MO-SAL: White solid. 1H-NMR(400 MHz, CDCl3) δ, ppm = 7.20 (s, H-7), 7.06 (d, H-12, J=6 Hz), 6.74 (d, H-11, J=6 Hz), 6.62 (s, H-9), 2.39 (t, H-3 and H-5), 1.79 (quintet, H-4), and 3.78 (s, -OCH3); 13C-NMR (100 MHz, CDCl3) δ, ppm = 154.5 (C13), 143.9 (C10), 136.9 (C11), 132.7.2 (C2, C6), 128.4 (C9), 124.3 (C8), 123.2 (C7), 12.07.0 (C12), 95.9 (C1), 55.7 (-OCH3), 32.0 (C3, C5), and 33.0 (C4); IR (KBr disc): 3065-w (alkene C-H stretch), 2919-m (aliphatic C-H stretch), 1614-s (C=C stretch), 1572-m, 1463-s (aromatic skeletal bands), 1438-s, 1372-s (aromatic C-H bend), 1325-s, 1272-s, 1117-s (C—O stretch), 908-s, 864-s, 768s (C-H oop bend); UV-vis (CHCl3) λmax nm: 240, 278; Mass: m/z [M + H]+= 349.1



CHX-5Cl-SAL: White solid. 1H-NMR(200 MHz, CDCl3) δ, ppm = 7.17 (d, H-9, J=2Hz), 7.10 (dd, H-11, J=2Hz, J=8Hz), 6.73 (d, H-12, J=8Hz), 6.61 (s, H-7), 2.51 (t, H-3 and H-5), and 1.81 (quintet, H-4); 13C-NMR (50 MHz, CDCl3) δ, ppm = 148.2 (C13), 133.1 (C10), 128.5 (C2, C6), 126.9 (C11), 125.8 (C9), 123.1 (C8), 121.4 (C7), 118.1 (C12), 96.0 (C1), 26.4 (C3, C5), and 20.3 (C4); IR (KBr disc): 3065-w (alkene C-H stretch), 2919-m (aliphatic C-H stretch), 1614-s (C=C stretch), 1572-m, 1463-s (aromatic skeletal bands), 1438-s, 1372-s (aromatic C-H bend), 1325-s, 1272-s, 1117-s (C—O stretch), 908-s, 864-s, 768s (C-H oop bend); UV-vis (CHCl3) λmax nm: 240, 278; Mass: m/z [M - H]+= 356, [M – H + 2]+= 358



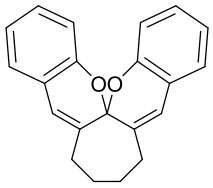
CHX-5Br-SAL: Pale yellow solid. 1H-NMR (400 MHz, CDCl3) δ, ppm = 7.40 (s, H-9), 7.30 (d, H-11, J=7.7 Hz), 6.70 (d, H-12, J=7.7 Hz), 6.60(s, H-7), 2.51 (t, H-3 and H-5), and 1.81 (quintet, H-5); 13C-NMR (100 MHz, CDCl3) δ, ppm = 149.2 (C13), 133.4 (C10), 128.9 (C2, C6), 126.3 (C11), 125.2 (C9), 123.1 (C8), 121.5 (C7), 118.4 (C12), 96.8 (C1), 26.4 (C3, C5), and 20.3 (C4); IR (KBr disc): 3059-w (aromatic C-H stretch); 2927-s (aliphatic C-H), 1633-m (C=C stretch); 1476 – s, 1419 -m (aromatic C-H bend), 1339-m (CH3 bend); 1286-m, 1228-m, 1179-m, 1126-m (C—O stretch); 1067-m, 1054-m (Ar-Br stretch); 852-s, 682-s (C-H oop). UV-vis (CHCl3) λmax nm: 242, 309; Mass: m/z [M]+ = 446.0 and [M+2]+ = 448.0

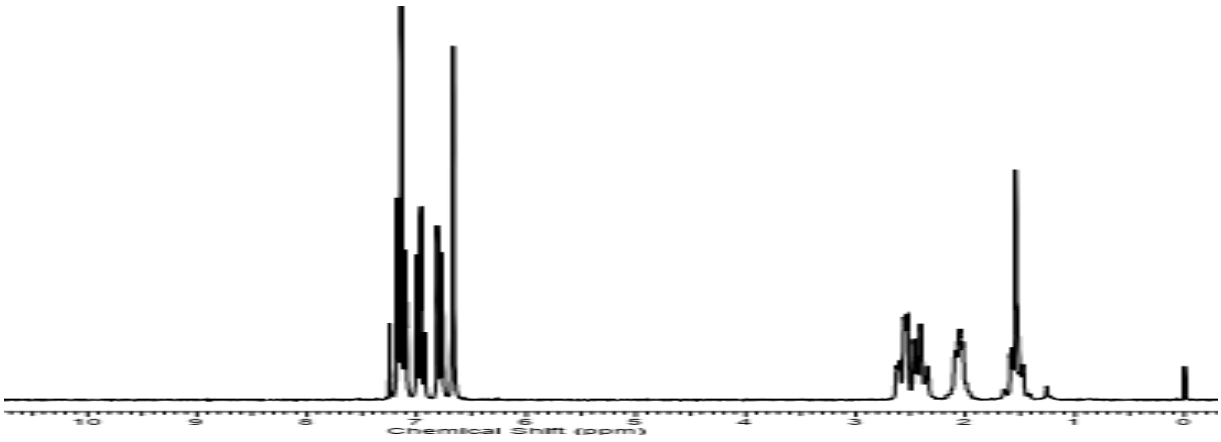


CHX-DiCl-SAL: Yellow solid. 1H-NMR(400 MHz, CDCl3) δ, ppm = 7.20 (d, H-11, J=2.8Hz), 7.06 (d, H-9, J=2.8Hz), 6.63 (s, H-7), 2.53 (4H, t, H-3 and H-5, J=6.5 Hz), and 1.82 (2H, m, H-4, J=6.5 Hz); 13C-NMR (100 MHz, CDCl3) δ, ppm = 144.0 (C13), 137.1 (C2, C6), 128.7 (C12), 126.8 (C10), 124.2 (C11), 123.3 (C9), 123.2 (C8), 122.4 (C7), 101.7 (C1), 33.4 (C3, C5), and 31.9 (C4); IR (KBr disc): 3040-w (alkene C-H stretch), 2920-m (aliphatic C-H stretch), 1610-s (C=C stretch), 1577-m, 1465-s (aromatic skeletal bands), 1440-s, 1373-s (aromatic C-H bend), 1320-s, 1275-s, 1110-s (C—O stretch), 910-s, 866-s, 770s (C-H oop bend); UV-vis (CHCl3) λmax nm: 240, 278; Mass: m/z [M - H]+= 439, [M – H + 2]+= 441

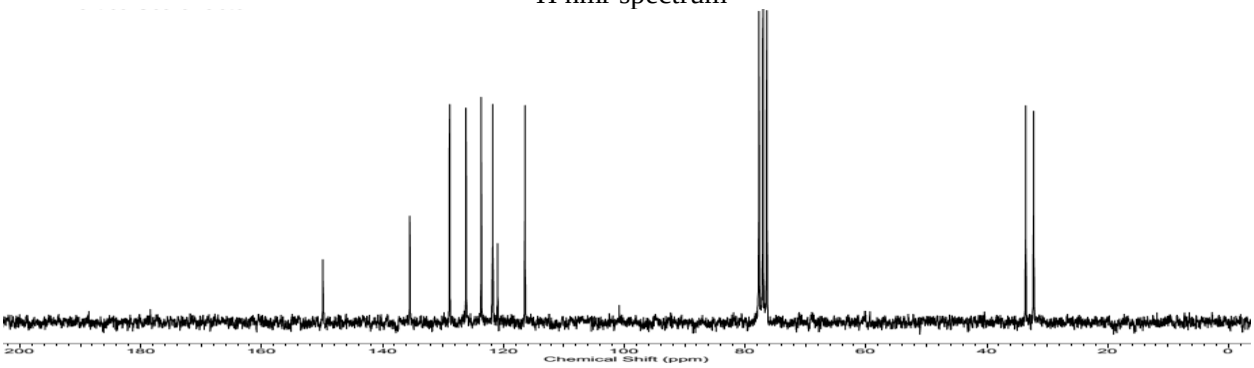
^{1}H-NMR, ^{13}C-NMR and Mass spectra of the spirobibenzopyrans

CHP-SAL

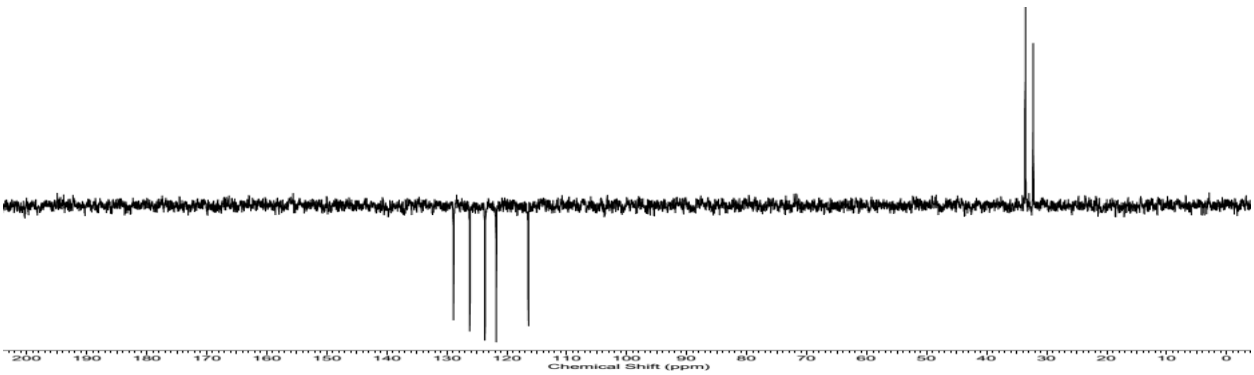




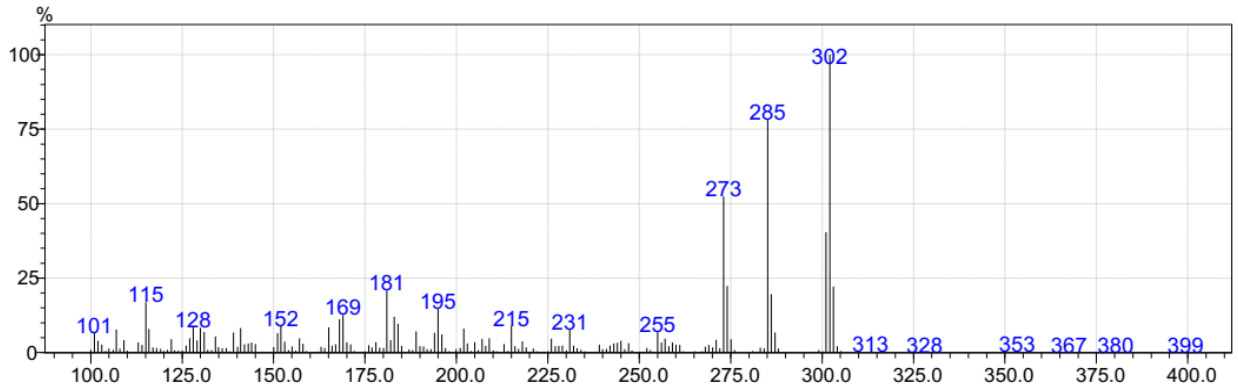
^{1}H nmr spectrum



^{13}C nmr spectrum

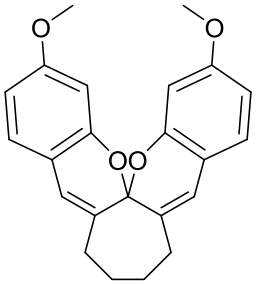


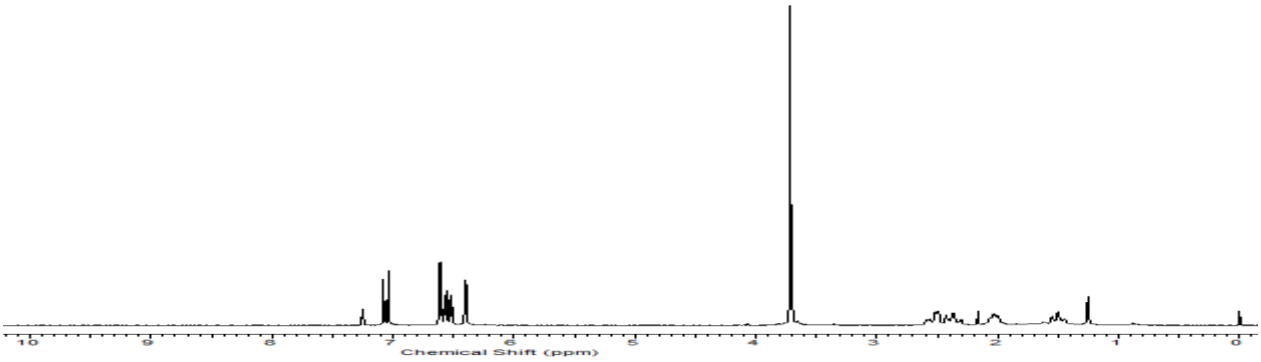
DEPT-135 ^{13}C nmr spectrum



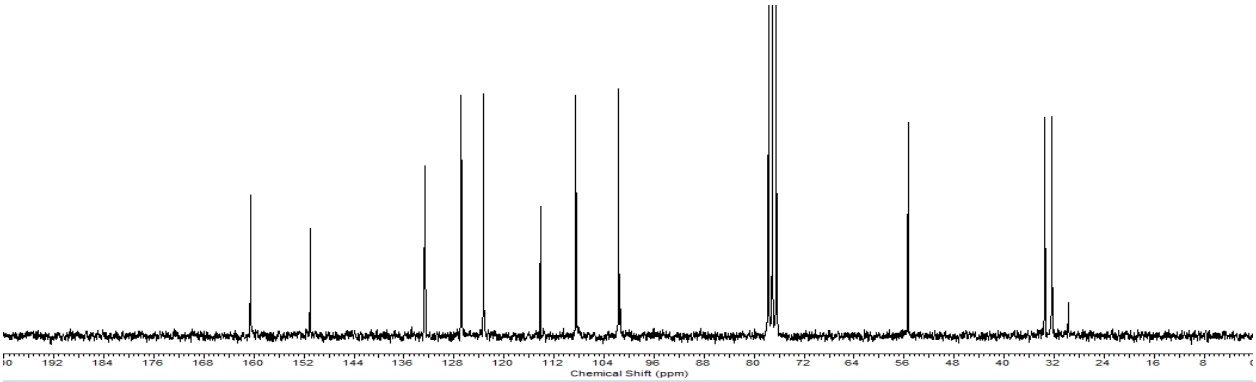
Mass spectrum

CHP-4MO-SAL

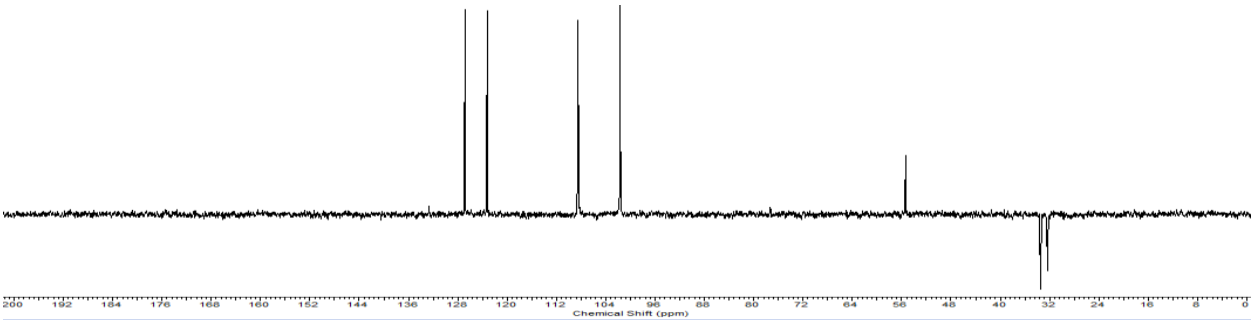




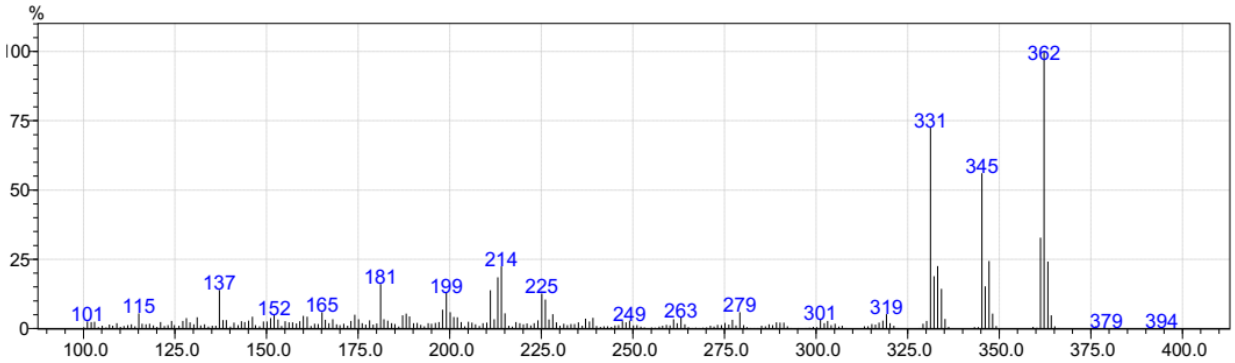
^{1}H nmr spectrum



^{13}C nmr spectrum

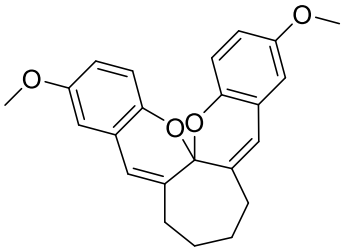


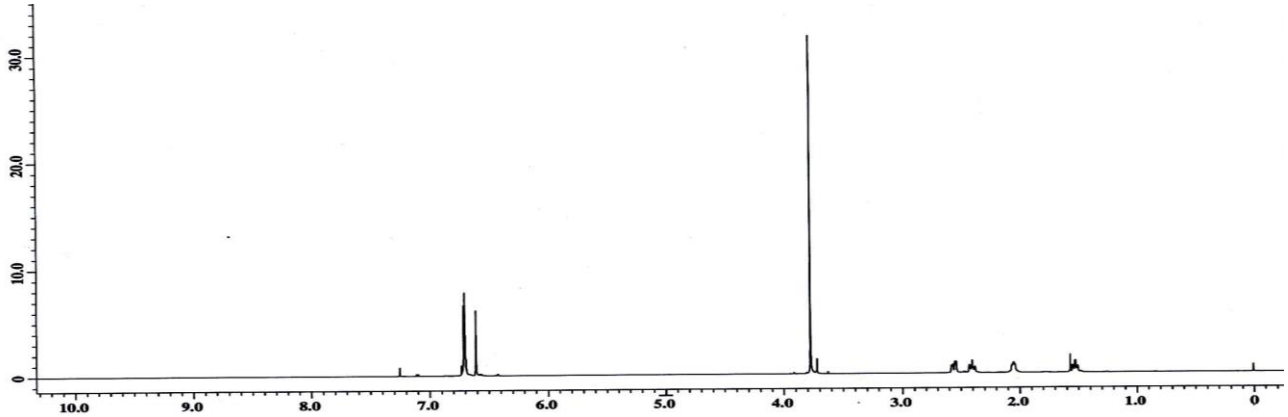
DEPT-135 ^{13}C nmr spectrum



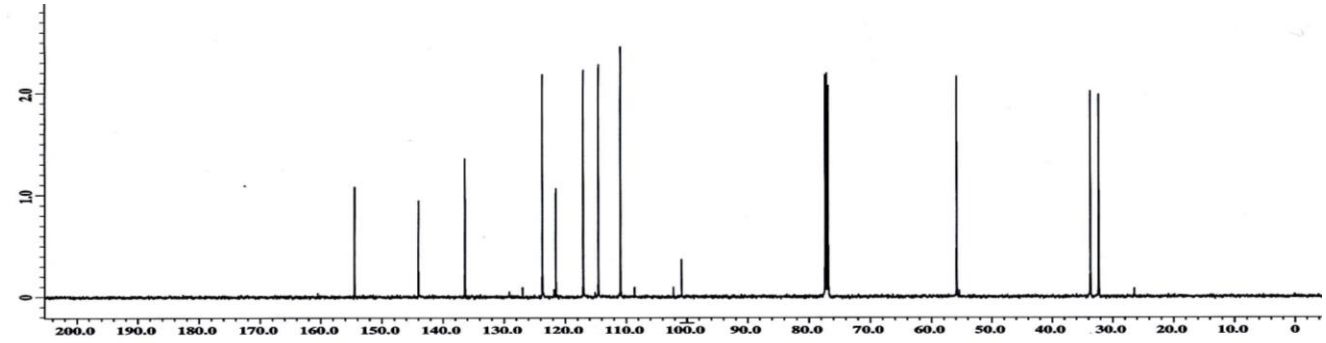
Mass spectrum

CHP-5MO-SAL

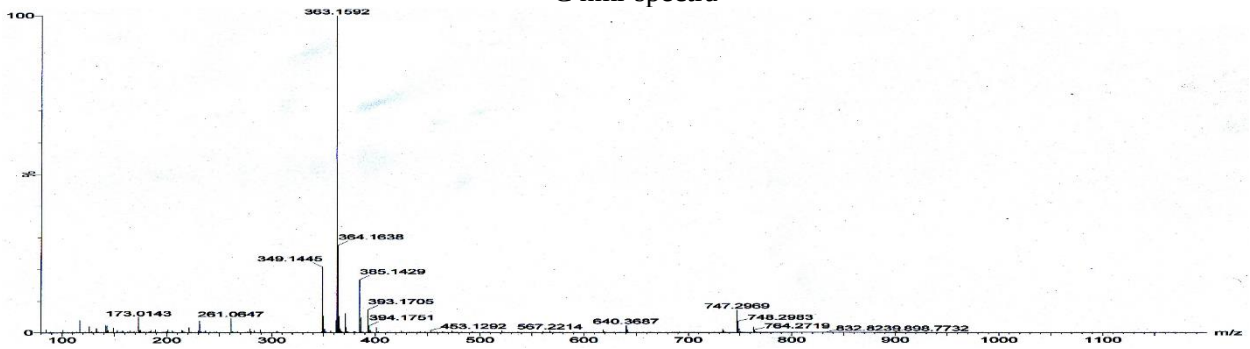




^{1}H nmr spectra

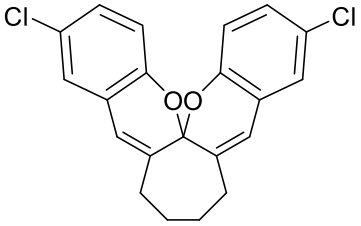


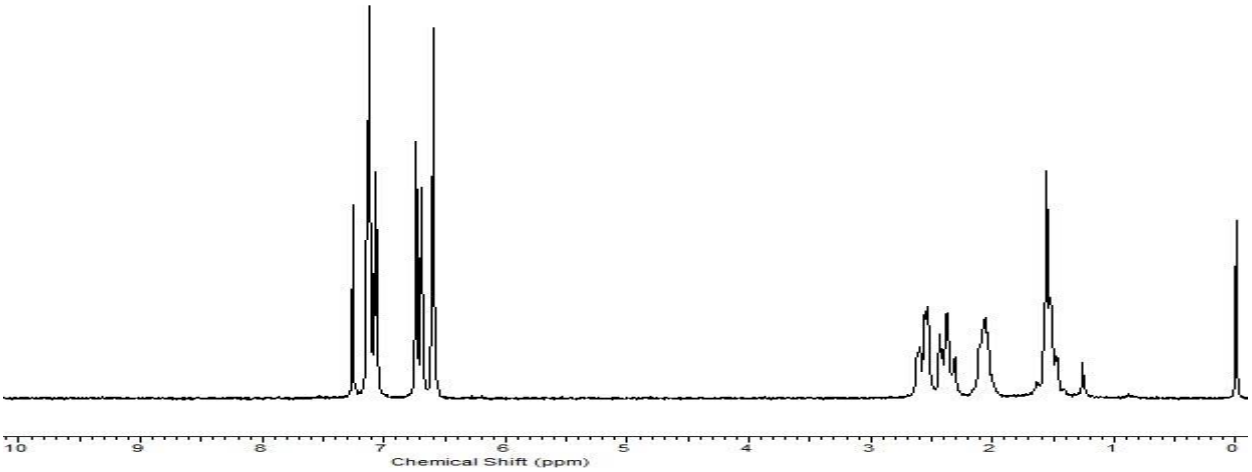
^{13}C nmr spectra



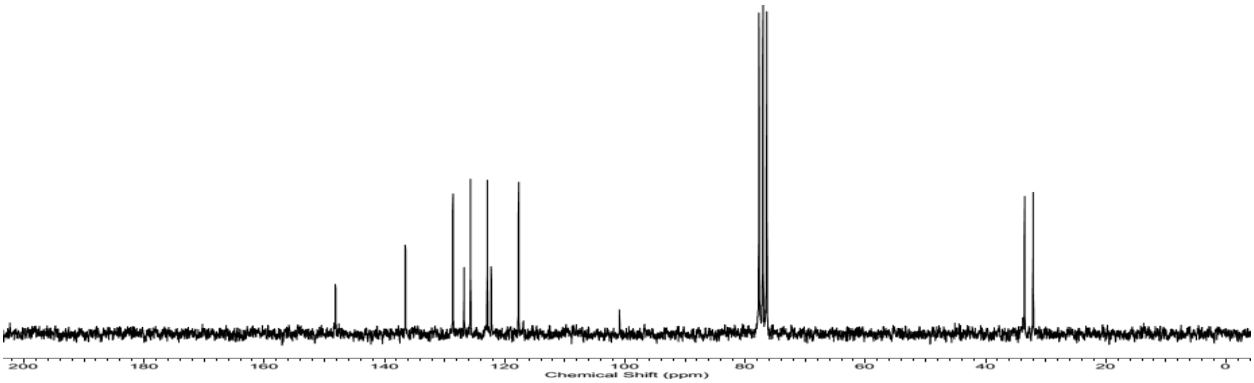
Mass spectrum

CHP-5Cl-SAL

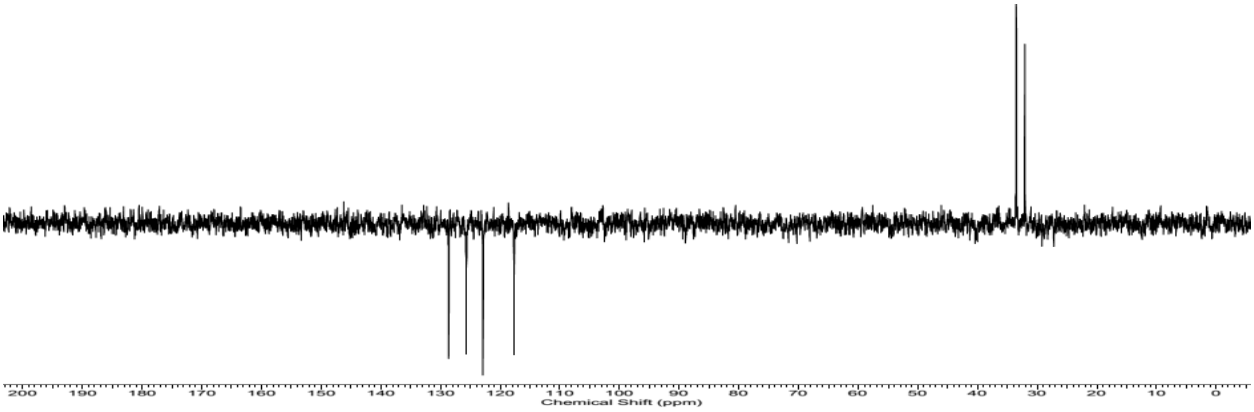




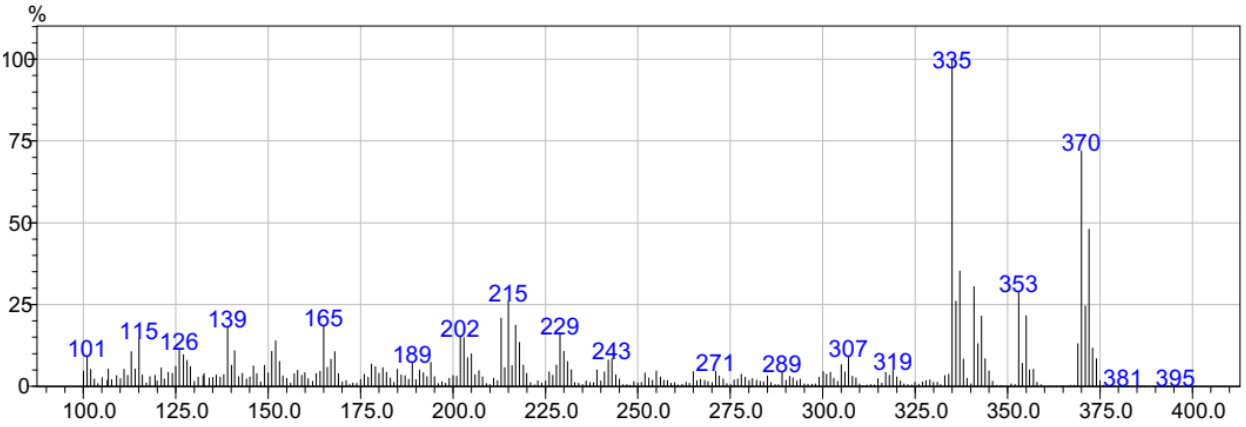
^{1}H nmr spectrum



^{13}C nmr spectrum

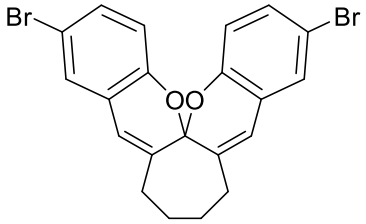


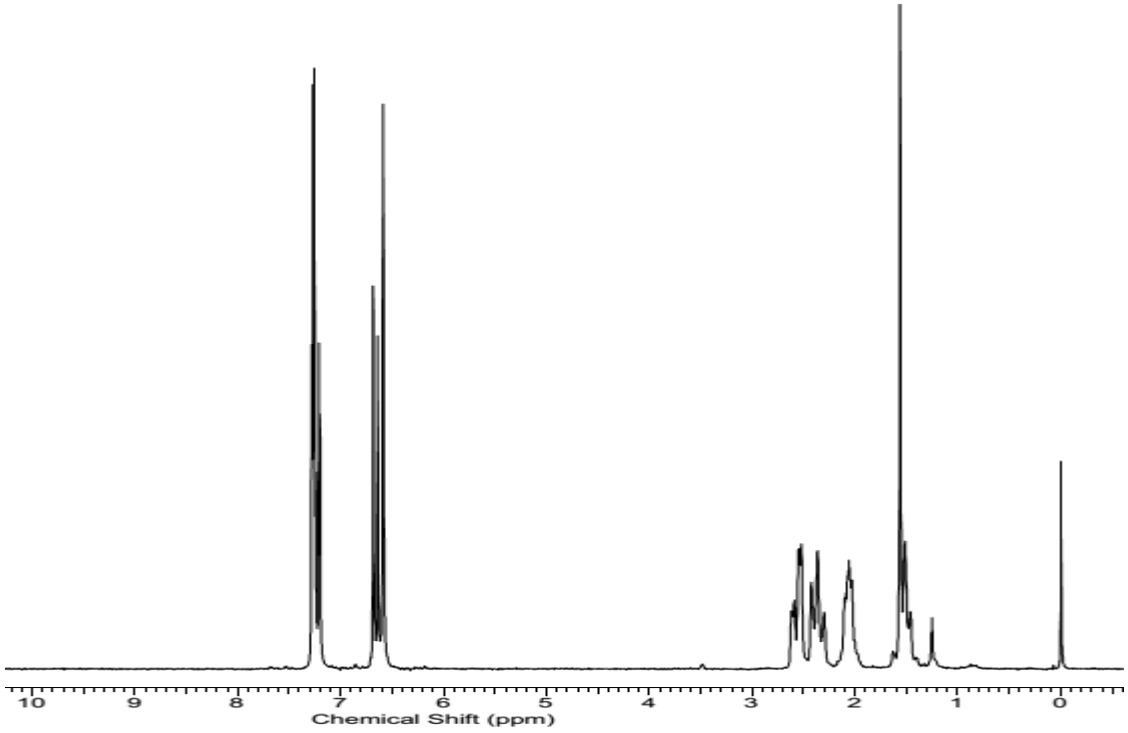
DEPT-135 ^{13}C nmr spectrum



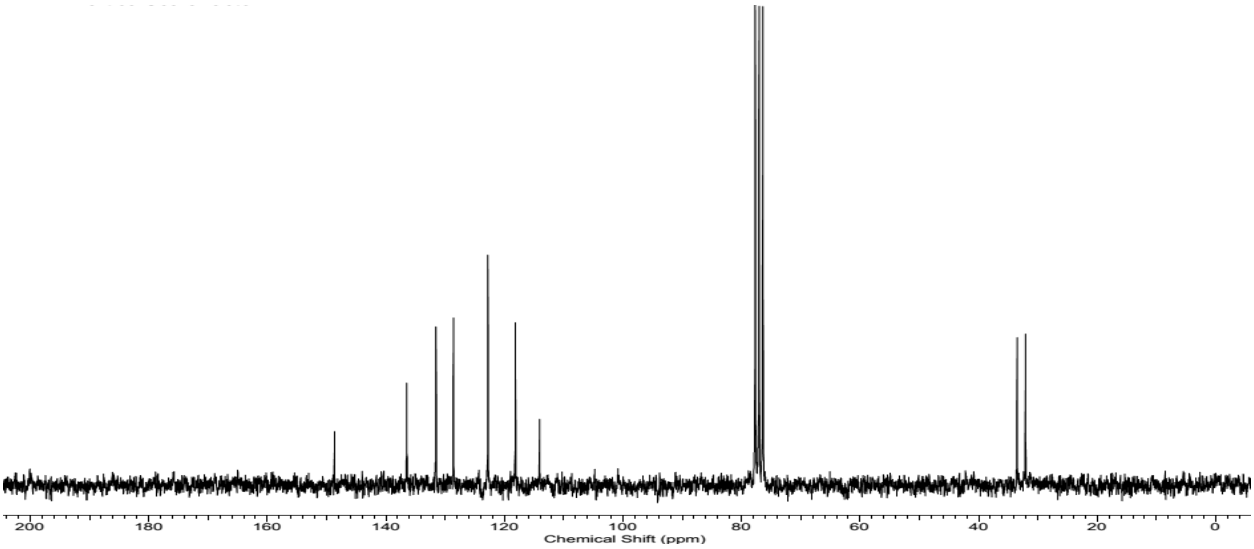
Mass spectrum

CHP-5Br-SAL

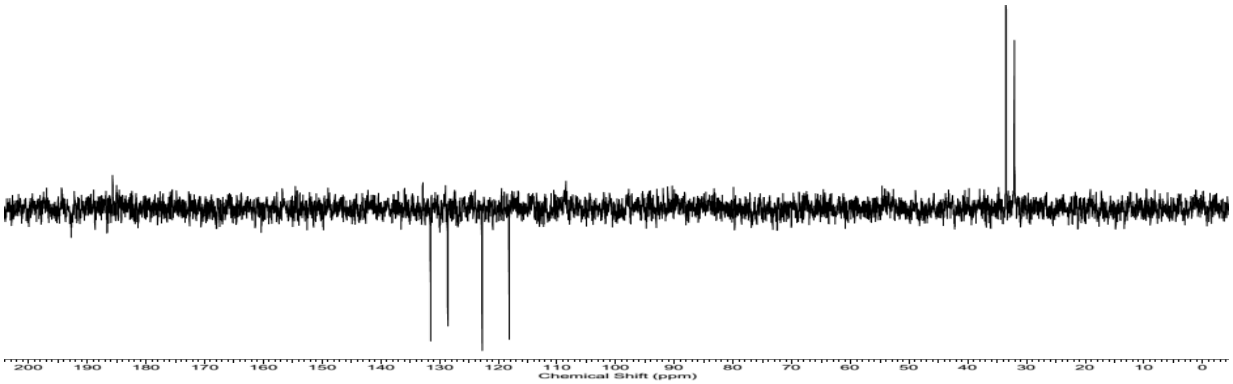




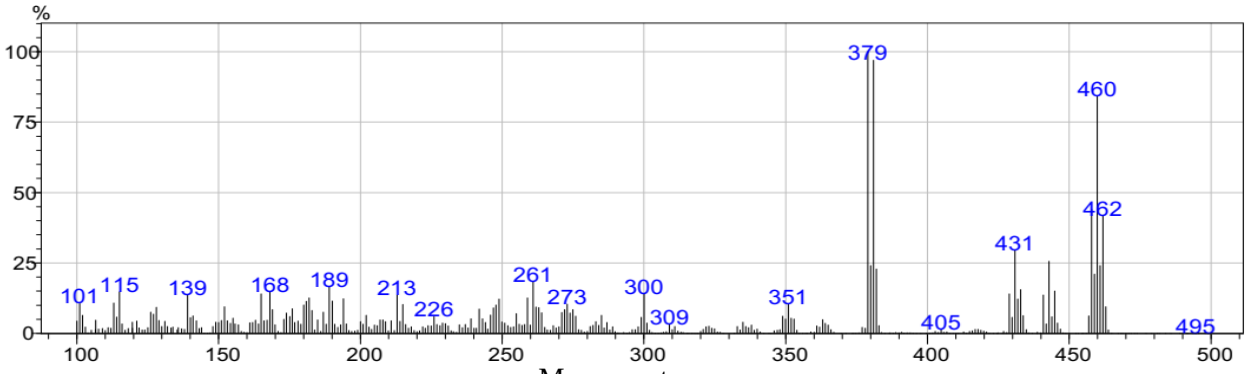
^{1}H nmr spectra



^{13}C nmr spectra

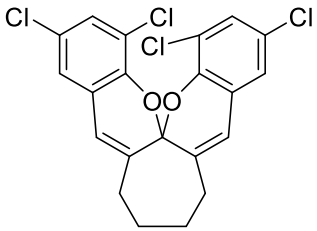


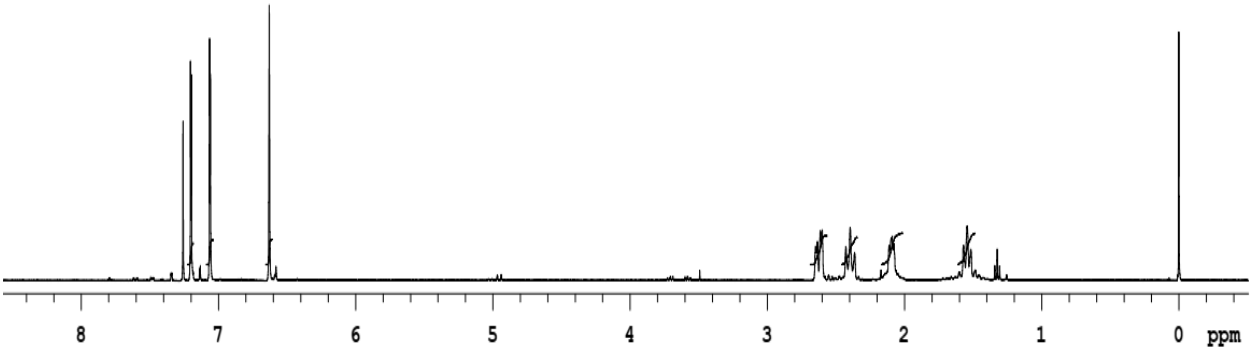
DEPT-135 ^{13}C nmr spectra



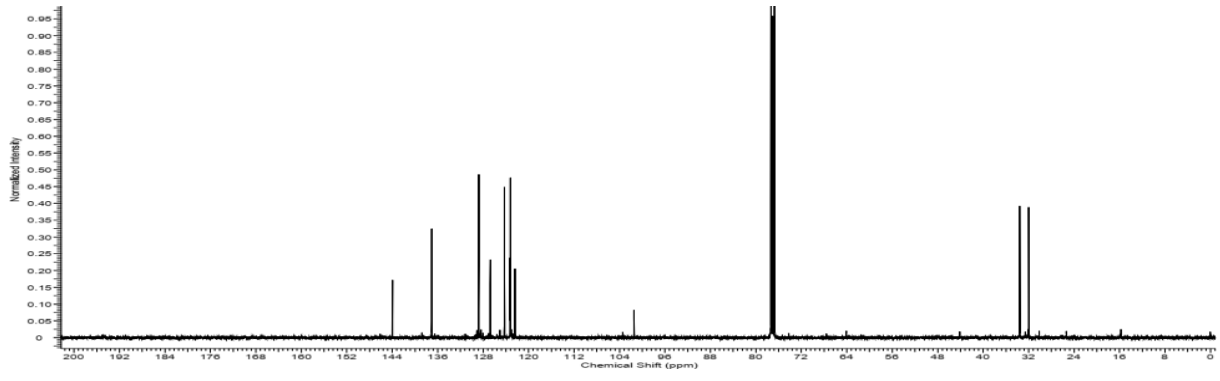
Mass spectrum

CHP-DiCl-SAL





^{1}H nmr spectrum



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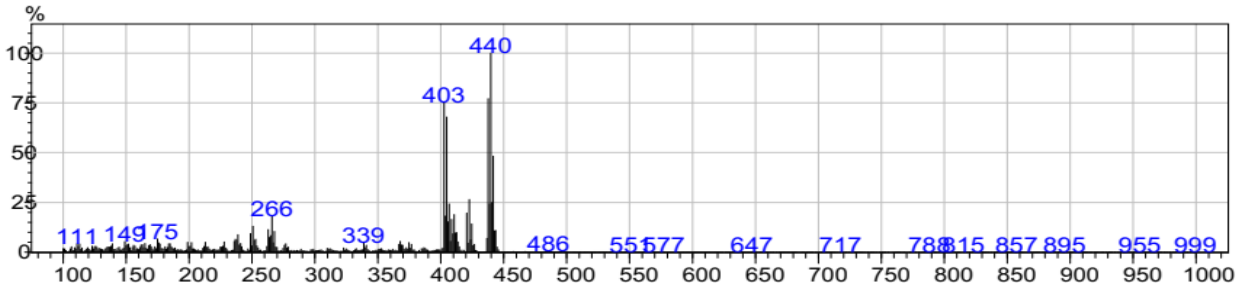
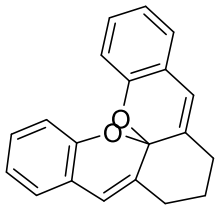
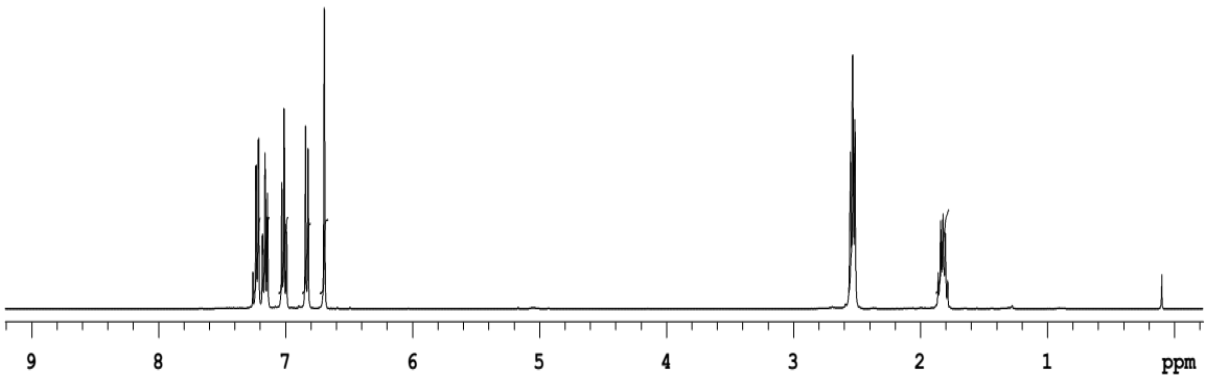


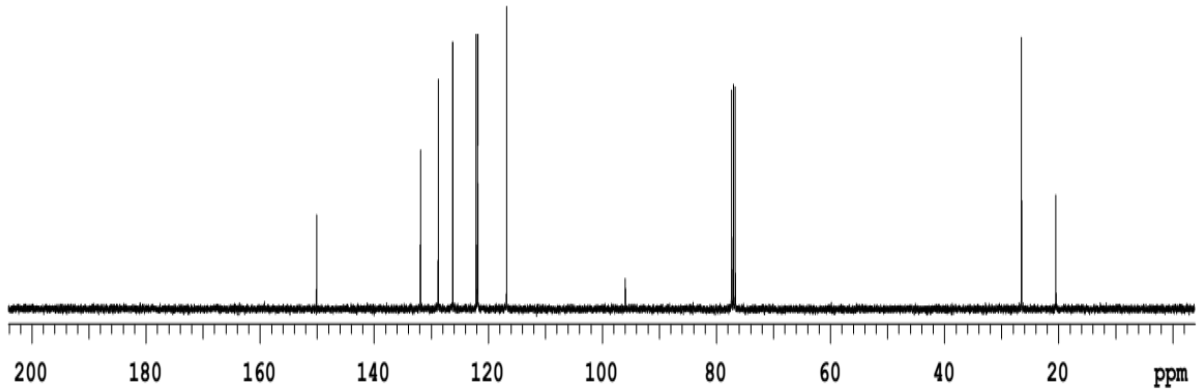
Mass spectrum

CHX-SAL

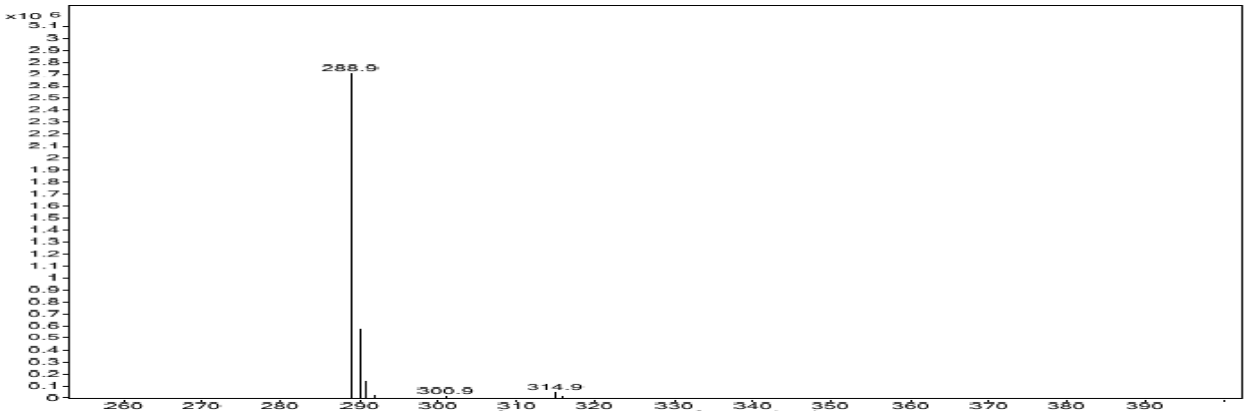




^{1}H nmr spectrum

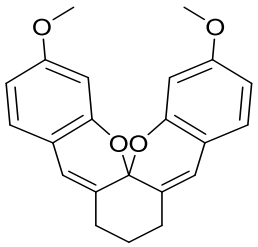


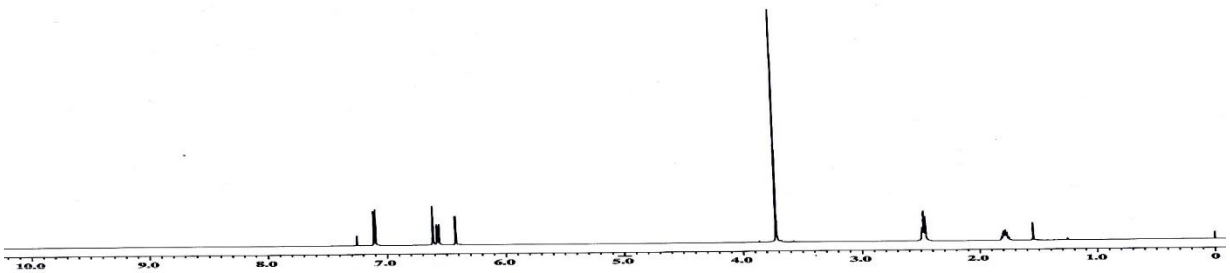
^{13}C nmr spectrum



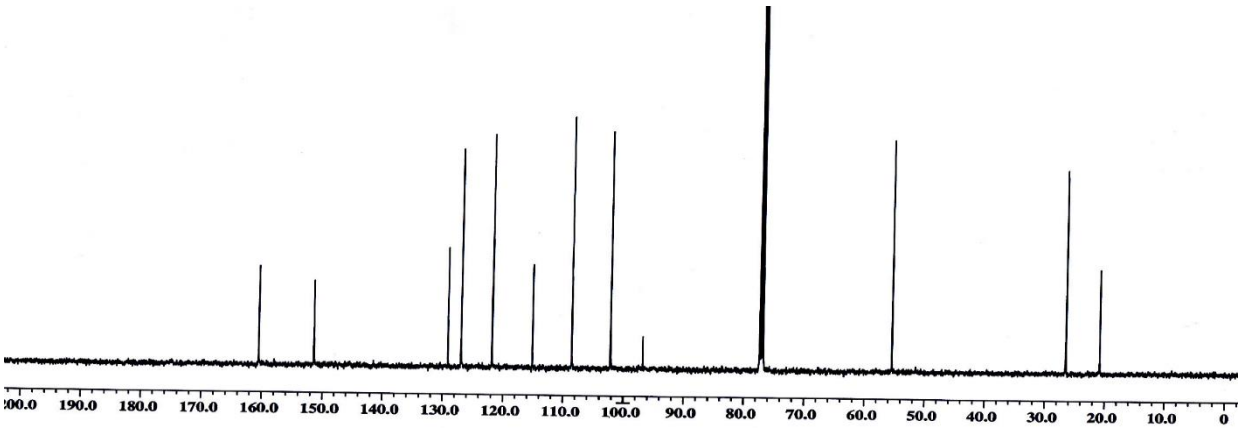
Mass spectrum

CHX-4MO-SAL





^{1}H nmr spectrum



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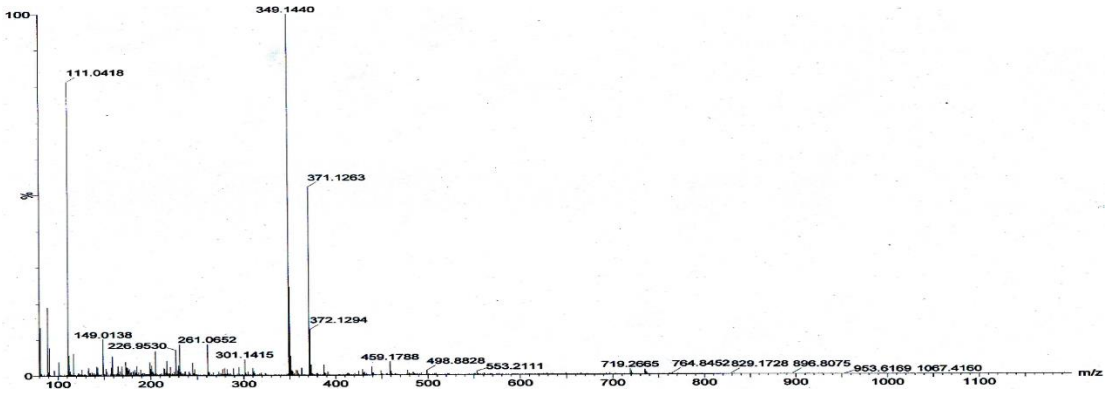
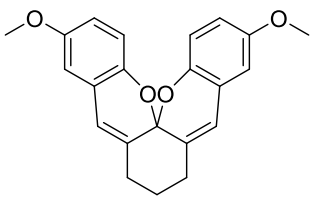
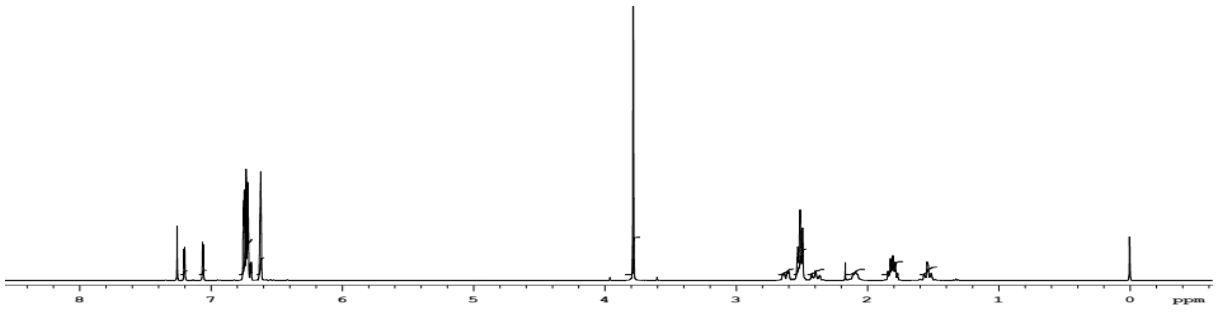


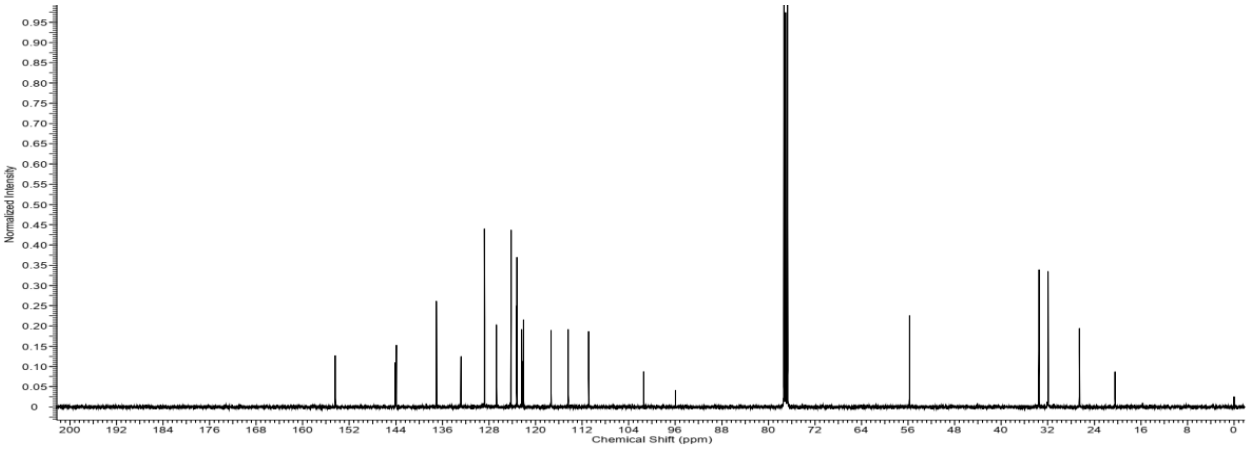
Mass spectra

CHX-5MO-SAL





^{1}H nmr spectrum



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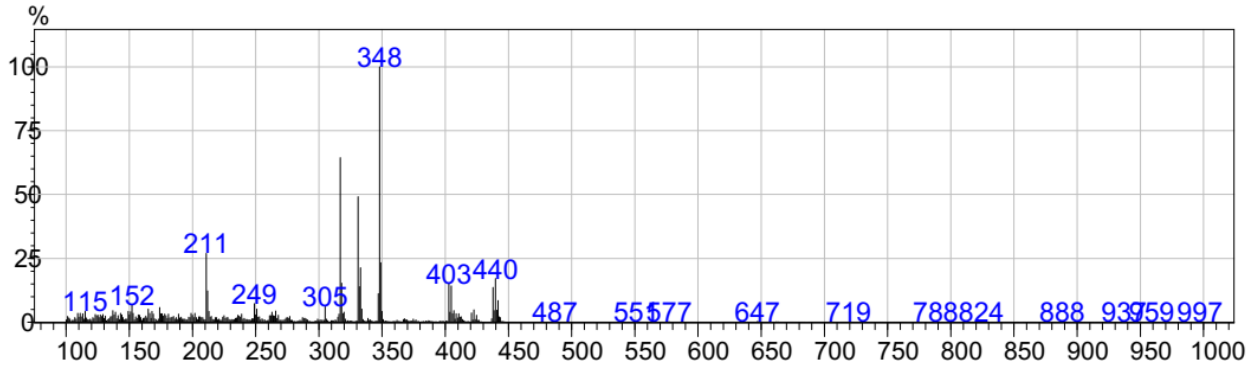
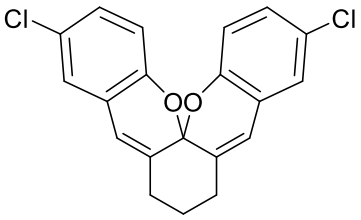
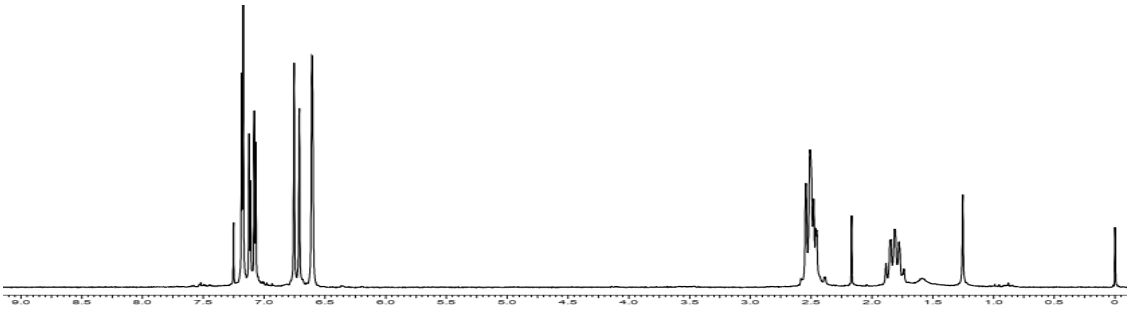


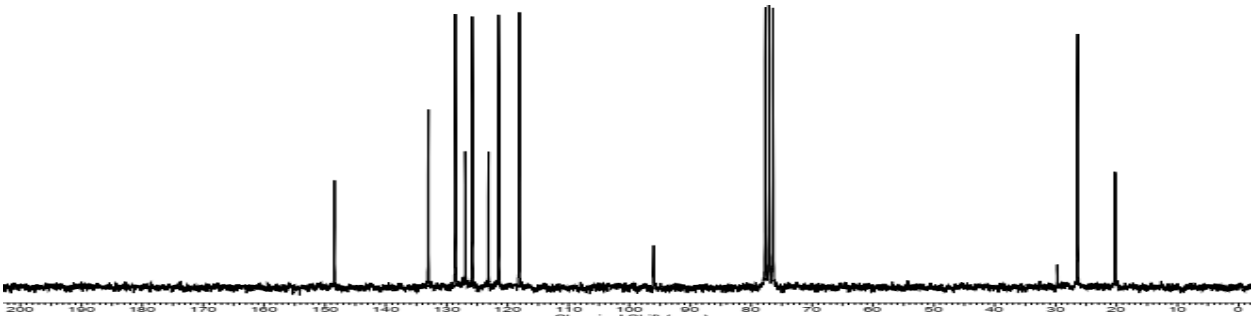
Mass spectrum

CHX-5Cl-SAL





^{1}H nmr spectrum



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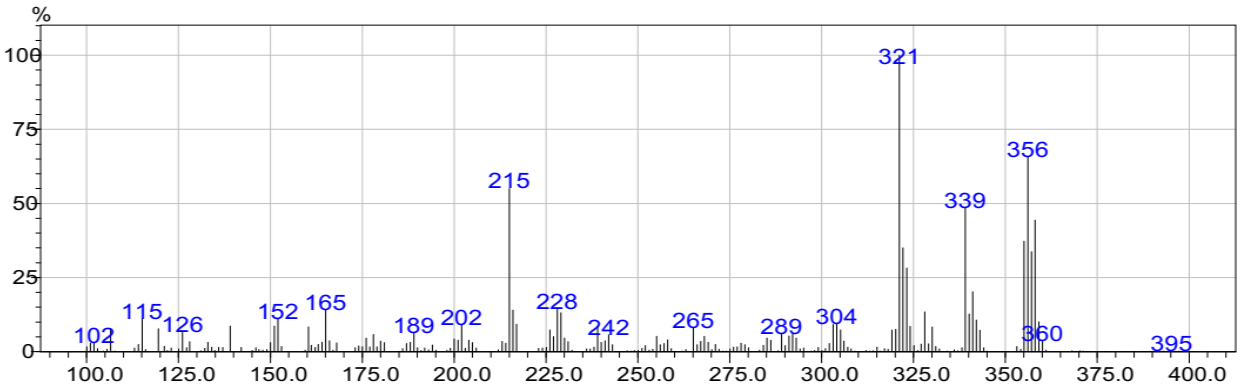
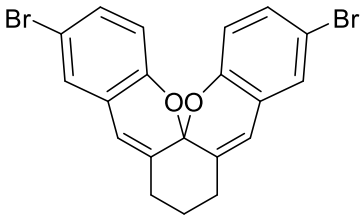
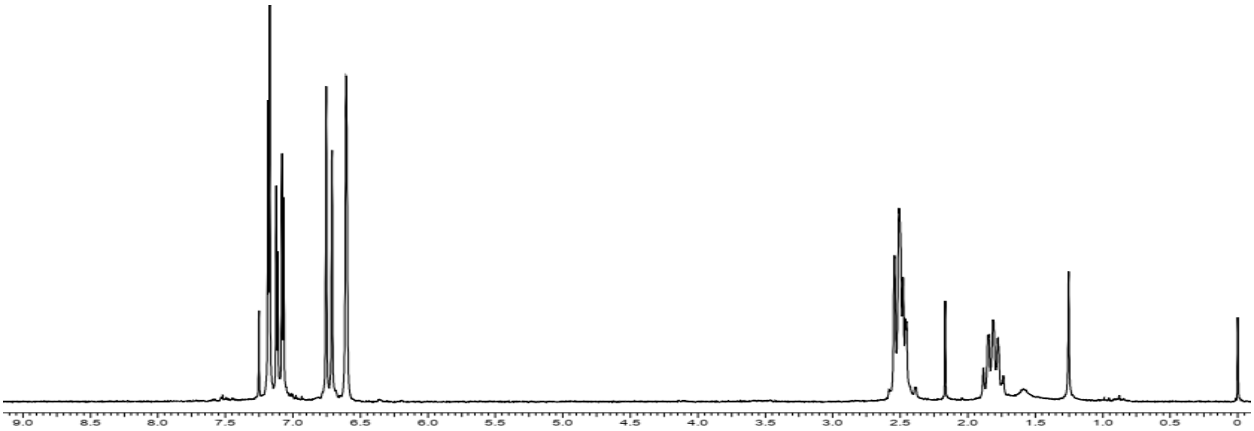


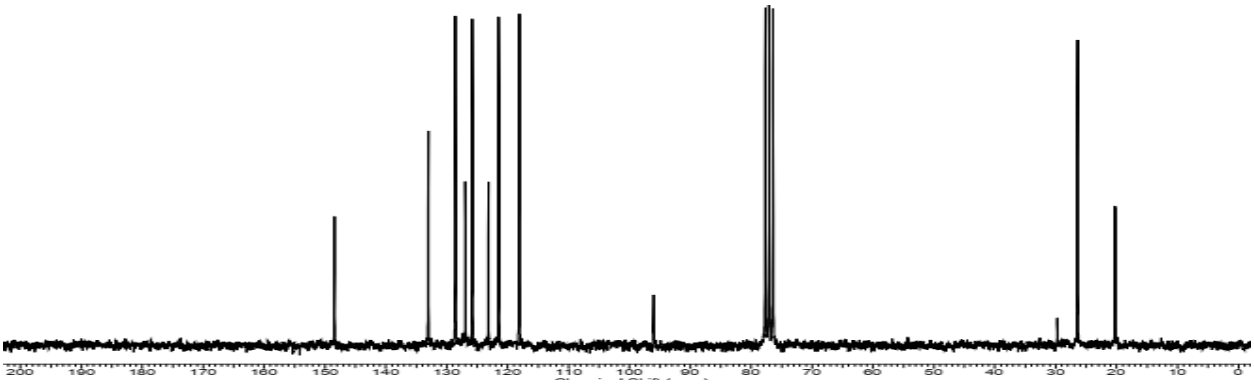
Mass spectrum

CHX-5Br-SAL

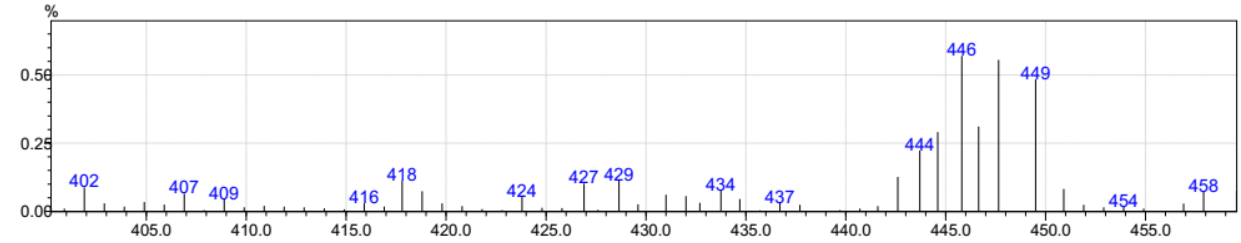




^{1}H nmr spectrum

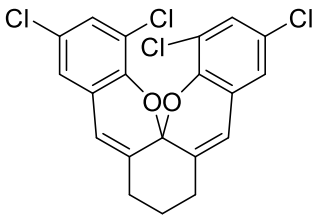


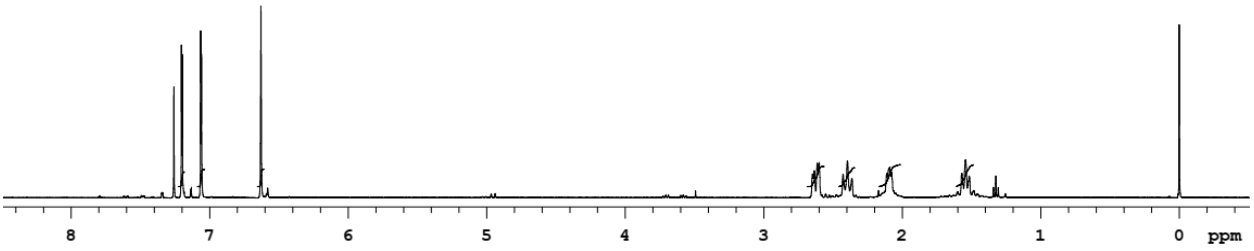
^{13}C nmr spectrum



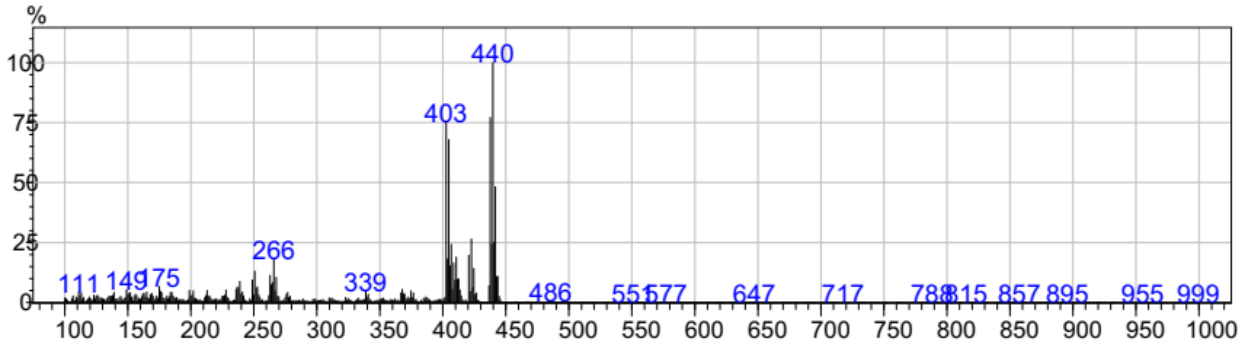
Mass spectrum

CHX-DiCl-SAL





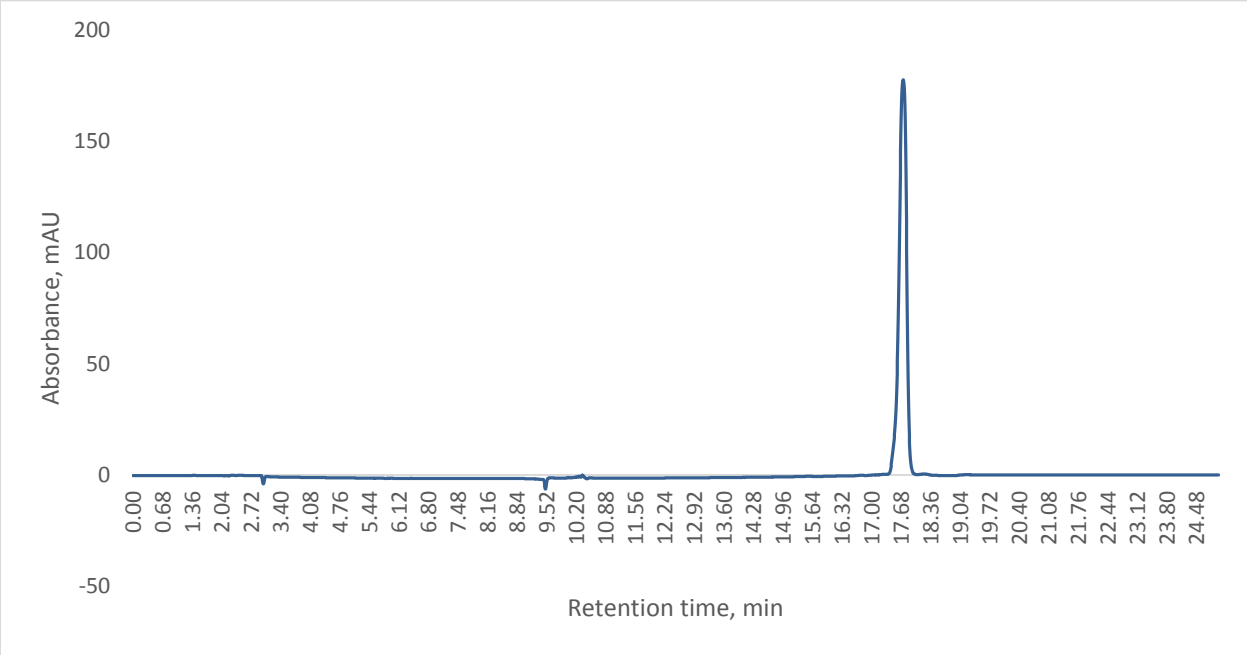
^{1}H nmr spectrum



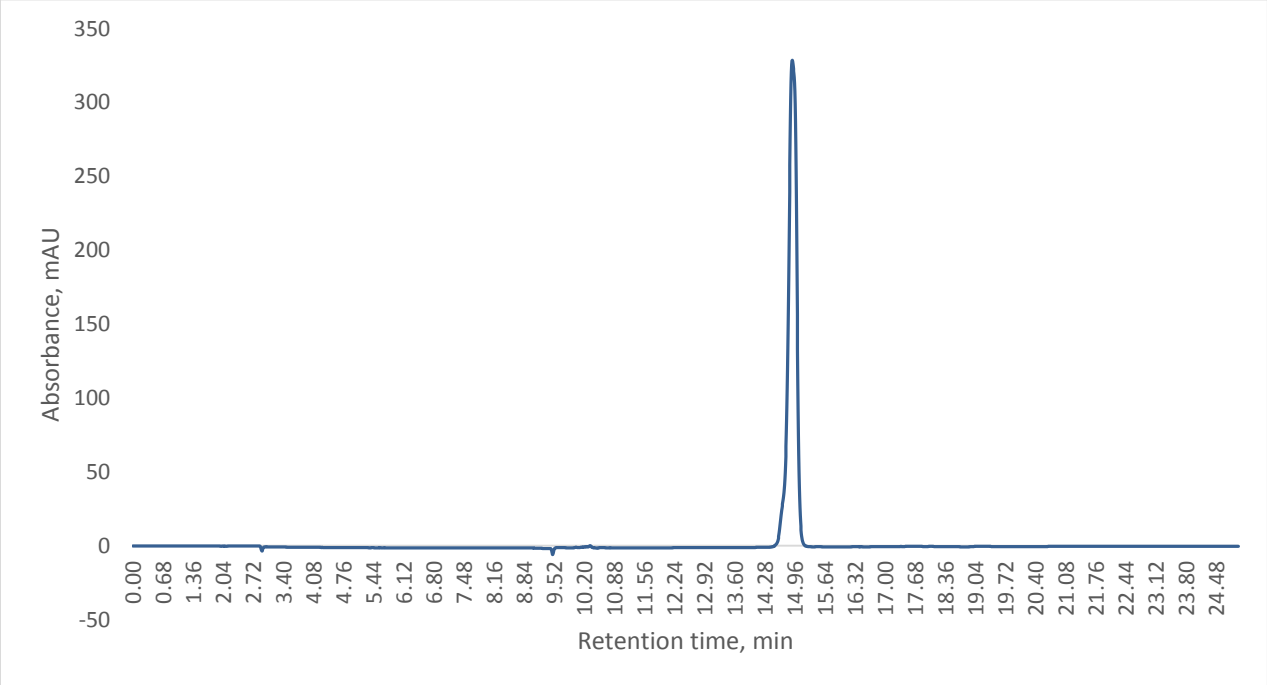
Mass Spectrum

HPLC DATA

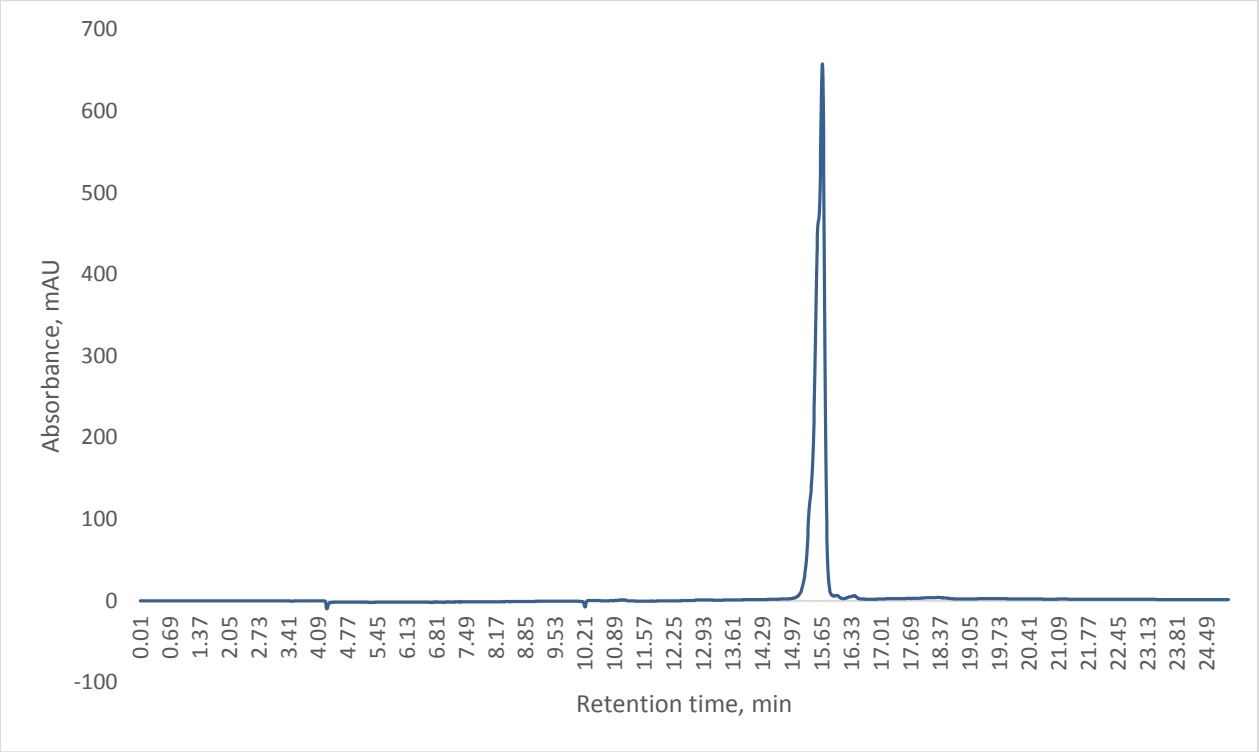
CHP-5Br-SAL, Signal at λ_{max} nm = 308



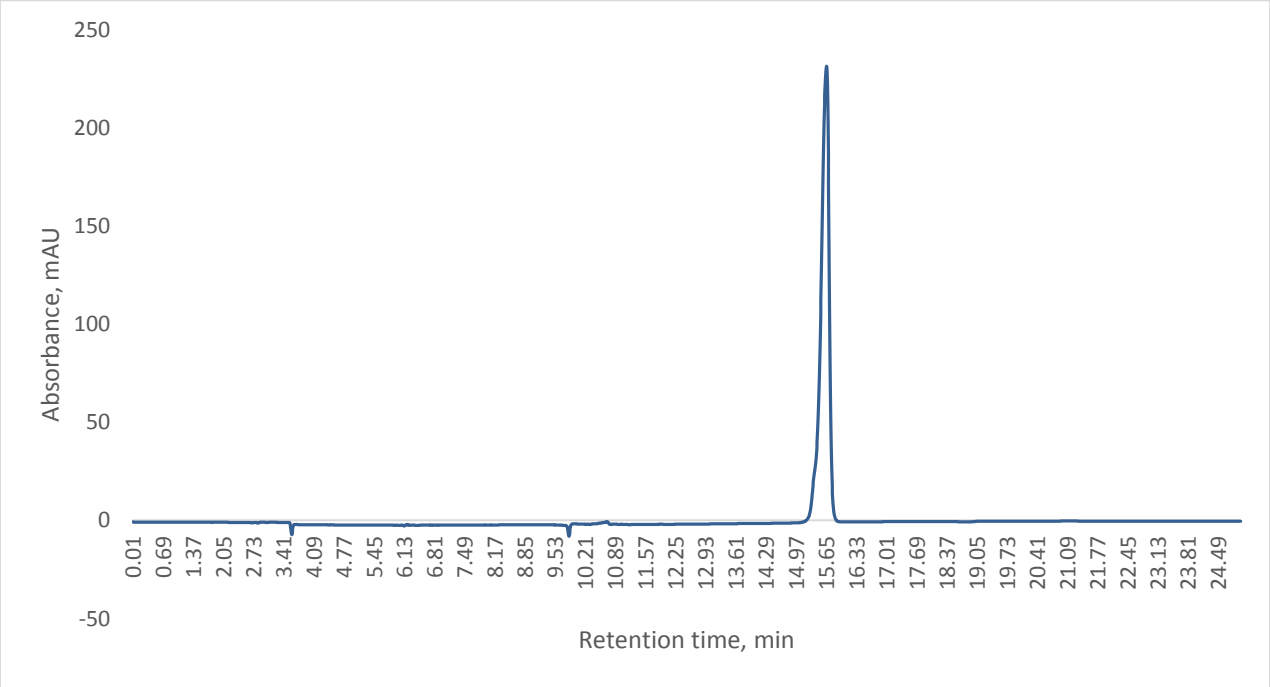
CHP-5MO-SAL, Signal at λ_{max} nm = 321



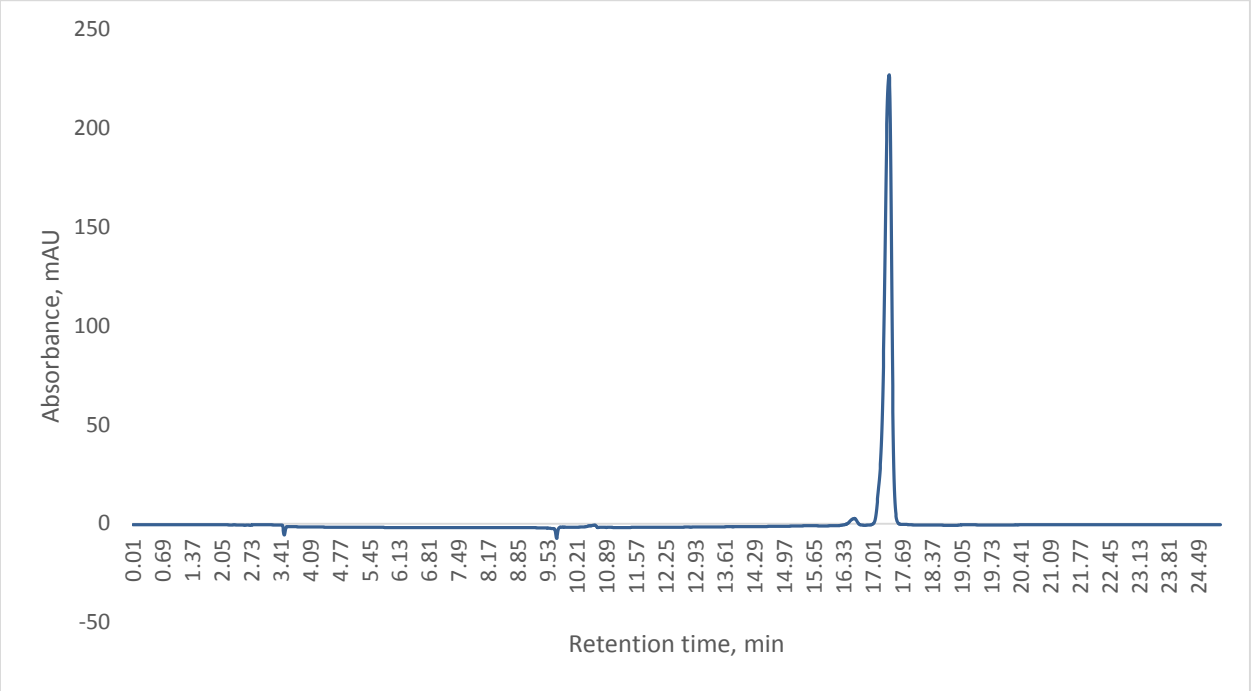
CHP-4MO-SAL, Signal at λ_{max} nm = 278



CHP-SAL, Signal at λ_{max} nm = 298



CHP-5Cl-SAL, Signal at λ_{max} nm = 298



Sample	Retention time
CHP-SAL	15.65
CHP-4MO-SAL	15.67
CHP-5MO-SAL	14.91
CHP-5Cl-SAL	17.34
CHP-5Br-SAL	17.74

SD Table II. Retention time of each spirobibenzopyran in minutes

Time (min)	Solvent A (%) (Water)	Solvent B (%) (ACN)
0	100	0
15	5	95
17	100	0

SD Table III: Mobile Phase program for Gradient Elution

XRD DATA

CHP-5Cl-SAL

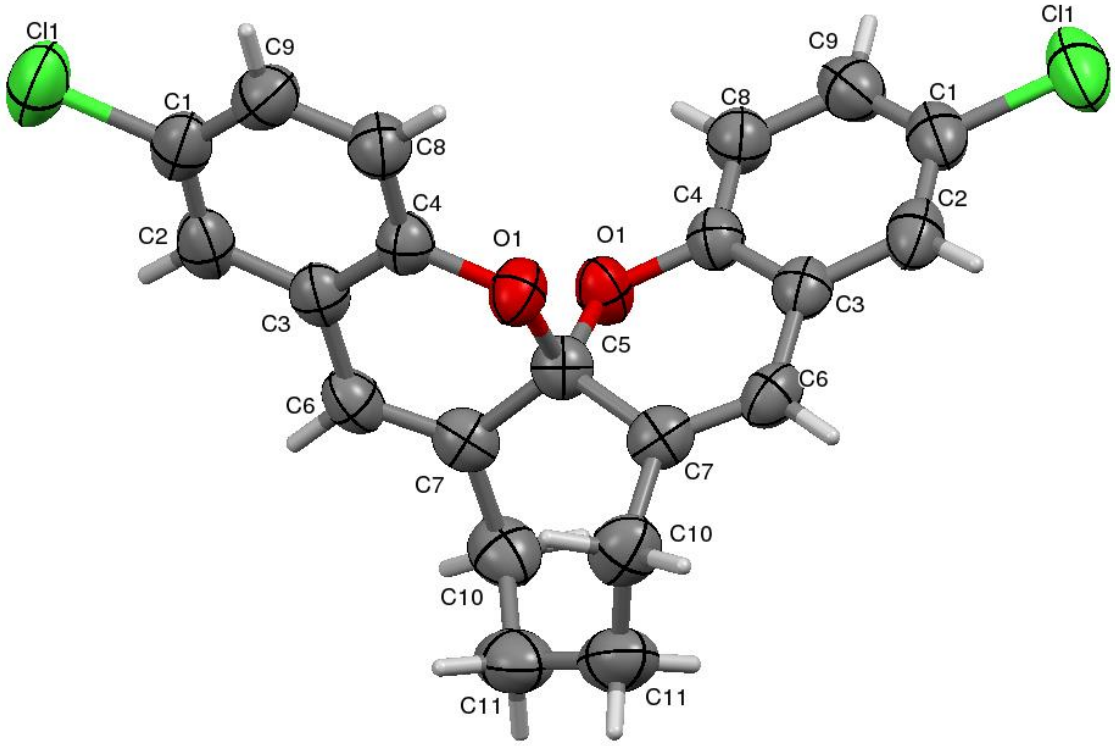


Table 1: Crystal data and structure refinement details.

CCDC Number	CCDC 1504427	
Empirical formula	$C_{21}H_{16}Cl_2O_2$	
Formula weight	185.62	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Reflns. for cell determination	1150	
θ range for above	4.61° to 63.68°	
Crystal system	Orthorhombic	
Space group	*Pbcn*	
Cell dimensions		
$a = 11.1071(6)$ Å	$b = 8.2385(4)$ Å	$c = 19.1755(9)$ Å
$\alpha = 90.00°$	$\beta = 90.00°$	$\gamma = 90.00°$
Volume	1754.67(15) Å^3	
Z	8	
Density(calculated)	1.405 Mg m^{-3}	
Absorption coefficient	3.416 mm^{-1}	
F_{000}	768	
Crystal size	0.29 × 0.26 × 0.23 mm	
θ range for data collection	4.61° to 63.68°	
Index ranges	$-12 \leq h \leq 12$	
	$-9 \leq k \leq 7$	
	$-21 \leq l \leq 22$	
Reflections collected	7530	
Independent reflections	1423 [$R_{\text{int}} = 0.0561$]	
Absorption correction	multi-scan	
Refinement method	Full matrix least-squares on F^2	
Data / restraints / parameters	1423 / 0 / 115	
Goodness-of-fit on F^2	1.121	
Final [$I > 2\sigma(I)$]	$R1 = 0.0729$, $wR2 = 0.1888$	
R indices (all data)	$R1 = 0.0820$, $wR2 = 0.2022$	
Extinction coefficient	0.0132(19)	
Largest diff. peak and hole	0.440 and −0.481 e Å^{-3}	

Table 2: Bond lengths (Å).

Atoms	Length	Atoms	Length
Cl1-C1	1.746(3)	C5-O1	1.440(3)
O1-C4	1.374(3)	C5-C7	1.505(3)
O1-C5	1.440(3)	C5-C7	1.505(3)
C1-C9	1.360(5)	C6-C7	1.327(4)
C1-C2	1.372(5)	C7-C10	1.509(4)
C2-C3	1.397(4)	C8-C9	1.388(4)
C3-C4	1.390(4)	C10-C11	1.529(5)
C3-C6	1.448(4)	C11-C11	1.510(7)
C4-C8	1.377(4)		

Table 3: Bond angles (°).

Atoms	Angle	Atoms	Angle
C4-O1-C5	118.88(16)	O1-C5-C7	103.38(13)
C9-C1-C2	121.8(3)	O1-C5-C7	103.38(13)
C9-C1-Cl1	119.2(3)	O1-C5-C7	113.19(13)
C2-C1-Cl1	119.0(3)	C7-C5-C7	116.2(3)
C1-C2-C3	119.7(3)	C7-C6-C3	122.0(3)
C4-C3-C2	118.0(3)	C6-C7-C5	119.2(2)
C4-C3-C6	117.5(2)	C6-C7-C10	123.8(3)
C2-C3-C6	124.4(3)	C5-C7-C10	116.9(2)
O1-C4-C8	117.1(2)	C4-C8-C9	119.2(3)
O1-C4-C3	121.2(2)	C1-C9-C8	119.6(3)
C8-C4-C3	121.6(2)	C7-C10-C11	113.1(3)
O1-C5-O1	107.5(3)	C11-C11-C10	115.2(2)
O1-C5-C7	113.19(13)		

CHP-5MO-SAL

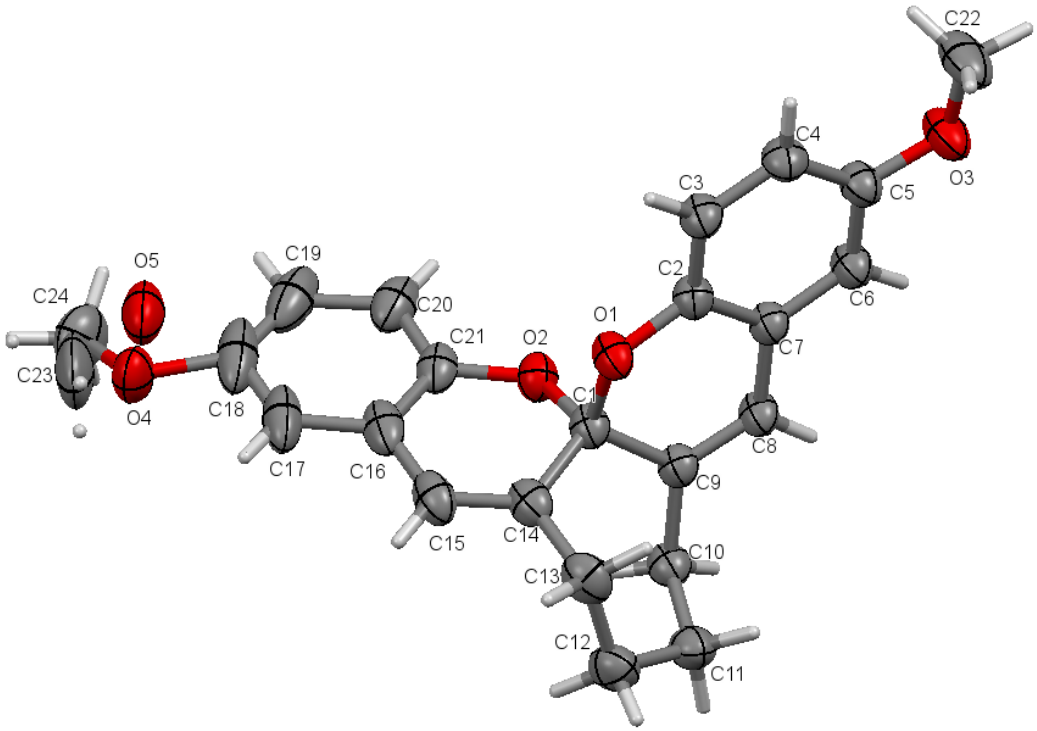

C22
O3
C4
C5
C3
C2
C6
C7
O1
C1
C8
C9
C10
C11
C12
C13
C14
C15
C16
C17
C18
C19
C20
C21
O2
O5
C24
C23
O4

Table 1: Crystal data and structure refinement details.

CCDC Number	CCDC 1504532	
Empirical formula	$C_{23}H_{22}O_4$	
Formula weight	362.41	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Reflns. for cell determination	1926	
θ range for above	5.76° to 64.30°	
Crystal system	Monoclinic	
Space group	Cc	
Cell dimensions		
$a = 8.029(2)$ Å	$b = 21.258(5)$ Å	$c = 11.349(3)$ Å
$\alpha = 90.00°$	$\beta = 101.660(19)°$	$\gamma = 90.00°$
Volume	1897.0(9) Å^3	
Z	4	
Density(calculated)	1.269 Mg m^{-3}	
Absorption coefficient	0.695 mm^{-1}	
F_{000}	768	
Crystal size	0.29 × 0.28 × 0.26 mm	
θ range for data collection	5.76° to 64.30°	
Index ranges	$-9 \leq h \leq 7$	
	$-22 \leq k \leq 24$	
	$-13 \leq l \leq 13$	
Reflections collected	6231	
Independent reflections	2376 [$R_{\text{int}} = 0.0453$]	
Absorption correction	multi-scan	
Refinement method	Full matrix least-squares on F^2	
Data / restraints / parameters	2376 / 8 / 266	
Goodness-of-fit on F^2	1.049	
Final [$I > 2\sigma(I)$]	$R1 = 0.0588$, $wR2 = 0.1552$	
R indices (all data)	$R1 = 0.0712$, $wR2 = 0.1659$	
Largest diff. peak and hole	0.204 and -0.208 e Å^{-3}	

Table 2: Bond lengths (Å).

Atoms	Length	Atoms	Length
O2-C21	1.380(4)	C21-C16	1.408(7)
O2-C1	1.436(4)	C14-C15	1.319(6)
O1-C2	1.376(4)	C14-C13	1.507(6)
O1-C1	1.433(4)	C3-C4	1.390(5)
O3-C5	1.371(4)	C11-C12	1.518(6)
O3-C22	1.383(5)	C11-C10	1.525(6)
C8-C9	1.314(4)	C20-C19	1.413(8)
C8-C7	1.446(5)	C15-C16	1.439(7)
C7-C6	1.382(5)	C16-C17	1.396(6)
C7-C2	1.395(4)	C12-C13	1.541(6)
C5-C6	1.380(5)	C17-C18	1.368(11)
C5-C4	1.386(5)	C18-C19	1.393(12)
C2-C3	1.374(5)	C18-O5	1.459(13)
C9-C1	1.504(5)	C18-O4	1.482(12)
C9-C10	1.512(5)	O4-C23	1.42(2)
C1-C14	1.518(5)	O5-C24	1.29(4)
C21-C20	1.381(7)		

Table 3: Bond angles (°).

Atoms	Angle	Atoms	Angle
C21-O2-C1	120.0(3)	C20-C21-C16	123.3(4)
C2-O1-C1	119.4(2)	C15-C14-C13	123.7(4)
C5-O3-C22	118.3(3)	C15-C14-C1	119.7(4)
C9-C8-C7	122.4(3)	C13-C14-C1	116.6(3)
C6-C7-C2	119.1(3)	C2-C3-C4	119.7(3)
C6-C7-C8	123.6(3)	C5-C4-C3	120.4(3)
C2-C7-C8	117.1(3)	C12-C11-C10	114.5(3)
O3-C5-C6	115.7(3)	C21-C20-C19	116.9(6)
O3-C5-C4	125.1(3)	C9-C10-C11	112.4(3)
C6-C5-C4	119.2(3)	C14-C15-C16	121.6(4)
C5-C6-C7	121.0(3)	C17-C16-C21	117.6(5)
C3-C2-O1	118.1(2)	C17-C16-C15	123.2(5)
C3-C2-C7	120.4(3)	C21-C16-C15	119.2(3)
O1-C2-C7	121.2(3)	C11-C12-C13	114.1(3)
C8-C9-C1	119.6(3)	C14-C13-C12	113.2(3)
C8-C9-C10	123.1(3)	C18-C17-C16	120.7(7)
C1-C9-C10	117.3(3)	C17-C18-C19	120.9(5)
O1-C1-O2	108.0(3)	C17-C18-O5	142.5(10)
O1-C1-C9	113.1(3)	C19-C18-O5	96.2(10)
O2-C1-C9	103.7(2)	C17-C18-O4	101.6(8)
O1-C1-C14	104.1(2)	C19-C18-O4	137.5(8)
O2-C1-C14	114.1(3)	O5-C18-O4	42.0(5)
C9-C1-C14	114.1(3)	C18-C19-C20	120.6(7)
O2-C21-C20	116.4(4)	C23-O4-C18	105.7(13)
O2-C21-C16	120.1(4)	C24-O5-C18	109(2)

4. *In-vitro* anti-cancer activity protocol

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) are reported as mean graph of the percent growth of the treated cells when compared with untreated control cells [1, 2]. The One-dose data (given below) is reported as a mean graph of the percent growth of treated cells. The number reported for the One-dose assay is growth relative to the no-drug control, and relative to the time zero number of cells. This allows detection of both growth inhibition (values between 0 and 100) and lethality

(values less than 0). For example, a value of 100 means no growth inhibition. A value of 40 would mean 60% growth inhibition. A value of 0 means no net growth over the course of the experiment. A value of -40 would mean 40% lethality. A value of -100 means all cells are dead.

SD Table IV. The *in vitro* anticancer analysis results for the CHP series

		Growth Percentage				
CANCER CELL	**SUB PANEL**	**CHP-SAL**	**CHP-4MO-SAL**	**CHP-5MO-SAL**	**CHP-5Cl-SAL**	**CHP-DiCl-SAL**
Leukemia	K-562	**58.35**	88.68	94.10	103.71	85.98
Non-Small Cell Lung Cancer	NCI-H460	**66.95**	94.39	113.07	105.60	105.82
	NCI-H522	82.42	**66.21**	96.24	76.64	95.79
Colon Cancer	HCT-116	**53.13**	73.44	100.36	97.30	78.22
	HCT-15	**45.96**	92.62	104.58	104.14	92.22
CNS Cancer	U251	**68.50**	89.65	103.20	93.56	96.84
Prostate Cancer	PC-3	**56.97**	69.59	102.01	84.41	92.15
Breast Cancer	T-47D	91.92	**67.62**	109.60	102.04	83.58

The results of the single dose study for the 5 selected spirobibenzopyrans from the **CHX** series have been tabulated below in **SD table V**.

CANCER CELL	***SUB PANEL***	***Growth Percentage***				
		CHX-SAL	***CHX-4MO-SAL***	***CHX-5MO-SAL***	***CHX-5Cl-SAL***	***CHX-DiCl-SAL***
Leukemia	CCRF-CEM	**18.28**	**5.97**	88.31	96.34	**45.36**
	HL-60(TB)	**8.47**	**7.56**	99.59	94.36	87.67
	K-562	**15.32**	**23.50**	94.85	87.10	75.88
	MOLT-4	**17.51**	**-3.56**	89.70	84.23	80.56
	RPMI-8226	**26.01**	**-20.58**	93.55	107.15	79.43
	SR	**6.44**	**4.94**	97.09	100.20	**63.19**
Non-Small Cell Lung Cancer	A549/ATCC	**32.65**	75.02	96.33	88.36	100.56
	EKVX	**57.76**	**39.65**	103.01	104.23	89.44
	HOP-62	**41.57**	**41.40**	101.21	105.83	104.91
	HOP-92	**61.42**	**26.64**	105.10	90.98	**55.63**
	NCI-H226	**56.44**	**64.09**	97.30	99.10	97.10
	NCI-H23	**42.30**	**48.27**	97.16	98.66	105.59
	NCI-H322M	**50.79**	80.84	106.32	108.23	87.65
	NCI-H460	**13.47**	**14.25**	105.25	103.73	108.43
	NCI-H522	**3.90**	**20.45**	101.58	76.84	102.48
Colon Cancer	COLO 205	**25.44**	**-9.95**	111.27	104.18	115.35
	HCC-2998	**58.40**	**57.94**	102.97	103.67	100.49

	HCT-116	**23.99**	**19.97**	94.74	93.46	96.55
	HCT-15	**20.14**	**12.83**	104.56	100.79	76.56
	HT29	**5.93**	**8.16**	97.57	88.84	112.44
	KM12	**19.78**	**-5.69**	91.22	102.25	96.39
	SW-620	**18.11**	**16.61**	94.58	98.47	99.99
CNS Cancer	SF-268	**31.56**	**38.52**	97.90	100.10	77.33
	SF-295	**11.30**	**78.63**	99.15	100.22	98.49
	SF-539	**7.81**	84.49	114.62	100.50	90.77
	SNB-19	**27.44**	**54.71**	105.09	102.91	88.84
	SNB-75	**22.99**	74.56	107.33	82.64	98.36
	U251	**26.46**	**34.95**	102.25	94.84	86.99
Melanoma	LOX IMVI	**22.99**	**-32.06**	97.19	97.45	83.75
	MALME-3M	**56.77**	**70.32**	111.16	109.43	103.68
	M14	**19.15**	**31.51**	96.01	102.54	98.79
	MDA-MB-435	**-41.60**	**-10.37**	103.06	109.31	105.19
	SK-MEL-2	**36.05**	**15.69**	117.14	89.48	108.02
	SK-MEL-28	**54.24**	**62.98**	97.48	114.26	95.27
	SK-MEL-5	**19.96**	**40.27**	98.77	99.67	97.86
	UACC-257	**40.07**	**52.52**	89.70	97.04	99.51
	UACC-62	**14.54**	**14.82**	103.55	99.18	95.13
Ovarian Cancer	IGROV1	**44.53**	**41.44**	109.88	104.31	88.19
	OVCAR-3	**3.51**	**5.62**	100.27	109.66	82.04
	OVCAR-4	**52.59**	**55.15**	105.13	112.87	90.73
	OVCAR-5	71.12	**47.18**	102.00	105.05	109.16
	OVCAR-8	**38.51**	**47.71**	99.51	96.66	89.11
	NCI/ADR-RES	**11.57**	**21.65**	102.73	105.49	95.20
	SK-OV-3	**30.85**	**60.13**	105.27	103.45	107.84
Renal Cancer	786-0	**26.44**	**38.70**	97.32	97.54	102.42
	A498	**5.61**	69.76	102.61	99.78	89.89
	ACHN	**47.34**	**25.30**	95.73	110.56	96.41
	CAKI-1	**27.21**	-	94.96	-	98.36
	RXF 393	**9.77**	**15.96**	101.32	96.52	106.92
	SN12C	**34.38**	**44.06**	110.33	100.10	96.28
	TK-10	**55.40**	**46.97**	112.95	91.51	111.64
	UO-31	**43.31**	**36.31**	95.56	86.54	84.11
Prostate Cancer	PC-3	**34.65**	**23.55**	93.86	86.42	69.95
	DU-145	**28.07**	**33.91**	109.02	108.75	105.70
Breast Cancer	MCF7	**13.51**	**8.63**	94.21	94.43	84.02
	MDA-MB-231/ATCC	**43.53**	**32.03**	121.22	101.04	98.52
	HS 578T	**33.37**	**45.03**	104.52	98.47	94.21
	BT-549	**26.39**	**35.03**	115.48	108.48	98.59

	T-47D	**31.86**	**44.67**	95.98	101.93	80.58
	MDA-MB-468	**25.53**	**56.33**	81.77	106.79	90.19

SD Table V. The *in vitro* anticancer analysis results for the CHX series.

The GI50 value (growth inhibitory activity) corresponds to the concentration of the compound causing 50% decrease in net cell growth, the TGI value (cytostatic activity) is the concentration of the compound resulting in total growth inhibition and LC50 value (cytotoxic activity) is the concentration of the compound causing net 50% loss of initial cells at the end of the incubation period of 48 h.

SD Table VI. The *in vitro* 5 dose analysis results for CHX-SAL and CHX-4MO-SAL.

		CHX-SAL	**CHX-4MO-SAL**	**CHX-SAL**	**CHX-4MO-SAL**	**CHX-SAL**	**CHX-4MO-SAL**
PANEL	CELL	**GI_{50}**		**TGI**		**LC_{50}**	
Leukemia	CCRF-CEM	*3.47*	*5.88*	*25.90*	>100	>100	>100
	HL-60(TB)	*3.24*	>100	>100	>100	>100	>100
	K-562	*3.54*	>100	>100	>100	>100	>100
	MOLT-4	*3.65*	*5.81*	>100	>100	>100	>100
	RPMI-8226	*3.38*	*6.12*	*15.00*	>100	>100	>100
	SR	*2.82*	*4.89*	>100	>100	>100	>100
Non-Small Cell Lung Cancer	A549/ATCC	*5.87*	>100	>100	>100	>100	>100
	EKVX	*5.49*	>100	>100	>100	>100	>100
	HOP-62	*3.80*	>100	>100	>100	>100	>100
	NCI-H226	>100	**4.46**	>100	>100	>100	>100
	NCI-H23	*6.20*	>100	>100	>100	>100	>100
	NCI-H322M	*3.92*	>100	>100	>100	>100	>100
	NCI-H460	*3.47*	>100	*16.40*	>100	>100	>100
	NCI-H522	*2.30*	>100	*6.20*	>100	>100	>100
Colon Cancer	COLO 205	*2.24*	>100	*5.04*	>100	>100	>100
	HCC-2998	**1.03**	>100	*60.70*	>100	>100	>100
	HCT-116	*4.34*	-	>100	>100	>100	>100
	HCT-15	*3.68*	>100	>100	>100	>100	>100
	HT29	*3.52*	>100	*17.90*	>100	>100	>100
	KM12	*3.61*	*18.70*	*56.70*	>100	>100	>100
	SW-620	*3.35*	>100	*53.60*	>100	>100	>100
CNS Cancer	SF-268	*4.74*	>100	>100	>100	>100	>100
	SF-295	*3.99*	>100	>100	>100	>100	>100
	SF-539	*1.92*	>100	*5.01*	>100	>100	>100
	SNB-19	*4.01*	>100	>100	>100	>100	>100
	SNB-75	*1.64*	-	*5.84*	>100	>100	>100
	U251	*4.54*	>100	>100	>100	>100	>100
Melanoma	LOX IMVI	*3.88*	>100	*28.00*	>100	>100	>100

	MALME-3M	*7.17*	>100	>100	>100	>100	>100
	M14	*3.37*	>100	>100	>100	>100	>100
	MDA-MB-435	*1.64*	*5.52*	*4.67*	>100	>100	>100
	SK-MEL-2	*4.31*	>100	*25.60*	>100	>100	>100
	SK-MEL-28	*5.22*	>100	>100	>100	>100	>100
	SK-MEL-5	*3.37*	*13.60*	*24.20*	>100	>100	>100
	UACC-257	*5.49*	>100	>100	>100	>100	>100
	UACC-62	*2.91*	*4.50*	*82.50*	>100	>100	>100
Ovarian Cancer	IGROV1	*5.36*	>100	>100	>100	>100	>100
	OVCAR-3	*3.06*	-	>100	>100	>100	>100
	OVCAR-4	*6.12*	>100	>100	>100	>100	>100
	OVCAR-5	*3.46*	>100	>100	>100	>100	>100
	OVCAR-8	*4.04*	>100	>100	>100	>100	>100
	NCI/ADR-RES	*3.18*	>100	*55.70*	>100	>100	>100
	SK-OV-3	*3.52*	>100	>100	>100	>100	>100
Renal Cancer	786-0	*6.41*	>100	>100	>100	>100	>100
	A498	*2.76*	>100	*13.10*	>100	>100	>100
	ACHN	*5.06*	>100	>100	>100	>100	>100
	CAKI-1	*3.71*	>100	>100	>100	>100	>100
	RXF 393	*2.85*	>100	*8.77*	>100	>100	>100
	SN12C	*4.42*	>100	>100	>100	>100	>100
	TK-10	*9.87*	>100	>100	>100	>100	>100
	UO-31	*4.86*	>100	>100	>100	>100	>100
Prostate Cancer	PC-3	*4.00*	>100	>100	>100	>100	>100
	DU-145	*3.73*	>100	*69.10*	>100	>100	>100
Breast Cancer	MCF7	*3.03*	>100	*60.60*	>100	>100	>100
	MDA-MB-231/ATCC	*4.23*	4.80	*45.50*	>100	>100	>100
	HS 578T	*3.03*	>100	-	>100	>100	>100
	BT-549	*3.73*	>100	*73.70*	>100	>100	>100
	T-47D	*2.46*	4.70	>100	>100	>100	>100
	MDA-MB-468	*5.42*	>100	*69.10*	>100	>100	>100

***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.(One dose study)**

CHP-SAL

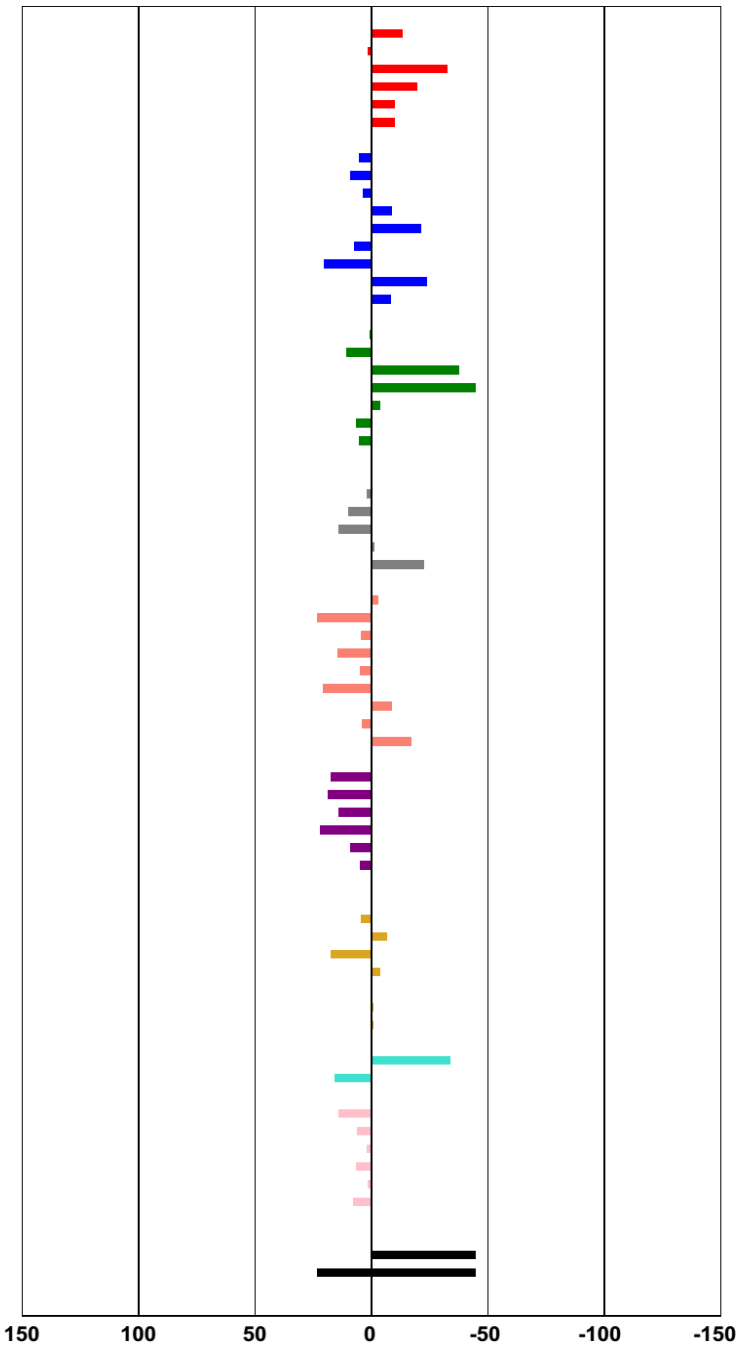
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-791127 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** May 31, 2016

Experiment ID: 1605OS20 | **Report Date:** Jun 15, 2016

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	77.69
HL-60(TB)	91.77
K-562	58.35
MOLT-4	71.20
RPMI-8226	80.77
SR	80.87
Non-Small Cell Lung Cancer	
A549/ATCC	95.86
EKVX	99.35
HOP-62	93.93
HOP-92	82.08
NCI-H226	69.69
NCI-H23	97.80
NCI-H322M	110.73
NCI-H460	66.95
NCI-H522	82.42
Colon Cancer	
COLO 205	91.09
HCC-2998	101.02
HCT-116	53.13
HCT-15	45.96
HT29	87.08
KM12	97.09
SW-620	95.58
CNS Cancer	
SF-268	90.50
SF-295	92.50
SF-539	100.48
SNB-19	104.40
SNB-75	89.73
U251	68.50
Melanoma	
LOX IMVI	88.11
MALME-3M	113.66
M14	94.77
MDA-MB-435	104.79
SK-MEL-2	95.09
SK-MEL-28	111.23
SK-MEL-5	82.22
UACC-257	94.34
UACC-62	73.71
Ovarian Cancer	
IGROV1	107.87
OVCAR-3	109.16
OVCAR-4	104.67
OVCAR-5	112.25
OVCAR-8	99.65
NCI/ADR-RES	95.23
SK-OV-3	90.58
Renal Cancer	
786-0	94.66
A498	84.40
ACHN	107.73
RXF 393	87.25
SN12C	90.71
TK-10	90.11
UO-31	90.20
Prostate Cancer	
PC-3	56.97
DU-145	106.03
Breast Cancer	
MCF7	104.66
MDA-MB-231/ATCC	96.59
HS 578T	92.18
BT-549	97.08
T-47D	91.92
MDA-MB-468	98.11
Mean	90.55
Delta	44.59
Range	67.70



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHP-4MO-SAL

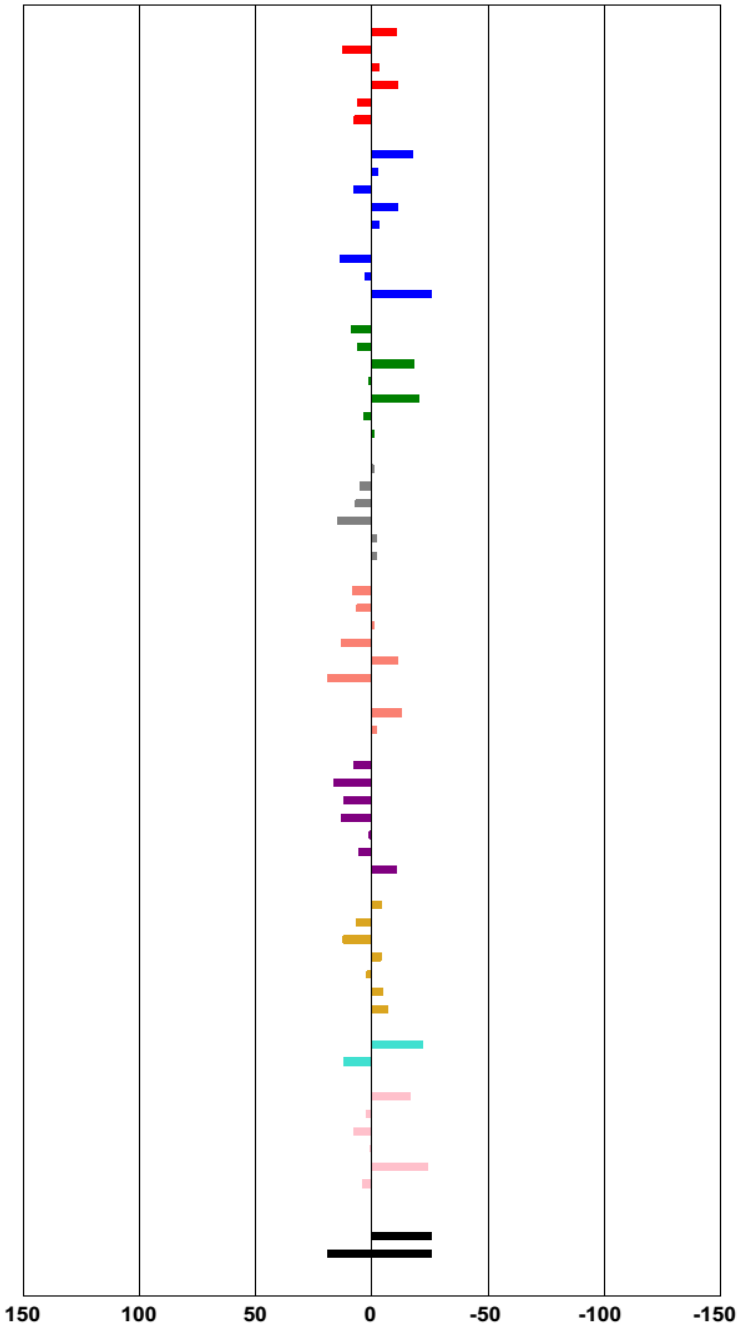
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-791125 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** May 31, 2016

Experiment ID: 1605OS20 | **Report Date:** Jun 15, 2016

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	80.87
HL-60(TB)	104.23
K-562	88.68
MOLT-4	80.57
RPMI-8226	97.78
SR	99.04
Non-Small Cell Lung Cancer	
A549/ATCC	73.81
EKVX	88.84
HOP-62	99.30
HOP-92	80.66
NCI-H226	88.39
NCI-H23	91.59
NCI-H322M	105.21
NCI-H460	94.39
NCI-H522	66.21
Colon Cancer	
COLO 205	100.51
HCC-2998	97.70
HCT-116	73.44
HCT-15	92.62
HT29	71.46
KM12	94.79
SW-620	90.68
CNS Cancer	
SF-268	90.74
SF-295	96.80
SF-539	98.43
SNB-19	106.20
SNB-75	89.83
U251	89.65
Melanoma	
LOX IMVI	99.83
MALME-3M	97.93
M14	90.43
MDA-MB-435	104.52
SK-MEL-2	80.22
SK-MEL-28	110.65
SK-MEL-5	91.48
UACC-257	78.61
UACC-62	89.36
Ovarian Cancer	
IGROV1	99.34
OVCAR-3	107.61
OVCAR-4	103.65
OVCAR-5	104.40
OVCAR-8	92.54
NCI/ADR-RES	96.92
SK-OV-3	80.83
Renal Cancer	
786-0	87.18
A498	98.24
ACHN	103.81
RXF 393	87.53
SN12C	93.64
TK-10	86.78
UO-31	84.69
Prostate Cancer	
PC-3	69.59
DU-145	103.52
Breast Cancer	
MCF7	75.18
MDA-MB-231/ATCC	93.80
HS 578T	99.44
BT-549	91.98
T-47D	67.62
MDA-MB-468	95.58
Mean	91.51
Delta	25.30
Range	44.44



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHP-5Cl-SAL

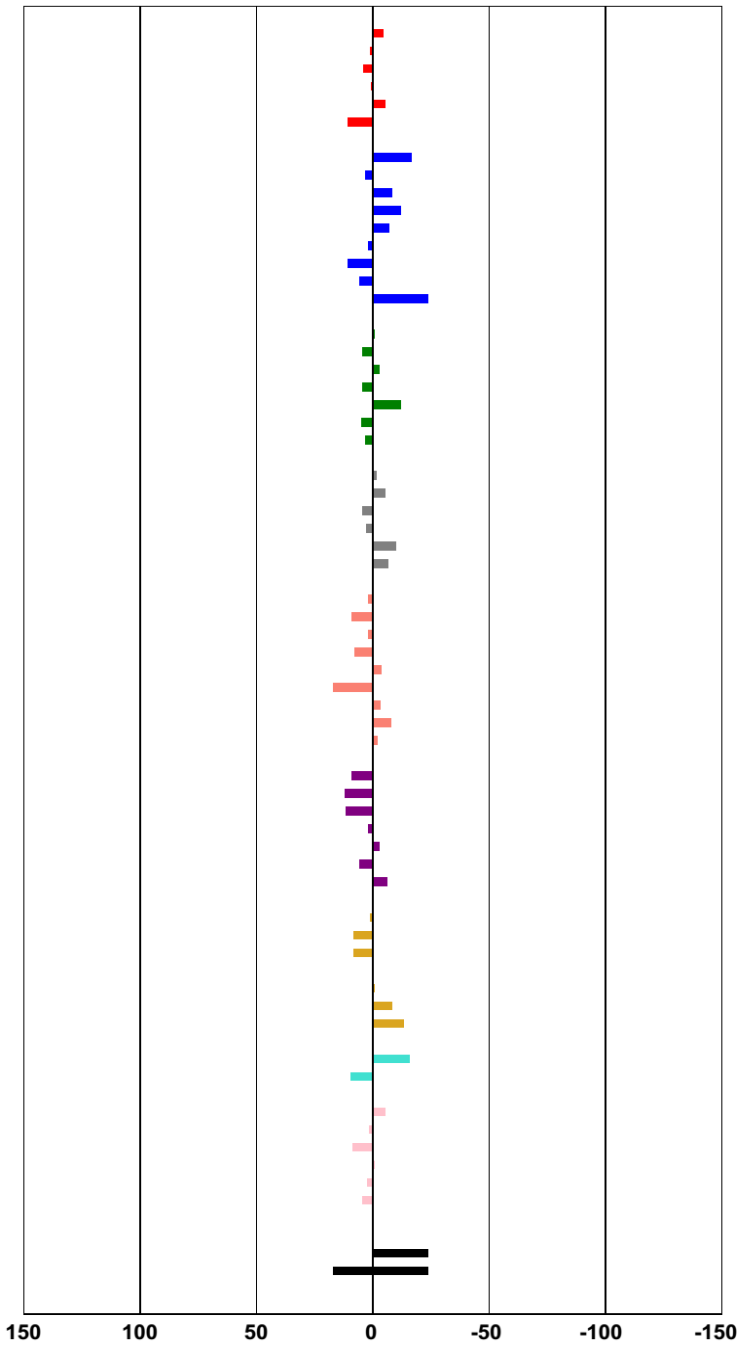
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-791126 / 1 **Conc:** 1.00E-5 Molar **Test Date:** May 31, 2016

Experiment ID: 1605OS20 **Report Date:** Jun 15, 2016

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	95.80
HL-60(TB)	100.68
K-562	103.71
MOLT-4	100.47
RPMI-8226	94.70
SR	110.41
Non-Small Cell Lung Cancer	
A549/ATCC	83.48
EKVX	103.09
HOP-62	91.93
HOP-92	88.02
NCI-H226	93.09
NCI-H23	101.53
NCI-H322M	110.57
NCI-H460	105.60
NCI-H522	76.64
Colon Cancer	
COLO 205	99.52
HCC-2998	104.19
HCT-116	97.30
HCT-15	104.14
HT29	88.33
KM12	104.67
SW-620	103.00
CNS Cancer	
SF-268	98.45
SF-295	94.95
SF-539	104.17
SNB-19	102.50
SNB-75	90.16
U251	93.56
Melanoma	
LOX IMVI	101.74
MALME-3M	109.01
M14	101.90
MDA-MB-435	107.71
SK-MEL-2	96.53
SK-MEL-28	116.92
SK-MEL-5	96.96
UACC-257	92.42
UACC-62	98.40
Ovarian Cancer	
IGROV1	108.85
OVCAR-3	111.83
OVCAR-4	111.26
OVCAR-5	101.54
OVCAR-8	97.54
NCI/ADR-RES	105.60
SK-OV-3	93.90
Renal Cancer	
786-0	100.96
A498	107.84
ACHN	108.19
RXF 393	99.86
SN12C	99.40
TK-10	92.02
UO-31	87.08
Prostate Cancer	
PC-3	84.41
DU-145	109.30
Breast Cancer	
MCF7	95.04
MDA-MB-231/ATCC	101.31
HS 578T	108.21
BT-549	99.47
T-47D	102.04
MDA-MB-468	104.19
Mean	99.93
Delta	23.29
Range	40.28



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHP-5MO-SAL

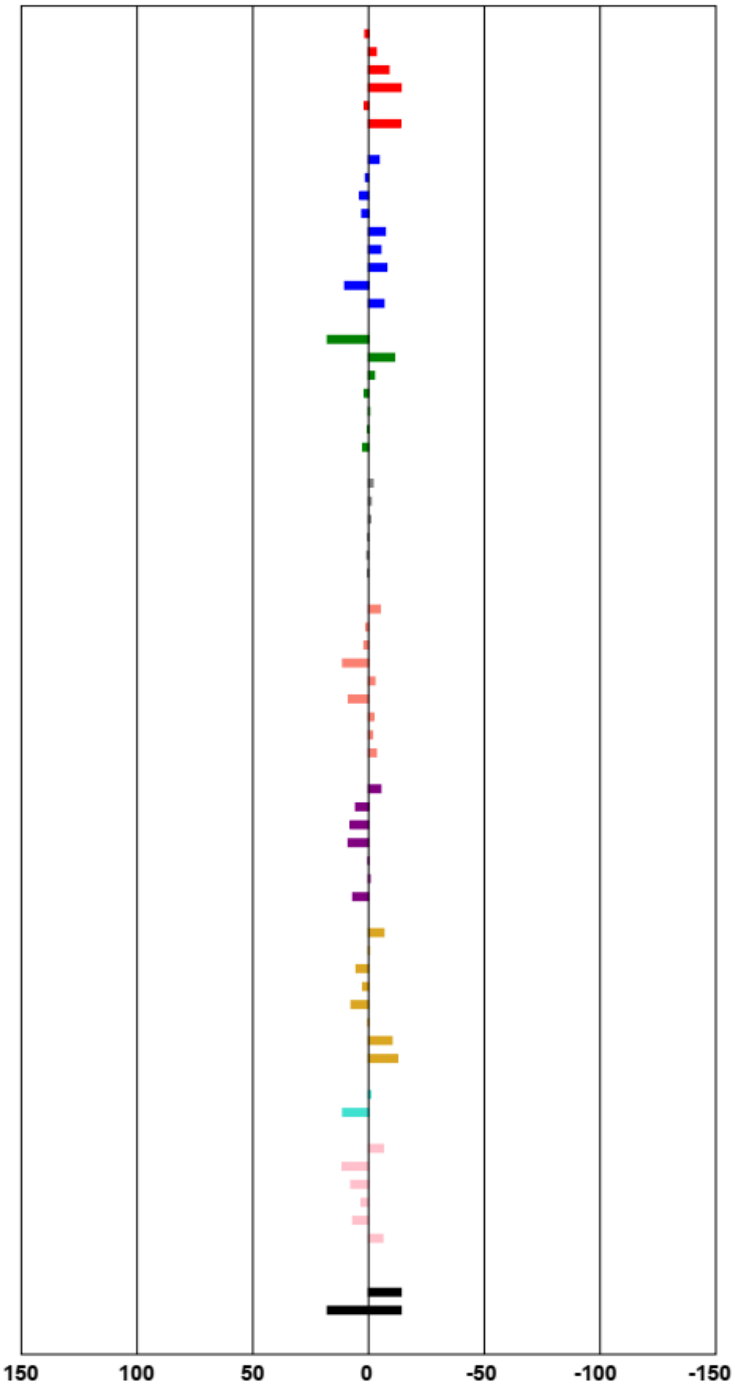
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-797140 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** Apr 10, 2017

Experiment ID: 1704OS85 | **Report Date:** Apr 26, 2017

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	104.35
HL-60(TB)	99.60
K-562	94.10
MOLT-4	88.84
RPMI-8226	104.65
SR	89.04
Non-Small Cell Lung Cancer	
A549/ATCC	98.34
EKVX	104.11
HOP-62	106.52
HOP-92	105.69
NCI-H226	95.65
NCI-H23	97.59
NCI-H322M	95.02
NCI-H460	113.07
NCI-H522	96.24
Colon Cancer	
COLO 205	120.58
HCC-2998	91.65
HCT-116	100.36
HCT-15	104.58
HT29	102.44
KM12	103.00
SW-620	105.30
CNS Cancer	
SF-268	100.93
SF-295	101.73
SF-539	102.09
SNB-19	102.95
SNB-75	103.50
U251	103.20
Melanoma	
LOX IMVI	97.83
MALME-3M	103.79
M14	104.74
MDA-MB-435	113.97
SK-MEL-2	100.16
SK-MEL-28	111.49
SK-MEL-5	100.72
UACC-257	101.19
UACC-62	99.55
Ovarian Cancer	
IGROV1	97.60
OVCAR-3	108.37
OVCAR-4	110.68
OVCAR-5	111.57
OVCAR-8	102.76
NCI/ADR-RES	102.28
SK-OV-3	109.59
Renal Cancer	
786-0	96.27
A498	102.52
ACHN	108.13
CAKI-1	105.31
RXF 393	110.30
SN12C	102.78
TK-10	92.77
UO-31	90.38
Prostate Cancer	
PC-3	102.01
DU-145	113.96
Breast Cancer	
MCF7	96.57
MDA-MB-231/ATCC	114.16
HS 578T	110.43
BT-549	105.95
T-47D	109.60
MDA-MB-468	96.72
Mean	102.82
Delta	13.98
Range	31.74



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHP-DiCl-SAL

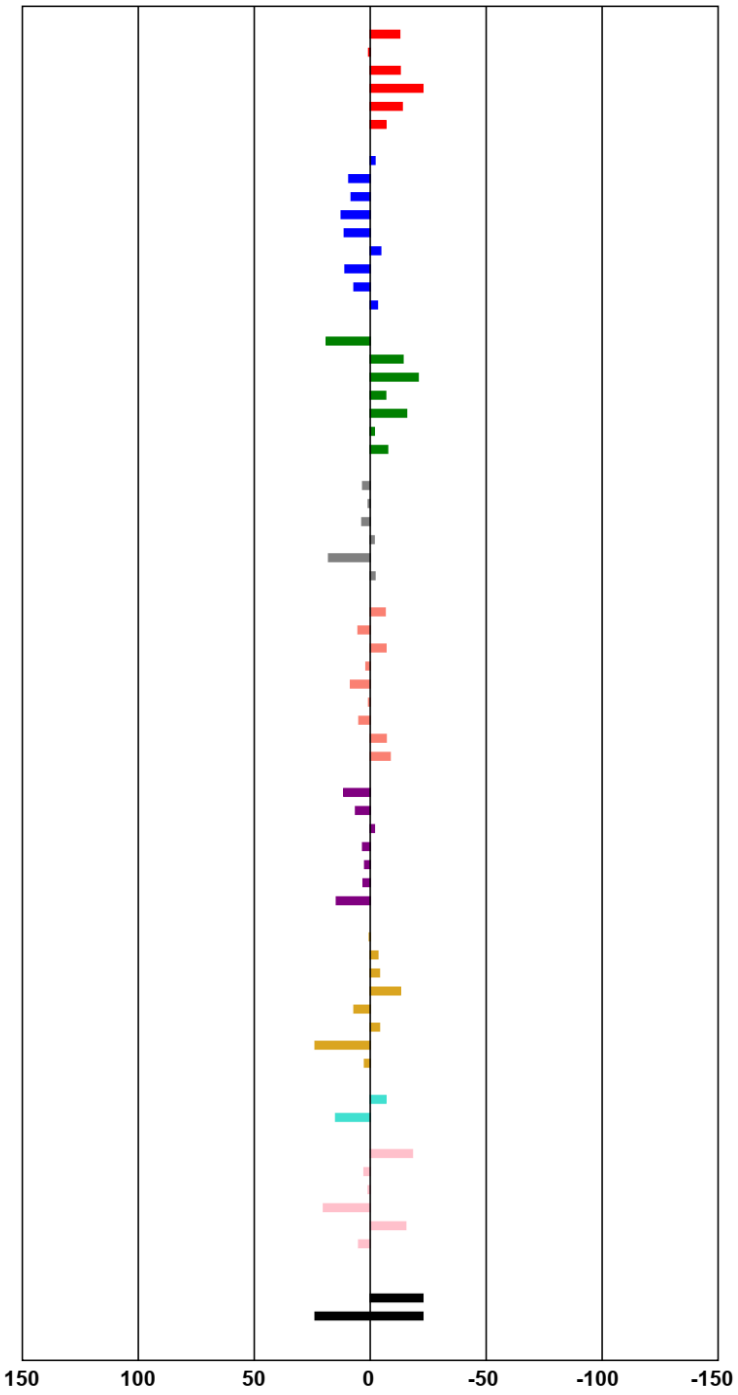
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-797139 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** Apr 10, 2017

Experiment ID: 1704OS85 | **Report Date:** Apr 26, 2017

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	86.18
HL-60(TB)	99.51
K-562	85.98
MOLT-4	76.19
RPMI-8226	85.10
SR	92.15
Non-Small Cell Lung Cancer	
A549/ATCC	96.84
EKVX	108.05
HOP-62	107.03
HOP-92	111.33
NCI-H226	110.00
NCI-H23	94.36
NCI-H322M	109.70
NCI-H460	105.82
NCI-H522	95.79
Colon Cancer	
COLO 205	117.75
HCC-2998	84.76
HCT-116	78.22
HCT-15	92.22
HT29	83.21
KM12	97.14
SW-620	91.39
CNS Cancer	
SF-268	102.08
SF-295	99.69
SF-539	102.43
SNB-19	97.19
SNB-75	116.77
U251	96.84
Melanoma	
LOX IMVI	92.45
MALME-3M	104.07
M14	92.10
MDA-MB-435	100.67
SK-MEL-2	107.33
SK-MEL-28	99.54
SK-MEL-5	103.70
UACC-257	92.01
UACC-62	90.30
Ovarian Cancer	
IGROV1	110.21
OVCAR-3	105.15
OVCAR-4	97.09
OVCAR-5	102.10
OVCAR-8	101.22
NCI/ADR-RES	101.90
SK-OV-3	113.42
Renal Cancer	
786-0	99.22
A498	95.60
ACHN	94.92
CAKI-1	85.88
RXF 393	105.82
SN12C	94.90
TK-10	122.59
UO-31	101.30
Prostate Cancer	
PC-3	92.15
DU-145	113.73
Breast Cancer	
MCF7	80.71
MDA-MB-231/ATCC	101.49
HS 578T	99.72
BT-549	118.99
T-47D	83.58
MDA-MB-468	103.80
Mean	98.86
Delta	22.67
Range	46.40



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHX-SAL

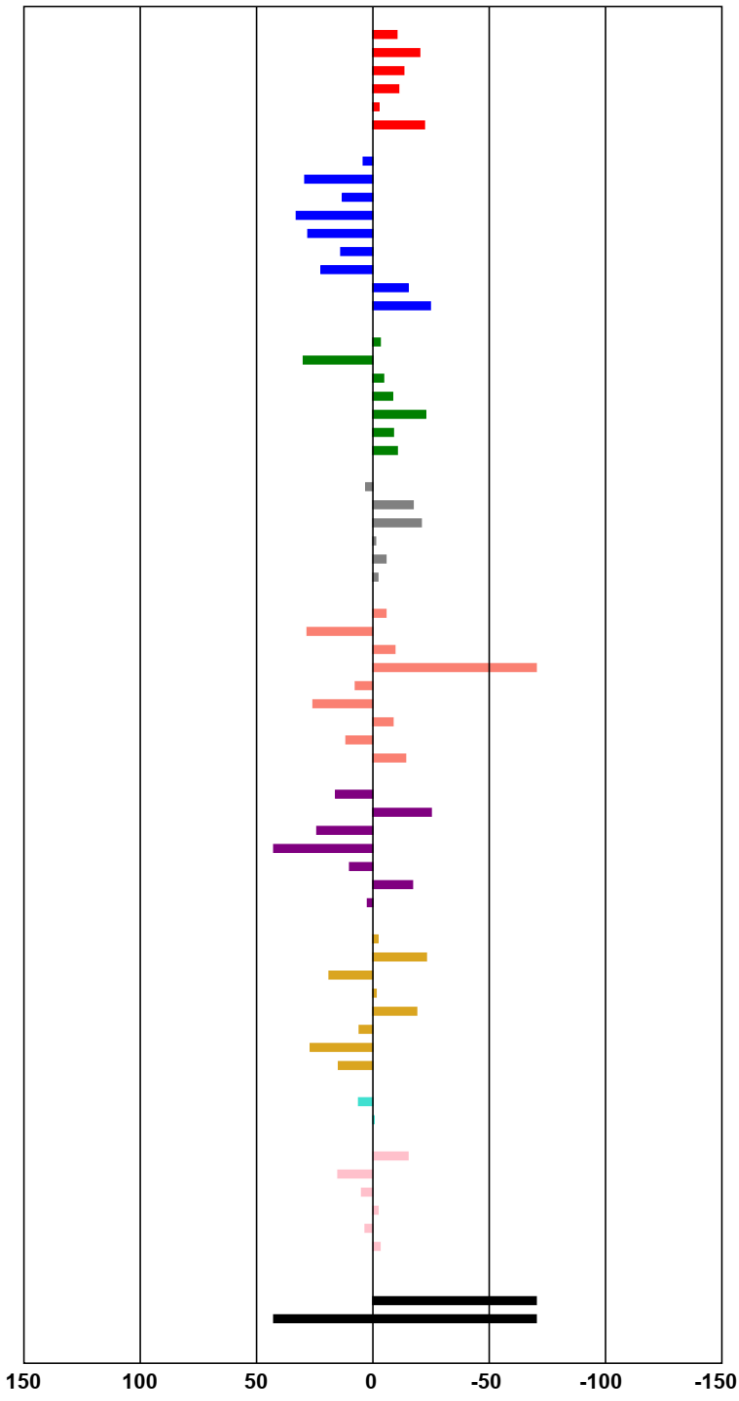
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-782680 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** Dec 01, 2014

Experiment ID: 1412OS98 | **Report Date:** Jun 15, 2016

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	18.28
HL-60(TB)	8.47
K-562	15.32
MOLT-4	17.51
RPMI-8226	26.01
SR	6.44
Non-Small Cell Lung Cancer	
A549/ATCC	32.65
EKVX	57.76
HOP-62	41.57
HOP-92	61.42
NCI-H226	56.44
NCI-H23	42.30
NCI-H322M	50.79
NCI-H460	13.47
NCI-H522	3.90
Colon Cancer	
COLO 205	25.44
HCC-2998	58.40
HCT-116	23.99
HCT-15	20.14
HT29	5.93
KM12	19.78
SW-620	18.11
CNS Cancer	
SF-268	31.56
SF-295	11.30
SF-539	7.81
SNB-19	27.44
SNB-75	22.99
U251	26.46
Melanoma	
LOX IMVI	22.99
MALME-3M	56.77
M14	19.15
MDA-MB-435	-41.60
SK-MEL-2	36.05
SK-MEL-28	54.24
SK-MEL-5	19.96
UACC-257	40.07
UACC-62	14.54
Ovarian Cancer	
IGROV1	44.53
OVCAR-3	3.51
OVCAR-4	52.59
OVCAR-5	71.12
OVCAR-8	38.51
NCI/ADR-RES	11.57
SK-OV-3	30.85
Renal Cancer	
786-0	26.44
A498	5.61
ACHN	47.34
CAKI-1	27.21
RXF 393	9.77
SN12C	34.38
TK-10	55.40
UO-31	43.31
Prostate Cancer	
PC-3	34.65
DU-145	28.07
Breast Cancer	
MCF7	13.51
MDA-MB-231/ATCC	43.53
HS 578T	33.37
BT-549	26.39
T-47D	31.86
MDA-MB-468	25.53
Mean	28.55
Delta	70.15
Range	112.72



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHX-4MO-SAL

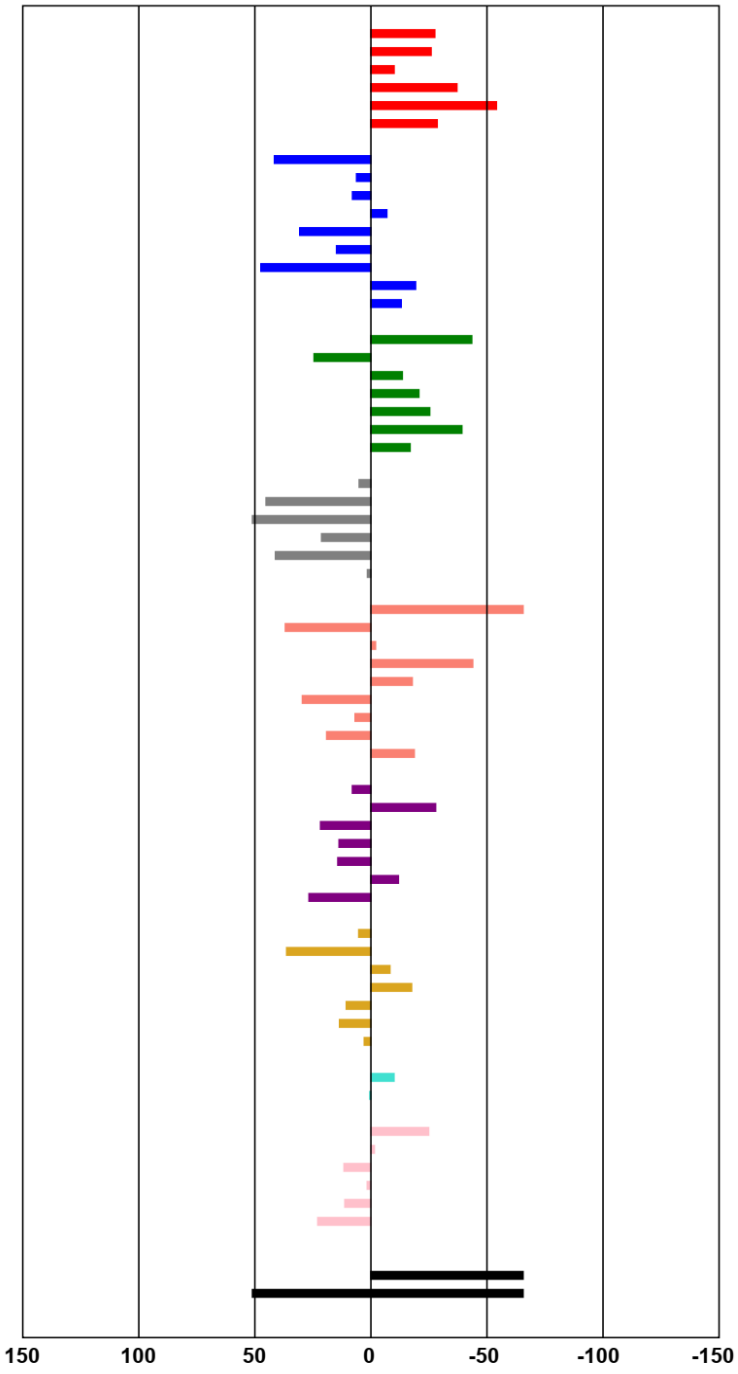
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-791128 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** May 31, 2016

Experiment ID: 1605OS20 | **Report Date:** Jun 15, 2016

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	5.97
HL-60(TB)	7.56
K-562	23.50
MOLT-4	-3.56
RPMI-8226	-20.58
SR	4.94
Non-Small Cell Lung Cancer	
A549/ATCC	75.02
EKVX	39.65
HOP-62	41.40
HOP-92	26.64
NCI-H226	64.09
NCI-H23	48.27
NCI-H322M	80.84
NCI-H460	14.25
NCI-H522	20.45
Colon Cancer	
COLO 205	-9.95
HCC-2998	57.94
HCT-116	19.97
HCT-15	12.83
HT29	8.16
KM12	-5.69
SW-620	16.61
CNS Cancer	
SF-268	38.52
SF-295	78.63
SF-539	84.49
SNB-19	54.71
SNB-75	74.56
U251	34.95
Melanoma	
LOX IMVI	-32.06
MALME-3M	70.32
M14	31.51
MDA-MB-435	-10.37
SK-MEL-2	15.69
SK-MEL-28	62.98
SK-MEL-5	40.27
UACC-257	52.52
UACC-62	14.82
Ovarian Cancer	
IGROV1	41.44
OVCAR-3	5.62
OVCAR-4	55.15
OVCAR-5	47.18
OVCAR-8	47.71
NCI/ADR-RES	21.65
SK-OV-3	60.13
Renal Cancer	
786-0	38.70
A498	69.76
ACHN	25.30
RXF 393	15.96
SN12C	44.06
TK-10	46.97
UO-31	36.31
Prostate Cancer	
PC-3	23.55
DU-145	33.91
Breast Cancer	
MCF7	8.63
MDA-MB-231/ATCC	32.03
HS 578T	45.03
BT-549	35.03
T-47D	44.67
MDA-MB-468	56.33
Mean	33.47
Delta	65.53
Range	116.55



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHX-5MO-SAL

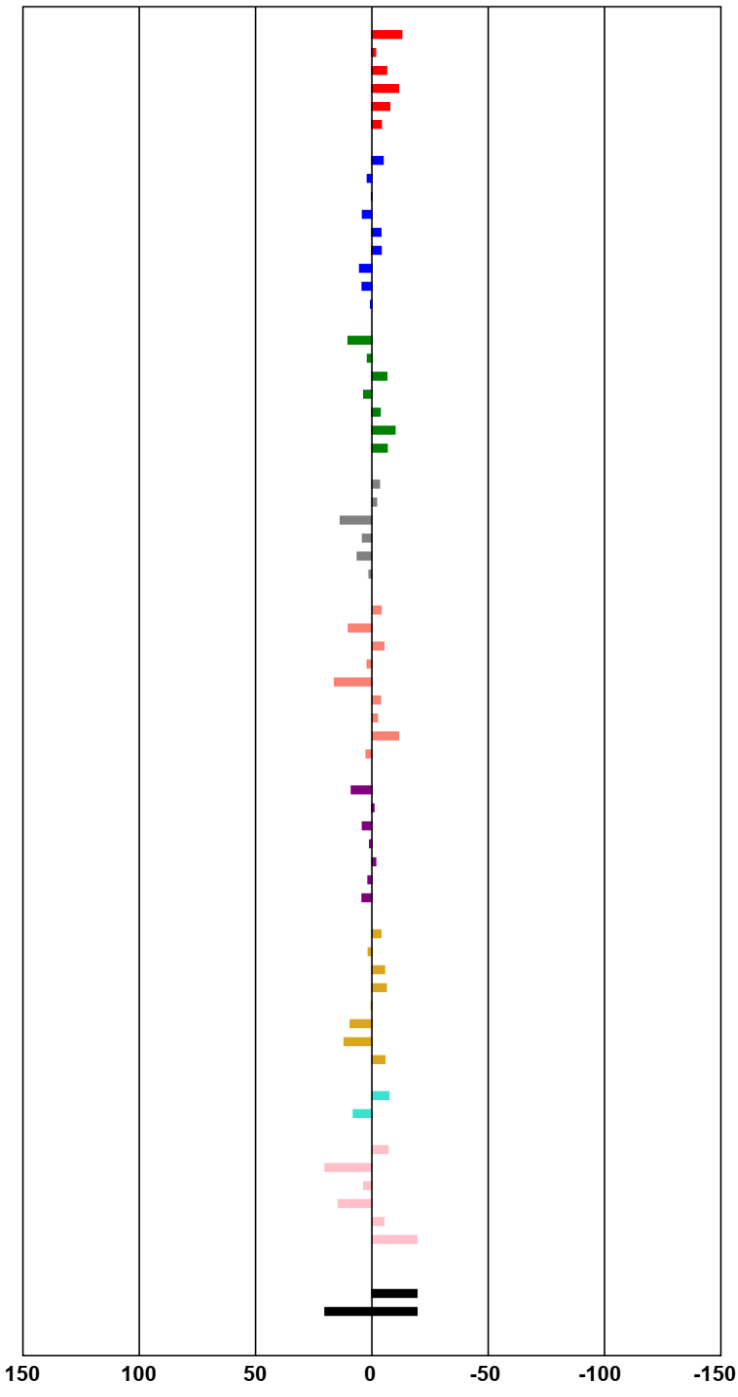
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-797137 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** Apr 10, 2017

Experiment ID: 1704OS85 | **Report Date:** Apr 26, 2017

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	88.31
HL-60(TB)	99.59
K-562	94.85
MOLT-4	89.70
RPMI-8226	93.55
SR	97.09
Non-Small Cell Lung Cancer	
A549/ATCC	96.33
EKVX	103.01
HOP-62	101.21
HOP-92	105.10
NCI-H226	97.30
NCI-H23	97.16
NCI-H322M	106.32
NCI-H460	105.25
NCI-H522	101.58
Colon Cancer	
COLO 205	111.27
HCC-2998	102.97
HCT-116	94.74
HCT-15	104.56
HT29	97.57
KM12	91.22
SW-620	94.58
CNS Cancer	
SF-268	97.90
SF-295	99.15
SF-539	114.62
SNB-19	105.09
SNB-75	107.33
U251	102.25
Melanoma	
LOX IMVI	97.19
MALME-3M	111.16
M14	96.01
MDA-MB-435	103.06
SK-MEL-2	117.14
SK-MEL-28	97.48
SK-MEL-5	98.77
UACC-257	89.70
UACC-62	103.55
Ovarian Cancer	
IGROV1	109.88
OVCAR-3	100.27
OVCAR-4	105.13
OVCAR-5	102.00
OVCAR-8	99.51
NCI/ADR-RES	102.73
SK-OV-3	105.27
Renal Cancer	
786-0	97.32
A498	102.61
ACHN	95.73
CAKI-1	94.96
RXF 393	101.32
SN12C	110.33
TK-10	112.95
UO-31	95.56
Prostate Cancer	
PC-3	93.86
DU-145	109.02
Breast Cancer	
MCF7	94.21
MDA-MB-231/ATCC	121.22
HS 578T	104.52
BT-549	115.48
T-47D	95.98
MDA-MB-468	81.77
Mean	101.09
Delta	19.32
Range	39.45



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHX-5Cl-SAL

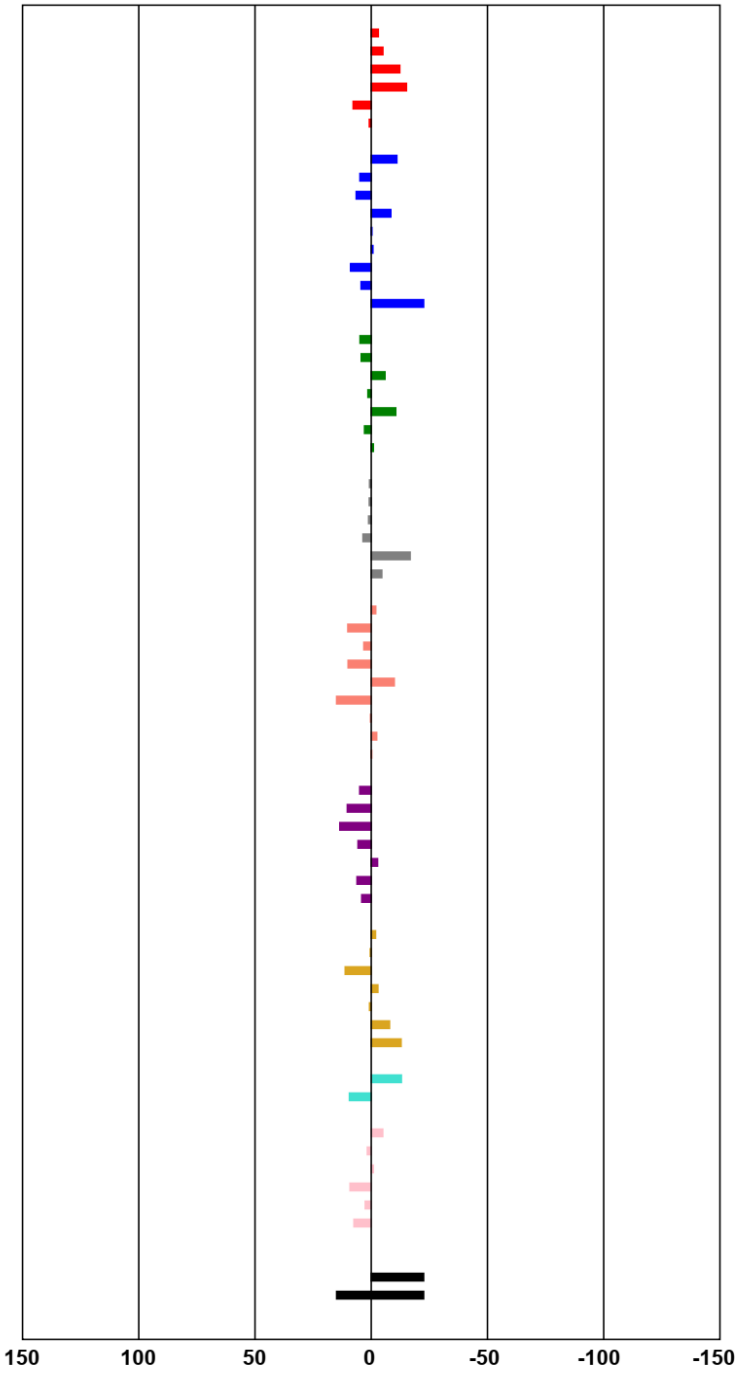
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-791129 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** May 31, 2016

Experiment ID: 1605OS20 | **Report Date:** Jun 15, 2016

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	96.34
HL-60(TB)	94.36
K-562	87.10
MOLT-4	84.23
RPMI-8226	107.15
SR	100.20
Non-Small Cell Lung Cancer	
A549/ATCC	88.36
EKVX	104.23
HOP-62	105.83
HOP-92	90.98
NCI-H226	99.10
NCI-H23	98.66
NCI-H322M	108.23
NCI-H460	103.73
NCI-H522	76.84
Colon Cancer	
COLO 205	104.18
HCC-2998	103.67
HCT-116	93.46
HCT-15	100.79
HT29	88.84
KM12	102.25
SW-620	98.47
CNS Cancer	
SF-268	100.10
SF-295	100.22
SF-539	100.50
SNB-19	102.91
SNB-75	82.64
U251	94.84
Melanoma	
LOX IMVI	97.45
MALME-3M	109.43
M14	102.54
MDA-MB-435	109.31
SK-MEL-2	89.48
SK-MEL-28	114.26
SK-MEL-5	99.67
UACC-257	97.04
UACC-62	99.18
Ovarian Cancer	
IGROV1	104.31
OVCAR-3	109.66
OVCAR-4	112.87
OVCAR-5	105.05
OVCAR-8	96.66
NCI/ADR-RES	105.49
SK-OV-3	103.45
Renal Cancer	
786-0	97.54
A498	99.78
ACHN	110.56
RXF 393	96.52
SN12C	100.10
TK-10	91.51
UO-31	86.54
Prostate Cancer	
PC-3	86.42
DU-145	108.75
Breast Cancer	
MCF7	94.43
MDA-MB-231/ATCC	101.04
HS 578T	98.47
BT-549	108.48
T-47D	101.93
MDA-MB-468	106.79
Mean	99.37
Delta	22.53
Range	37.42



***In-vitro* anti-cancer activity at 10µM against NCI 60 cell line panel.**

CHX-DiCl-SAL

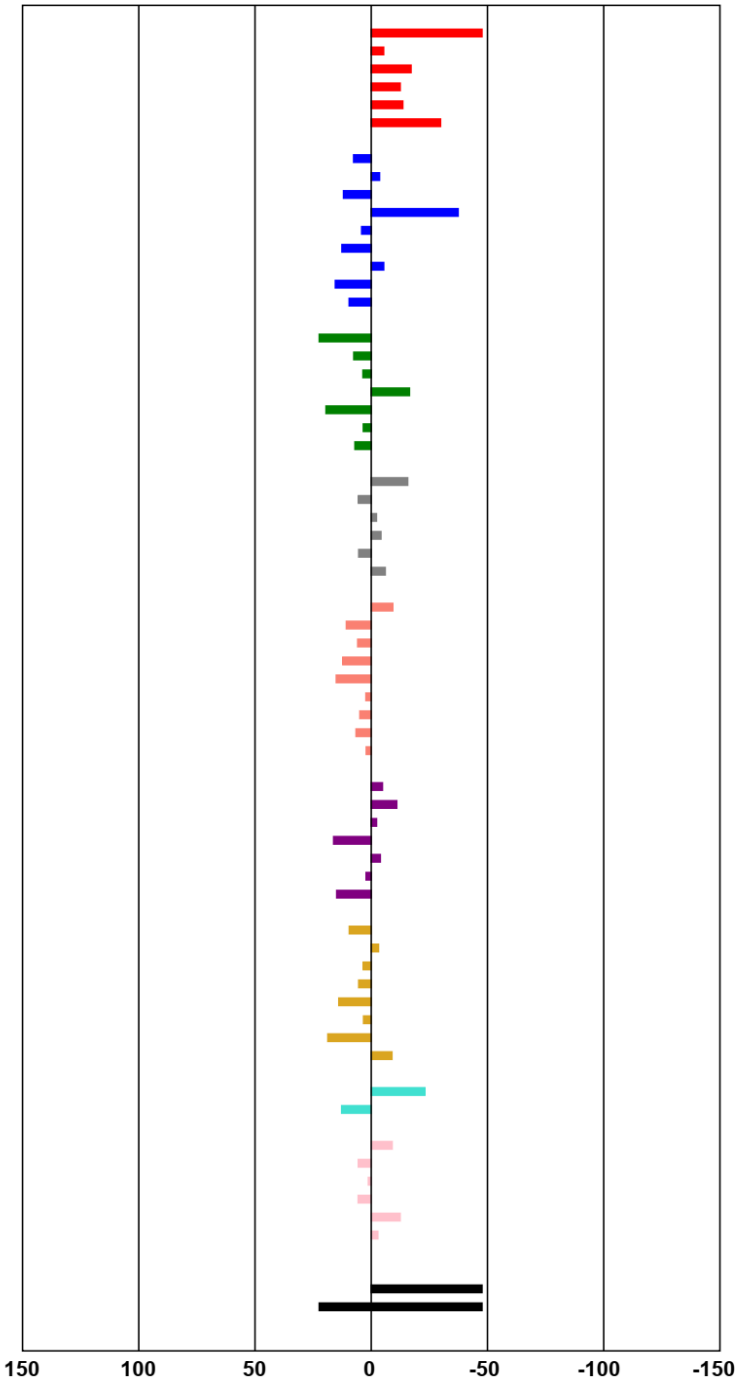
Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-797138 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** Apr 10, 2017

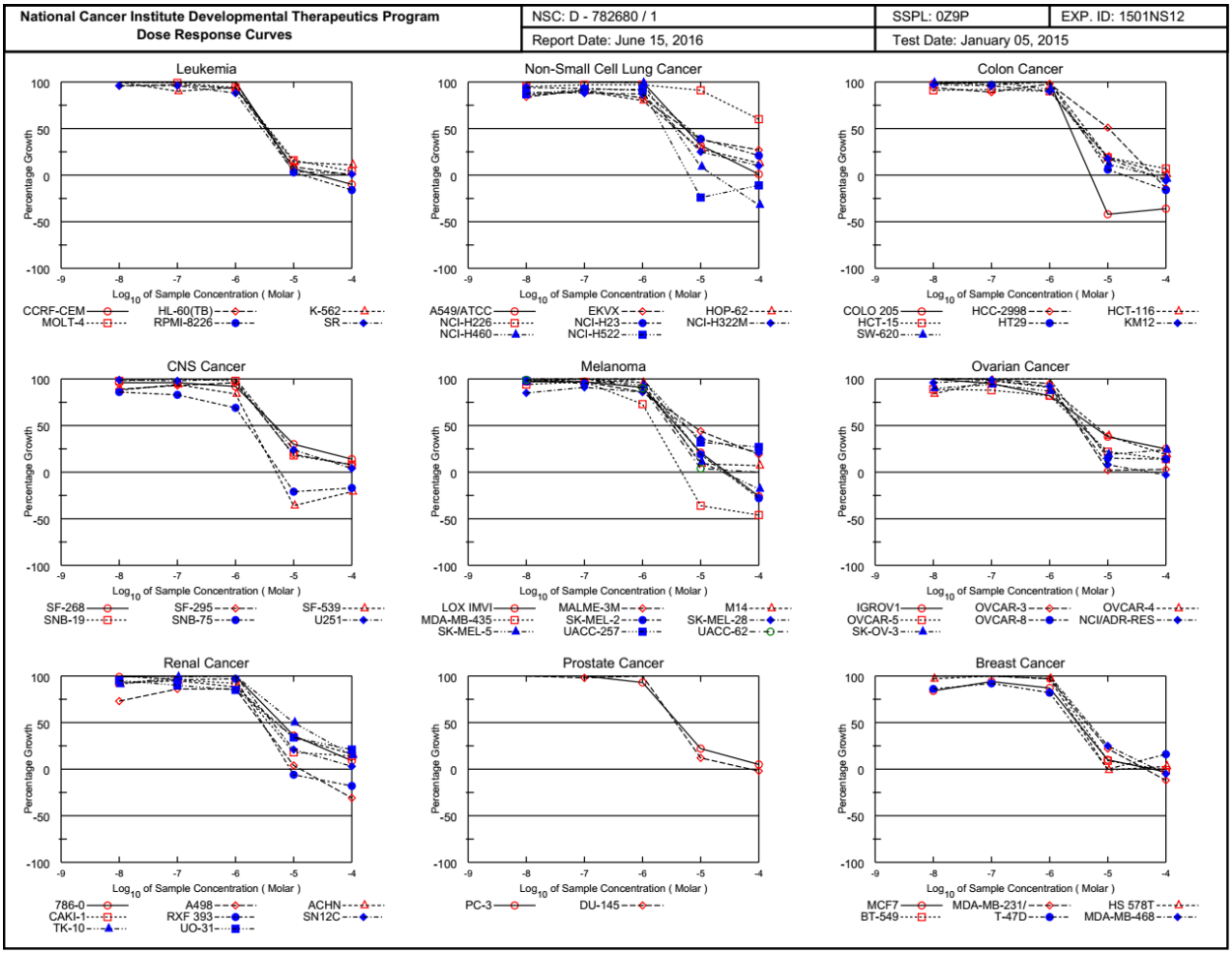
Experiment ID: 1704OS85 | **Report Date:** Apr 26, 2017

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	45.36
HL-60(TB)	87.67
K-562	75.88
MOLT-4	80.56
RPMI-8226	79.43
SR	63.19
Non-Small Cell Lung Cancer	
A549/ATCC	100.56
EKVX	89.44
HOP-62	104.91
HOP-92	55.63
NCI-H226	97.10
NCI-H23	105.59
NCI-H322M	87.65
NCI-H460	108.43
NCI-H522	102.48
Colon Cancer	
COLO 205	115.35
HCC-2998	100.49
HCT-116	96.55
HCT-15	76.56
HT29	112.44
KM12	96.39
SW-620	99.99
CNS Cancer	
SF-268	77.33
SF-295	98.49
SF-539	90.77
SNB-19	88.84
SNB-75	98.36
U251	86.99
Melanoma	
LOX IMVI	83.75
MALME-3M	103.68
M14	98.79
MDA-MB-435	105.19
SK-MEL-2	108.02
SK-MEL-28	95.27
SK-MEL-5	97.86
UACC-257	99.51
UACC-62	95.13
Ovarian Cancer	
IGROV1	88.19
OVCAR-3	82.04
OVCAR-4	90.73
OVCAR-5	109.16
OVCAR-8	89.11
NCI/ADR-RES	95.20
SK-OV-3	107.84
Renal Cancer	
786-0	102.42
A498	89.89
ACHN	96.41
CAKI-1	98.36
RXF 393	106.92
SN12C	96.28
TK-10	111.64
UO-31	84.11
Prostate Cancer	
PC-3	69.95
DU-145	105.70
Breast Cancer	
MCF7	84.02
MDA-MB-231/ATCC	98.52
HS 578T	94.21
BT-549	98.59
T-47D	80.58
MDA-MB-468	90.19
Mean	93.00
Delta	47.64
Range	69.99



In-vitro anti-cancer activity against NCI 60 cell line panel – five dose study.

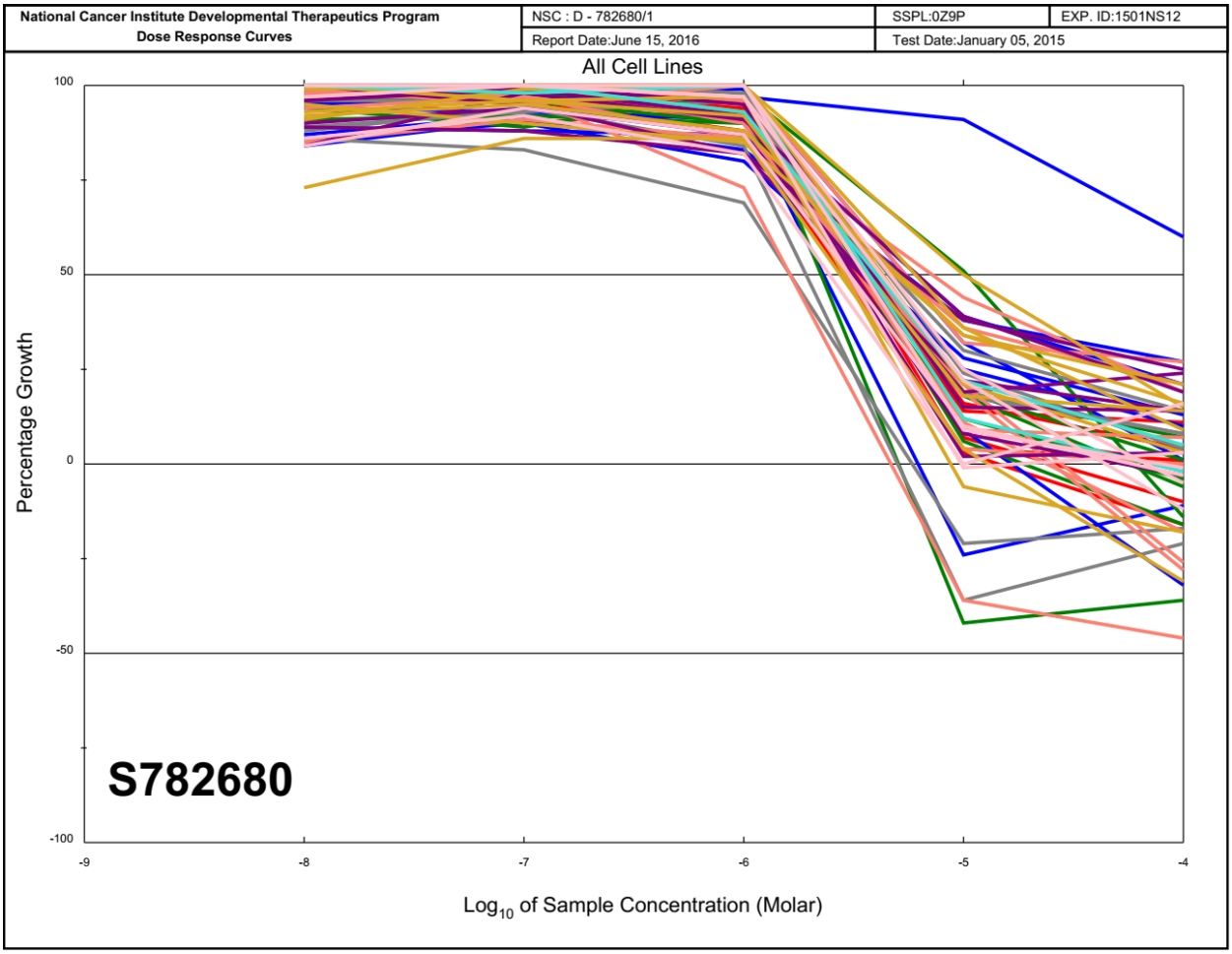
CHX-SAL



National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 782680 / 1	Experiment ID : 1501NS12	Test Type : 08	Units : Molar
Report Date : June 15, 2016	Test Date : January 05, 2015	QNS :	MC :
COMI : G6_SSSIHL	Stain Reagent : SRB Dual-Pass Related	SSPL : 0Z9P	

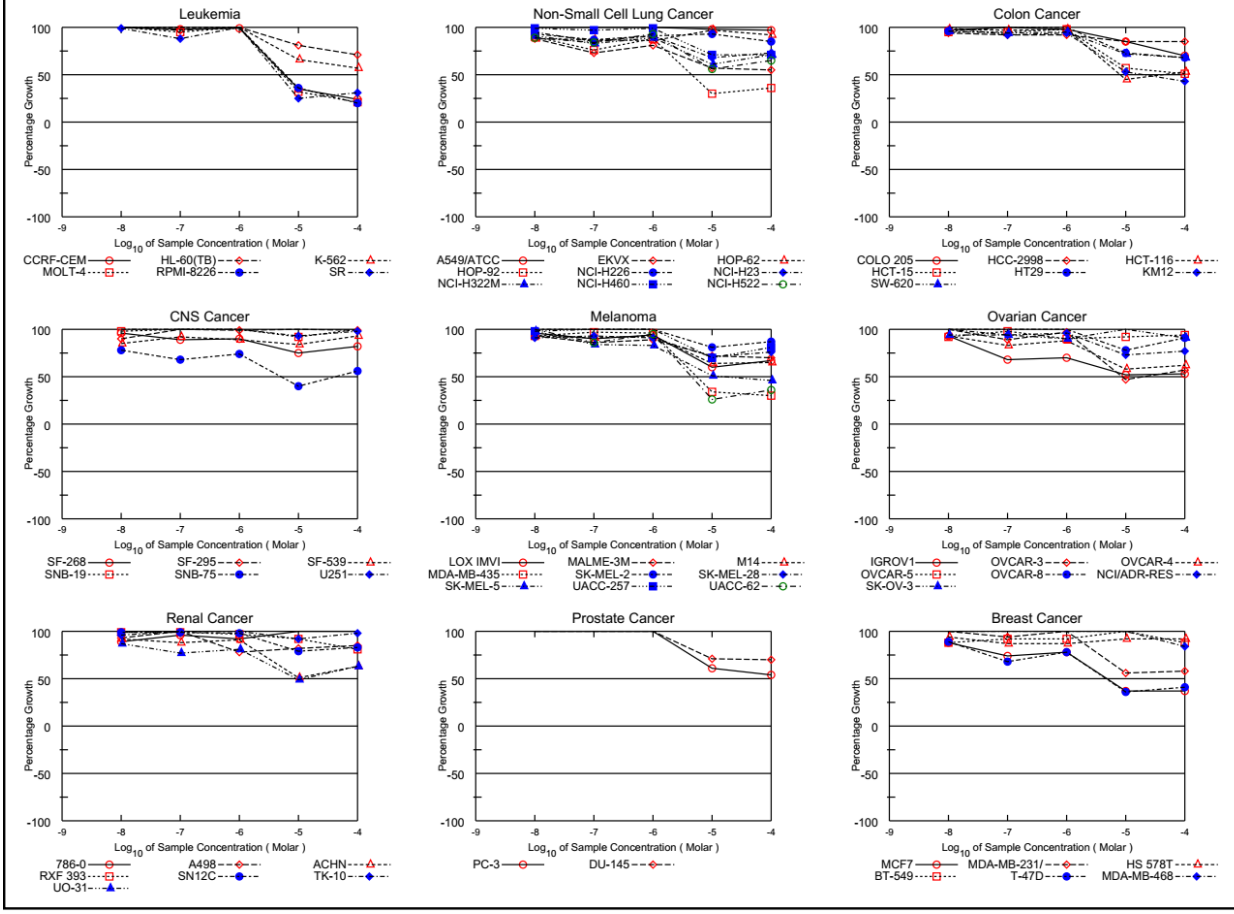
			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.496	2.229	2.260	2.311	2.234	0.623	0.445	102	105	100	7	-10	3.47E-6	2.59E-5	> 1.00E-4
HL-60(TB)	0.691	2.646	2.568	2.594	2.507	0.867	0.698	96	97	93	9	.	3.24E-6	> 1.00E-4	> 1.00E-4
K-562	0.237	2.010	2.005	1.829	1.913	0.477	0.428	100	90	94	14	11	3.54E-6	> 1.00E-4	> 1.00E-4
MOLT-4	0.509	2.362	2.376	2.339	2.255	0.800	0.581	101	99	94	16	4	3.65E-6	> 1.00E-4	> 1.00E-4
RPMI-8226	0.852	2.363	2.406	2.457	2.400	0.903	0.717	103	106	102	3	-16	3.38E-6	1.50E-5	> 1.00E-4
SR	0.305	1.673	1.620	1.620	1.504	0.359	0.317	96	96	88	4	1	2.82E-6	> 1.00E-4	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.370	1.850	1.844	1.905	1.976	0.849	0.378	100	104	108	32	1	5.87E-6	> 1.00E-4	> 1.00E-4
EKVX	0.671	1.906	1.703	1.797	1.701	1.144	1.001	84	91	83	38	27	5.49E-6	> 1.00E-4	> 1.00E-4
HOP-62	0.818	1.980	1.820	1.859	1.744	1.149	0.972	86	90	80	28	13	3.80E-6	> 1.00E-4	> 1.00E-4
NCI-H226	1.554	2.568	2.521	2.537	2.539	2.477	2.164	95	97	97	91	60	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H23	0.697	1.951	1.870	1.858	1.840	1.189	0.957	94	93	91	39	21	6.20E-6	> 1.00E-4	> 1.00E-4
NCI-H322M	0.786	1.916	1.791	1.786	1.766	1.068	0.897	89	88	87	25	10	3.92E-6	> 1.00E-4	> 1.00E-4
NCI-H460	0.354	3.068	3.096	3.121	3.028	0.592	0.241	101	102	99	9	-32	3.47E-6	1.64E-5	> 1.00E-4
NCI-H522	1.013	2.190	2.042	2.097	2.095	0.769	0.900	87	92	92	-24	-11	2.30E-6	6.20E-6	> 1.00E-4
Colon Cancer															
COLO 205	0.375	1.455	1.436	1.495	1.454	0.216	0.240	98	104	100	-42	-36	2.24E-6	5.04E-6	> 1.00E-4
HCC-2998	0.850	2.600	2.498	2.416	2.572	1.740	0.731	94	89	98	51	-14	1.03E-5	6.07E-5	> 1.00E-4
HCT-116	0.219	1.890	1.896	1.923	1.974	0.533	0.244	100	102	105	19	1	4.34E-6	> 1.00E-4	> 1.00E-4
HCT-15	0.372	2.139	1.988	2.006	1.960	0.716	0.492	91	92	90	19	7	3.68E-6	> 1.00E-4	> 1.00E-4
HT29	0.210	1.293	1.315	1.265	1.334	0.270	0.176	102	97	104	6	-16	3.52E-6	1.79E-5	> 1.00E-4
KM12	0.488	2.727	2.651	2.649	2.498	0.902	0.459	97	96	90	18	-6	3.61E-6	5.67E-5	> 1.00E-4
SW-620	0.344	2.307	2.292	2.341	2.158	0.575	0.329	99	102	92	12	-4	3.35E-6	5.36E-5	> 1.00E-4
CNS Cancer															
SF-268	0.637	2.296	2.225	2.224	2.169	1.130	0.877	96	96	92	30	14	4.74E-6	> 1.00E-4	> 1.00E-4
SF-295	0.829	3.049	2.806	2.898	2.959	1.262	1.002	89	93	96	19	8	3.99E-6	> 1.00E-4	> 1.00E-4
SF-539	0.882	2.587	2.388	2.487	2.317	0.563	0.699	88	94	84	-36	-21	1.92E-6	5.01E-6	> 1.00E-4
SNB-19	0.553	1.832	1.807	1.835	1.809	0.787	0.655	98	100	98	18	8	4.01E-6	> 1.00E-4	> 1.00E-4
SNB-75	0.932	1.899	1.766	1.732	1.603	0.735	0.771	86	83	69	-21	-17	1.64E-6	5.84E-6	> 1.00E-4
U251	0.446	2.015	2.005	1.977	2.017	0.820	0.512	99	98	100	24	4	4.54E-6	> 1.00E-4	> 1.00E-4
Melanoma															
LOX IMVI	0.409	2.584	2.519	2.508	2.397	0.867	0.303	97	97	91	21	-26	3.88E-6	2.80E-5	> 1.00E-4
MALME-3M	0.807	1.735	1.712	1.710	1.607	1.214	0.986	98	97	86	44	19	7.17E-6	> 1.00E-4	> 1.00E-4
M14	0.436	1.752	1.719	1.804	1.704	0.549	0.529	97	104	96	9	7	3.37E-6	> 1.00E-4	> 1.00E-4
MDA-MB-435	0.577	2.767	2.641	2.706	2.186	0.368	0.312	94	97	73	-36	-46	1.64E-6	4.67E-6	> 1.00E-4
SK-MEL-2	0.851	1.522	1.516	1.490	1.547	0.979	0.615	99	95	104	19	-28	4.31E-6	2.56E-5	> 1.00E-4
SK-MEL-28	0.643	2.055	1.850	1.924	1.858	1.149	0.938	85	91	86	36	21	5.22E-6	> 1.00E-4	> 1.00E-4
SK-MEL-5	0.874	2.579	2.624	2.624	2.467	1.064	0.718	103	103	93	11	-18	3.37E-6	2.42E-5	> 1.00E-4
UACC-257	0.978	1.945	1.922	1.979	1.968	1.283	1.241	98	104	102	32	27	5.49E-6	> 1.00E-4	> 1.00E-4
UACC-62	0.695	2.269	2.260	2.270	2.109	0.757	0.693	99	100	90	4	.	2.91E-6	8.25E-5	> 1.00E-4
Ovarian Cancer															
IGROV1	0.598	2.197	2.245	2.124	1.917	1.205	0.996	103	95	82	38	25	5.36E-6	> 1.00E-4	> 1.00E-4
OVCAR-3	0.778	2.147	2.183	2.145	2.081	0.808	0.816	103	100	95	2	3	3.06E-6	> 1.00E-4	> 1.00E-4
OVCAR-4	0.826	1.851	1.692	1.835	1.763	1.224	1.019	84	98	91	39	19	6.12E-6	> 1.00E-4	> 1.00E-4
OVCAR-5	0.568	1.666	1.544	1.534	1.473	0.813	0.724	89	88	82	22	14	3.46E-6	> 1.00E-4	> 1.00E-4
OVCAR-8	0.456	1.933	1.942	2.013	1.989	0.678	0.659	101	105	104	15	14	4.04E-6	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.577	1.881	1.826	1.865	1.776	0.687	0.561	96	99	92	8	-3	3.18E-6	5.57E-5	> 1.00E-4
SK-OV-3	1.108	2.301	2.184	2.225	2.148	1.337	1.399	90	94	87	19	24	3.52E-6	> 1.00E-4	> 1.00E-4
Renal Cancer															
786-0	0.713	2.230	2.218	2.323	2.353	1.261	0.847	99	106	108	36	9	6.41E-6	> 1.00E-4	> 1.00E-4
A498	1.498	2.427	2.180	2.299	2.298	1.536	1.033	73	86	86	4	-31	2.76E-6	1.31E-5	> 1.00E-4
ACHN	0.591	2.157	2.026	2.085	1.968	1.125	0.839	92	95	88	34	16	5.06E-6	> 1.00E-4	> 1.00E-4
CAKI-1	0.685	3.163	2.990	3.065	2.958	1.141	1.020	93	96	92	18	14	3.71E-6	> 1.00E-4	> 1.00E-4
RXF 393	1.265	1.840	1.844	1.820	1.821	1.191	1.037	101	96	97	-6	-18	2.85E-6	8.77E-6	> 1.00E-4
SN12C	0.521	1.588	1.605	1.658	1.610	0.749	0.557	102	107	102	21	3	4.42E-6	> 1.00E-4	> 1.00E-4
TK-10	0.883	1.795	1.710	1.786	2.061	1.335	1.017	91	99	129	50	15	9.87E-6	> 1.00E-4	> 1.00E-4
UO-31	0.771	2.816	2.711	2.621	2.504	1.470	1.198	95	90	85	34	21	4.86E-6	> 1.00E-4	> 1.00E-4
Prostate Cancer															
PC-3	0.585	2.071	2.083	2.085	1.961	0.911	0.665	101	101	93	22	5	4.00E-6	> 1.00E-4	> 1.00E-4
DU-145	0.448	2.020	2.021	1.987	2.026	0.641	0.438	100	98	100	12	-2	3.73E-6	6.91E-5	> 1.00E-4
Breast Cancer															
MCF7	0.329	1.916	1.666	1.815	1.706	0.494	0.320	84	94	87	10	-3	3.03E-6	6.06E-5	> 1.00E-4
MDA-MB-231/ATCC	0.605	1.474	1.508	1.505	1.445	0.798	0.535	104	104	97	22	-12	4.23E-6	4.55E-5	> 1.00E-4
HS 578T	1.110	2.150	2.123	2.156	2.124	1.097	1.140	97	101	97	-1	3	3.03E-6	.	> 1.00E-4
BT-549	0.925	1.965	2.021	2.059	2.011	1.021	0.912	105	109	104	9	-1	3.73E-6	7.37E-5	> 1.00E-4
T-47D	0.740	1.585	1.466	1.517	1.431	0.744	0.874	86	92	82	.	16	2.46E-6	> 1.00E-4	> 1.00E-4
MDA-MB-468	1.040	1.656	1.697	1.729	1.776	1.193	0.991	107	112	119	25	-5	5.42E-6	6.91E-5	> 1.00E-4



In-vitro **anti-cancer activity against NCI 60 cell line panel – five dose study.**

CHX--4MO-SAL

National Cancer Institute Developmental Therapeutics Program Dose Response Curves	NSC: D - 791128 / 1	SSPL: 0Z9P	EXP. ID: 1607NS41
	Report Date: August 28, 2016	Test Date: July 11, 2016	

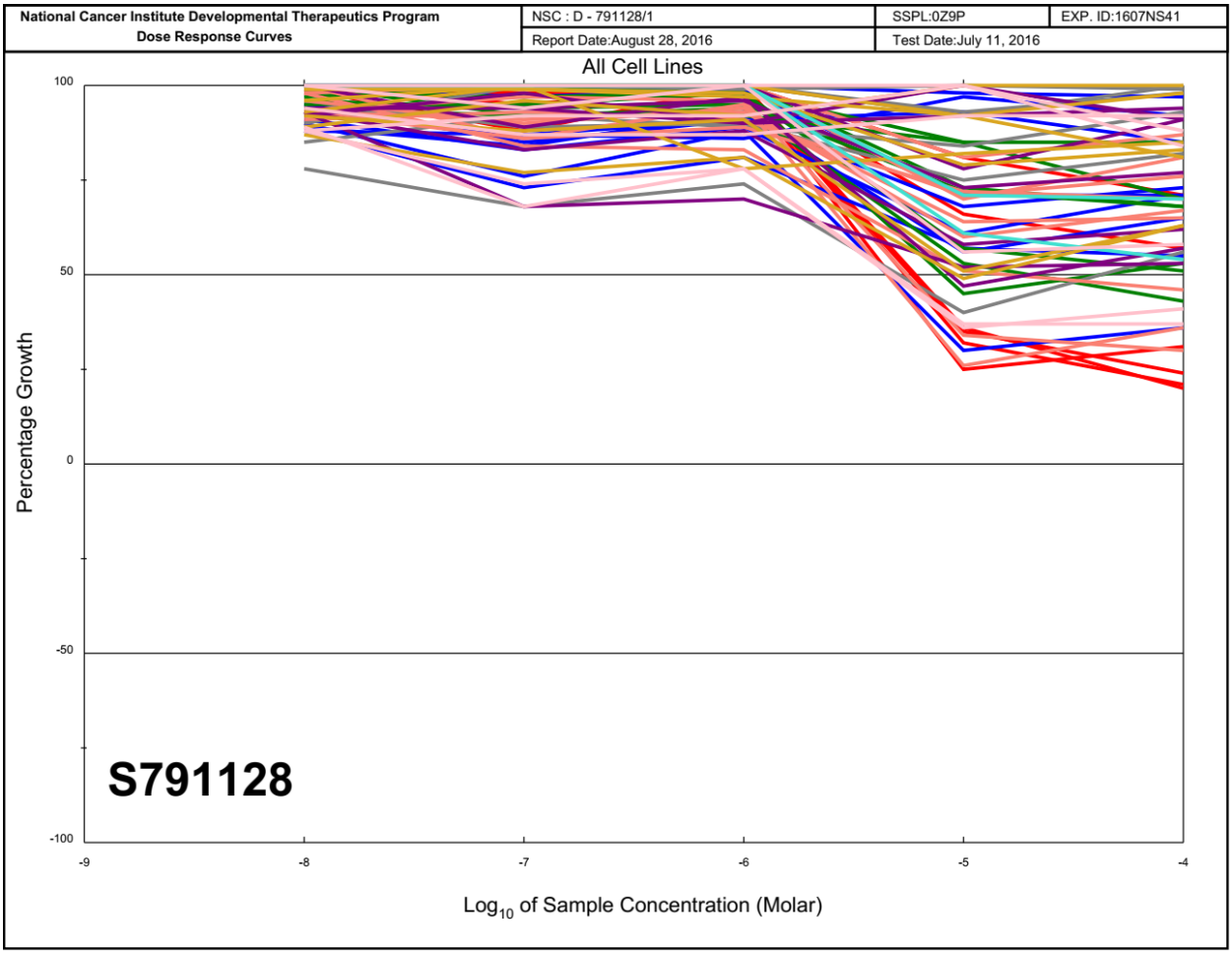


National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 791128 / 1	Experiment ID : 1607NS41	Test Type : 08	Units : Molar
Report Date : August 28, 2016	Test Date : July 11, 2016	QNS :	MC :
COMI : chx-4-MO-sal	Stain Reagent : SRB Dual-Pass Related	SSPL : 0Z9P	

Log10 Concentration

	Time	Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.560	2.979	2.995	2.931	2.958	1.414	1.142	101	98	99	35	24	5.88E-6	> 1.00E-4	> 1.00E-4
HL-60(TB)	0.721	2.386	2.578	2.343	2.569	2.064	1.910	111	97	111	81	71	> 1.00E-4	> 1.00E-4	> 1.00E-4
K-562	0.257	2.307	2.597	2.399	2.445	1.618	1.422	114	105	107	66	57	> 1.00E-4	> 1.00E-4	> 1.00E-4
MOLT-4	0.573	2.695	2.764	2.594	2.878	1.250	1.027	103	95	109	32	21	5.81E-6	> 1.00E-4	> 1.00E-4
RPMI-8226	0.830	2.741	2.800	2.750	2.796	1.512	1.212	103	100	103	36	20	6.12E-6	> 1.00E-4	> 1.00E-4
SR	0.414	2.080	2.070	1.889	2.163	0.834	0.927	99	88	105	25	31	4.89E-6	> 1.00E-4	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.572	2.364	2.374	2.442	2.461	2.324	2.314	101	104	105	98	97	> 1.00E-4	> 1.00E-4	> 1.00E-4
EKVX	0.708	2.284	2.092	1.866	1.981	1.608	1.580	88	73	81	57	55	> 1.00E-4	> 1.00E-4	> 1.00E-4
HOP-62	0.724	1.926	1.776	1.775	1.759	1.886	1.826	88	87	86	97	92	> 1.00E-4	> 1.00E-4	> 1.00E-4
HOP-92	1.331	1.770	1.728	1.665	1.716	1.462	1.491	90	76	88	30	36	4.46E-6	> 1.00E-4	> 1.00E-4
NCI-H226	0.704	1.789	1.718	1.645	1.695	1.715	1.628	93	87	91	93	85	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H23	0.615	2.025	1.947	1.810	1.903	1.573	1.644	95	85	91	68	73	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H322M	0.893	2.307	2.186	2.069	2.150	1.757	1.898	91	83	89	61	71	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H460	0.289	2.506	2.487	2.430	2.481	1.867	1.863	99	97	99	71	71	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H522	1.018	2.357	2.211	2.138	2.266	1.762	1.888	89	84	93	56	65	> 1.00E-4	> 1.00E-4	> 1.00E-4
Colon Cancer															
COLO 205	0.516	2.131	2.077	2.186	2.102	1.896	1.650	97	103	98	85	70	> 1.00E-4	> 1.00E-4	> 1.00E-4
HCC-2998	0.855	2.729	2.618	2.582	2.571	2.454	2.448	94	92	92	85	85	> 1.00E-4	> 1.00E-4	> 1.00E-4
HCT-116	0.220	2.101	2.058	2.054	2.056	1.066	1.224	98	97	98	45	53	.	> 1.00E-4	> 1.00E-4
HCT-15	0.398	2.545	2.439	2.435	2.494	1.615	1.484	95	95	98	57	51	> 1.00E-4	> 1.00E-4	> 1.00E-4
HT29	0.306	2.070	2.000	2.127	2.091	1.598	1.510	96	103	101	73	68	> 1.00E-4	> 1.00E-4	> 1.00E-4
KM12	0.420	2.427	2.420	2.268	2.302	1.475	1.287	100	92	94	53	43	1.87E-5	> 1.00E-4	> 1.00E-4
SW-620	0.278	1.567	1.511	1.491	1.501	1.202	1.161	96	94	95	72	68	> 1.00E-4	> 1.00E-4	> 1.00E-4
CNS Cancer															
SF-268	0.698	2.194	2.135	2.028	2.050	1.825	1.927	96	89	90	75	82	> 1.00E-4	> 1.00E-4	> 1.00E-4
SF-295	0.788	2.527	2.346	2.534	2.507	2.728	2.504	90	100	99	112	99	> 1.00E-4	> 1.00E-4	> 1.00E-4
SF-539	1.002	2.842	2.562	2.693	2.642	2.556	2.716	85	92	89	84	93	> 1.00E-4	> 1.00E-4	> 1.00E-4
SNB-19	0.681	2.275	2.249	2.315	2.314	2.151	2.321	98	102	102	92	103	> 1.00E-4	> 1.00E-4	> 1.00E-4
SNB-75	0.838	1.482	1.342	1.275	1.313	1.099	1.198	78	68	74	40	56	.	> 1.00E-4	> 1.00E-4
U251	0.525	2.256	2.304	2.322	2.330	2.135	2.228	103	104	104	93	98	> 1.00E-4	> 1.00E-4	> 1.00E-4
Melanoma															
LOX IMVI	0.576	3.111	3.014	2.864	2.961	2.098	2.278	96	90	94	60	67	> 1.00E-4	> 1.00E-4	> 1.00E-4
MALME-3M	0.705	1.410	1.362	1.308	1.329	1.212	1.199	93	86	89	72	70	> 1.00E-4	> 1.00E-4	> 1.00E-4
M14	0.492	2.082	1.976	1.932	1.973	1.511	1.522	93	91	93	64	65	> 1.00E-4	> 1.00E-4	> 1.00E-4
MDA-MB-435	0.428	2.194	2.077	2.134	2.118	1.031	0.962	93	97	96	34	30	5.52E-6	> 1.00E-4	> 1.00E-4
SK-MEL-2	0.890	1.872	1.967	1.868	1.885	1.690	1.740	110	100	101	81	87	> 1.00E-4	> 1.00E-4	> 1.00E-4
SK-MEL-28	0.871	2.639	2.480	2.510	2.481	2.124	2.221	91	93	91	71	76	> 1.00E-4	> 1.00E-4	> 1.00E-4
SK-MEL-5	0.679	2.836	2.790	2.497	2.469	1.769	1.680	98	84	83	51	46	1.36E-5	> 1.00E-4	> 1.00E-4
UACC-257	1.088	2.302	2.280	2.347	2.374	1.934	2.074	98	104	106	70	81	> 1.00E-4	> 1.00E-4	> 1.00E-4
UACC-62	0.834	3.040	3.030	2.730	2.936	1.406	1.630	100	86	95	26	36	4.50E-6	> 1.00E-4	> 1.00E-4
Ovarian Cancer															
IGROV1	0.614	2.171	2.058	1.672	1.709	1.420	1.440	93	68	70	52	53	> 1.00E-4	> 1.00E-4	> 1.00E-4
OVCAR-3	0.500	1.734	1.757	1.593	1.692	1.080	1.208	102	89	97	47	57	.	> 1.00E-4	> 1.00E-4
OVCAR-4	0.604	1.326	1.273	1.201	1.242	1.026	1.050	93	83	88	58	62	> 1.00E-4	> 1.00E-4	> 1.00E-4
OVCAR-5	0.704	1.648	1.570	1.625	1.557	1.575	1.590	92	98	90	92	94	> 1.00E-4	> 1.00E-4	> 1.00E-4
OVCAR-8	0.501	2.179	2.200	2.218	2.242	1.812	2.035	101	102	104	78	91	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.525	1.910	1.924	1.825	1.851	1.541	1.593	101	94	96	73	77	> 1.00E-4	> 1.00E-4	> 1.00E-4
SK-OV-3	0.965	2.344	2.265	2.259	2.208	2.348	2.221	94	94	90	100	91	> 1.00E-4	> 1.00E-4	> 1.00E-4
Renal Cancer															
786-0	0.688	2.348	2.169	2.284	2.209	2.517	2.378	89	96	92	110	102	> 1.00E-4	> 1.00E-4	> 1.00E-4
A498	1.433	2.016	1.973	2.014	1.889	1.909	1.927	93	100	78	82	85	> 1.00E-4	> 1.00E-4	> 1.00E-4
ACHN	0.468	2.005	1.881	1.817	1.861	1.252	1.438	92	88	91	51	63	> 1.00E-4	> 1.00E-4	> 1.00E-4
RXF 393	0.889	1.677	1.669	1.672	1.651	1.615	1.525	99	99	97	92	81	> 1.00E-4	> 1.00E-4	> 1.00E-4
SN12C	0.730	2.811	2.782	2.798	2.762	2.381	2.453	99	99	98	79	83	> 1.00E-4	> 1.00E-4	> 1.00E-4
TK-10	1.141	2.387	2.338	2.634	2.642	2.286	2.366	96	120	120	92	98	> 1.00E-4	> 1.00E-4	> 1.00E-4
UO-31	0.869	2.383	2.190	2.038	2.090	1.611	1.818	87	77	81	49	63	.	> 1.00E-4	> 1.00E-4
Prostate Cancer															
PC-3	0.617	1.893	1.928	1.938	1.954	1.402	1.309	103	104	105	61	54	> 1.00E-4	> 1.00E-4	> 1.00E-4
DU-145	0.444	1.843	1.881	1.840	1.846	1.434	1.420	103	100	100	71	70	> 1.00E-4	> 1.00E-4	> 1.00E-4
Breast Cancer															
MCF7	0.382	2.362	2.117	1.848	1.933	1.110	1.123	88	74	78	37	37	4.80E-6	> 1.00E-4	> 1.00E-4
MDA-MB-231/ATCC	0.774	1.788	1.869	1.727	1.819	1.347	1.358	108	94	103	56	58	> 1.00E-4	> 1.00E-4	> 1.00E-4
HS 578T	1.046	1.721	1.679	1.634	1.633	1.666	1.666	94	87	87	92	92	> 1.00E-4	> 1.00E-4	> 1.00E-4
BT-549	1.111	2.415	2.263	2.310	2.314	2.582	2.261	88	92	92	113	88	> 1.00E-4	> 1.00E-4	> 1.00E-4
T-47D	0.835	1.895	1.783	1.552	1.667	1.218	1.266	89	68	78	36	41	4.70E-6	> 1.00E-4	> 1.00E-4
MDA-MB-468	0.681	1.602	1.599	1.619	1.625	1.603	1.457	100	102	102	100	84	> 1.00E-4	> 1.00E-4	> 1.00E-4



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5. Computational studies

The spirobibenzopyrans used for the studies namely: CHP-5Cl-SAL, and CHP-5MO-SAL were modelled using GaussView (5.0.8) [5]. The energy minimization of these molecules has been carried out using DFT theory in Gaussian 09 [6], along with frequency studies. The 10 spirobibenzopyrans selected for the *in vitro* analysis were then evaluated for their drug likeness by testing their Lipinski's parameters at:

http://www.scfbioiitd.res.in/software/drugdesign/lipinski.jsp [7,8].

Label	Experimental	Gaussian	
H-12	7.20	7.54	
H-10	7.10	7.47	
H-11	6.95	7.36	
H-13	6.80	7.15	
H-8	6.70	7.05	
H-6	2.40	2.70	3.28
H-3	2.60	2.57	2.88
H-4	2.10	1.97	
H-5	1.55	1.62	

SD table VII: ^{1}H-NMR comparison for CHP-SAL

Bond lengths (in Å)	EXPT	Gaussian
Cl1-C1	1.75	1.76
O1-C4	1.37	1.37
O1-C5	1.44	1.44
C1-C9	1.36	1.39
C1-C2	1.37	1.39
C2-C3	1.40	1.40
C3-C4	1.39	1.40
C3-C6	1.45	1.45
C4-C8	1.38	1.39
C5-C7	1.51	1.52
C6-C7	1.33	1.34
C7-C10	1.51	1.51
C8-C9	1.33	1.39
C10-C11	1.53	1.56
C11-C11	1.51	1.53

SD table VIIIa: Bond lengths comparison for CHP-5Cl-SAL

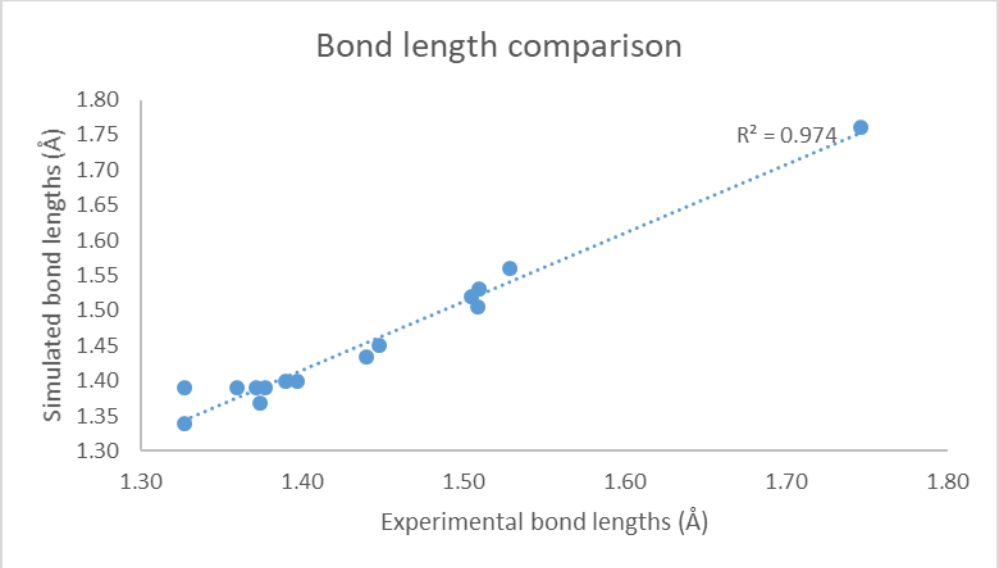

Figure III: Bond lengths comparison for CHP-5Cl-SAL with regression analysis

Bond angles (in degrees)	EXPT	Gaussian
C4-O1-C5	118.9	119.2
C9-C1-C2	121.8	121.2
C9-C1-Cl1	119.2	119.4
C2-C1-Cl1	119.0	119.4
C1-C2-C3	119.7	119.8
C4-C3-C2	118.0	118.7
C4-C3-C6	117.5	117.7
C2-C3-C6	124.4	123.5
O1-C4-C8	117.1	118.0
O1-C4-C3	121.2	120.7
C8-C4-C3	121.6	121.2
O1-C5-O1	107.5	108.3
O1-C5-C7	113.2	112.8
O1-C5-C7	103.4	104.6
C7-C5-C7	116.2	114.3
C7-C6-C3	122.0	121.7
C6-C7-C5	119.2	118.5
C6-C7-C10	123.8	124.0
C5-C7-C10	116.9	117.2
C4-C8-C9	119.2	119.7
C1-C9-C8	119.6	119.4
C7-C10-C11	113.1	114.9
C11-C11-C10	115.2	113.8

SD table VIIIb: Bond angles comparison for CHP-5Cl-SAL

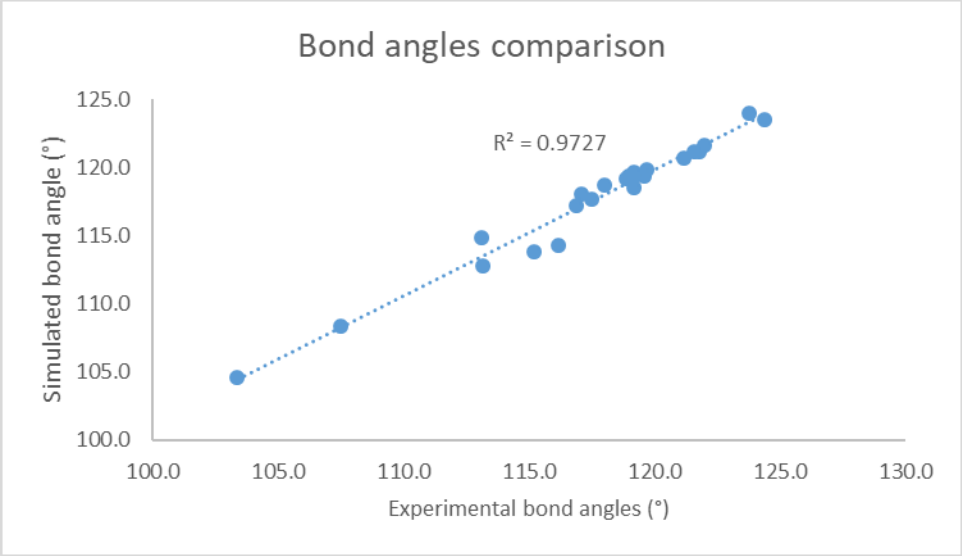

Figure IV: Bond angles comparison for CHP-5Cl-SAL with regression analysis

Bond lengths (in Å)	EXPT	Gaussian
O2-C21	1.38	1.38
O2-C1	1.44	1.43
O1-C2	1.38	1.37
O1-C1	1.43	1.43
O3-C5	1.37	1.37
O3-C22	1.38	1.41
C8-C9	1.31	1.34
C8-C7	1.45	1.45
C7-C6	1.38	1.40
C7-C2	1.40	1.40
C5-C6	1.38	1.39
C5-C4	1.39	1.40
C2-C3	1.37	1.39
C9-C1	1.50	1.51
C9-C10	1.51	1.51
C1-C14	1.52	1.52
C21-C20	1.38	1.39
C21-C16	1.41	1.40
C14-C15	1.32	1.34
C14-C13	1.51	1.50
C3-C4	1.39	1.39
C11-C12	1.52	1.53
C11-C10	1.53	1.56
C20-C19	1.41	1.39
C15-C16	1.44	1.45

C16-C17	1.40	1.40
C12-C13	1.54	1.56
C17-C18	1.37	1.39
C18-C19	1.39	1.40
C18-O4	1.48	1.37
O4-C23	1.42	1.41

SD table IXa: Bond lengths comparison for CHP-5MO-SAL

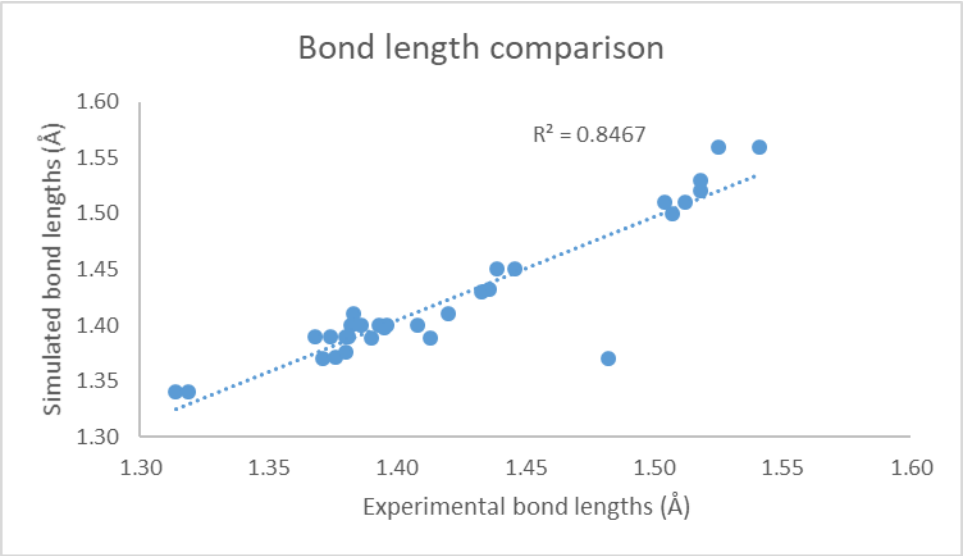

Figure V: Bond lengths comparison for CHP-5MO-SAL with regression analysis

Bond angles (in degrees)	EXPT	Gaussian
C21-O2-C1	120.0	121.0
C2-O1-C1	119.4	117.9
C5-O3-C22	118.3	118.0
C9-C8-C7	122.4	121.3
C6-C7-C2	119.1	119.1
C6-C7-C8	123.6	123.3
C2-C7-C8	117.1	117.5
O3-C5-C6	115.7	115.5
O3-C5-C4	125.1	124.7
C6-C5-C4	119.2	119.7
C5-C6-C7	121.0	120.3
C3-C2-O1	118.1	118.2
C3-C2-C7	120.4	120.7
O1-C2-C7	121.2	120.9
C8-C9-C1	119.6	119.1
C8-C9-C10	123.1	125.1
C1-C9-C10	117.3	116.5
O1-C1-O2	108.0	108.8

O1-C1-C9	113.1	112.2
O2-C1-C9	103.7	103.0
O1-C1-C14	104.1	105.4
O2-C1-C14	114.1	112.9
C9-C1-C14	114.1	114.4
O2-C21-C20	116.4	118.2
O2-C21-C16	120.1	120.8
C20-C21-C16	123.3	120.7
C15-C14-C13	123.7	121.1
C15-C14-C1	119.7	119.2
C13-C14-C1	116.6	116.5
C2-C3-C4	119.7	119.7
C5-C4-C3	120.4	120.4
C12-C11-C10	114.5	114.0
C21-C20-C19	116.9	119.6
C9-C10-C11	112.4	113.0
C14-C15-C16	121.6	122.7
C17-C16-C21	117.6	119.3
C17-C16-C15	123.2	123.4
C21-C16-C15	119.2	117.2
C11-C12-C13	114.1	115.6
C14-C13-C12	113.2	113.0
C18-C17-C16	120.7	120.1
C17-C18-C19	120.9	119.7
C18-C19-C20	120.6	120.5

SD table IXb: Bond angles comparison for CHP-5MO-SAL

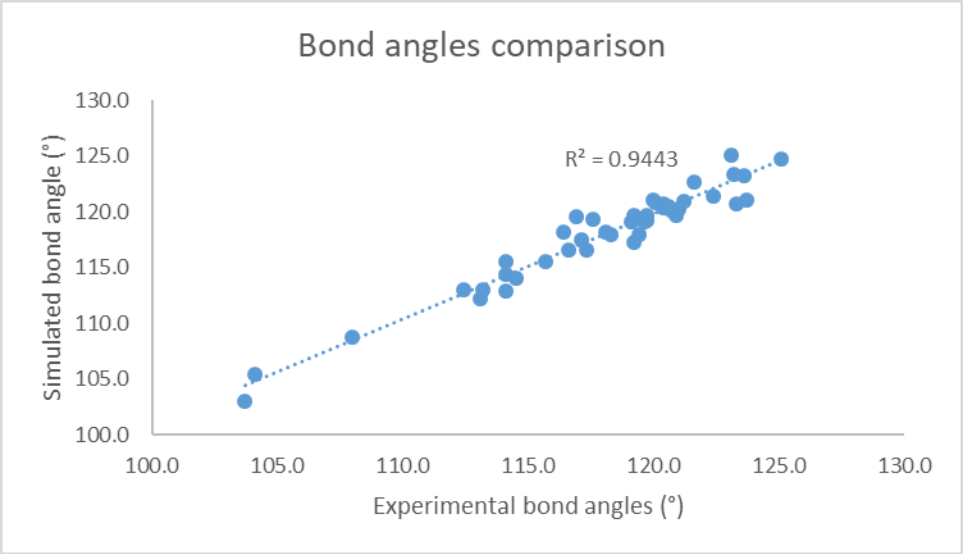

Figure VI: Bond angles comparison for CHP-5MO-SAL with regression analysis

SD Table X. Regression analysis of the observed IR values vs the computed IR values

Molecule	R^2 value for Observed IR vs Computed IR
CHP-5MO-SAL	0.8176
CHP-5Cl-SAL	0.7940

SD Table XI. Drug likeness score of the spirobibenzopyrans on the basis of Lipinski parameters

Spirobibenzopyrans	Molecular mass	No. of hydrogen bond donors	No. of hydrogen bond acceptors	Log P	Molar refractivity
CHP-SAL	302	0	2	5.21	91.29
CHP-4MO-SAL	362	0	4	5.23	104.40
CHP-5Cl-SAL	371	0	2	4.97	95.45
CHP-5MO-SAL	362	0	4	5.23	104.40
CHP-DiCl-SAL	440	0	2	4.73	99.61
CHX-SAL	288	0	2	4.82	86.68
CHX-4MO-SAL	348	0	4	4.84	99.78
CHX-5MO-SAL	348	0	4	4.84	99.78
CHX-5Cl-SAL	357	0	2	4.58	90.83
CHX-DiCl-SAL	426	0	2	4.34	94.99

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