Tetracycline analogues with a selective inhibitory effect on HIF-1α

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

Supporting Information

General Experimental Details

All reagents and solvents used were supplied from commercial sources unless otherwise indicated. Reactions requiring anhydrous conditions were conducted in glassware, which had been oven-dried overnight and used the following day. All reactions were carried under dry N_2 conditions unless otherwise stated. All reactions were monitored by analytical thin-layer chromatography (TLC) performed using indicated solvent on silica gel 60 (0.25 mm). TLC plates were visualized using UV light (254 or 360nm) and/or staining with a cerium sulfate-ammonium molybdate solution or basic potassium permanganate $KMnO_4$ followed by heating. LC-MS, liquid chromatography coupled with mass spectrophotometer, was also used to monitor the progress of the reactions. Solvents were removed by rotary evaporator at or below 40 ºC and the compounds further dried using low-pressure vacuum pumps. Compounds with low boiling points such as bromo-pentadiene, pendienol and the trienes were dried at 100 mmHg at 30 ºC. An immersion cooler was used to perform overnight reactions at very low temperatures e.g. -45 ºC. The purification of the compounds was achieved by column chromatography using silica gel (230 – 400mesh). ^1H and ^{13}C NMR were recorded at 400MHz or 500MHz for ^1H NMR and 100MHz or 125MHz for ^{13}C NMR. Chemical shifts (δ H) are quoted in ppm (parts per million) and referenced to $CDCl_3$ residual chloroform signal ^1H δ = 7.26, ^{13}C δ = 77.2 or *d6*-DMSO residual dimethyl-sulphoxide signal ^1H δ = 2.54, ^{13}C δ = 40.45. Multiplicities in ^1H NMR spectra are quoted as: s = singlet, d = doublet, q = quartet, m = multiplet, dd = double doublet, ddd = double double doublet, dt = double triplet, td = triple doublet, ddt = double double triplet. High resolution mass spectra (HRMS) were obtained on a mass spectrometer coupled with to LC using electrospray (ES) ionization and time-of-flight (TOF) mass spectrometry. Infrared spectra were recorded 1000 using neat conditions. All the reactions were carried out under N_2 flow, and in anhydrous conditions and dry solvents, unless water was used as solvent or co-solvent.

High Throughput Screening Protocol of Tetracycline Analogues

HIF-1 targeted cell-based high-throughput screens (HTS) utilise the ability of HIF-1 to bind to the hypoxia responsive element (HRE), a recognition sequence in the DNA, in order to trigger transcription. Generally, almost all mammalian cell-lines that have been deprived of oxygen, either under natural or induced conditions, respond by inducing HIF-1 transcriptional activity. Cell-based screens are performed by growing cells under hypoxic conditions (0.1-1% O_2) or by treating them with HIF-1 inducers, such as CoCl and DFO (desferoxamine). It is important to note that hypoxia mimetic agents do not mimic the hypoxic state overall but simply work as HIF-1α activators, and an understanding of this is crucial for interpreting the results.

Luciferase is the most commonly used reporter gene in screening assays. It offers easy measurement by non-invasive imaging of bioluminescence. One way it can be introduced is by stable transfection of HRE-luciferase reporter plasmids in cancer cell lines. In his review, Melillo has observed that this technique cannot be compared with transient transfection experiments, but is still robust enough to be used in HTS. The technique was validated initially by comparing the induction of luciferase expression when U251-HRE cells generated in Melillo's lab were subjected to hypoxia. An 8- to 12- fold induction was noted compared with untreated normoxic cells.

The detailed cell-based HTS protocol has been reported in Melillo's review. U251 human glioma cells co-transfected with pGL2-TK-HRE containing the inducible nitric oxide synthase (iNOS). The cells are maintained under normoxic conditions and hypoxia is induced by flushing the incubating flask with 1% O_2, 5%CO_2, and 94% N_2. Plasmids with mutated HRE (p-GL3-HRE) containing luciferase were used to transfect U251 cells which were employed as a secondary screen to evaluate the specificity for HIF-1 inhibition. A bright luciferase reagent is added, and, after 3 min, luminescence is measured. The toxicity of the compounds is also assayed in parallel using a fluorescent dye exclusion technique. When multiple doses of the compounds are used, the ratio of the EC_{50} observed in control versus HRE cells (e.g., U251-pGL3/U251-HRE) sould provide a fairly reliable indicator of specificity, as well as a measure of toxicity of the compounds.

Cell-based HIF-1–targeted HTS also allows for the identification of small molecules that inhibit unidentified components of the hypoxic cell signaling pathway. As a result, a number of validation assays are required to fully elucidate the mechanism of action of potential inhibitors identified in the HTS.

Hits from the HTS are first evaluated for their effect on inducing messenger RNA (mRNA) expression of endogenous HIF-1 target genes in hypoxic cells. A number of genes that are generally expressed in a HIF-1-dependent fashion in the majority of mammalian cells, such as vascular endothelial growth factor (VEGF), glucose transporter 1 (Glut-1) and glycolytic enzymes are assessed.

The following experiments were carried out in Professor G. Melillo's lab and the experimental procedures are reported as previously described in Cell Cycle 5:16, 1847-1853, 15 August 2006.

Cell Culture and Reagents

U251 human glioma cells were maintained in RPMI 1640 medium containing 5% FBS and 2 mM glutamine in a humidified incubator at 37℃ in 5% CO2. Stably transfected cell lines,

U251-HRE and U251-pGL3, were maintained as described before with 100 μg/ml of G418.16 293 Human embryonic kidney cells were maintained in DMEM medium containing 10% FBS. For hypoxic conditions, cells were cultured in an Invivo2 400 hypoxic workstation (Ruskin Technologies Cincinnati, OH) at an oxygen concentration of 1%. Compounds for screening were obtained from the Developmental Therapeutics Program, NCI.

Plasmids and Proteins

The bHLH (amino acids 1–86) and PAS-A (amino acids 86–165) domains of the human HIF-1α cDNA were PCR amplified and cloned into pET28b(+)-His tag expression vector (Novagen, Madison, WI). For expression in mammalian cells, the PAS-A and bHLH-PAS (amino acids 1–380) domains were cloned into pTriEx-4 vector (Novagen). The PAS-A (amino acids 159–240) and bHLH-PAS (amino acids 1–475) domains of the human HIF-1β cDNA were PCR amplified and cloned into pFlag1 expression vector (Sigma, St. Louis, MO). All plasmids were verified by sequencing (LMT, SAIC Frederick, Inc, NCI-Frederick).

Recombinant HIF-1α proteins were expressed in E. coli BL21 (DE3) cells with isopropyl-β-D-thiogalactopyranoside (IPTG). HIF-1α recombinant proteins were extracted using a commercially available kit (Bugbuster protein extraction regent, Novagen) following the manufacturer's protocol and were purified by FPLC with HisTrapTM-HP (Amersham Biosciences, Uppsala, Sweden) and by HPLC with C18 column (4.6 x 250 mm, VydacTM) (Grace Vydac, Columbia, MD). The amino acid sequence of N-terminal end of HIF-1α-PAS-A protein was confirmed by microsequencing. Recombinant HIF-1β proteins were expressed in E. coli DH5α cells in the presence of IPTG. The soluble fractions of HIF-1β proteins were prepared by CelLyticTM B-II (Sigma) regent and purified by anti-Flag-M2 agarose affinity chromatography (Sigma). The molecular weight of expressed HIF-1α-bHLH, HIF-1α-PAS-A, HIF-1β-PAS-A and HIF-1β-bHLH-PAS protein was 10, 12, 11 and 56 KDa, respectively.

Immunoprecipitation

Purified HIF-1α-PAS-A-His protein and soluble fraction of Flag-HIF-1β-PAS-A were incubated with RIPA buffer for 2 hr at 4 C. The binding complex was pulled down with anti-Flag-M2 monoclonal antibody for 1 hr at 4 ℃ with rotation. Protein complex was immobilized on GammaBindTM G SepharoseTM (Amersham Biosciences, Uppsala, Sweden) with 1% BSA solution for 1 hr. Sepharose beads were extensively washed with 0.1% (w/v) Triton X-100, 50 mM tri-HCl, pH 7.4, 30 mM NaCl, 5 mM EDTA, and protease inhibitors (Roche Diagnostics, Mannheim, Germany).

For immunoprecipitation experiments using U251 cells, nuclear extracts were prepared as previously described. Nuclear proteins (100 μg) were incubated with anti-HIF-1α monoclonal antibody (Novus Biologicals, Littletone, CO) for 2 hr at 4 C and immobilized on GammaBindTM G SepharoseTM for 1 hr. HIF-1α-PAS-A-His and HIF-1β proteins were detected by Immunoblot using anti-His-monoclonal antibody and anti-HIF-1β monoclonal antibody (Novus Biologicals), respectively.

Mammalian Two-Hybrid System

HIF-1α-PAS-A and HIF-1β- PAS-A domains were cloned into pBind and pAct vectors, containing the GAL4 DNA binding domain and VP16 transcriptional activation domain, respectively (Promega, Inc., Madison, WI). HIF-1α-PAS-A and HIF-1β-PAS-A plasmids along with the pG5luc luciferase reporter vector were transfected in HeLa and 293 cells

seeded in a 48-well plate. Cells were incubated for 24 hr at 37 C and luciferase activity was measured using Dual-Luciferase® Reporter assay system (Promega, Inc., Madison, WI). Results of luciferase expression were normalized to protein amount and Renilla luciferase activity. Cells were also transfected with pBind and pAct empty vectors as negative control. Stably transfected cells, 293-P3 and 293-N4 were generated by cotransfection of pBind-HIF-1α-PAS-A/pAct-HIF-1β-PAS-A and empty vectors, respectively.

Transient Transfection Experiments

U251 cells seeded in 48-well plates were transfected with pTriEx-4-HIF-1α-PAS-A, pTriEx-4-HIF-1α-bHLH-PAS and pGL2-TK-HRE plasmid, containing the luciferase reporter gene under control of three tandem copies of a hypoxia responsive element. Eighteen hours following transfection, cells were incubated for 24 hr under normoxic or hypoxic conditions and luciferase activity was measured using Steady Glo luciferase assay reagents (Promega, Inc.). Results of luciferase activity were normalized by protein concentration.

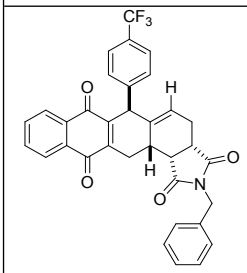
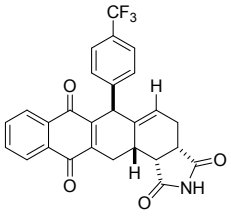
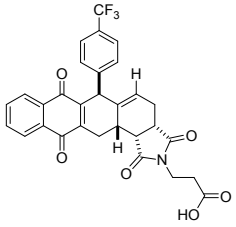
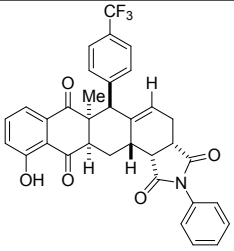
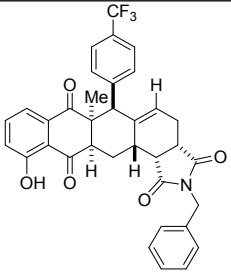
Validation assays to exclude compounds that interfere with the detection system were developed by immobilizing HIF-1α-PAS-A protein, in the absence of HIF-1β-PAS-A, on 96-well plate at 4 ℃ for 16 hr. After blocking with 3% BSA/PBS, compounds were added in 0.5X buffer for 1 hr at room temperature. Anti-His-HRP conjugate/TMB reagent was added to detect HIF-1α-PAS-A-His protein in the absence or presence of test compounds.

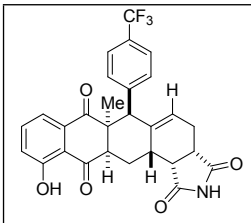
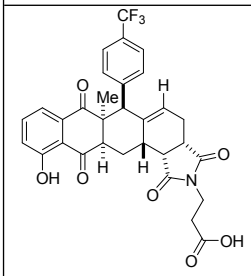
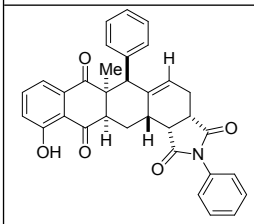
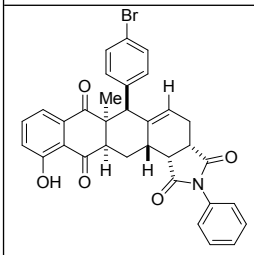
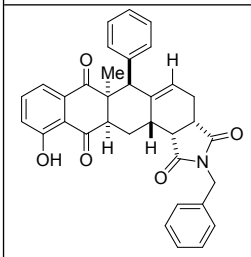
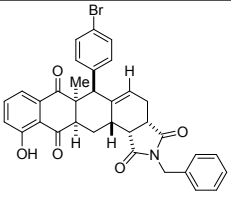
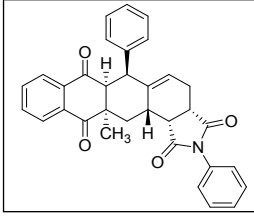
The NCI-diversity set and the “HIF-1 library”, composed of approximately 120 compounds previously identified in a cell-based HTS, were from the Developmental Therapeutics Program, NCI. Final concentration of compounds was 10 μM in 1% DMSO. Inhibitory activity of compounds was compared to DMSO control Compounds that inhibited HIF-1α/HIF-1β complex formation by >50% were further tested using the validation assays described.

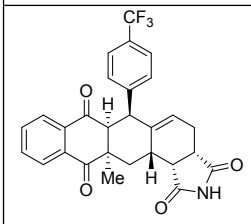
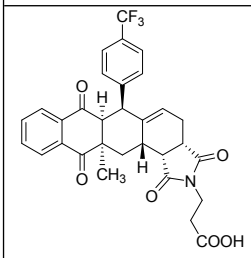
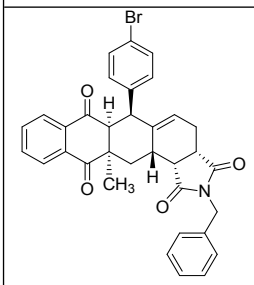
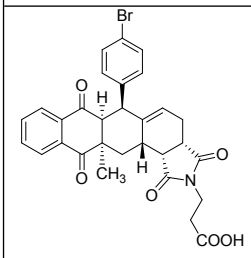
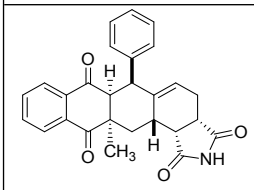
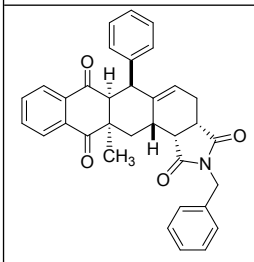
HRE Luciferase Assay

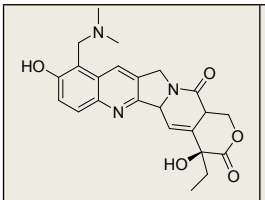
U251-HRE and U251- pGL3 cells were seeded onto 96-well plates the day before treatment. Cells were then cultured for additional 24 hours in the absence or presence of test compounds. Luciferase assay was performed as previously described.16 Luminescence reading was normalized by protein concentration and expressed as relative luciferase unit compared to untreated cells cultured under hypoxia.

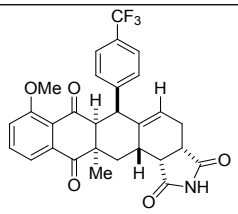
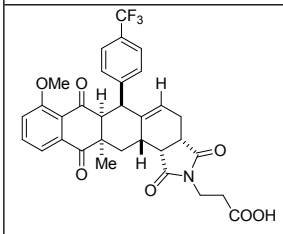
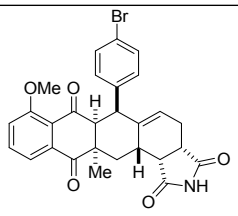
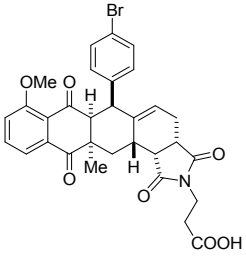
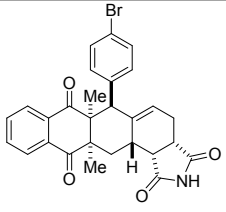
Table S1: Results of the U251-HRE cell-based screen for tetracycline analogues

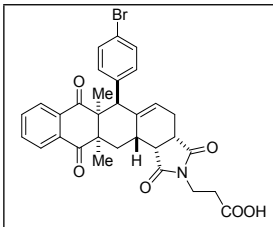
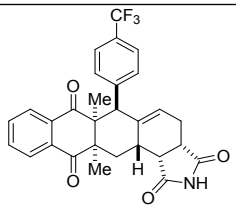
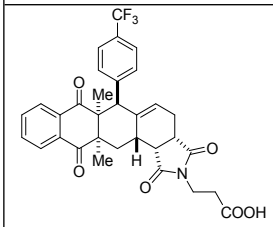
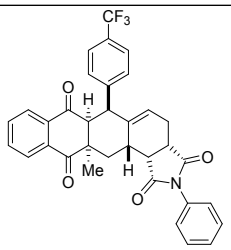
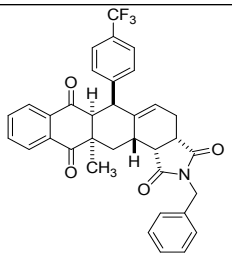
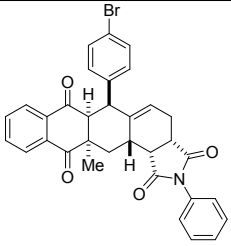
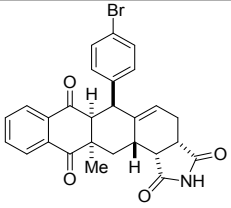
Structure	Code	MW	Formula	EC_{50} HRE (µM)	EC_{50} pGL3 (µM)	pGL3/HRE
	**5.79** [YB021]	567.55	$C_{34}H_{24}F_3NO_4$	>20	>20	<1
	**5.80** [YB027]	477.43	$C_{27}H_{18}F_3NO_4$	>20	>20	<1
	**5.81** [YB028]	549.49	$C_{30}H_{22}F_3NO_6$	>20	>20	<1
	**5.82** [YB022]	585.57	$C_{34}H_{26}F_3NO_5$	>20	>20	<1
	**5.83** [YB023]	599.60	$C_{35}H_{28}F_3NO_5$	>20	>20	<1

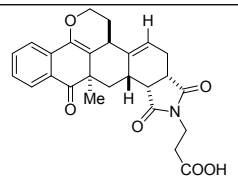
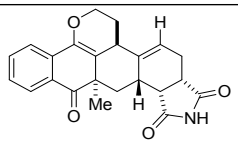
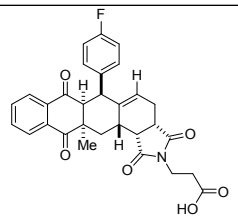
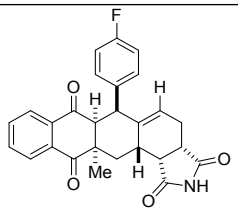
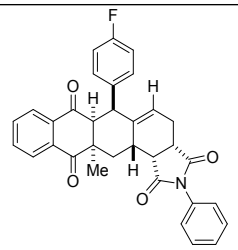
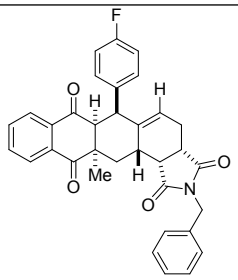
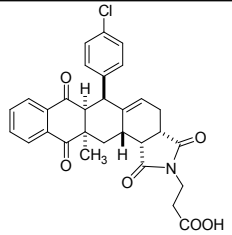
	**5.84** [YB024] **5a**	509.47	$C_{28}H_{22}F_3NO_5$	6.7	>20	>3
	**5.85** [YB025]	581.54	$C_{31}H_{26}F_3NO_7$	>20	>20	<1
	**5.86** [YB029]	517.57	$C_{33}H_{28}NO_5$	>20	>20	<1
	**5.87** [YB030]	596.47	$C_{33}H_{26}BrNO_5$	>20	>20	<1
	**5.88** [YB031]	531.60	$C_{34}H_{29}NO_5$	>20	>20	<1
	**5.89** [YB032]	610.49	$C_{34}H_{28}BrNO_5$	>20	>20	<1
	**5.98** [YB026]	501.57	$C_{33}H_{27}NO_4$	>20	>20	<1

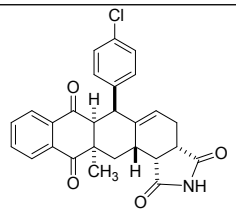
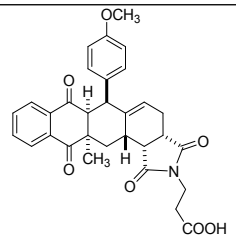
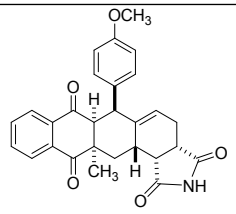
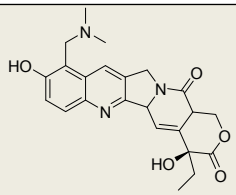
	**5.99** [YB036] **5b**	493.47	$C_{28}H_{22}F_3NO_4$	2.3	>20	>8.6
	**5.100** [YB037]	565.53	$C_{31}H_{26}F_3NO_6$	>20	>20	<1
	**5.101** [YB038]	594.49	$C_{34}H_{28}BrNO_4$	>20	>20	<1
	**5.102** [YB039] **5c**	576.43	$C_{30}H_{26}BrNO_6$	1.4	>20	>14
	**5.103** [YB040]	425.47	$C_{27}H_{23}NO_4$	>20	>20	<1
	**5.104** [YB041]	515.60	$C_{34}H_{29}NO_4$	>20	>20	<1

	**NSC-2609699**	423.46	$C_{23}H_{25}N_3O_5$	0.012	>20	>1700

Structure	Code	MW	Formula	EC_{50} HRE (µM)	EC_{50} pGL3 (µM)	pGL3/HRE
	**5.90** [YB071] **5d**	523.50	$C_{29}H_{24}F_3NO_5$	6.7	>20	>3
	**5.91** [YB072]	595.56	$C_{32}H_{28}F_3NO_7$	>20	>20	<1
	**5.92** [YB073]	534.40	$C_{28}H_{24}BrNO_5$	>20	>20	<1
	**5.93** [YB074] **5e**	606.46	$C_{31}H_{28}BrNO_7$	15.5	>20	>1.4
	**5.94** [YB077]	518.40	$C_{28}H_{24}BrNO_4$	>20	>20	<1

	**5.95** [YB078]	590.46	$C_{31}H_{26}BrNO_6$	>20	>20	<1
	**5.96** [YB081] **5f**	507.17	$C_{29}H_{24}F_3NO_4$	7.8	>20	>2.7
	**5.97** [YB082]	579.56	$C_{32}H_{28}F_3NO_6$	>20	>20	<1
	**5.105** [YB063a]	569.57	$C_{34}H_{26}F_3NO_4$	>20	>20	<1
	**5.106** [YB063b]	583.60	$C_{34}H_{26}F_3NO_4$	>20	>20	<1
	**5.107** [YB064a]	580.47	$C_{35}H_{26}BrNO_4$	>20	>20	<1
	**5.108** [YB064b]	504.37	$C_{27}H_{22}BrNO_4$	>20	>20	<1

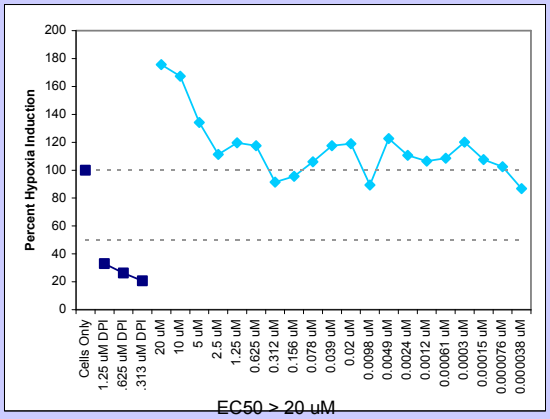
	**5.109** [YB085]	465.50	$C_{26}H_{27}NO_7$	>20	>20	<1
	**5.110** [YB086]	393.43	$C_{23}H_{23}NO_5$	>20	>20	<1
	**5.115** [KSN011] **5g**	515.53	$C_{30}H_{26}FNO_6$	4.1	8.7	2.15
	**5.116** [KSN012]	443.47	$C_{27}H_{22}FNO_4$	>20	>20	<1
	**5.117** [KSN013]	519.56	$C_{33}H_{26}FNO_4$	>20	>20	<1
	**5.118** [KSN014]	533.59	$C_{34}H_{28}FNO_4$	>20	>20	<1
	**5.124** [001-DA-022-01]	531.98	$C_{30}H_{26}ClNO_6$	>20	>20	<1

	**5.125** [001-DA-023-01]	459.92	$C_{27}H_{22}ClNO_4$	>20	>20	<1
	**5.126** [001-DA-025-01]	527.56	$C_{31}H_{29}NO_7$	>20	>20	<1
	**5.127** [001-DA-024-01]	455.50	$C_{28}H_{25}NO_5$	>20	>20	<1
	NSC 2609699	423.46	$C_{23}H_{25}N_3O_5$	0.047	>20	>4200

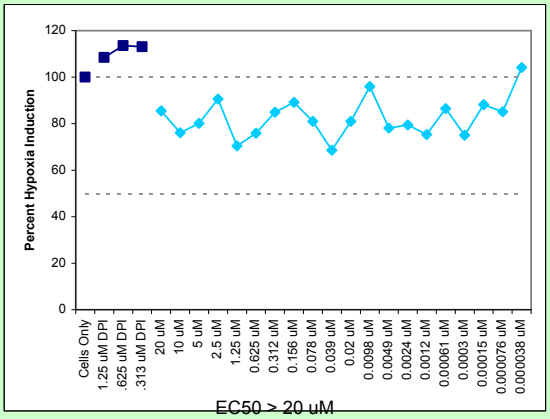
Calculated Values for 20 Dose Titration of NSC# ThurstonYB021 from Well A01 of Plate 3202008921

Exp Date 3/20/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

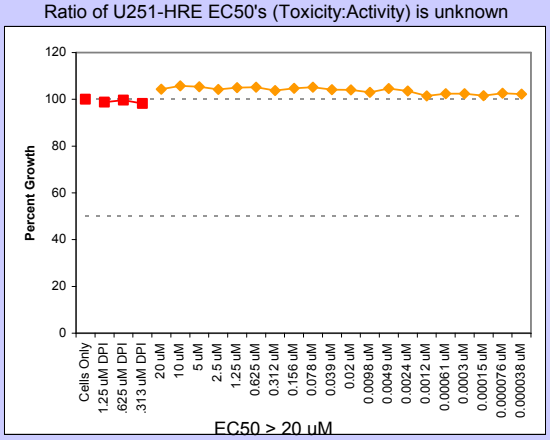


EC50 > 20 uM

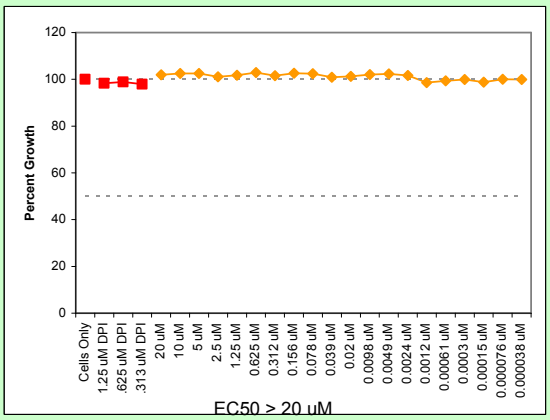


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



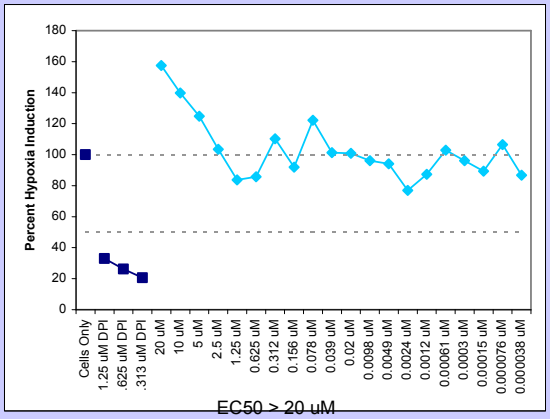
EC50 > 20 uM

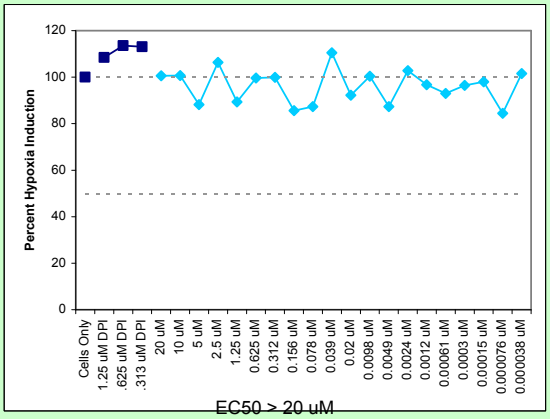
	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	33	26	21	176	167	134	111	120	117	91	96	106	117	119	89	123	111	107	109	120	108	102	87	10
HRE Growth	99	100	98	104	106	105	104	105	105	104	105	105	104	104	103	105	104	101	102	102	102	103	102	10
				Z 'DPI = 0.428								Z Prime = 0.517						Cell Only Ind = 5.217						
PG3 Activity	109	114	113	86	76	80	91	70	76	85	89	81	69	81	96	78	79	75	87	75	88	85	104	10
PG3 Growth	98	99	98	102	102	103	101	102	103	102	103	102	101	101	102	102	102	99	99	100	99	100	100	10

Calculated Values for 20 Dose Titration of NSC# ThurstonYB022 from Well B01 of Plate 3202008921

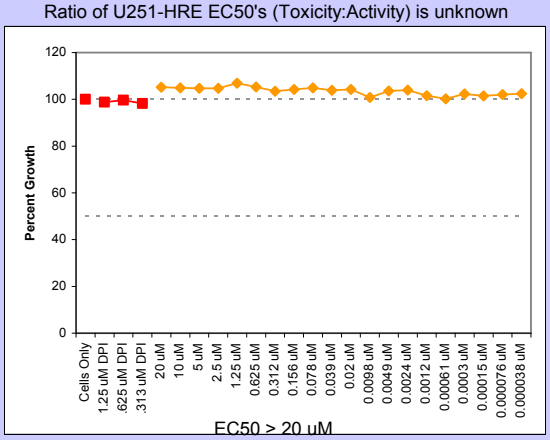
Exp Date 3/20/2008

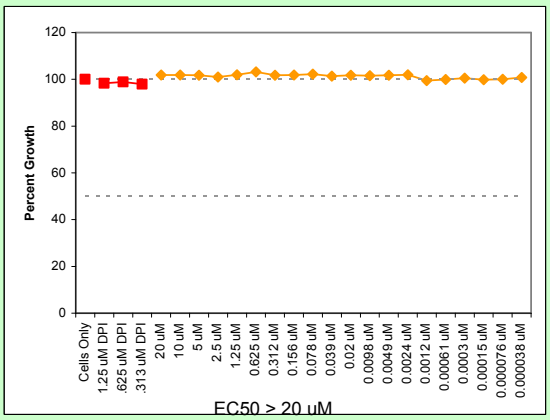
U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**





Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



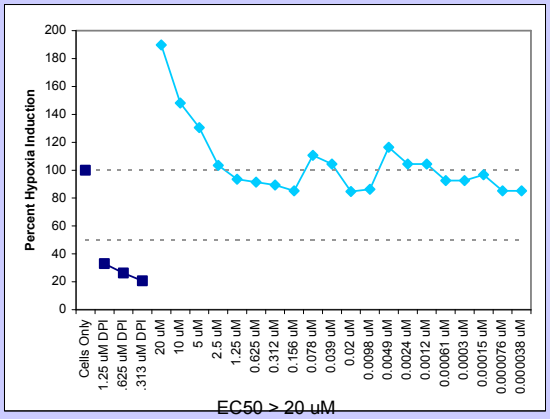


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	33	26	21	158	140	125	103	84	86	110	92	122	101	101	96	94	77	87	103	96	89	107	87	10
HRE Growth	99	100	98	105	105	105	105	107	105	103	104	105	104	104	101	104	104	102	100	102	101	102	102	10
				Z 'DPI = 0.428							Z Prime = 0.517							Cell Only Ind = 5.217						
PG3 Activity	109	114	113	101	101	88	106	89	100	100	86	87	111	92	100	87	103	97	93	96	98	84	102	10
PG3 Growth	98	99	98	102	102	102	101	102	103	102	102	102	101	102	102	102	102	99	100	101	100	100	101	10

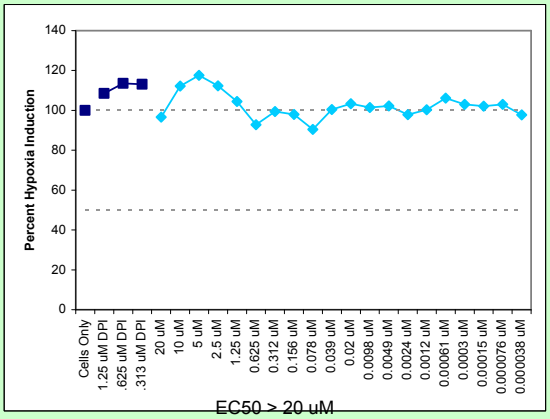
Calculated Values for 20 Dose Titration of NSC# ThurstonYB023 from Well C01 of Plate 3202008921

Exp Date 3/20/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

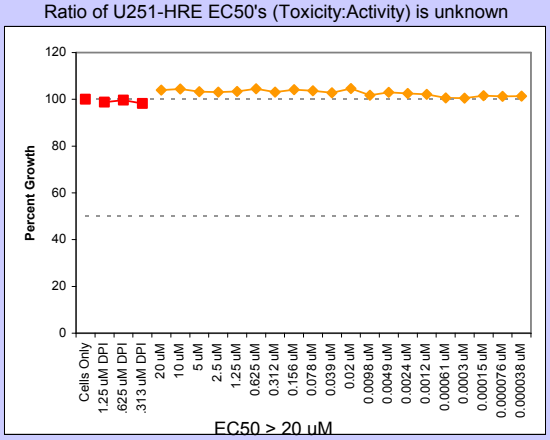


EC50 > 20 uM

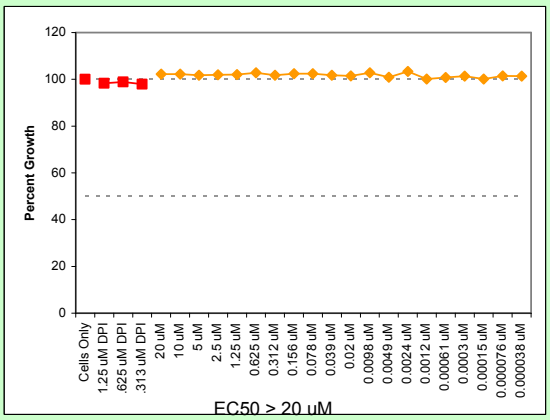


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



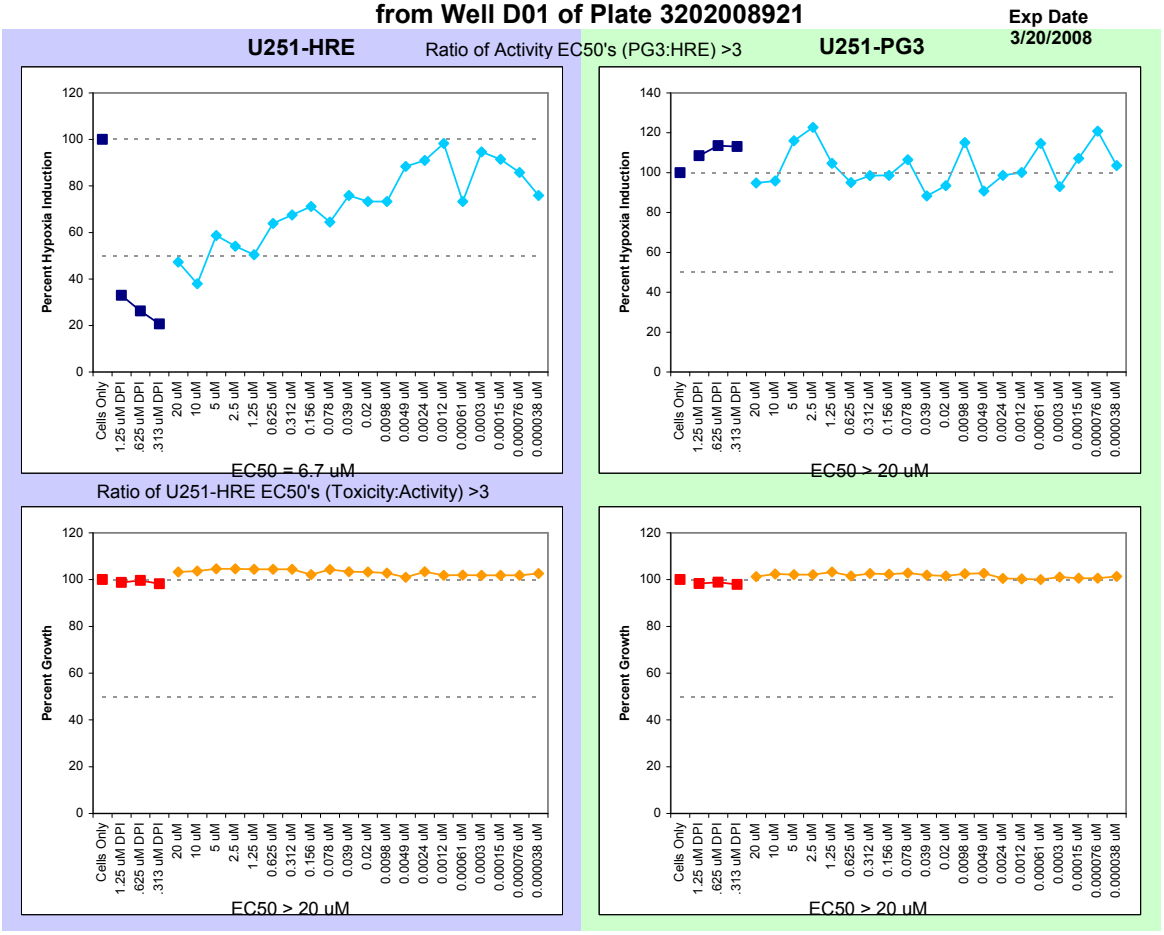
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	33	26	21	190	148	130	103	94	91	89	85	111	104	85	86	116	104	104	93	93	97	85	85	10
HRE Growth	99	100	98	104	104	103	103	103	105	103	104	104	103	105	102	103	103	102	101	100	102	101	101	10
				Z 'DPI = 0.428								Z Prime = 0.517						Cell Only Ind = 5.217						
PG3 Activity	109	114	113	97	112	118	112	105	93	99	98	90	100	103	101	102	98	100	106	103	102	103	98	10
PG3 Growth	98	99	98	102	102	102	102	102	103	102	102	102	102	101	103	101	103	100	101	101	100	101	101	10

5a-yb024

Calculated Values for 20 Dose Titration of NSC# ThurstonYB024
from Well D01 of Plate 3202008921

Exp Date
3/20/2008

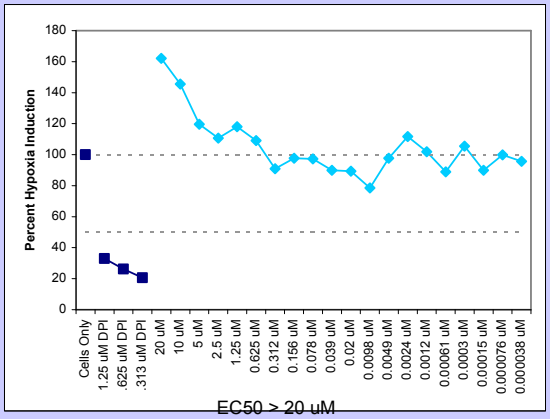


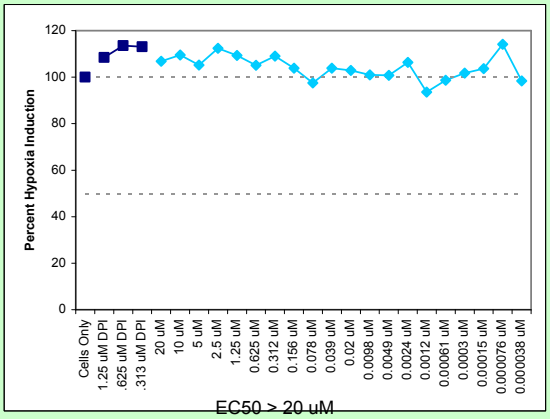
	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	33	26	21	47	38	59	54	50	64	68	71	64	76	73	73	88	91	98	73	95	91	86	76	10
HRE Growth	99	100	98	103	104	105	105	104	104	104	102	104	103	103	103	101	103	102	102	102	102	102	103	10
				Z 'DPI = 0.428							Z Prime = 0.517								Cell Only Ind = 5.217					
PG3 Activity	109	114	113	95	96	116	123	105	95	98	99	106	88	94	115	91	99	100	115	93	107	121	104	10
PG3 Growth	98	99	98	101	102	102	102	103	102	103	102	103	102	102	103	103	100	100	100	101	101	101	101	10

Calculated Values for 20 Dose Titration of NSC# ThurstonYB025 from Well E01 of Plate 3202008921

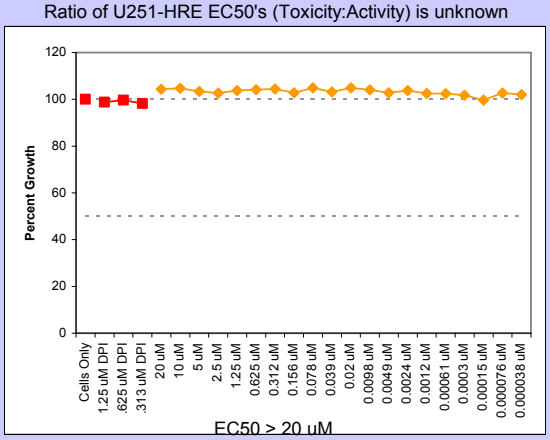
Exp Date 3/20/2008

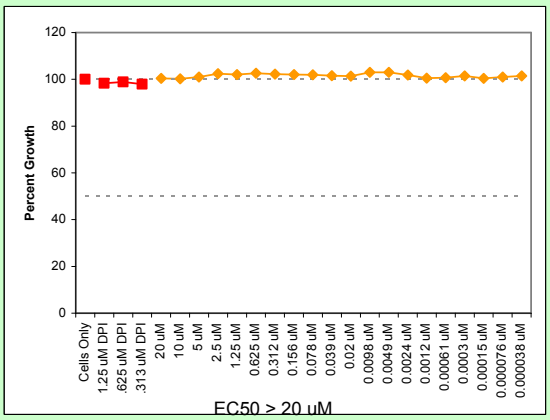
U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**





Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



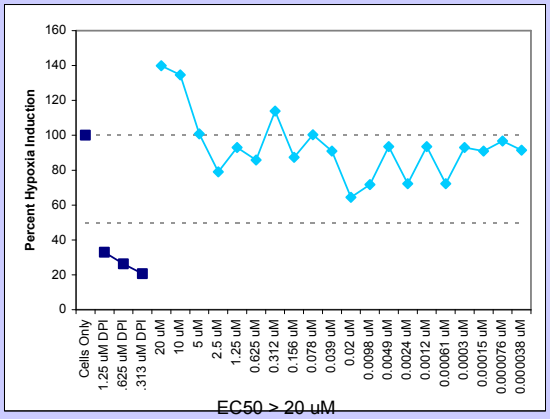


	1.25 uM DPI	625 uM DPI	313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	33	26	21	162	146	120	111	118	109	91	98	97	90	89	78	98	112	102	89	106	90	100	96	10
HRE Growth	99	100	98	104	105	103	103	104	104	104	103	105	103	105	104	103	104	103	102	102	100	103	102	10
				Z 'DPI = 0.428								Z Prime = 0.517							Cell Only Ind = 5.217						
PG3 Activity	109	114	113	107	110	105	112	109	105	109	104	97	104	103	101	101	106	94	99	102	104	114	98	10
PG3 Growth	98	99	98	100	100	101	102	102	103	102	102	102	102	101	103	103	102	100	101	101	100	101	101	10

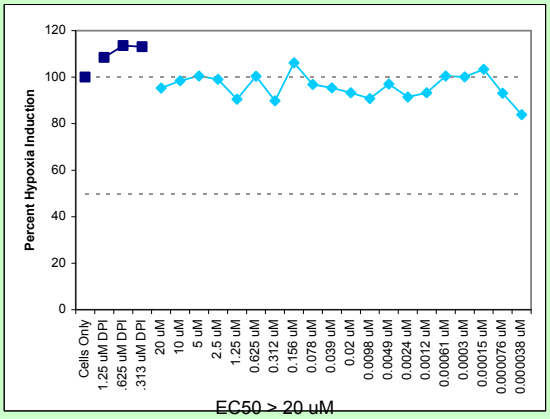
Calculated Values for 20 Dose Titration of NSC# ThurstonYB026 from Well F01 of Plate 3202008921

Exp Date 3/20/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

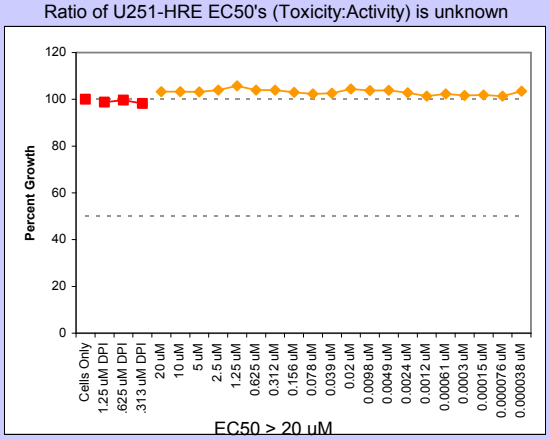


EC50 > 20 uM

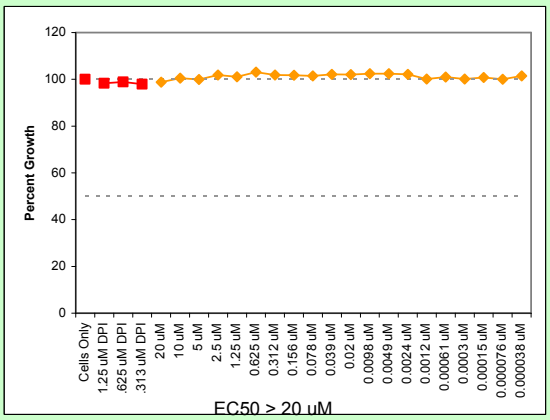


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



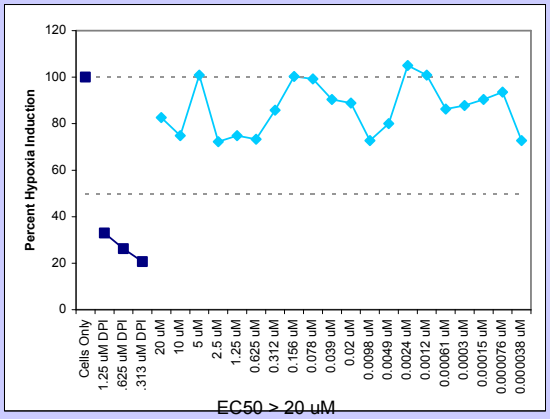
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	33	26	21	140	135	101	79	93	86	114	87	100	91	64	72	94	72	94	72	93	91	97	91	10
HRE Growth	99	100	98	103	103	103	104	106	104	104	103	102	103	104	104	104	103	101	102	102	102	101	103	10
				Z 'DPI = 0.428								Z Prime = 0.517							Cell Only Ind = 5.217					
PG3 Activity	109	114	113	95	98	100	99	91	100	90	106	97	95	93	91	97	91	93	100	100	103	93	84	10
PG3 Growth	98	99	98	99	100	100	102	101	103	102	102	101	102	102	102	102	102	100	101	100	101	100	102	10

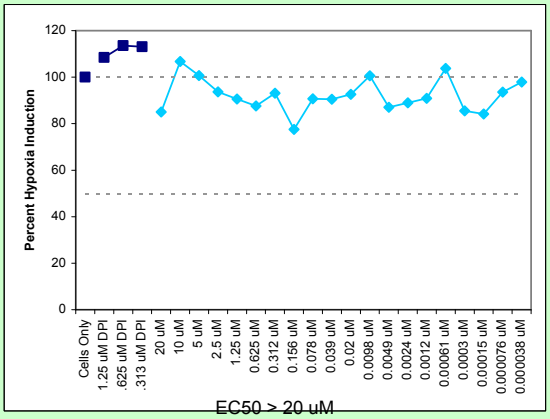
Calculated Values for 20 Dose Titration of NSC# ThurstonYB027 from Well G01 of Plate 3202008921

Exp Date 3/20/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

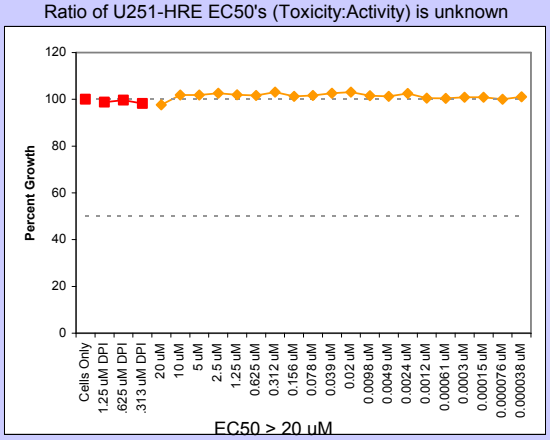


EC50 > 20 uM

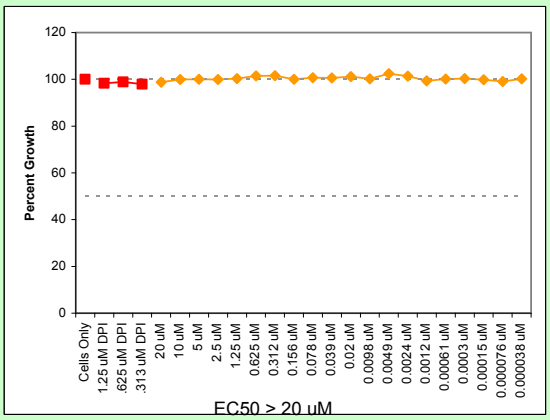


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



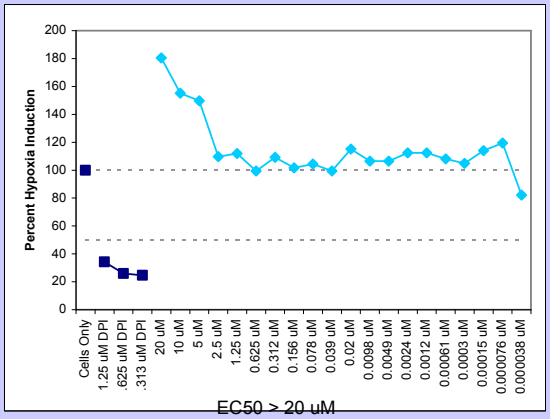
EC50 > 20 uM

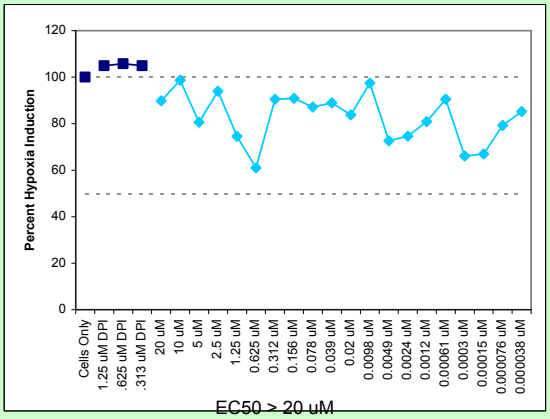
	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	33	26	21	83	75	101	72	75	73	86	100	99	90	89	73	80	105	101	86	88	90	94	73	10
HRE Growth	99	100	98	98	102	102	103	102	102	103	101	102	103	103	102	101	102	101	100	101	101	100	101	10
				Z 'DPI = 0.428								Z Prime = 0.517							Cell Only Ind = 5.217					
PG3 Activity	109	114	113	85	107	101	94	91	88	93	78	91	90	93	101	87	89	91	104	86	84	94	98	10
PG3 Growth	98	99	98	99	100	100	100	100	101	102	100	101	101	101	100	102	101	99	100	100	100	99	100	10

Calculated Values for 20 Dose Titration of NSC# ThurstonYB028 from Well A01 of Plate 3202008928

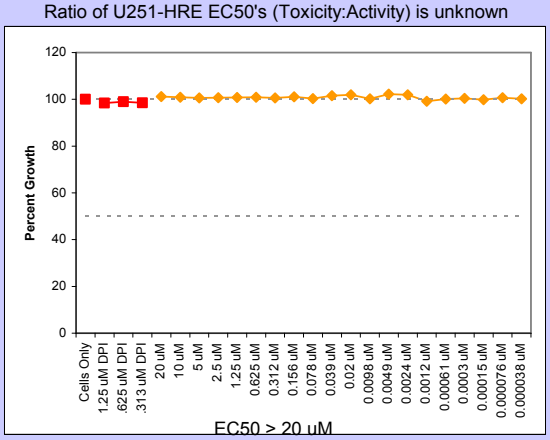
Exp Date 3/20/2008

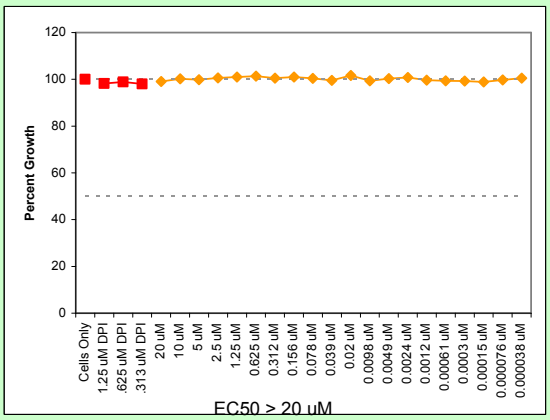
U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**





Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



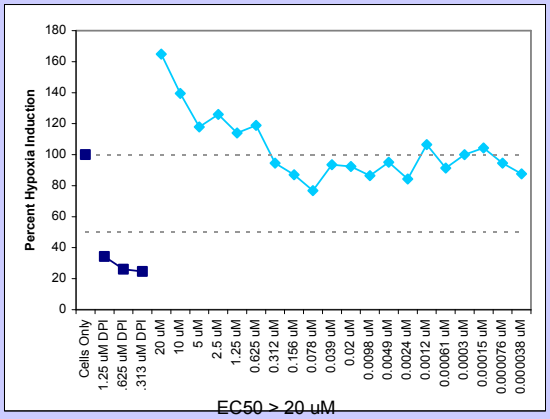


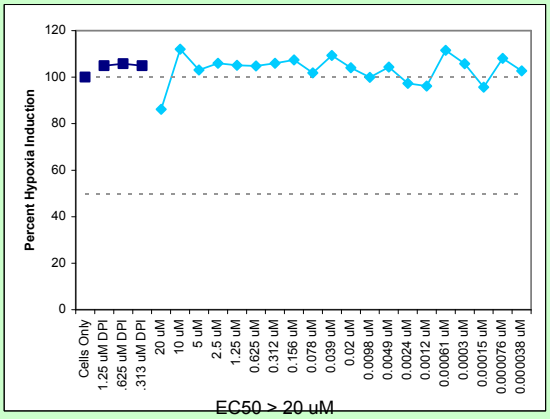
	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	34	26	25	181	155	150	110	112	99	109	102	104	99	115	106	106	112	112	108	105	114	119	82	10
HRE Growth	98	99	99	101	101	101	101	101	101	101	101	100	102	102	100	102	102	99	100	100	100	101	100	10
				Z 'DPI = 0.233							Z Prime = 0.361								Cell Only Ind = 5.017					
PG3 Activity	105	106	105	90	99	81	94	75	61	90	91	87	89	84	97	73	75	81	91	66	67	79	85	10
PG3 Growth	98	99	98	99	100	100	101	101	101	101	101	100	100	102	99	100	101	100	99	99	99	100	100	10

Calculated Values for 20 Dose Titration of NSC# ThurstonYB029 from Well B01 of Plate 3202008928

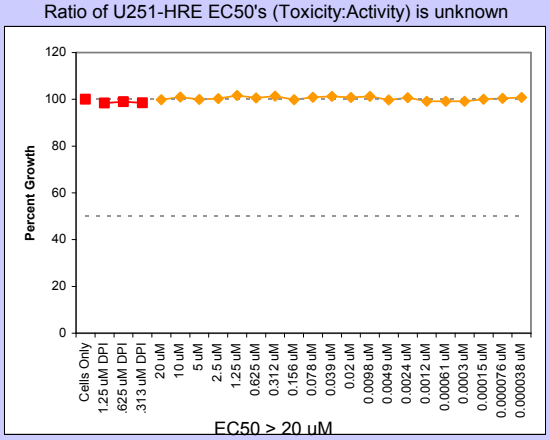
Exp Date 3/20/2008

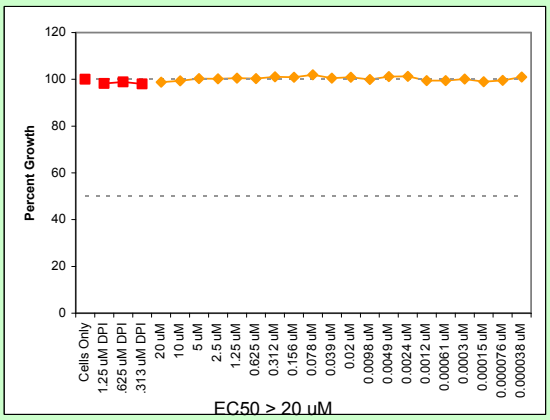
U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**





Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



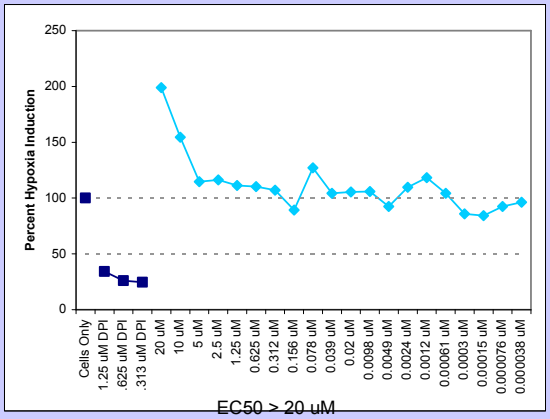


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	34	26	25	165	139	118	126	114	119	95	87	77	94	92	86	95	84	106	91	100	104	95	88	10
HRE Growth	98	99	99	100	101	100	100	102	101	101	100	101	101	101	101	100	101	99	99	99	100	100	101	10
				Z 'DPI = 0.233							Z Prime = 0.361								Cell Only Ind = 5.017					
PG3 Activity	105	106	105	86	112	103	106	105	105	106	107	102	109	104	100	104	97	96	112	106	96	108	103	10
PG3 Growth	98	99	98	99	99	100	100	101	100	101	101	102	101	101	100	101	101	99	99	100	99	100	101	10

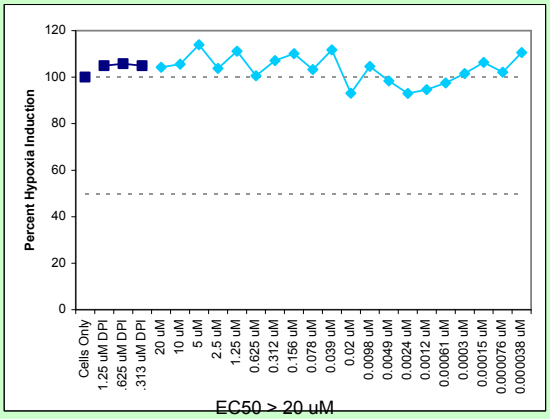
Calculated Values for 20 Dose Titration of NSC# ThurstonYB030 from Well C01 of Plate 3202008928

Exp Date 3/20/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

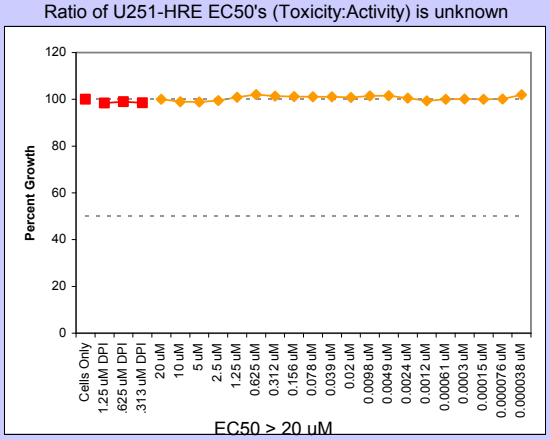


EC50 > 20 uM

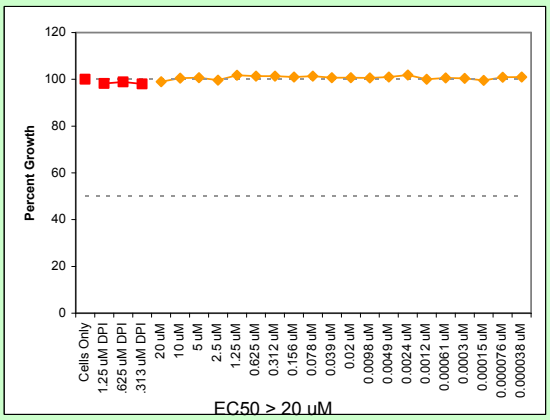


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



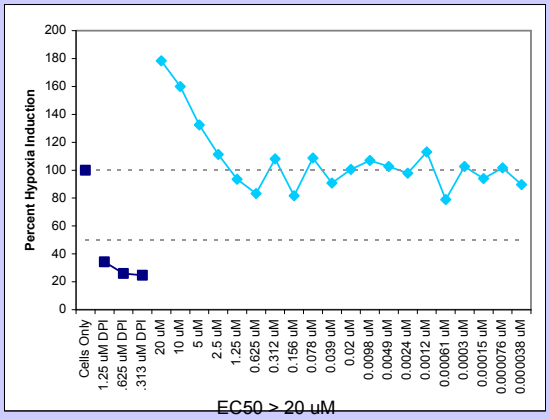
EC50 > 20 uM

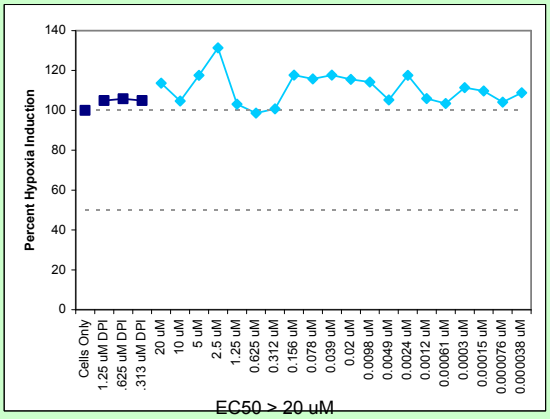
	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	34	26	25	199	155	115	116	111	110	107	89	127	104	105	106	92	110	118	104	86	84	92	96	10
HRE Growth	98	99	99	100	99	99	99	101	102	101	101	101	101	101	101	102	100	99	100	100	100	100	102	10
				Z 'DPI = 0.233				Z Prime = 0.361										Cell Only Ind = 5.017						
PG3 Activity	105	106	105	104	106	114	104	111	101	107	110	103	112	93	105	98	93	95	98	102	106	102	111	10
PG3 Growth	98	99	98	99	101	101	100	102	101	101	101	101	101	101	101	101	102	100	101	100	100	101	101	10

Calculated Values for 20 Dose Titration of NSC# ThurstonYB031 from Well D01 of Plate 3202008928

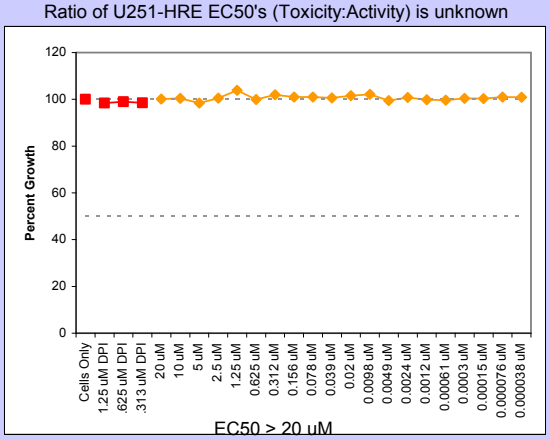
Exp Date 3/20/2008

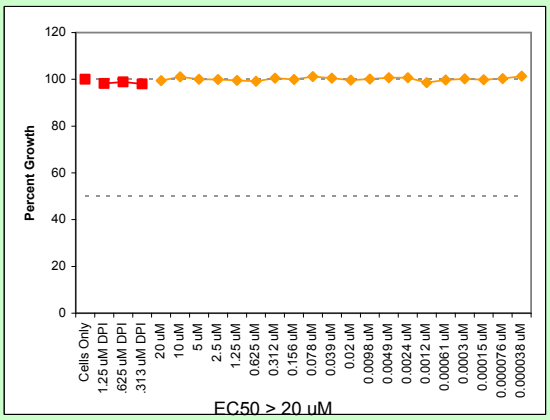
U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**





Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown

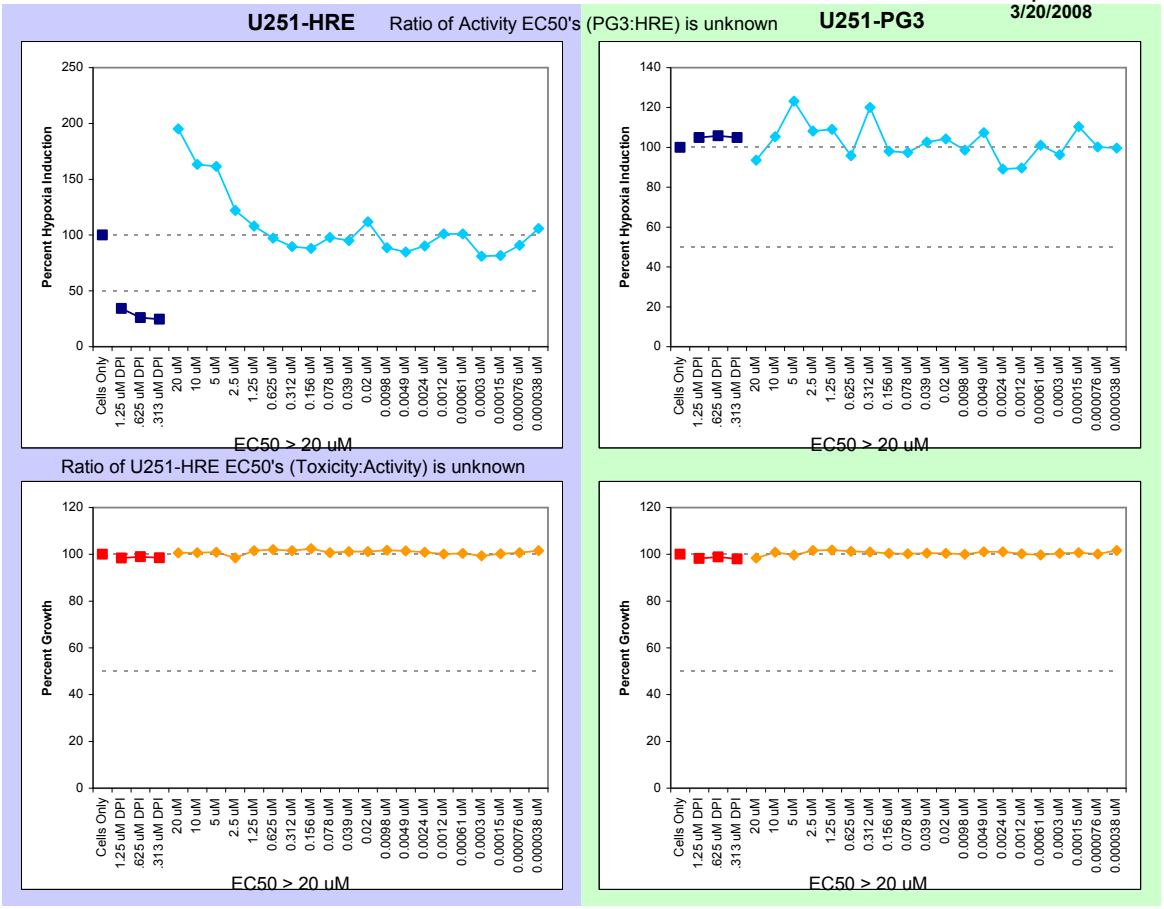




	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	34	26	25	178	160	132	111	94	83	108	82	109	91	101	107	103	98	113	79	103	94	102	90	10
HRE Growth	98	99	99	100	100	98	101	104	100	102	101	101	101	102	102	99	101	100	100	100	100	101	101	10
				Z 'DPI = 0.233							Z Prime = 0.361							Cell Only Ind = 5.017						
PG3 Activity	105	106	105	114	105	118	131	103	99	101	118	116	118	116	114	105	118	106	103	111	110	104	109	10
PG3 Growth	98	99	98	99	101	100	100	100	99	100	100	101	100	100	100	101	101	99	100	100	100	100	101	10

Calculated Values for 20 Dose Titration of NSC# ThurstonYB032 from Well E01 of Plate 3202008928

Exp Date 3/20/2008

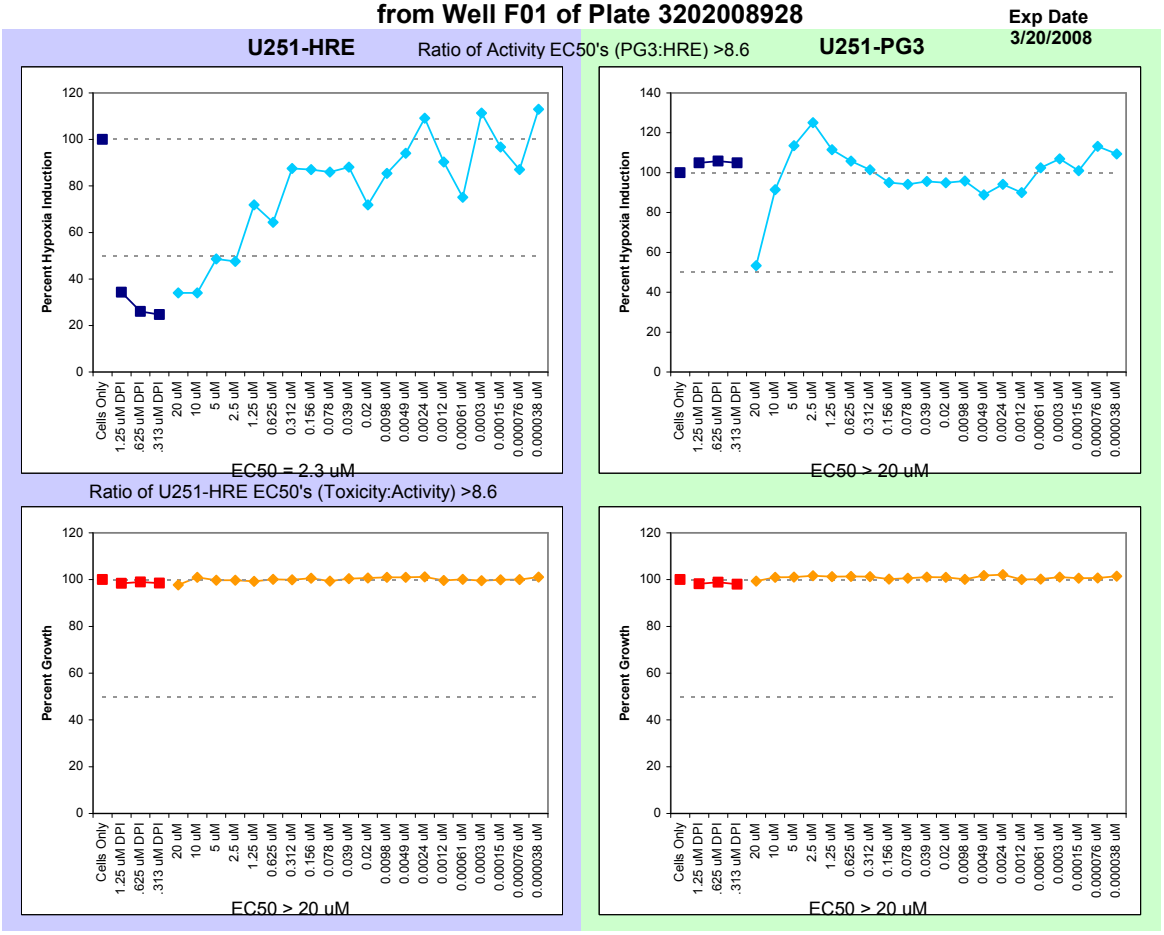


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	34	26	25	195	163	162	122	108	97	90	88	98	95	112	89	85	90	101	101	81	82	91	106	10
HRE Growth	98	99	99	101	101	101	98	102	102	102	102	101	101	101	102	101	101	100	100	99	100	101	102	10
				Z 'DPI = 0.233							Z Prime = 0.361								Cell Only Ind = 5.017					
PG3 Activity	105	106	105	94	105	123	108	109	96	120	98	97	103	104	99	107	89	90	101	96	110	100	100	10
PG3 Growth	98	99	98	98	101	100	102	102	101	101	100	100	101	100	100	101	101	100	100	100	101	100	102	10

5b – yb036

Calculated Values for 20 Dose Titration of NSC# ThurstonYB036 from Well F01 of Plate 3202008928

Exp Date 3/20/2008

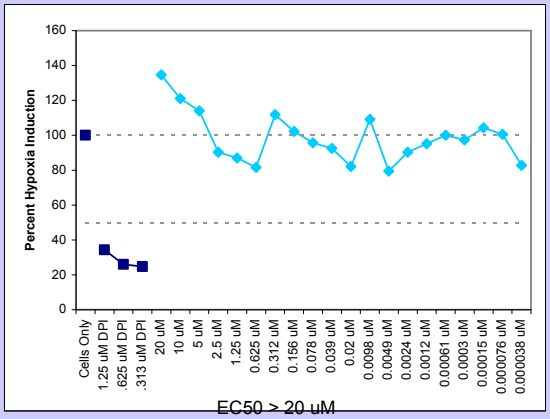


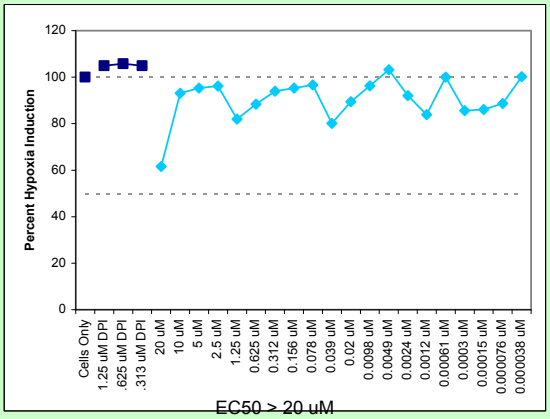
	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	34	26	25	34	34	49	48	72	64	88	87	86	88	72	85	94	109	90	75	111	97	87	113	10
HRE Growth	98	99	99	98	101	100	100	99	100	100	101	99	100	101	101	101	101	100	100	100	100	100	101	10
				Z 'DPI = 0.233							Z Prime = 0.361								Cell Only Ind = 5.017					
PG3 Activity	105	106	105	53	91	113	125	112	106	101	95	94	96	95	96	89	94	90	102	107	101	113	109	10
PG3 Growth	98	99	98	99	101	101	102	101	101	101	100	101	101	101	100	102	102	100	100	101	101	101	101	10

Calculated Values for 20 Dose Titration of NSC# ThurstonYB037 from Well G01 of Plate 3202008928

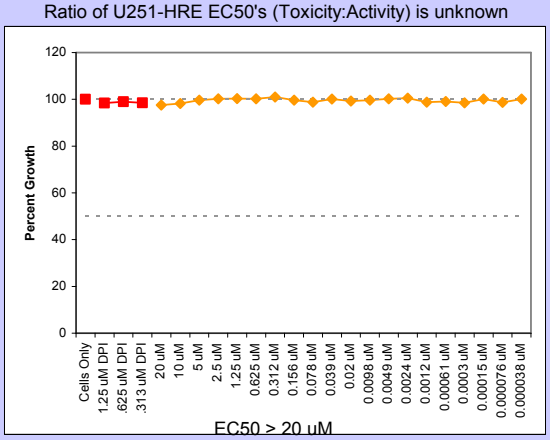
Exp Date 3/20/2008

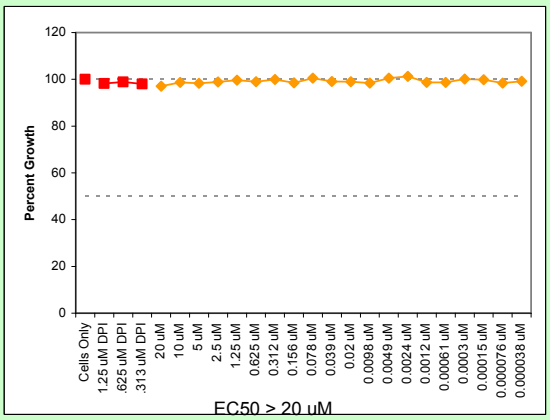
U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**





Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



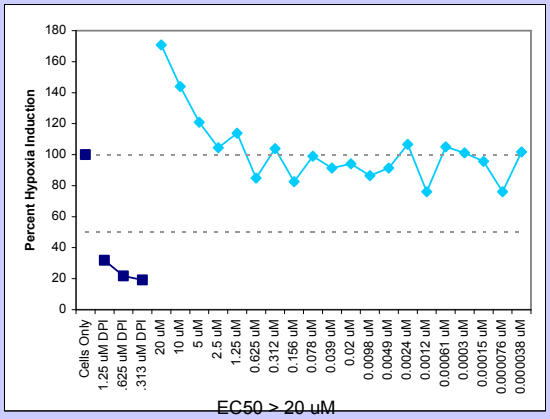


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	34	26	25	135	121	114	90	87	82	112	102	96	92	82	109	79	90	95	100	97	104	101	83	10
HRE Growth	98	99	99	98	98	100	100	100	100	101	100	99	100	99	100	100	101	99	99	99	100	99	100	10
				Z 'DPI = 0.233							Z Prime = 0.361								Cell Only Ind = 5.017					
PG3 Activity	105	106	105	62	93	95	96	82	88	94	95	97	80	89	96	103	92	84	100	86	86	89	100	10
PG3 Growth	98	99	98	97	99	98	99	100	99	100	98	100	99	99	98	100	101	99	99	100	100	98	99	10

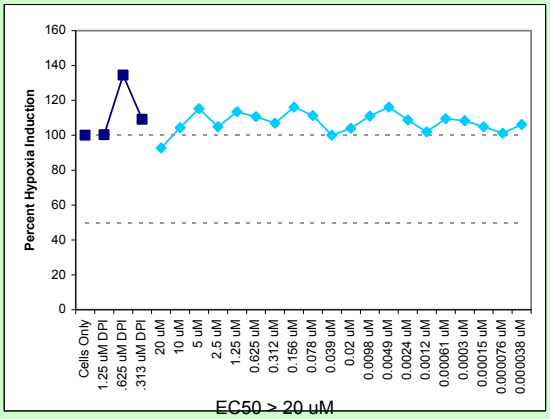
Calculated Values for 20 Dose Titration of NSC# ThurstonYB038 from Well D01 of Plate 3202008911

Exp Date 3/20/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

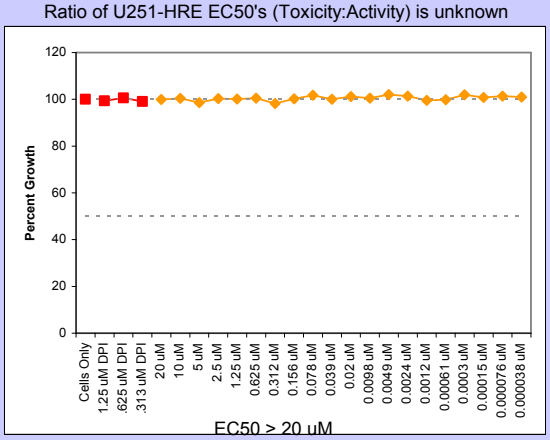


EC50 > 20 uM

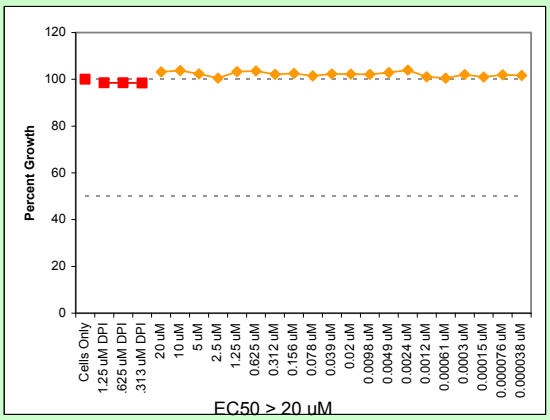


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



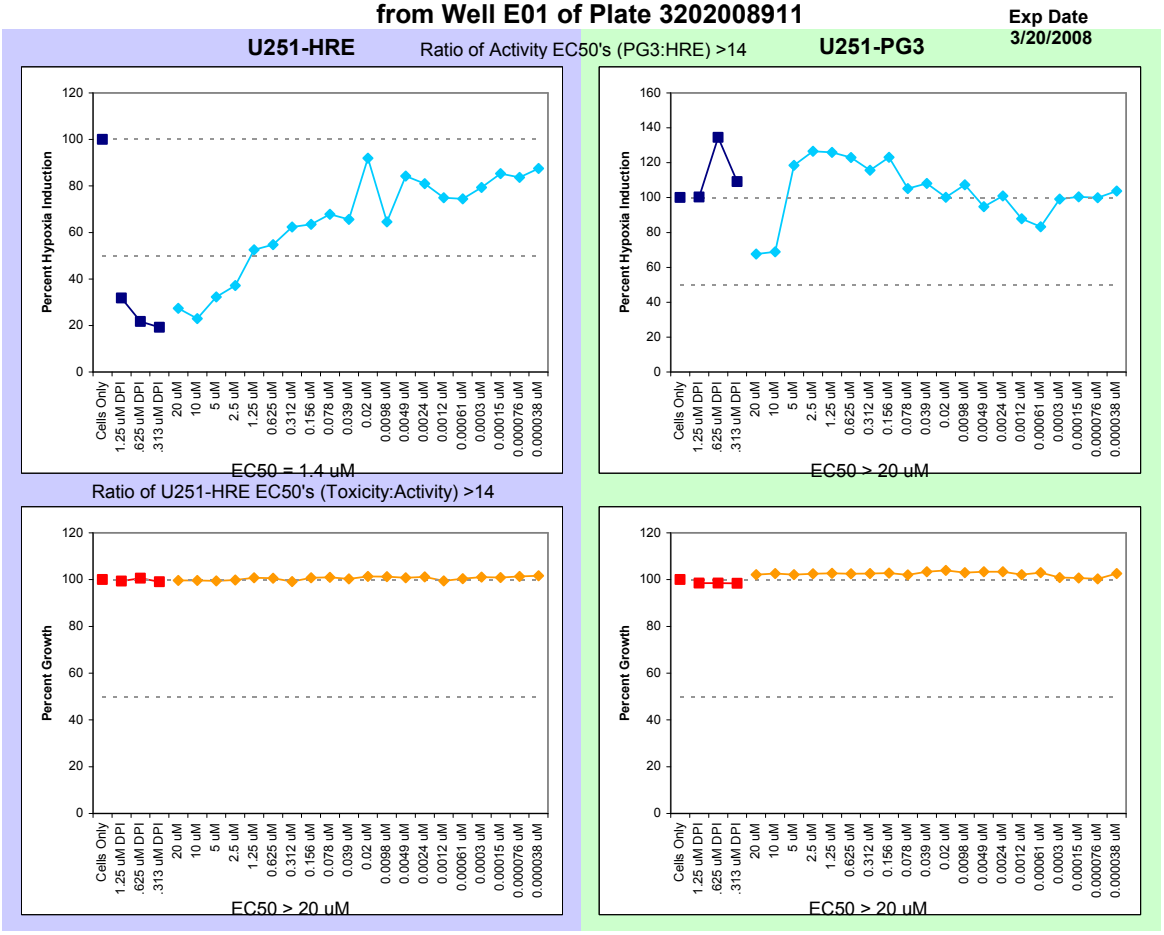
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	32	22	19	171	144	121	105	114	85	104	83	99	91	94	86	91	107	76	105	101	96	76	102	10
HRE Growth	99	101	99	100	100	99	100	100	101	98	100	102	100	101	100	102	101	100	100	102	101	101	101	10
				Z 'DPI = 0.255								Z Prime = 0.35							Cell Only Ind = 4.956					
PG3 Activity	100	135	109	93	104	115	105	114	111	107	116	111	100	104	111	116	109	102	110	108	105	101	106	10
PG3 Growth	99	99	98	103	104	102	100	103	104	102	103	101	102	102	102	103	104	101	101	102	101	102	102	10

5c – yb039

Calculated Values for 20 Dose Titration of NSC# ThurstonYB039 from Well E01 of Plate 3202008911

Exp Date 3/20/2008

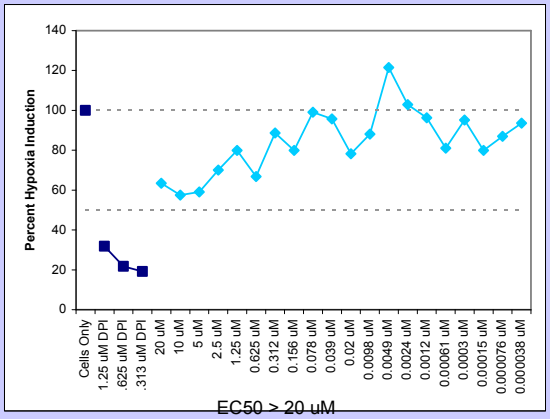


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	32	22	19	27	23	32	37	53	55	62	63	68	66	92	65	84	81	75	74	79	85	84	88	10
HRE Growth	99	101	99	100	100	99	100	101	101	99	101	101	100	101	101	101	101	99	100	101	101	101	102	10
				Z 'DPI = 0.255							Z Prime = 0.35								Cell Only Ind = 4.956					
PG3 Activity	100	135	109	68	69	118	127	126	123	116	123	105	108	100	107	95	101	88	83	99	100	100	104	10
PG3 Growth	99	99	98	102	103	102	103	103	102	103	103	102	103	104	103	103	103	102	103	101	101	100	103	10

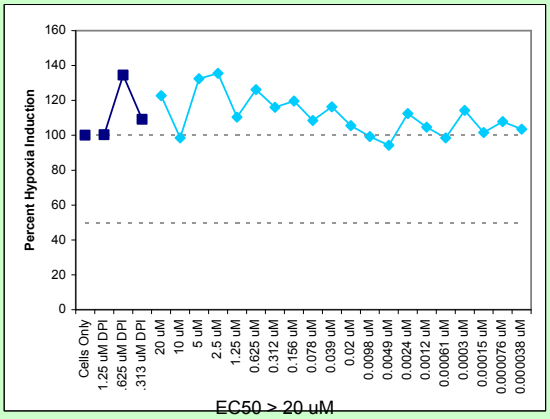
Calculated Values for 20 Dose Titration of NSC# ThurstonYB040 from Well F01 of Plate 3202008911

Exp Date 3/20/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

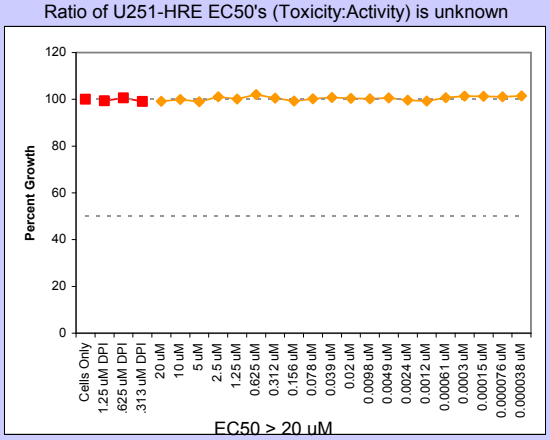


EC50 > 20 uM

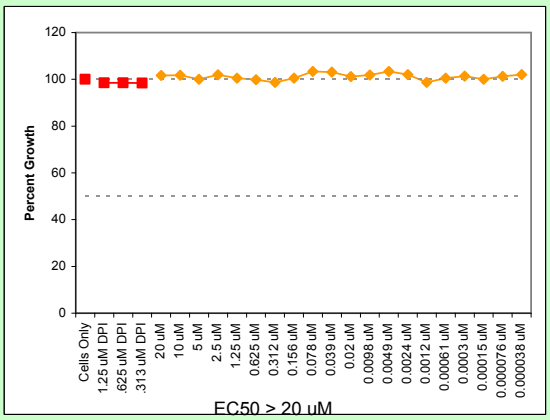


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



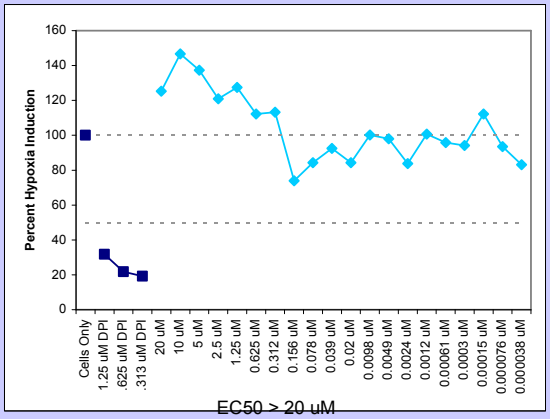
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	32	22	19	63	57	59	70	80	67	89	80	99	96	78	88	121	103	96	81	95	80	87	94	10
HRE Growth	99	101	99	99	100	99	101	100	102	101	99	100	101	100	100	101	100	99	101	101	101	101	101	10
				Z 'DPI = 0.255								Z Prime = 0.35						Cell Only Ind = 4.956						
PG3 Activity	100	135	109	123	99	132	136	110	126	116	120	108	116	106	99	94	113	105	99	114	102	108	104	10
PG3 Growth	99	99	98	102	102	100	102	100	100	99	101	103	103	101	102	103	102	99	100	101	100	101	102	10

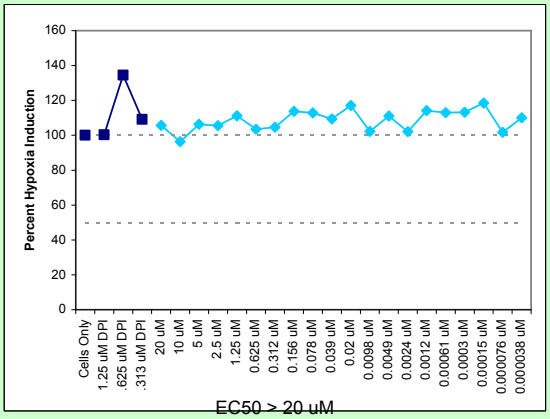
Calculated Values for 20 Dose Titration of NSC# ThurstonYB041 from Well G01 of Plate 3202008911

Exp Date 3/20/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

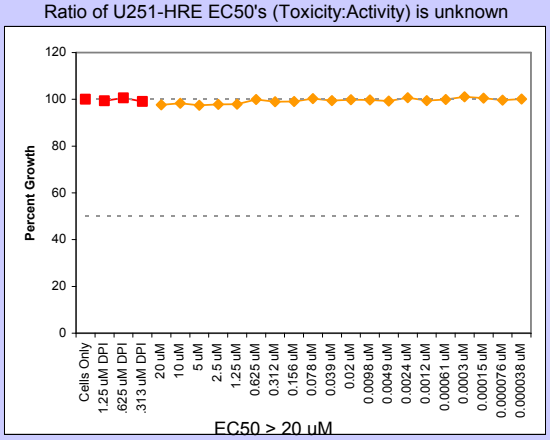


EC50 > 20 uM

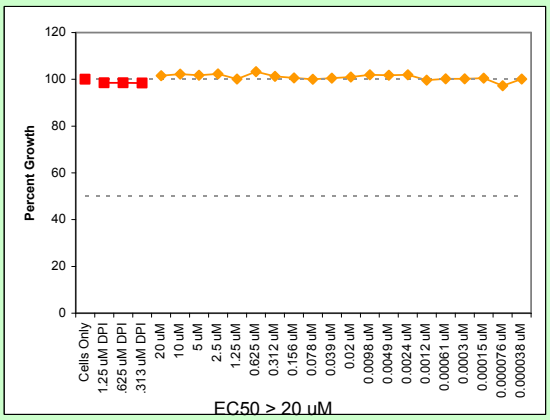


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



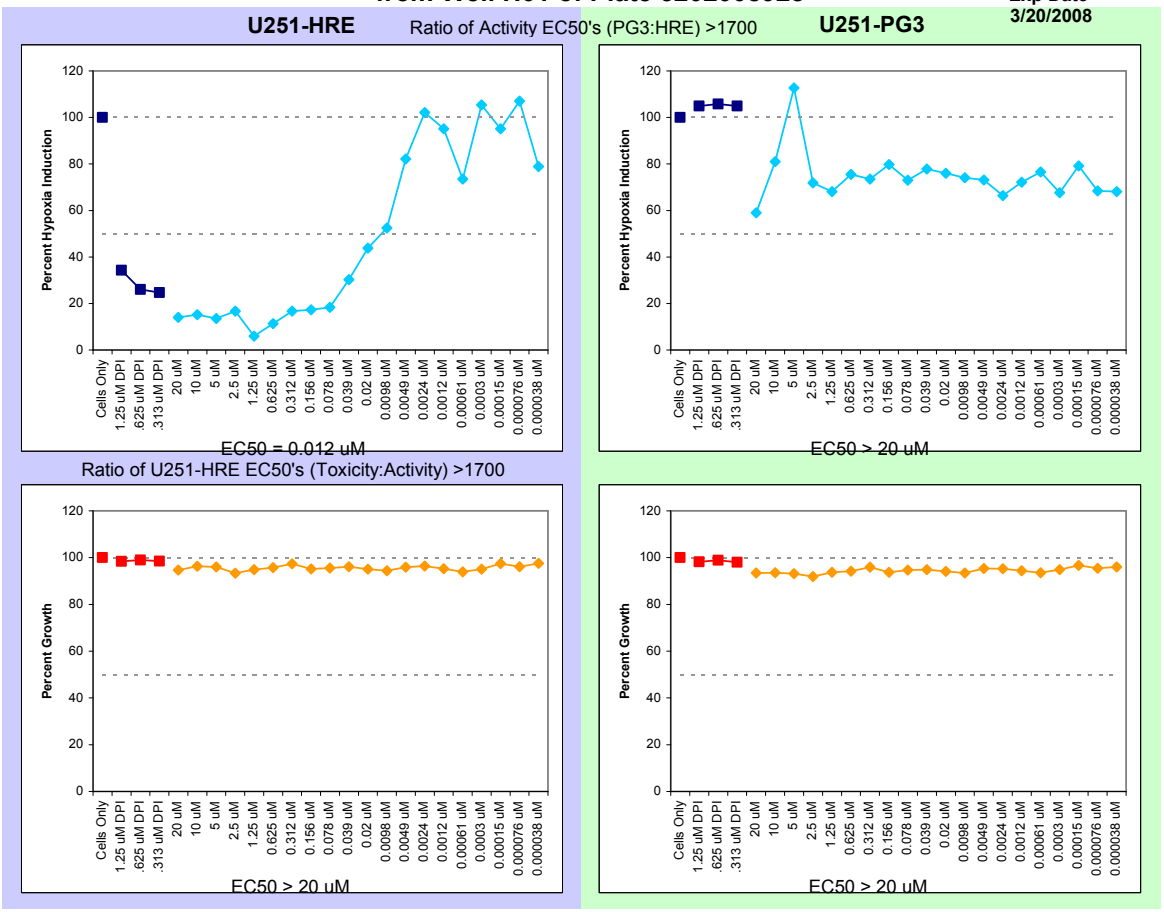
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	32	22	19	125	147	137	121	127	112	113	74	84	92	84	100	98	84	101	96	94	112	94	83	10
HRE Growth	99	101	99	98	98	97	98	98	100	99	99	100	99	100	100	99	101	99	100	101	100	100	100	10
				Z 'DPI = 0.255							Z Prime = 0.35							Cell Only Ind = 4.956						
PG3 Activity	100	135	109	106	96	106	106	111	103	105	114	113	109	117	102	111	102	114	113	113	119	102	110	10
PG3 Growth	99	99	98	102	102	102	102	100	103	101	101	100	101	101	102	102	102	100	100	100	101	97	100	10

Topotecan 01

Calculated Values for 20 Dose Titration of NSC# S609699 from Well H01 of Plate 3202008928

Exp Date 3/20/2008

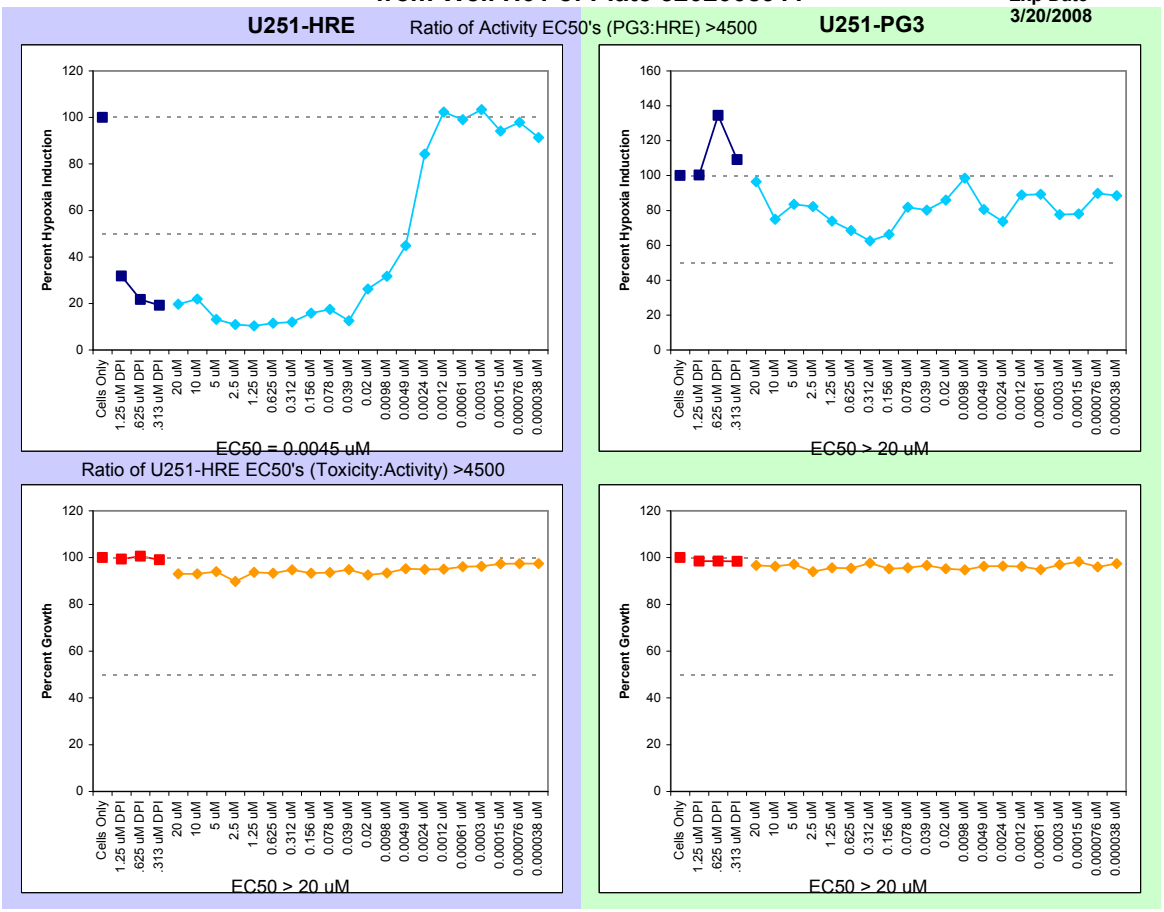


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	34	26	25	14	15	14	17	6	11	17	17	18	30	44	52	82	102	95	74	105	95	107	79	10
HRE Growth	98	99	99	95	96	96	93	95	96	97	95	96	96	95	94	96	96	95	94	95	97	96	98	10
				Z 'DPI = 0.233					Z Prime = 0.361									Cell Only Ind = 5.017						
PG3 Activity	105	106	105	59	81	113	72	68	75	73	80	73	78	76	74	73	66	72	77	68	79	68	68	10
PG3 Growth	98	99	98	93	94	93	92	94	94	96	94	95	95	94	93	95	95	94	93	95	97	95	96	10

Topotecan 02

Calculated Values for 20 Dose Titration of NSC# S609699
from Well H01 of Plate 3202008911

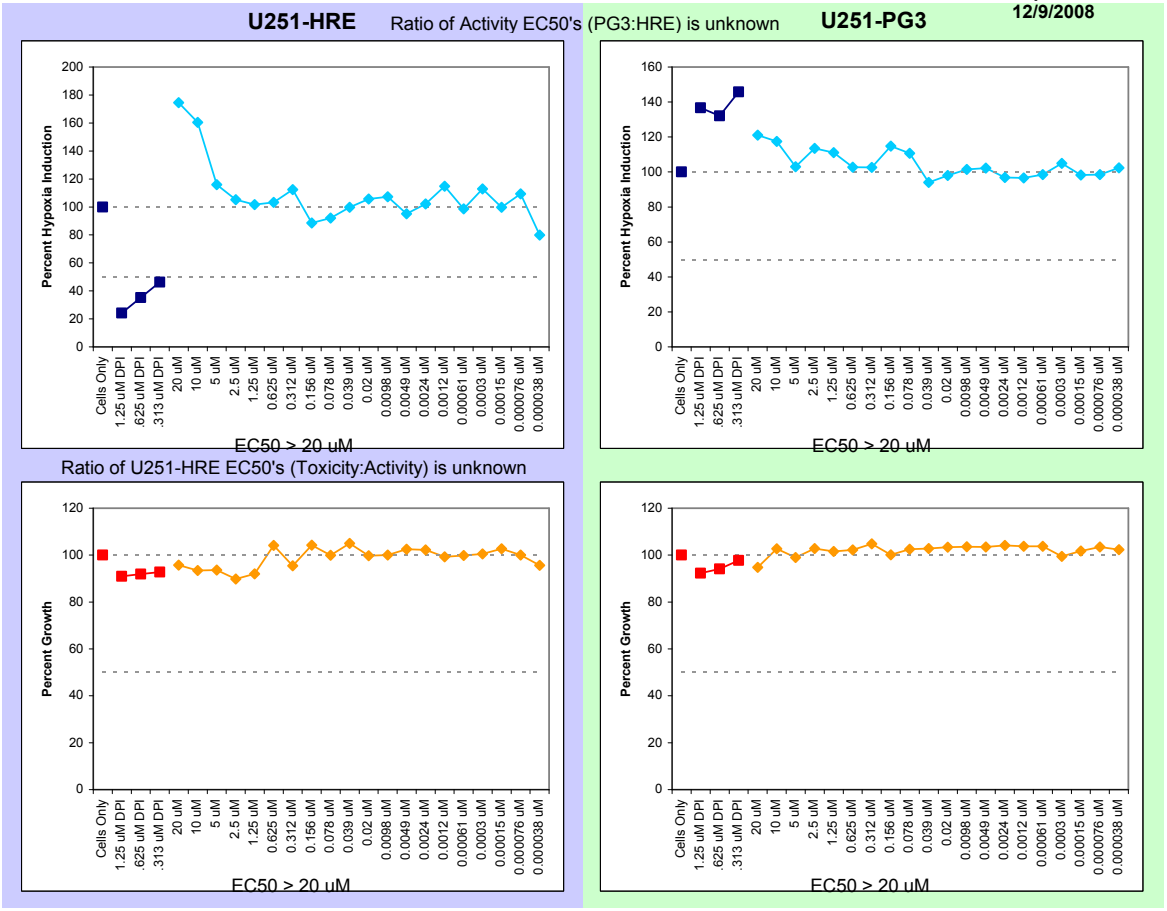
Exp Date
3/20/2008



	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	32	22	19	20	22	13	11	10	11	12	16	18	13	26	32	45	84	102	99	103	94	98	91	10
HRE Growth	99	101	99	93	93	94	90	94	93	95	93	94	95	93	93	95	95	95	96	96	97	97	97	10
				Z 'DPI = 0.255							Z Prime = 0.35								Cell Only Ind = 4.956					
PG3 Activity	100	135	109	96	75	84	82	74	69	63	66	82	80	86	99	81	74	89	89	78	78	90	88	10
PG3 Growth	99	99	98	97	96	97	94	96	95	98	95	96	97	95	95	96	96	96	95	97	98	96	97	10

Calculated Values for 20 Dose Titration of NSC# Thurston 001-DA-022-01 from Well C01 of Plate 12092008002

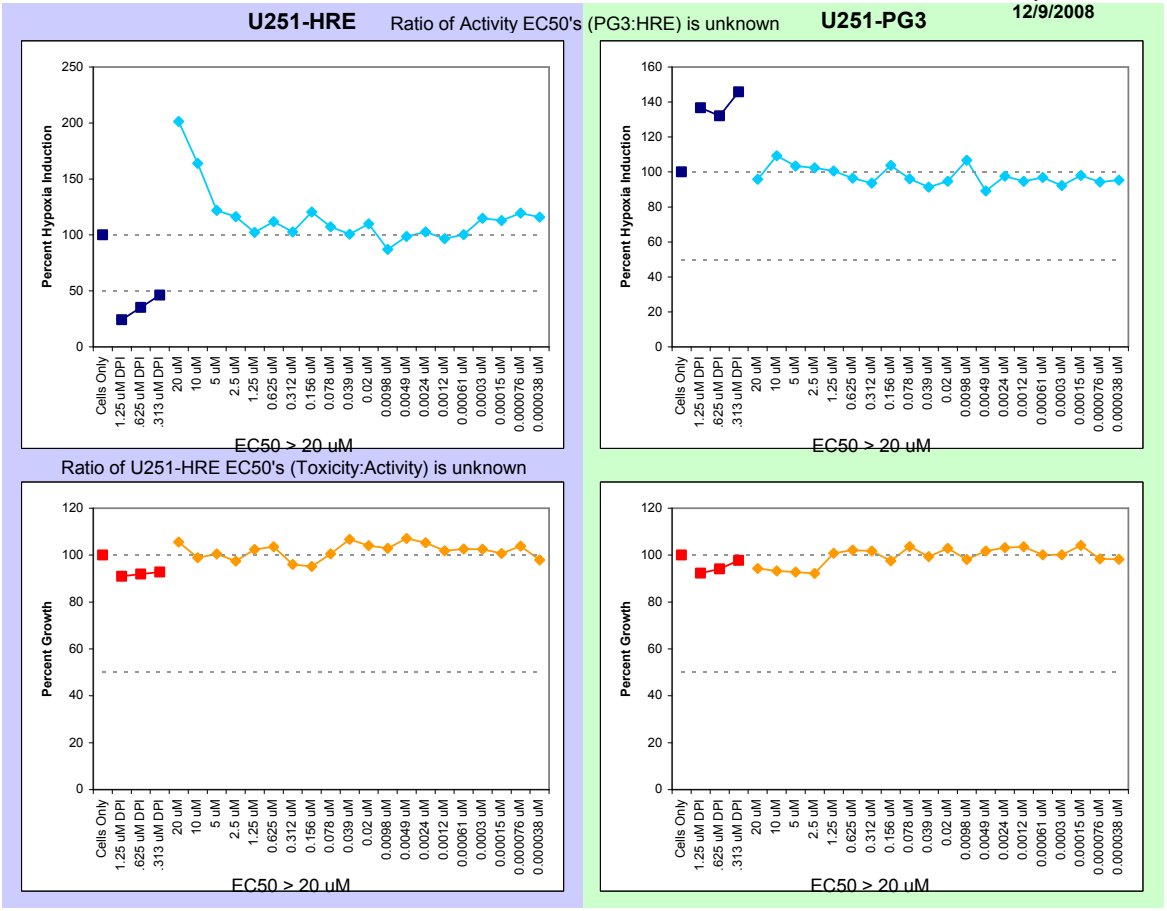
Exp Date 12/9/2008



	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	35	46	175	160	116	105	102	103	112	89	92	100	106	107	95	102	115	99	113	100	109	80	100
HRE Growth	91	92	93	96	93	94	90	92	104	95	104	100	105	100	100	103	102	99	100	100	103	100	96	100
				Z 'DPI = 0.1								Z Prime = 0.276							Cell Only Ind = 3.764					
PG3 Activity	137	132	146	121	117	103	113	111	103	103	115	111	94	98	101	102	97	97	99	105	98	99	102	100
PG3 Growth	92	94	98	95	103	99	103	102	102	105	100	103	103	103	104	103	104	104	104	99	102	103	102	100

Calculated Values for 20 Dose Titration of NSC# Thurston 001-DA-024-01 from Well E01 of Plate 12092008002

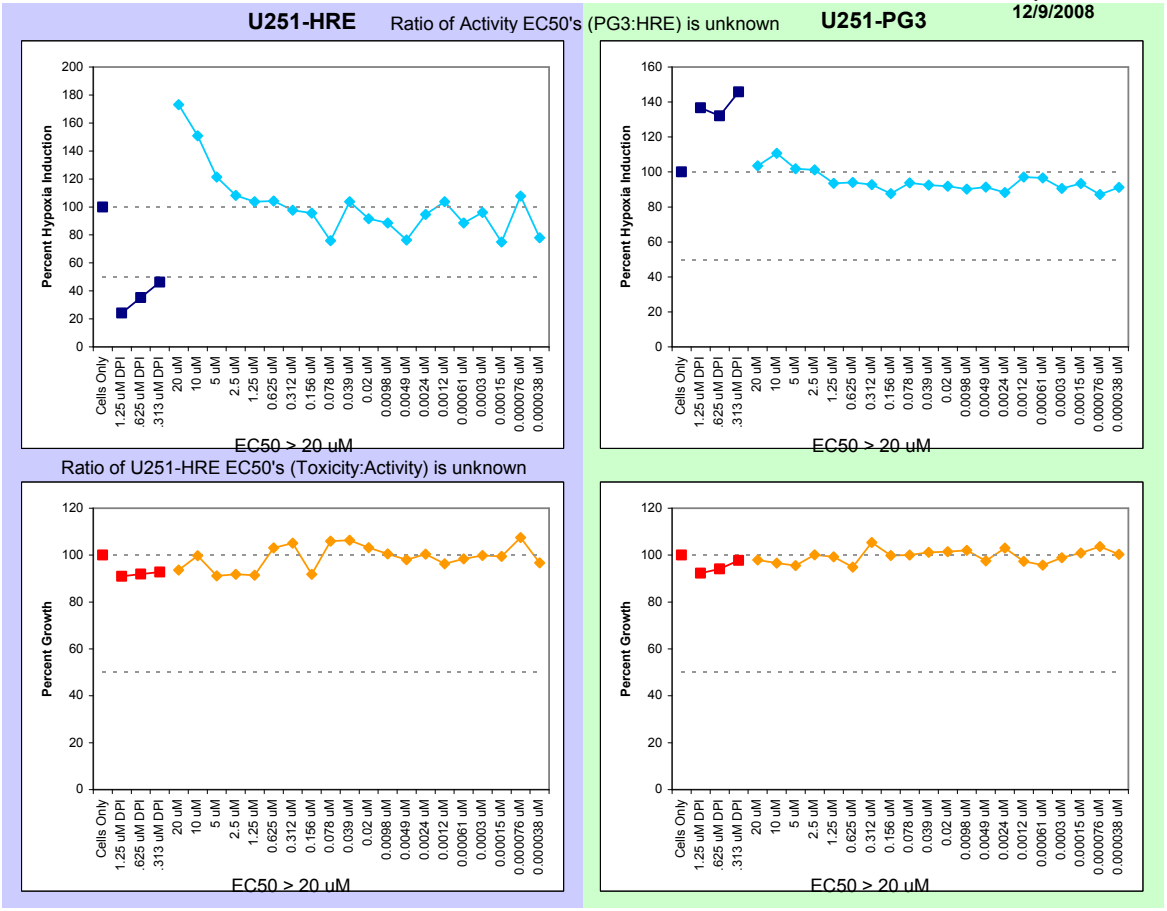
Exp Date 12/9/2008



	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	35	46	201	164	122	116	102	112	103	120	107	101	110	87	99	103	97	100	115	113	119	116	100
HRE Growth	91	92	93	106	99	100	97	102	104	96	95	101	107	104	103	107	105	102	103	103	101	104	98	100
				Z 'DPI = 0.1								Z Prime = 0.276							Cell Only Ind = 3.764					
PG3 Activity	137	132	146	96	109	103	102	101	96	94	104	96	91	95	107	89	98	95	97	92	98	94	95	100
PG3 Growth	92	94	98	94	93	93	92	101	102	102	98	104	99	103	98	102	103	104	100	100	104	98	98	100

Calculated Values for 20 Dose Titration of NSC# Thurston 001-DA-025-01 from Well F01 of Plate 12092008002

Exp Date 12/9/2008

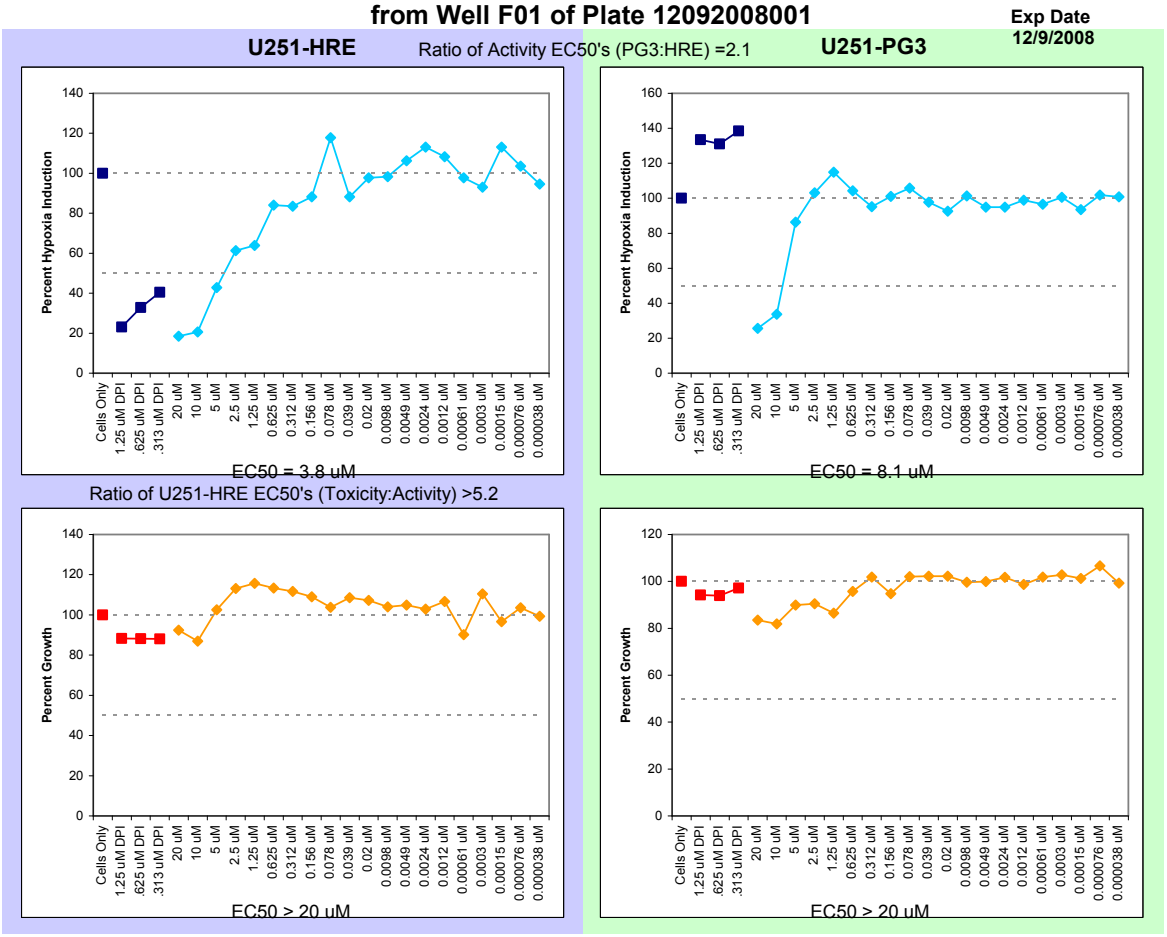


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	35	46	173	151	121	108	104	104	98	96	76	104	92	89	76	95	104	89	96	75	108	78	100
HRE Growth	91	92	93	94	100	91	92	91	103	105	92	106	106	103	100	98	100	96	98	100	99	108	97	100
				Z 'DPI = 0.1								Z Prime = 0.276							Cell Only Ind = 3.764					
PG3 Activity	137	132	146	103	111	102	101	94	94	93	88	94	93	92	90	91	88	97	97	91	93	87	91	100
PG3 Growth	92	94	98	98	97	96	100	99	95	105	100	100	101	101	102	98	103	97	96	99	101	104	100	100

5g – ksn011

Calculated Values for 20 Dose Titration of NSC# Thurston KSN011
from Well F01 of Plate 12092008001

Exp Date 12/9/2008

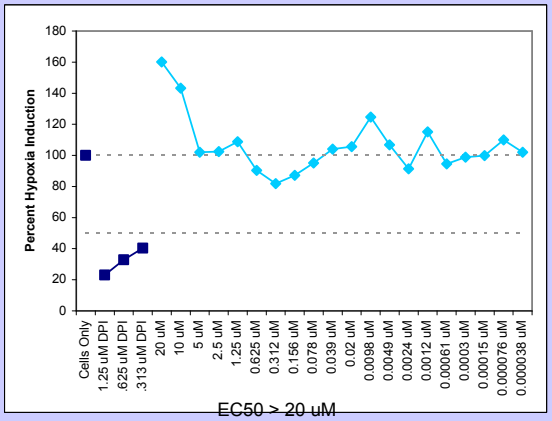


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	23	33	40	18	21	43	61	64	84	83	88	118	88	98	98	106	113	108	98	93	113	104	95	100
HRE Growth	88	88	88	92	87	103	113	116	113	112	109	104	109	107	104	105	103	107	90	110	97	104	99	100
				Z 'DPI = 0.157								Z Prime = 0.205							Cell Only Ind = 3.605					
PG3 Activity	133	131	138	26	34	86	103	115	104	95	101	106	98	93	101	95	95	99	97	101	94	102	101	100
PG3 Growth	94	94	97	84	82	90	90	86	96	102	95	102	102	102	100	100	102	99	102	103	101	107	99	100

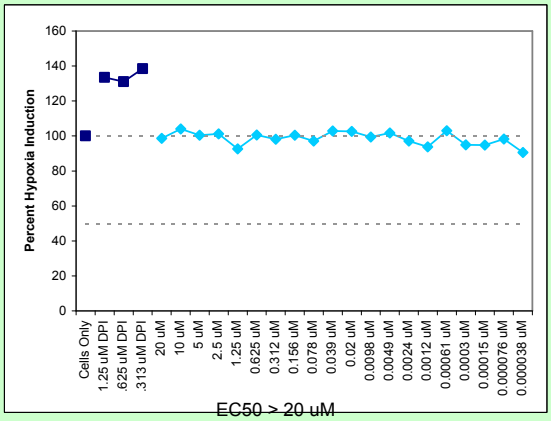
Calculated Values for 20 Dose Titration of NSC# Thurston KSN012 from Well G01 of Plate 12092008001

Exp Date 12/9/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

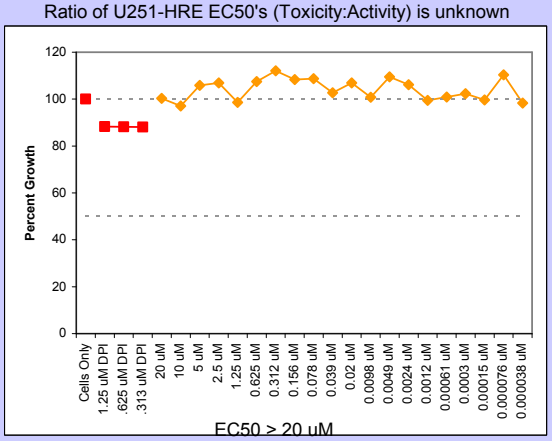


EC50 > 20 uM

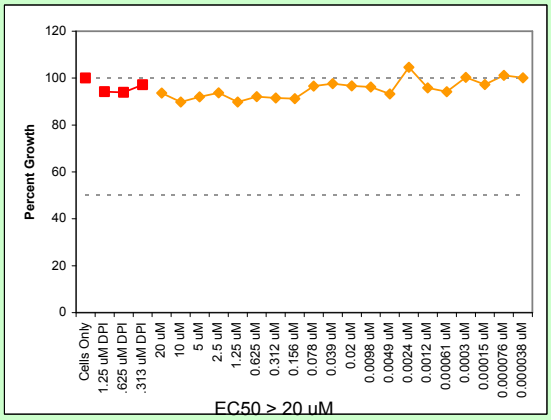


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	23	33	40	160	143	102	103	109	90	82	87	95	104	106	125	107	91	115	95	99	100	110	102	100
HRE Growth	88	88	88	100	97	106	107	99	107	112	108	109	103	107	101	109	106	99	101	102	100	110	98	100

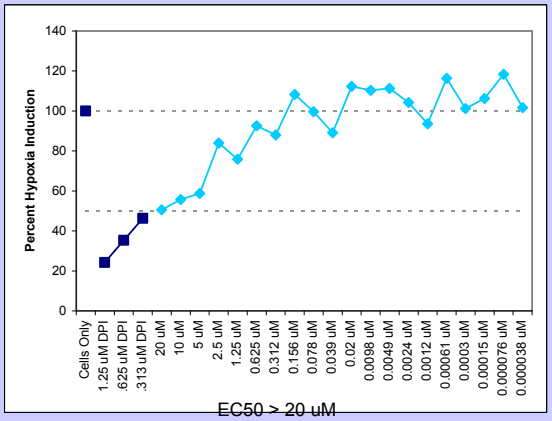
Z 'DPI = 0.157 | Z Prime = 0.205 | Cell Only Ind = 3.605

PG3 Activity	133	131	138	99	104	100	101	93	101	98	100	97	103	103	99	102	97	94	103	95	95	98	91	100
PG3 Growth	94	94	97	94	90	92	94	90	92	92	91	97	98	97	96	93	105	96	94	100	97	101	100	100

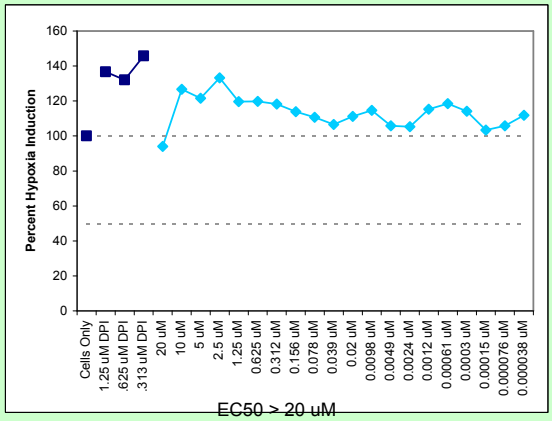
Calculated Values for 20 Dose Titration of NSC# Thurston KSN013 from Well A01 of Plate 12092008002

Exp Date 12/9/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

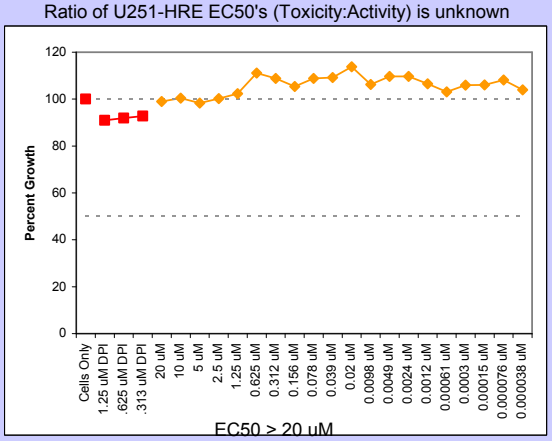


EC50 > 20 uM

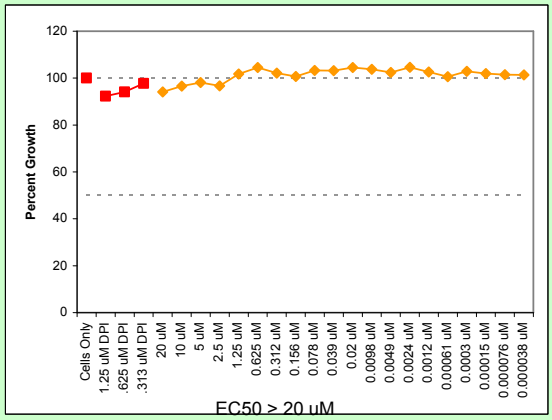


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



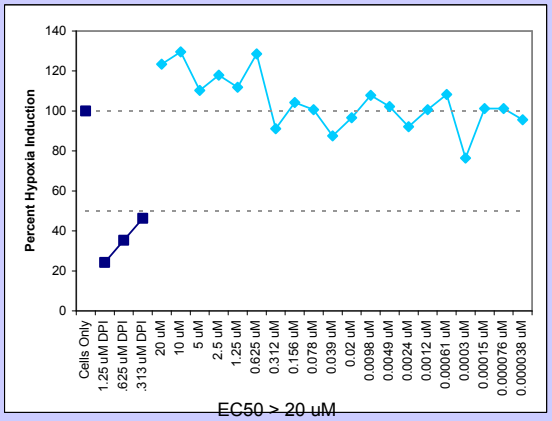
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	35	46	51	56	59	84	76	93	88	108	100	89	112	110	111	104	94	116	101	106	118	102	100
HRE Growth	91	92	93	99	100	98	100	102	111	109	105	109	109	114	106	110	110	106	103	106	106	108	104	100
				Z 'DPI = 0.1								Z Prime = 0.276						Cell Only Ind = 3.764						
PG3 Activity	137	132	146	94	127	122	133	120	120	118	114	111	107	111	115	106	105	115	118	114	103	106	112	100
PG3 Growth	92	94	98	94	97	98	97	102	105	102	101	103	103	105	104	102	105	103	101	103	102	101	101	100

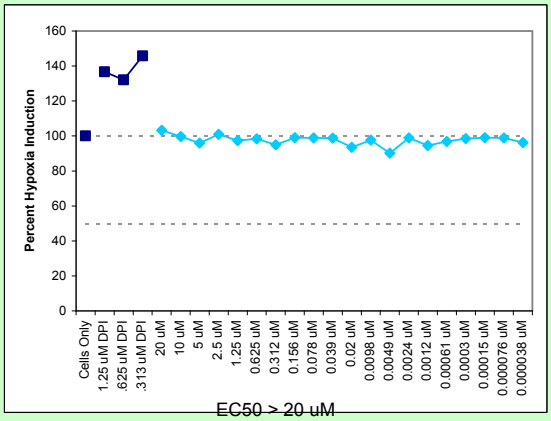
Calculated Values for 20 Dose Titration of NSC# Thurston KSN014 from Well B01 of Plate 12092008002

Exp Date 12/9/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

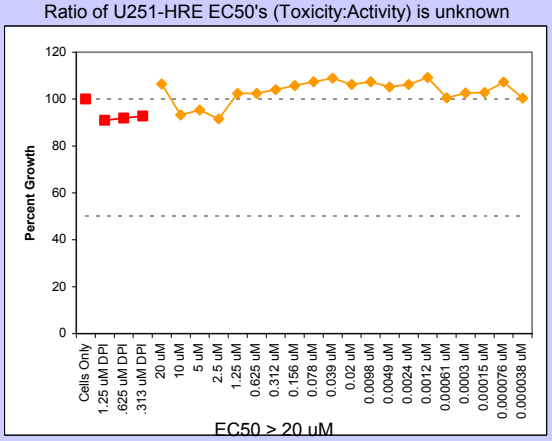


EC50 > 20 uM

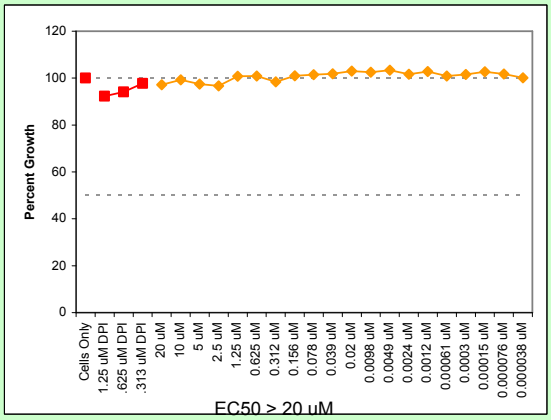


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



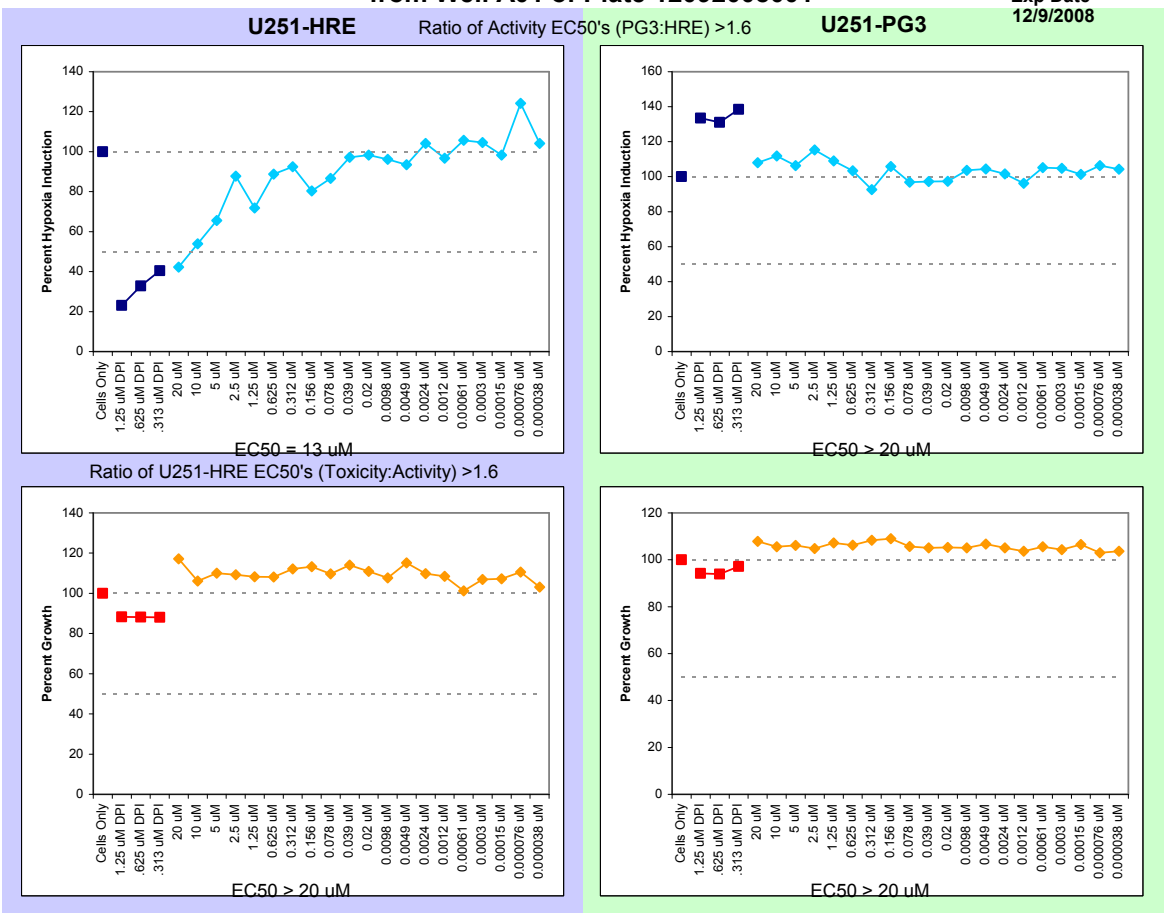
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	35	46	123	130	110	118	112	129	91	104	101	88	97	108	102	92	101	108	76	101	101	96	100
HRE Growth	91	92	93	106	93	95	92	102	102	104	106	107	109	106	107	105	106	109	100	103	103	107	100	100
				Z 'DPI = 0.1								Z Prime = 0.276						Cell Only Ind = 3.764						
PG3 Activity	137	132	146	103	100	96	101	97	98	95	99	99	99	93	98	90	99	95	97	99	99	99	96	100
PG3 Growth	92	94	98	97	99	97	97	101	101	98	101	101	102	103	102	103	102	103	101	102	103	102	100	100

5e– yb074

Calculated Values for 20 Dose Titration of NSC# Thurston YB074
from Well A01 of Plate 1209208001

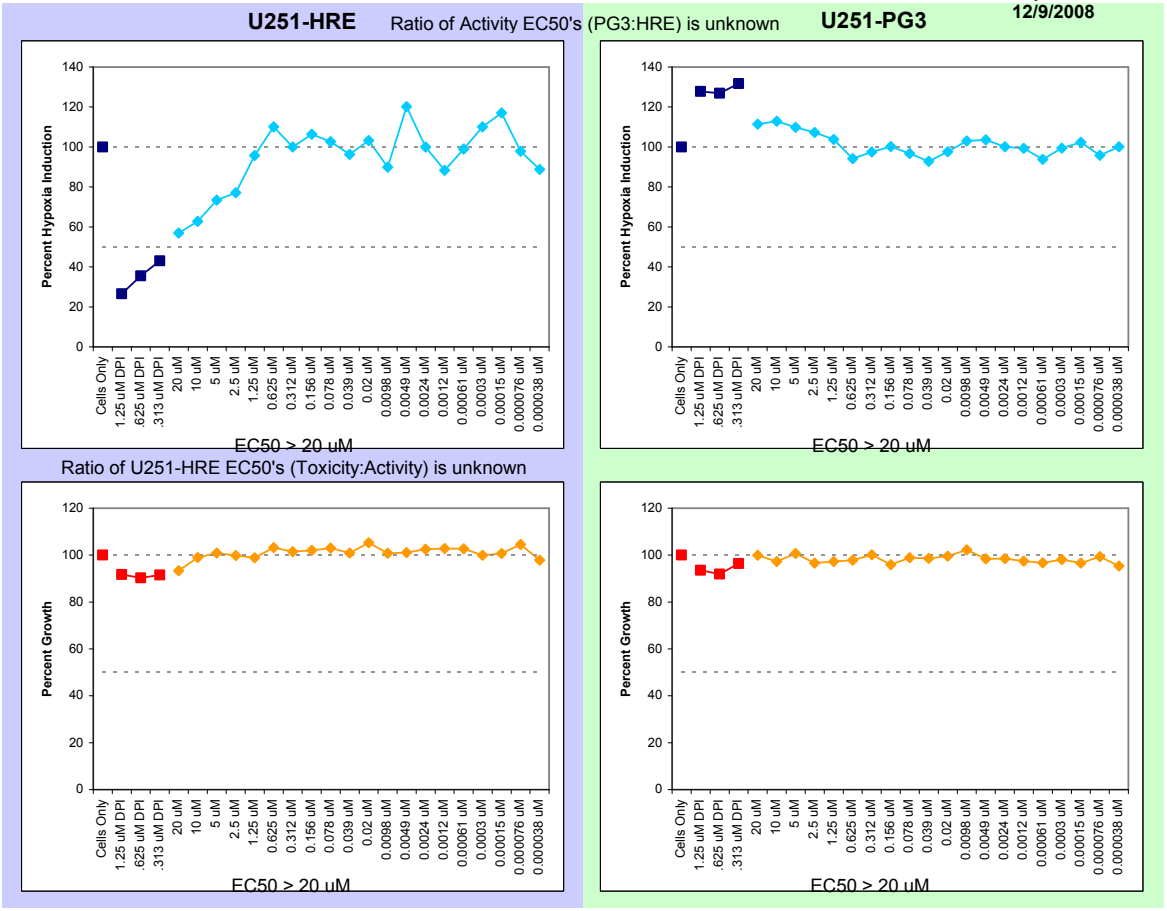
Exp Date 12/9/2008



	1.25 uM DPI	625 uM DPI	313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	23	33	40	42	54	66	88	72	89	92	80	87	97	98	96	94	104	97	106	105	98	124	104	100
HRE Growth	88	88	88	117	106	110	109	108	108	112	113	110	114	111	108	115	110	108	101	107	107	111	103	100
				Z 'DPI = 0.157						Z Prime = 0.205								Cell Only Ind = 3.605						
PG3 Activity	133	131	138	108	112	106	115	109	103	93	106	97	97	97	104	104	102	96	105	105	101	106	104	100
PG3 Growth	94	94	97	108	106	106	105	107	106	108	109	106	105	105	105	107	105	104	106	104	107	103	104	100

Calculated Values for 20 Dose Titration of NSC# Thurston YB077 from Well B01 of Plate 12092008003

Exp Date 12/9/2008

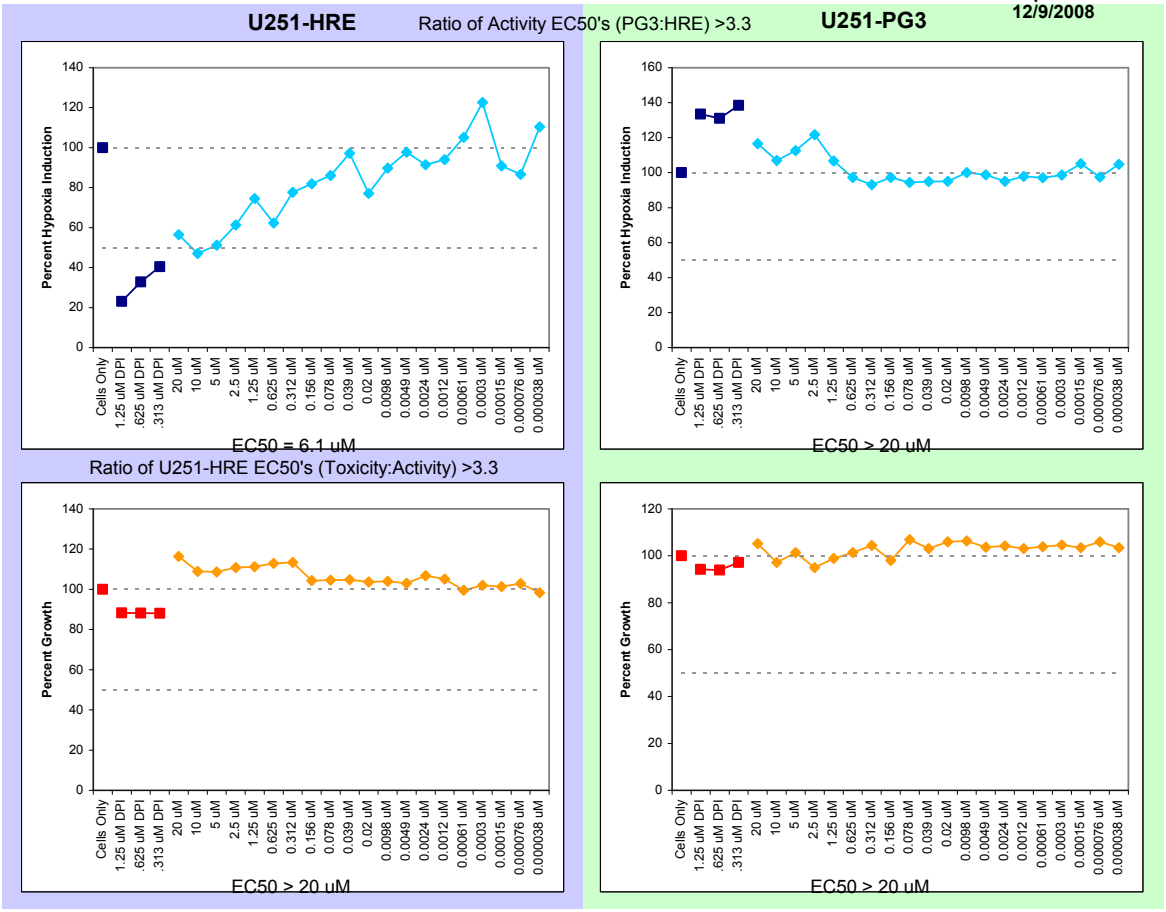


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	27	36	43	57	63	73	77	96	110	100	106	103	96	103	90	120	100	88	99	110	117	98	89	100
HRE Growth	92	90	91	93	99	101	100	99	103	101	102	103	101	105	101	101	102	103	103	100	101	104	98	100
				Z 'DPI = 0.12							Z Prime = 0.238								Cell Only Ind = 3.581					
PG3 Activity	128	127	132	111	113	110	107	104	94	98	100	97	93	98	103	104	100	99	94	99	102	96	100	100
PG3 Growth	94	92	96	100	97	101	97	97	98	100	96	99	99	100	102	98	99	97	97	98	97	99	95	100

5f– yb081

Calculated Values for 20 Dose Titration of NSC# Thurston YB081 from Well C01 of Plate 12092008001

Exp Date 12/9/2008

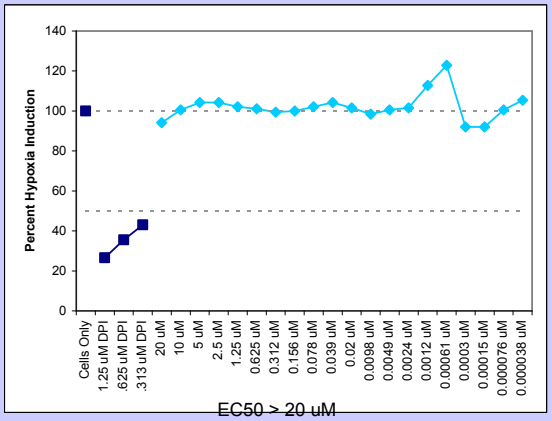


	1.25 uM DPI	625 uM DPI	313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	23	33	40	57	47	51	61	75	62	78	82	86	97	77	90	98	91	94	105	123	91	87	110	100
HRE Growth	88	88	88	116	109	109	111	111	113	113	104	105	105	104	104	103	107	105	99	102	101	103	98	100
				Z 'DPI = 0.157					Z Prime = 0.205									Cell Only Ind = 3.605						
PG3 Activity	133	131	138	117	107	113	122	107	97	93	97	94	95	95	100	99	95	98	97	99	105	97	105	100
PG3 Growth	94	94	97	105	97	101	95	99	101	104	98	107	103	106	106	104	104	103	104	105	103	106	103	100

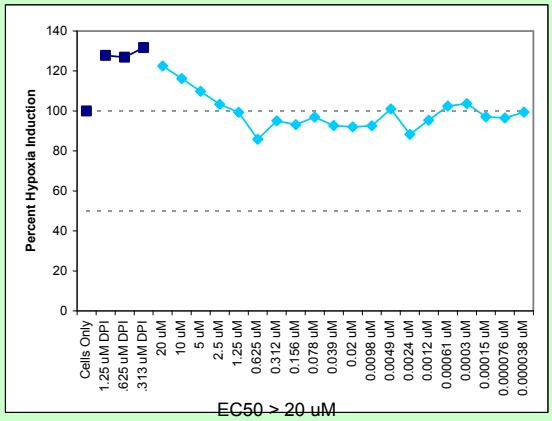
Calculated Values for 20 Dose Titration of NSC# Thurston YB085 from Well D01 of Plate 12092008003

Exp Date 12/9/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

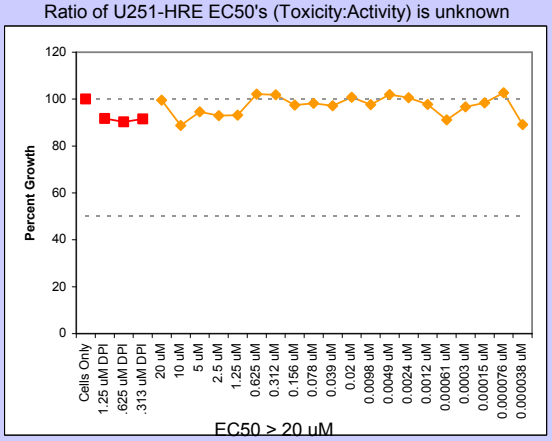


EC50 > 20 uM

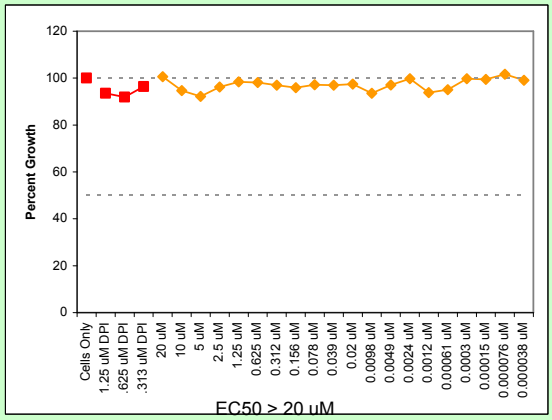


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



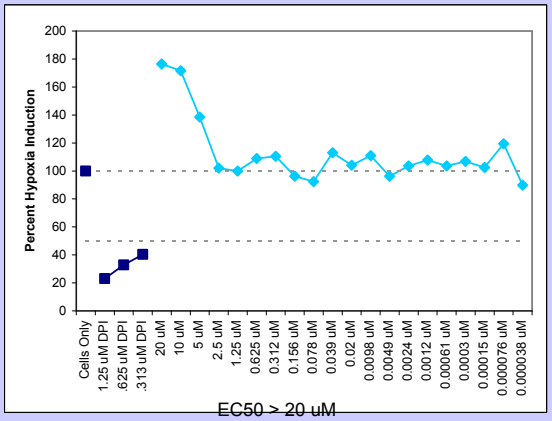
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	27	36	43	94	101	104	104	102	101	99	100	102	104	102	98	101	102	113	123	92	92	101	105	100
HRE Growth	92	90	91	100	89	95	93	93	102	102	97	98	97	101	98	102	101	98	91	97	98	103	89	100
				Z 'DPI = 0.12							Z Prime = 0.238							Cell Only Ind = 3.581						
PG3 Activity	128	127	132	123	116	110	103	99	86	95	93	97	93	92	93	101	88	95	102	104	97	96	99	100
PG3 Growth	94	92	96	101	95	92	96	98	98	97	96	97	97	97	94	97	100	94	95	100	99	102	99	100

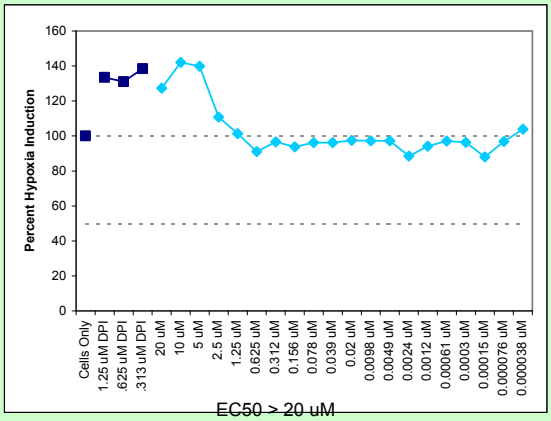
Calculated Values for 20 Dose Titration of NSC# Thurston YB086 from Well E01 of Plate 12092008001

Exp Date 12/9/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

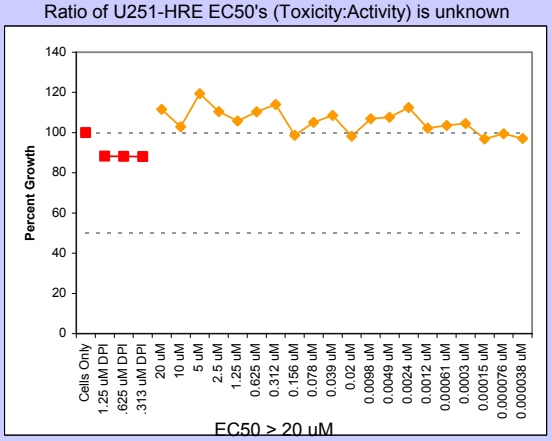


EC50 > 20 uM

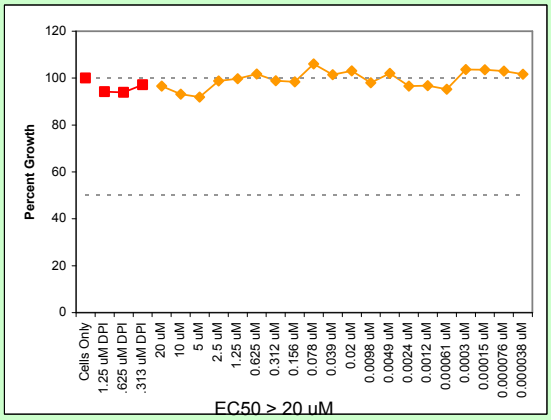


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	23	33	40	176	172	138	102	100	109	110	96	92	113	104	111	96	104	108	104	107	103	119	90	100
HRE Growth	88	88	88	112	103	119	110	106	110	114	99	105	109	98	107	108	113	102	104	105	97	99	97	100
				Z 'DPI = 0.157								Z Prime = 0.205						Cell Only Ind = 3.605						
PG3 Activity	133	131	138	127	142	140	111	101	91	97	94	96	96	98	97	97	89	94	97	96	88	97	104	100
PG3 Growth	94	94	97	97	93	92	99	100	102	99	98	106	101	103	98	102	97	97	95	104	104	103	102	100

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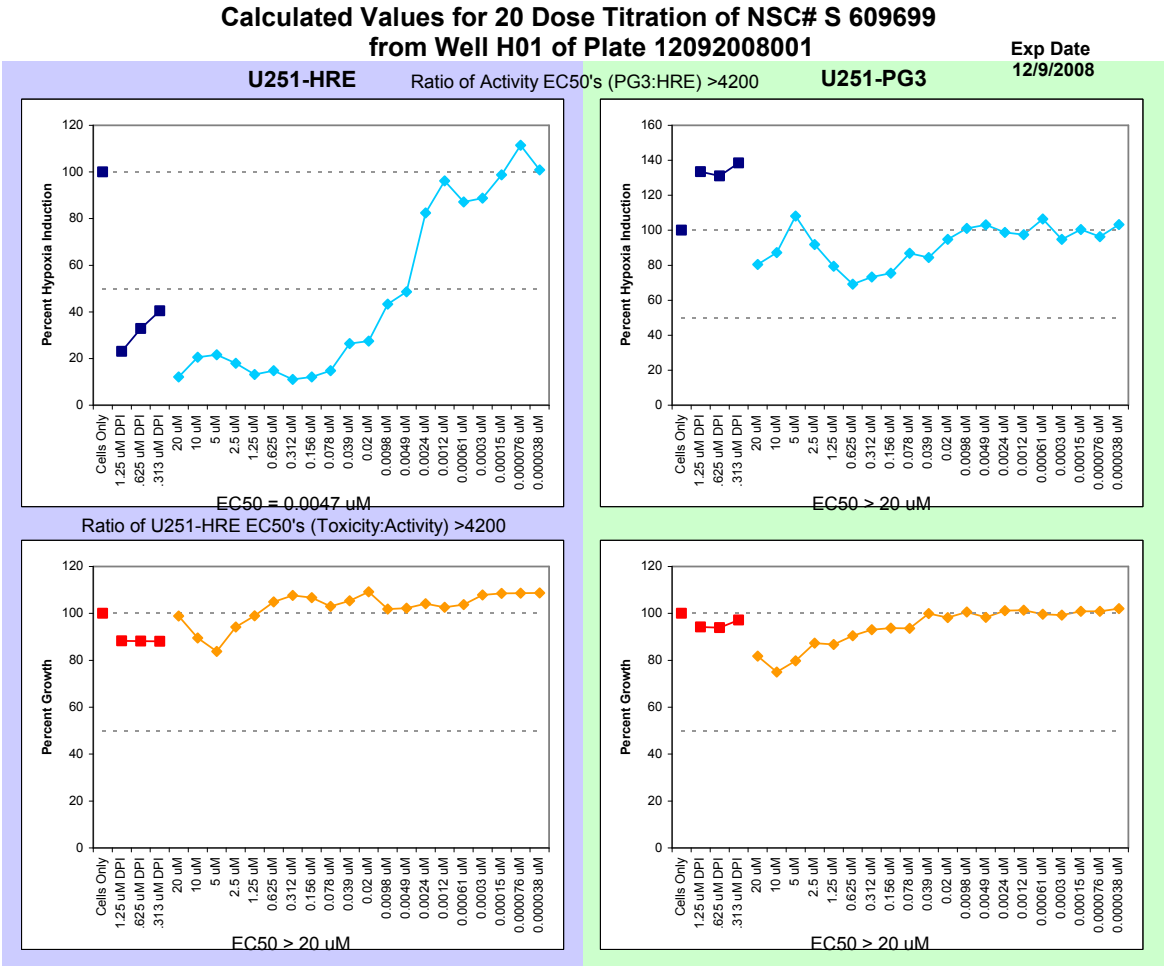
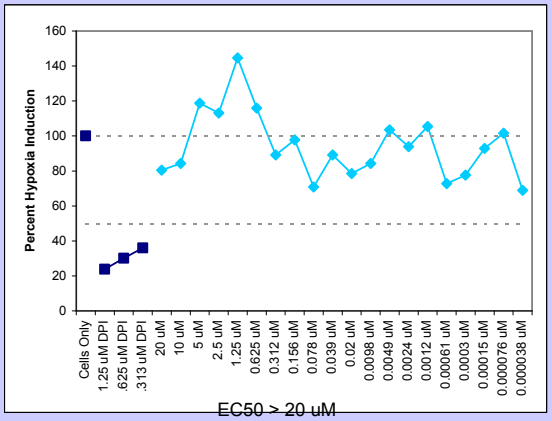


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	23	33	40	12	21	22	18	13	15	11	12	15	26	27	43	49	82	96	87	89	99	111	101	100
HRE Growth	88	88	88	99	90	84	94	99	105	108	107	103	105	109	102	102	104	103	104	108	109	109	109	100
				Z 'DPI = 0.157								Z Prime = 0.205						Cell Only Ind = 3.605						
PG3 Activity	133	131	138	80	87	108	92	79	69	73	76	87	84	95	101	103	99	98	106	95	100	96	103	100
PG3 Growth	94	94	97	82	75	80	87	87	90	93	94	94	100	98	101	98	101	101	100	99	101	101	102	100

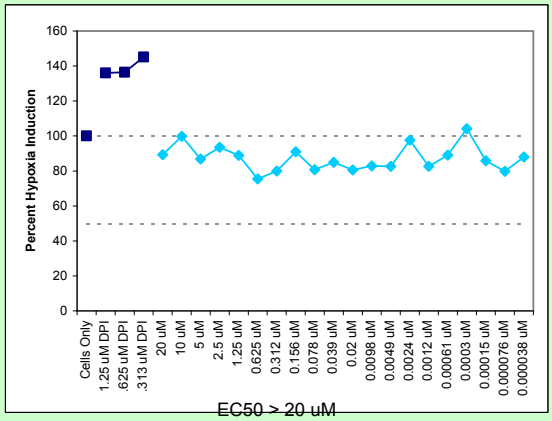
Calculated Values for 20 Dose Titration of NSC# Thurston YB082 from Well G01 of Plate 12022008005

Exp Date 12/2/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

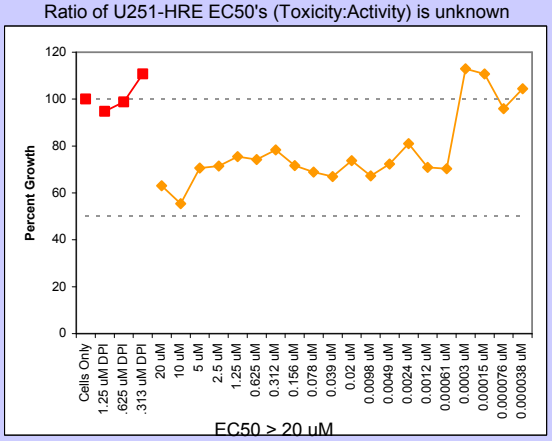


EC50 > 20 uM

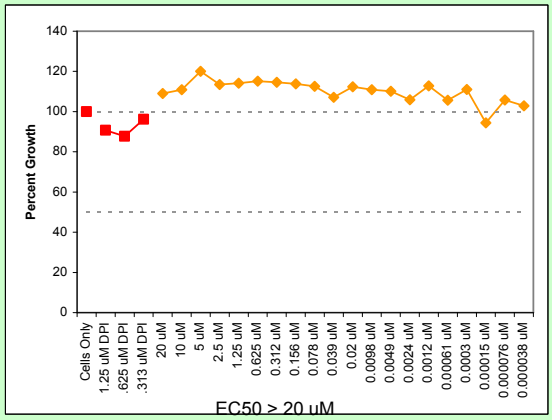


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



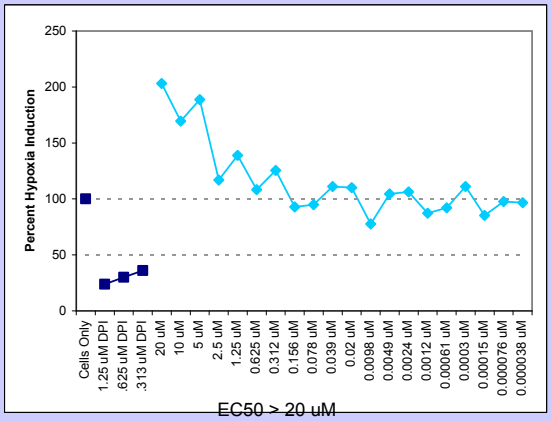
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	30	36	80	84	119	113	145	116	89	98	71	89	79	84	103	94	105	73	78	93	102	69	100
HRE Growth	95	99	111	63	55	71	71	75	74	78	72	69	67	74	67	72	81	71	70	113	111	96	104	100
				Z 'DPI = -0.73								Z Prime = -0.463							Cell Only Ind = 4.014					
PG3 Activity	136	136	145	89	100	87	93	89	75	80	91	81	85	81	83	83	98	83	89	104	86	80	88	100
PG3 Growth	91	88	96	109	111	120	113	114	115	115	114	113	107	112	111	110	106	113	106	111	94	106	103	100

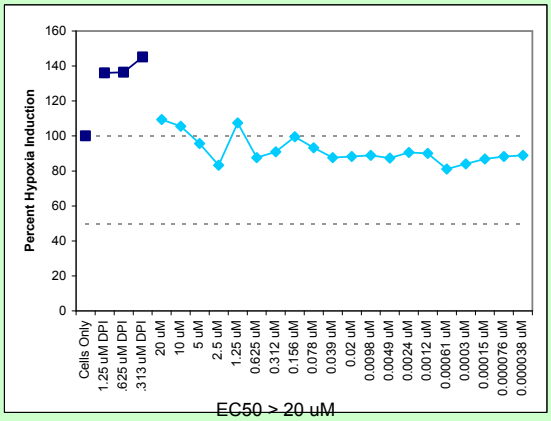
Calculated Values for 20 Dose Titration of NSC# Thurston YB078 from Well E01 of Plate 12022008005

Exp Date 12/2/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

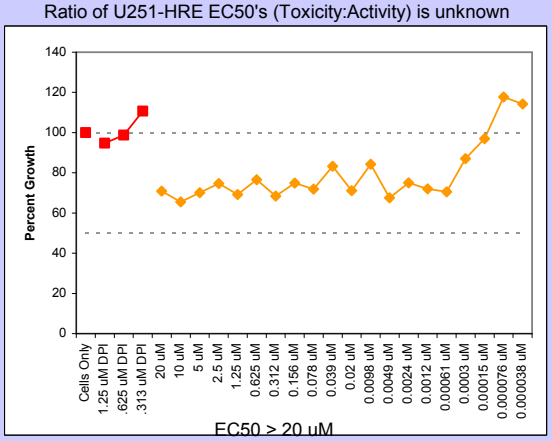


EC50 > 20 uM

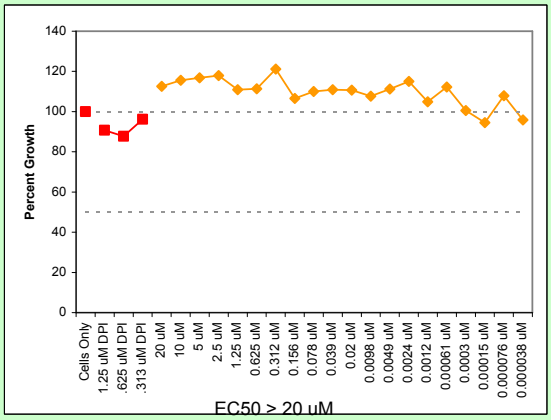


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



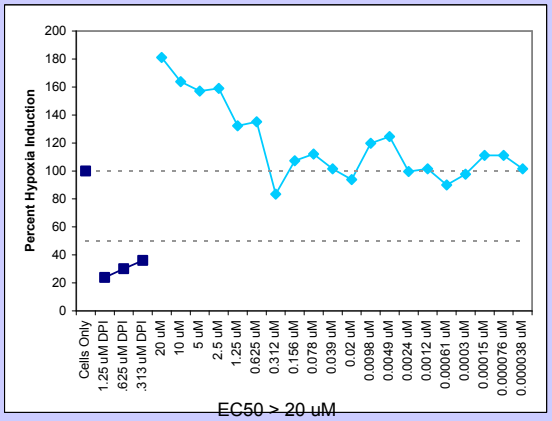
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	30	36	203	170	189	117	139	108	126	93	95	111	110	78	104	106	87	92	111	85	98	97	100
HRE Growth	95	99	111	71	65	70	75	69	77	68	75	72	83	71	84	68	75	72	71	87	97	118	114	100
				Z 'DPI = -0.73								Z Prime = -0.463						Cell Only Ind = 4.014						
PG3 Activity	136	136	145	109	106	96	83	107	88	91	100	93	88	88	89	87	91	90	81	84	87	88	89	100
PG3 Growth	91	88	96	113	116	117	118	111	111	121	107	110	111	111	108	111	115	105	112	101	94	108	96	100

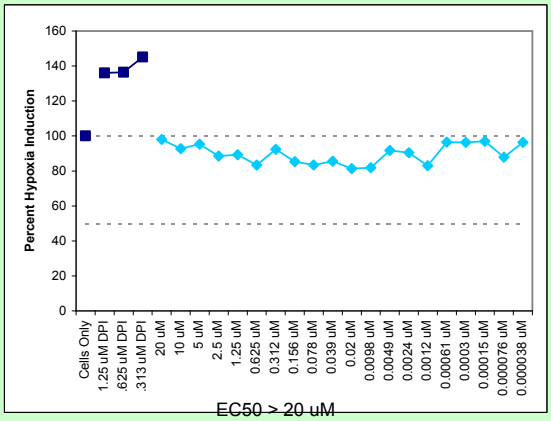
Calculated Values for 20 Dose Titration of NSC# Thurston YB073 from Well B01 of Plate 12022008005

Exp Date 12/2/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

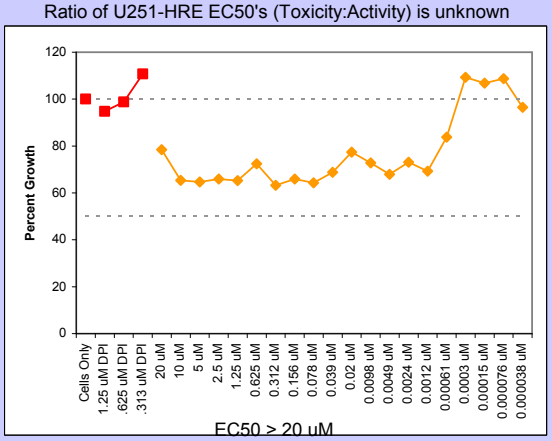


EC50 > 20 uM

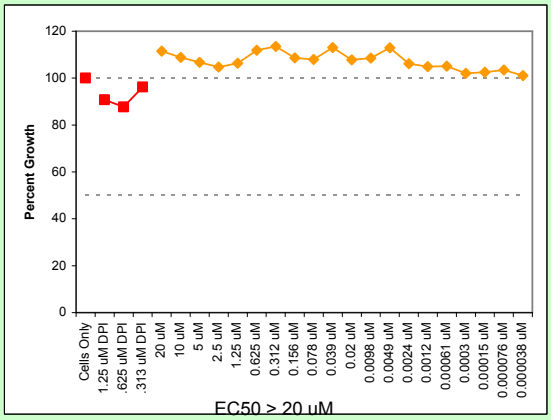


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



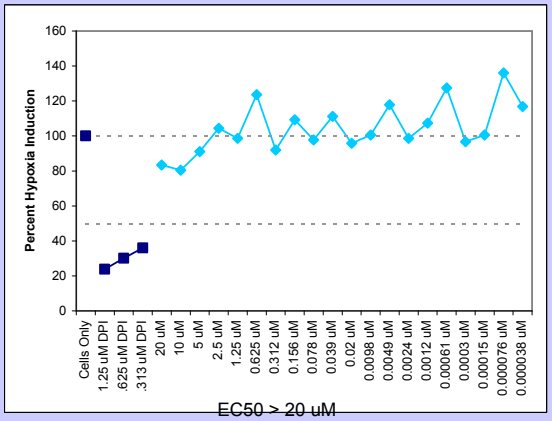
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	30	36	181	164	157	159	132	135	83	107	112	102	94	120	125	100	102	90	98	111	111	102	100
HRE Growth	95	99	111	78	65	65	66	65	72	63	66	64	69	77	73	68	73	69	84	109	107	109	96	100
				Z 'DPI = -0.73								Z Prime = -0.463						Cell Only Ind = 4.014						
PG3 Activity	136	136	145	98	93	95	88	89	83	92	85	83	86	81	82	92	90	83	96	96	97	88	96	100
PG3 Growth	91	88	96	111	109	107	105	106	112	114	109	108	113	108	108	113	106	105	105	102	103	103	101	100

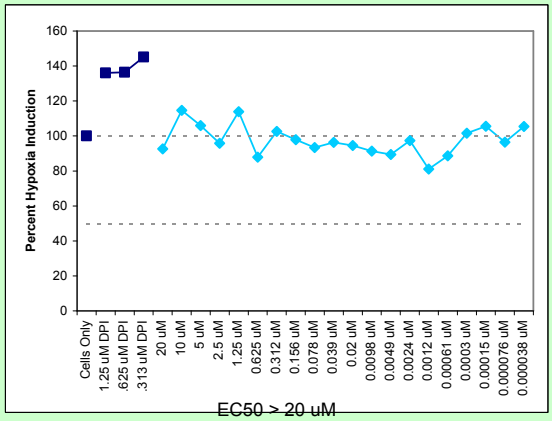
Calculated Values for 20 Dose Titration of NSC# Thurston YB072 from Well A01 of Plate 12022008005

Exp Date 12/2/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

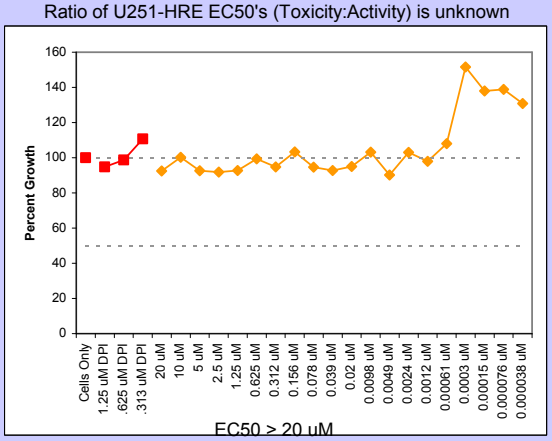


EC50 > 20 uM

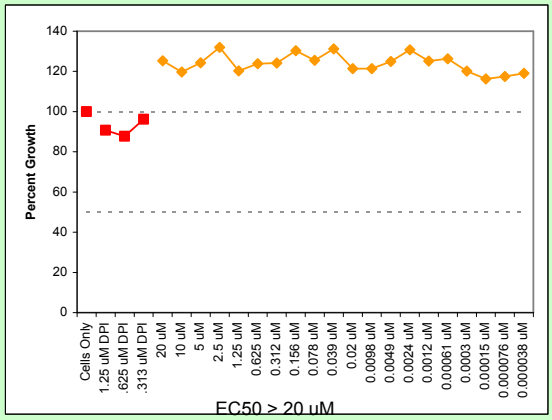


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



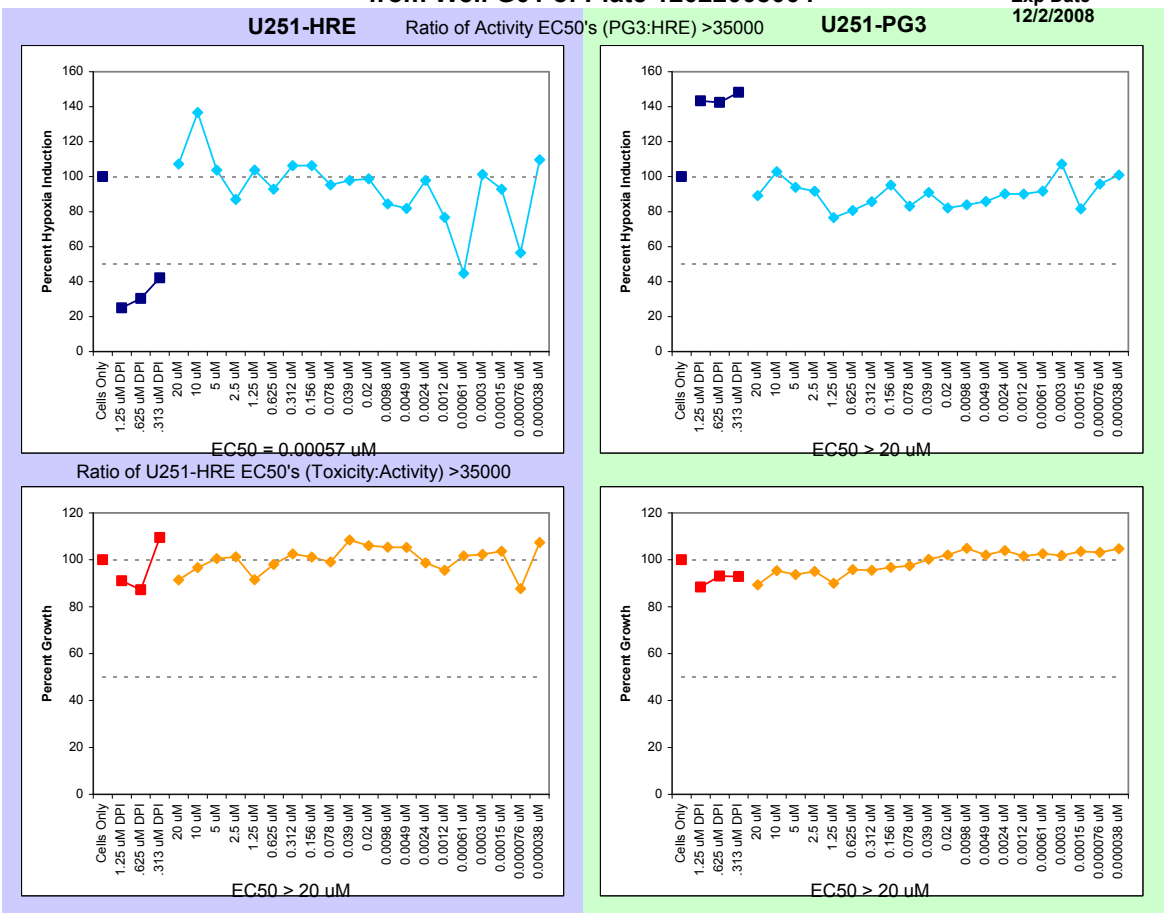
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	30	36	83	80	91	104	99	124	92	109	98	111	96	101	118	99	107	127	97	101	136	117	100
HRE Growth	95	99	111	92	100	93	92	93	99	95	103	95	93	95	103	90	103	98	108	152	138	139	131	100
				Z 'DPI = -0.73								Z Prime = -0.463						Cell Only Ind = 4.014						
PG3 Activity	136	136	145	93	115	106	96	114	88	103	98	93	96	95	91	89	97	81	89	102	106	96	105	100
PG3 Growth	91	88	96	125	120	124	132	120	124	124	130	126	131	121	121	125	131	125	126	120	116	118	119	100

5d– yb071

Calculated Values for 20 Dose Titration of NSC# Thurston YB071 from Well G01 of Plate 12022008004

Exp Date 12/2/2008

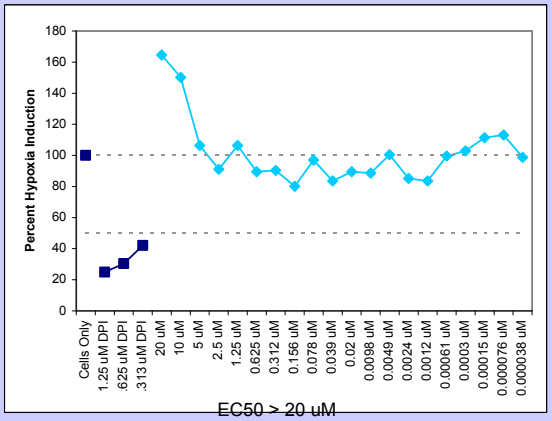


	1.25 uM DPI	625 uM DPI	313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	25	30	42	107	137	104	87	104	93	106	106	95	98	99	84	82	98	77	45	101	93	57	110	100
HRE Growth	91	87	109	91	97	101	101	91	98	103	101	99	108	106	105	105	99	96	102	102	104	88	107	100
				Z 'DPI = -0.302						Z Prime = -0.041								Cell Only Ind = 4.558						
PG3 Activity	143	142	148	89	103	94	92	77	81	86	95	83	91	82	84	86	90	90	92	107	82	96	101	100
PG3 Growth	88	93	93	89	95	94	95	90	96	96	97	97	100	102	105	102	104	102	103	102	104	103	105	100

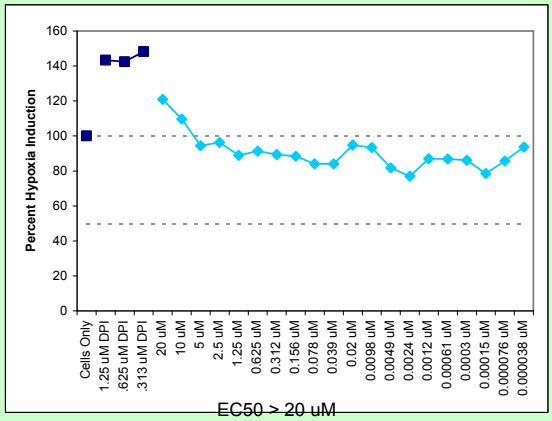
Calculated Values for 20 Dose Titration of NSC# Thurston YB064B from Well F01 of Plate 12022008004

Exp Date 12/2/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

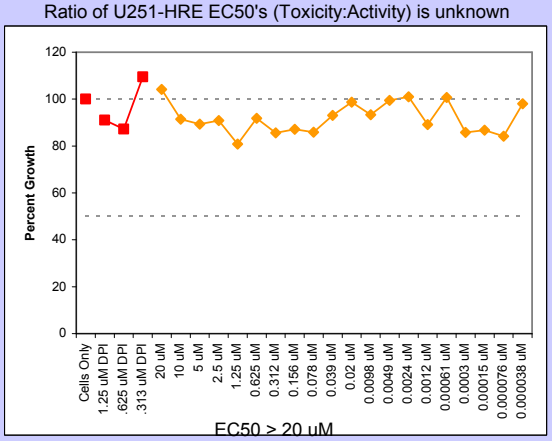


EC50 > 20 uM

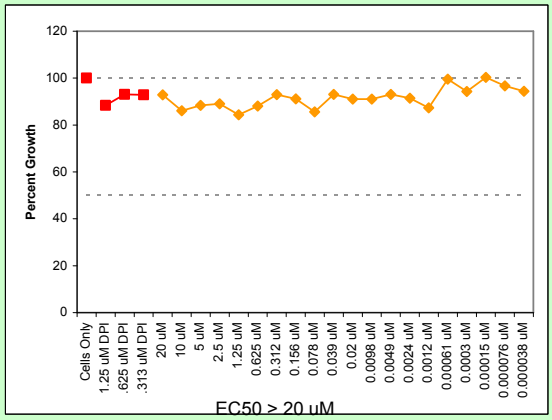


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



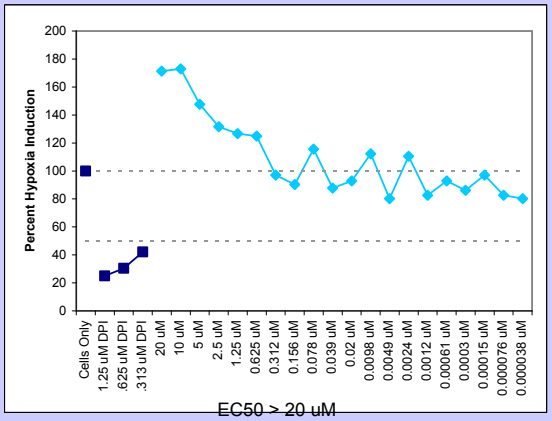
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	25	30	42	165	150	106	91	106	89	90	80	97	84	89	89	100	85	84	100	103	111	113	99	100
HRE Growth	91	87	109	104	91	89	91	81	92	86	87	86	93	99	93	99	101	89	101	86	87	84	98	100
				Z 'DPI = -0.302								Z Prime = -0.041							Cell Only Ind = 4.558					
PG3 Activity	143	142	148	121	110	94	96	89	91	89	88	84	84	95	93	82	77	87	87	86	79	86	94	100
PG3 Growth	88	93	93	93	86	88	89	84	88	93	91	86	93	91	91	93	91	87	100	94	100	97	94	100

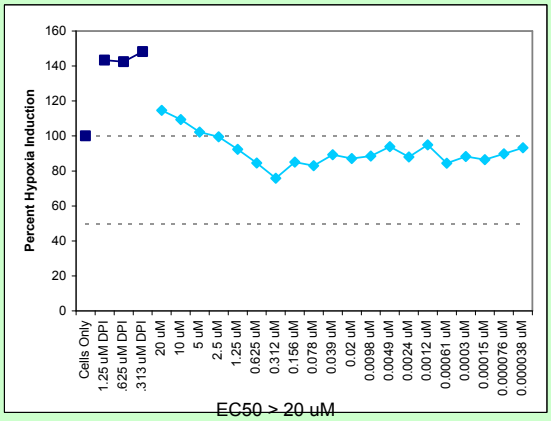
Calculated Values for 20 Dose Titration of NSC# Thurston YB064A from Well E01 of Plate 12022008004

Exp Date 12/2/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

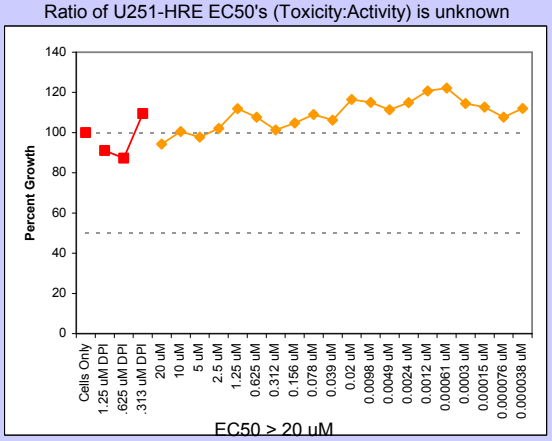


EC50 > 20 uM

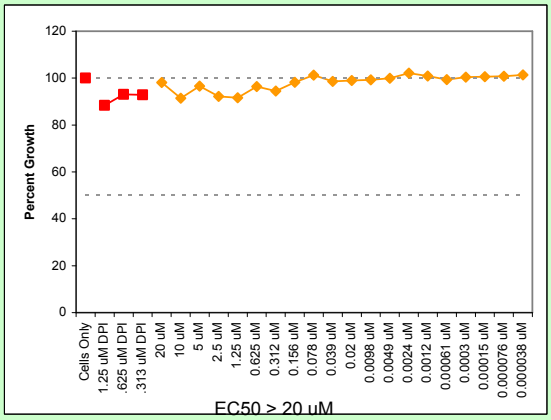


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	25	30	42	171	173	148	132	127	125	97	90	116	88	93	112	80	111	83	93	86	97	83	80	100
HRE Growth	91	87	109	94	101	98	102	112	108	101	105	109	106	117	115	111	115	121	122	114	113	108	112	100

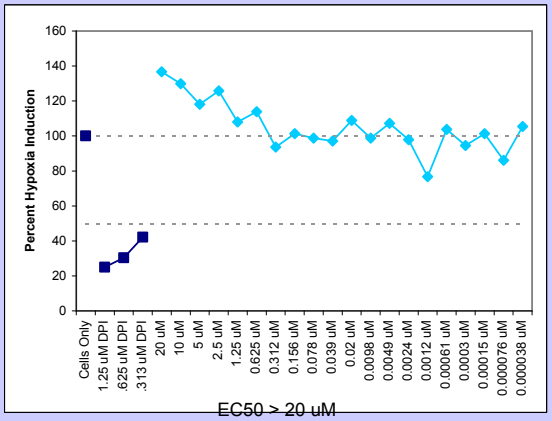
Z 'DPI = -0.302 | Z Prime = -0.041 | Cell Only Ind = 4.558

PG3 Activity	143	142	148	115	109	102	100	92	84	76	85	83	89	87	88	94	88	95	84	88	86	90	93	100
PG3 Growth	88	93	93	98	91	97	92	92	96	95	98	101	99	99	99	100	102	101	99	100	101	101	101	100

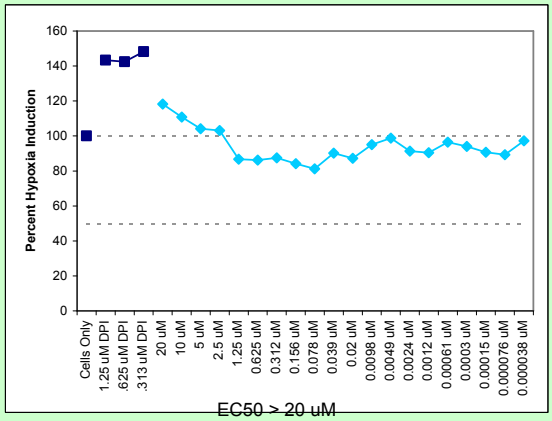
Calculated Values for 20 Dose Titration of NSC# Thurston YB063B from Well D01 of Plate 12022008004

Exp Date 12/2/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

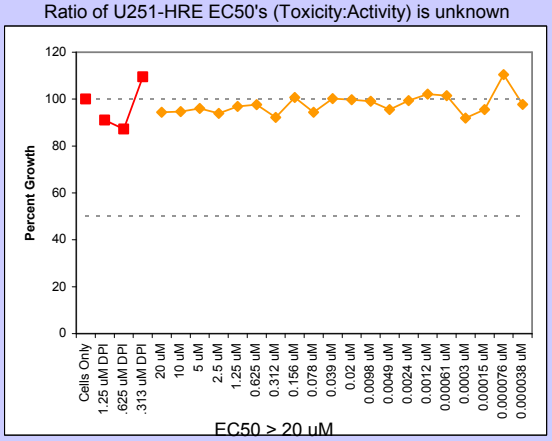


EC50 > 20 uM

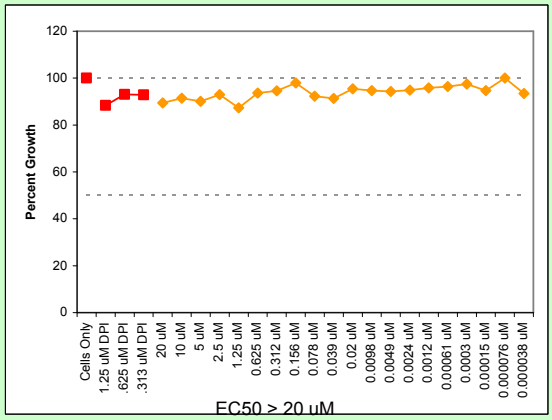


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	25	30	42	137	130	118	126	108	114	94	101	99	97	109	99	107	98	77	104	95	101	86	105	100
HRE Growth	91	87	109	94	95	96	94	97	98	92	101	94	100	100	99	96	99	102	101	92	96	110	98	100

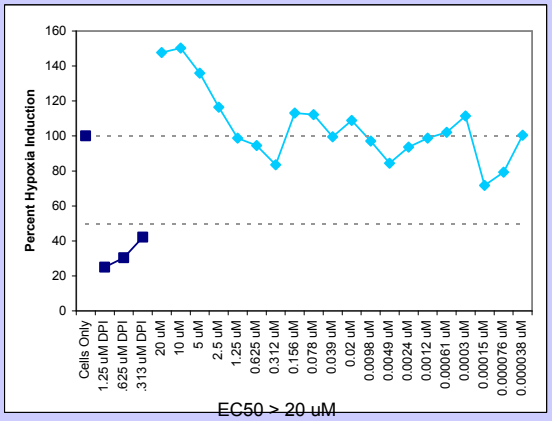
Z 'DPI = -0.302 | Z Prime = -0.041 | Cell Only Ind = 4.558

PG3 Activity	143	142	148	118	111	104	103	87	86	87	84	81	90	87	95	99	91	90	96	94	91	89	97	100
PG3 Growth	88	93	93	89	91	90	93	87	94	95	98	92	91	95	95	94	95	96	96	97	95	100	93	100

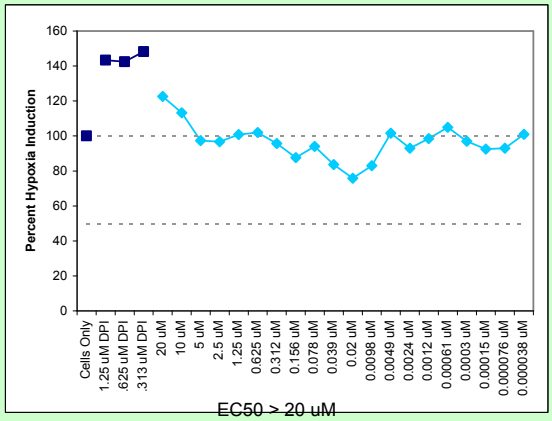
Calculated Values for 20 Dose Titration of NSC# Thurston YB063A from Well C01 of Plate 12022008004

Exp Date 12/2/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

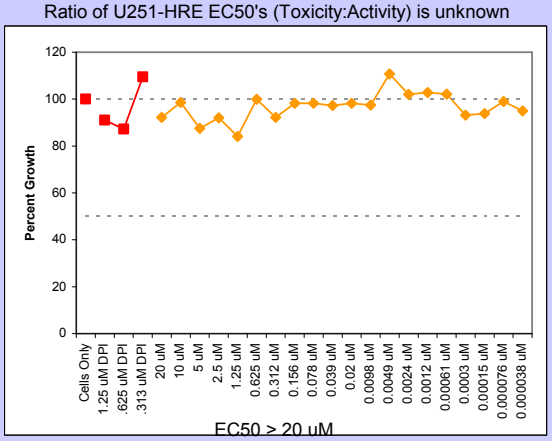


EC50 > 20 uM

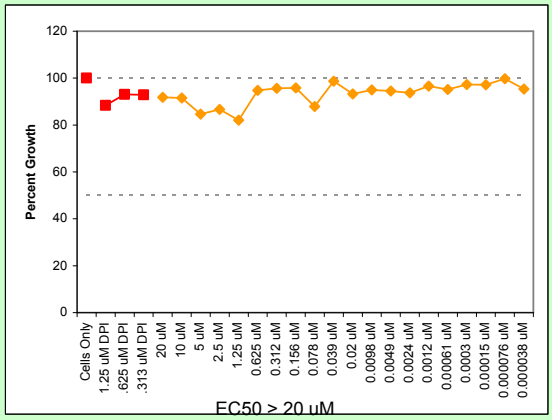


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM



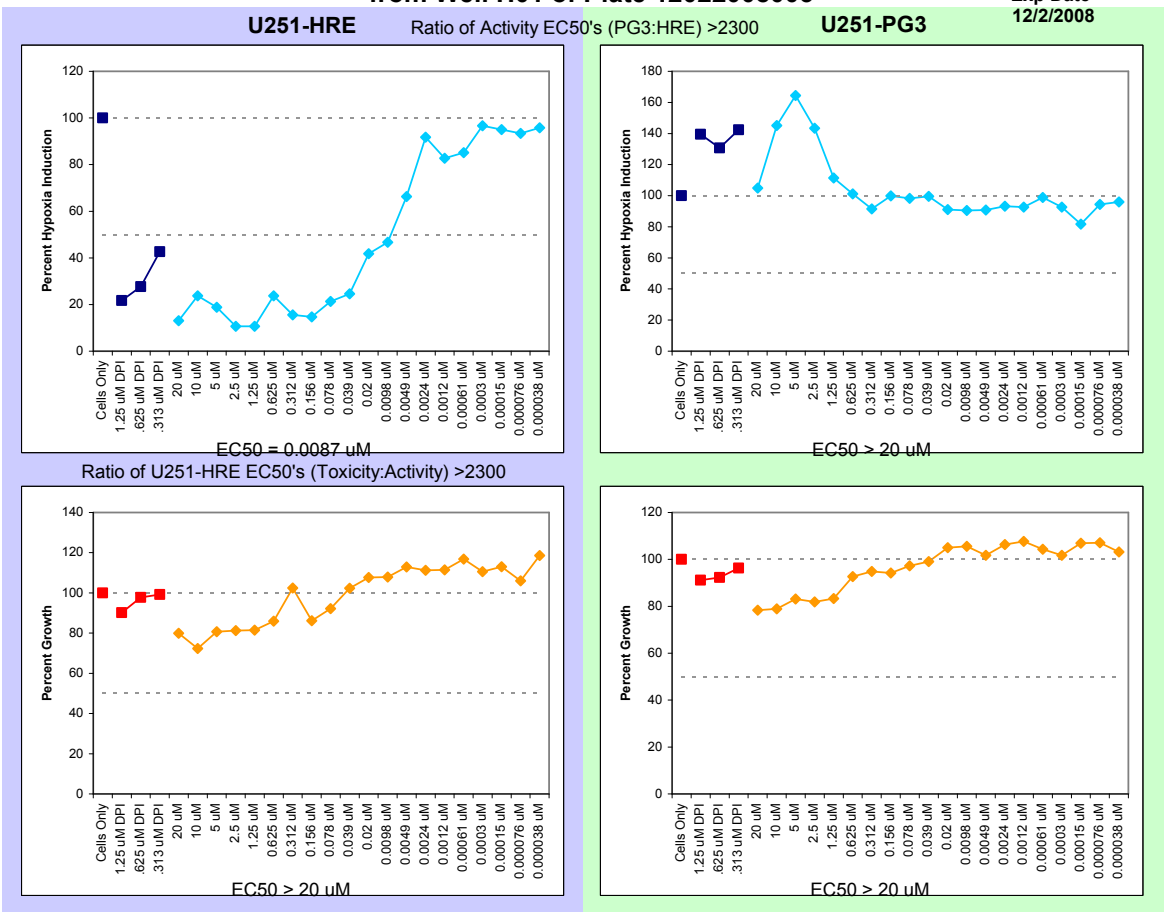
EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	25	30	42	148	150	136	116	99	95	84	113	112	100	109	97	84	94	99	102	111	72	79	100	100
HRE Growth	91	87	109	92	99	88	92	84	100	92	98	98	97	98	97	111	102	103	102	93	94	99	95	100
				Z 'DPI = -0.302							Z Prime = -0.041							Cell Only Ind = 4.558						
PG3 Activity	143	142	148	123	113	97	97	101	102	96	88	94	84	76	83	102	93	98	105	97	92	93	101	100
PG3 Growth	88	93	93	92	92	85	87	82	95	96	96	88	99	93	95	94	94	97	95	97	97	100	95	100

Topotecan 04

Calculated Values for 20 Dose Titration of NSC# S 609699 from Well H01 of Plate 12022008003

Exp Date 12/2/2008

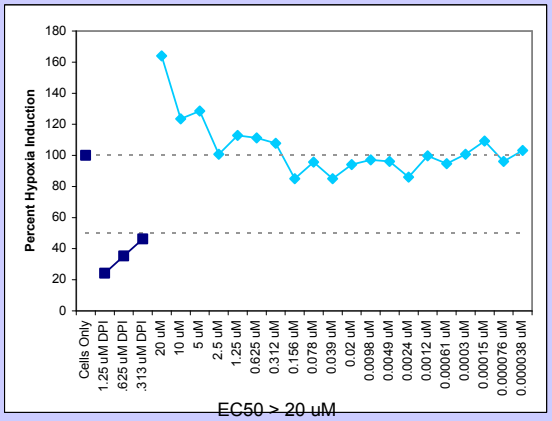


	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	22	28	43	13	24	19	11	11	24	16	15	21	25	42	47	66	92	83	85	97	95	93	96	100
HRE Growth	90	98	99	80	72	81	81	81	86	102	86	92	102	108	108	113	111	111	117	111	113	106	119	100
				Z 'DPI = -0.059								Z Prime = 0.045						Cell Only Ind = 4.697						
PG3 Activity	139	131	142	105	145	164	143	111	101	92	100	98	100	91	91	91	93	93	99	93	82	94	96	100
PG3 Growth	91	92	96	78	79	83	82	83	93	95	94	97	99	105	106	102	106	108	104	102	107	107	103	100

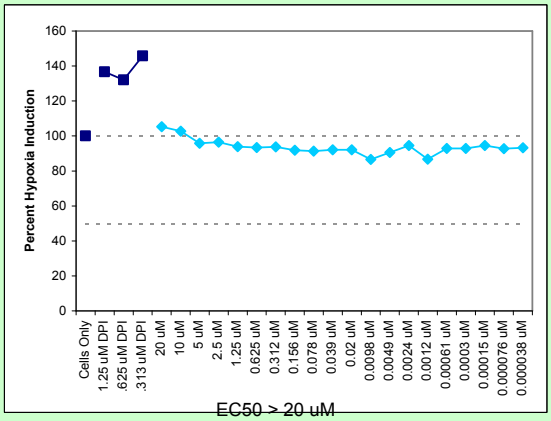
Calculated Values for 20 Dose Titration of NSC# Thurston 001-DA-023-01 from Well D01 of Plate 12092008002

Exp Date 12/9/2008

U251-HRE Ratio of Activity EC50's (PG3:HRE) is unknown **U251-PG3**

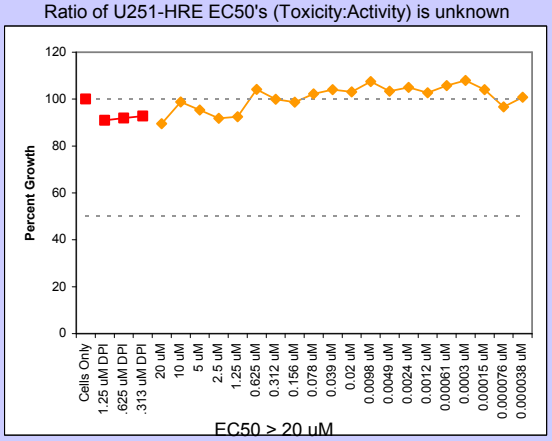


EC50 > 20 uM

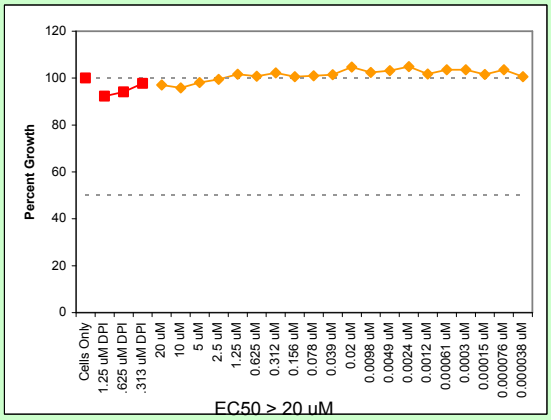


EC50 > 20 uM

Ratio of U251-HRE EC50's (Toxicity:Activity) is unknown



EC50 > 20 uM

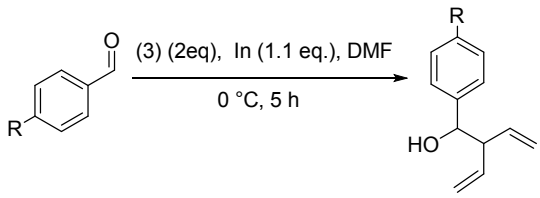


EC50 > 20 uM

	1.25 uM DPI	.625 uM DPI	.313 uM DPI	20 uM	10 uM	5 uM	2.5 uM	1.25 uM	0.625 uM	0.312 uM	0.156 uM	0.078 uM	0.039 uM	0.02 uM	0.0098 uM	0.0049 uM	0.0024 uM	0.0012 uM	0.00061 uM	0.0003 uM	0.00015 uM	0.000076 uM	0.000038 uM	Cells Only
HRE Activity	24	35	46	164	123	129	101	113	111	108	85	96	85	94	97	96	86	100	95	101	109	96	103	100
HRE Growth	91	92	93	90	99	95	92	92	104	100	99	102	104	103	107	103	105	103	106	108	104	97	101	100
				Z 'DPI = 0.1								Z Prime = 0.276							Cell Only Ind = 3.764					
PG3 Activity	137	132	146	105	103	96	96	94	93	94	92	91	92	92	87	91	95	87	93	93	95	93	93	100
PG3 Growth	92	94	98	97	96	98	99	102	101	102	101	101	102	105	102	103	105	102	104	104	102	104	101	100

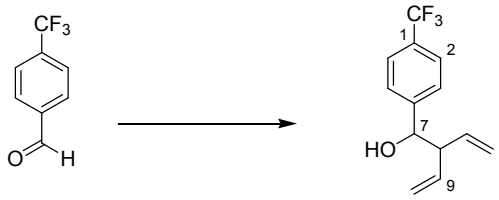
Synthesis of Cross-Conjugated Trienes

1) Preparation of the indium-mediated γ-pentadienylation of benzaldehydes



General procedure for the preparation of phenyl-vinylbutenol compounds as previously reported by Bendiabdellah & Zinzalla[1] and references therein.

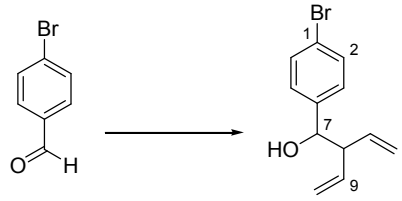
7-(1-(trifluoromethyl)phenyl)-8-vinylbut-9-en-7-ol



$C_{13}H_{13}F_3O$
MW: 242.24

The product was isolated as a clear yellow oil; **Y** = 74%; $\boldsymbol{R_f}$ 0.16 (Silicagel, *n*-hexane/EtOAc 10:1); **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.59 (2H, d, *J* =8.2Hz, $H^{2,6}$),7.43(2H, d, *J* =8.2Hz, $H^{3,5}$),5.82 (1H, ddd, *J* =17.2, 10.3, 8.2 Hz, H^9),5.70 (1H, ddd, *J* =17.2, 10.2, 7.2 Hz, H^9),5.25 (1H, dd, *J* = 10.2, 1.0Hz, H^{11}),5.17 (1H, dt, *J* = 17.2, 1.1Hz, H^{11}), 5.09 (1H, dt, *J* = 10.4, 1.2Hz, H^{11}), 5.02 (1H, dt, *J* = 17.2, 1.2Hz, H^{11}), 4.66 (1H, dd, *J* = 6.8, 2.9Hz, H^8), 3.08 (1H, q, *J* = 7.2Hz, H^7),2.32 (1H, d, *J* = 3.2Hz,OH);**^{13}C NMR**(100MHz, $CDCl_3$): δ144.7 (C^4), 135.1 (C^9), 134.9 (C^9), 128.6 (C1, q, *J* = 32Hz), 126.1 (C^3&C^5), 123.95 (C^2&C^6), 123.2 (CF_3, q, *J* = 270Hz), 117.8 (C^{10}), 116.7(C^{10}), 74.5 (C^8), 55.2 (C^7); **HRMS**: Found 281.0547 $[M+K]^+$, $C_{13}H_{13}F_3KO$ theoretical mass = 281.0556; **Elemental analysis**, calculated for $C_{13}H_{13}F_3O$: C 64.46%, H 5.41%; found: C 64.48%, H 5.21%.

7-(1-bromophenyl)-8-vinylbut-9-en-7-ol

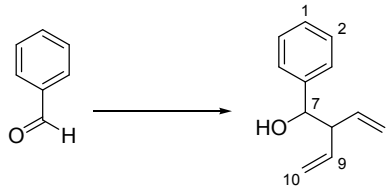


$C_{12}H_{13}BrO$
MW: 253.14

The product was isolated as clear, yellow oil; **Y** = 85%; $\boldsymbol{R_f}$ 0.13 (Silicagel, *n*-hexane/EtOAc 10:1); **^{1}H NMR** (400MHz, $CDCl_3$):δ 7.46 (2H, d, *J* =8.4Hz, $H^{2,6}$),7.19(2H, d, *J* =8.4Hz, $H^{3,5}$), 5.80 (1H, ddd, *J* =17.2, 10.3, 8.2 Hz, H^9), 5.64 (1H, ddd, *J* =17.2, 10.2, 7.2 Hz, H^9), 5.25 (1H, dd, *J* = 10.2, 1.0Hz, H^{10}), 5.17 (1H, dt, *J* = 17.2, 1.1Hz, H^{10}), 5.07 (1H, dt, *J* = 10.4, 1.2Hz, H^{10}), 5.01 (1H, dt, *J* = 17.2, 1.2Hz, H^{10}), 4.56 (1H, dd, *J* = 6.8, 2.9Hz, H^8), 3.04 (1H, q, *J* =

7.2Hz, H^7), 2.18 (1H, d, *J* = 3.2Hz, OH);**MS** (ESI): *m/z* = 251.19 [M-H^+, 100%], calculated for same isomer = 253.022 $[M+H]^+$.

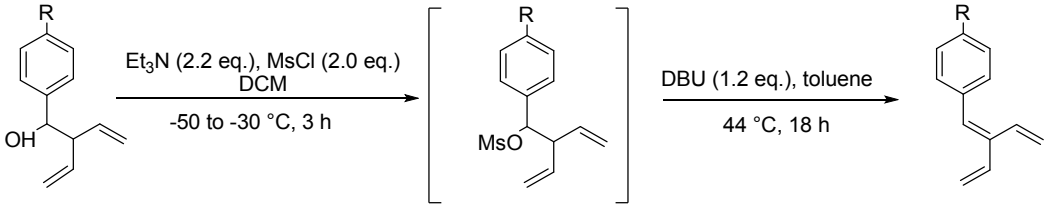
7-phenyl-8-vinylbut-9-en-7-ol



$C_{12}H_{14}O$
MW: 174.24

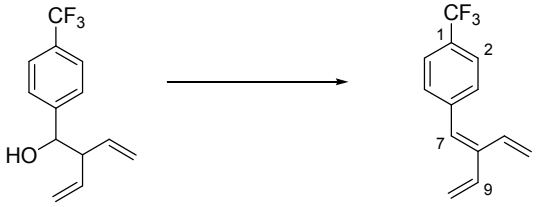
The product was isolated as a clear, yellow oil; $\boldsymbol{R_f}$ 0.18 (Silica gel, *n*-hexane/EtOAc 10:1). Spectroscopic data in accordance with those reported in literature.

2) Formation of the cross-conjugated triene system



General procedure as previously reported by Bendiabdellah and Zinzalla.[1]

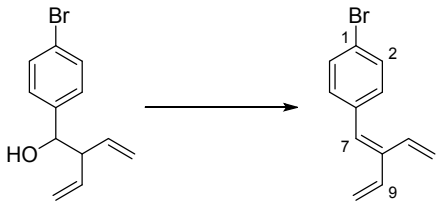
1-(trifluoromethyl)-4-(8-vinylbuta-7,9-dienyl)benzol



$C_{13}H_{11}F_3$
MW: 224.22

The product was isolated as a clear oil; **Y** = 88%; $\boldsymbol{R_f}$ 0.11 (Silicagel, *n*-hexane/EtOAc 10:1); **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.59 (2H, d, *J* =8.2Hz, $H^{2,6}$), 7.43(2H, d, *J* =8.2Hz, $H^{3,5}$), 6.71-6.63 (1H, dd, *J* =17.1, 11.2 Hz, $H^{9/9'}$), 6.65 (1H, s, H^7), 6.63-6.55 (1H, ddd, *J* = 17.2, 10.7, 0.7Hz, $H^{9/9'}$), 5.61 (1H, dd, *J* = 17.2, 1.3Hz, $H^{10/10'}$), 5.52 (1H, dd, *J* = 17.6, 1.2Hz, $H^{10/10'}$), 5.44 (1H, dt, *J* = 11.2, 1.2Hz, $H^{10/10'}$), 5.30 (1H, dd, *J* = 10.7, 1.3Hz, $H^{1010'}$); **^{13}C NMR** (100MHz, $CDCl_3$): δ140.67 (C^4), 139.9 (C^8), 137.7 (C^9), 132.8 (C^9), 129.7 (C^3&C^5), 129.2 (C1, q, J = 32Hz), 127.8 (C^7), 125.0 (C^2&C^6), 124.2 (CF_3, q, *J* = 270Hz), 119.6 (C^{10}), 117.4 (C^{10}).

1-bromo-4-(2-vinylbuta-1,3-dienyl)benzene

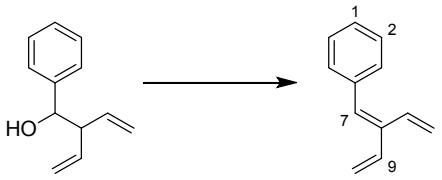


$C_{12}H_{13}BrO$
MW: 253.14

$C_{12}H_{11}Br$
MW: 235.12

The product was isolated as a clear oil; **Y** = 92%; $\boldsymbol{R_f}$ 0.06 (Silicagel, *n*-hexane/EtOAc 10:1);**^{1}H NMR** (400MHz, $CDCl_3$): δ 7.46 (2H, d, *J* =8.5Hz, $H^{2,6}$), 7.23 (2H, d, *J* =8.5Hz, $H^{3,5}$), 6.62 (1H, dd, *J* =17.6, 11.0 Hz, $H^{9/9'}$), 6.54 (1H, s, H^{7}), 6.53 (1H, ddd, *J* = 17.3, 10.7, 0.9Hz, $H^{9/9'}$), 5.55 (1H, dd, *J* = 17.3, 1.3Hz, $H^{10/10'}$), 5.48 (1H, dd, *J* = 17.6, 1.2Hz, $H^{10/10'}$), 5.38 (1H, dt, *J* = 11.2, 1.2Hz, $H^{10/10'}$), 5.23 (1H, dd, *J* = 10.7, 1.3Hz, $H^{10/10'}$);**^{13}C NMR**(100MHz, $CDCl_3$): δ138.6 (C^4), 137.7 (C^7), 133.1 (C^9), 132.8 (C^9), 131.3 (C^3, C^5), 131.2 (C^2, C^6), 128.2 (C^9), 121.0 (C1), 119.1 (C^{10}), 116.5 (C^{10}); **MS (EI)**: *m/z* = 233.60 [M-H^+, 100%], calculated = 235.0122 $[M+H]^+$.

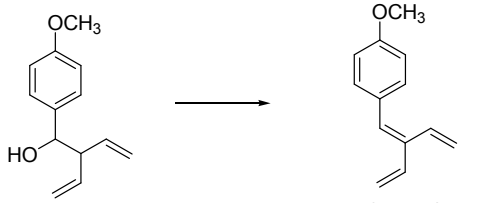
(8-vinylbuta-7,9-dienyl)benzene



$C_{12}H_{12}$
MW: 156.22

The product was isolated as clear oil. **Y** = 88%;$\boldsymbol{R_f}$ 0.12 (Silicagel, *n*-hexane/EtOAc 10:1).Spectroscopic data in accordance with those reported in literature.

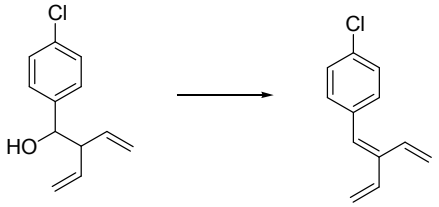
Synthesis of 1-methoxy-4-(2-vinylbuta-1,3-dienyl)benzene



$C_{13}H_{14}O$
Mol. Wt.: 186.25

The product was isolated as clear oil (900 mg, 44%). **IR** (cm^{-1}): 3082, 3003, 2956, 2835, 1601, 1505, 1301, 1247, 1174, 1033, 989, 908, 828. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 3.85 (s, 3 H, OCH_3), 5.20 (dd of a AMX system, 1 H, *J* = 1.68, 10.74 Hz, H4'*E*), 5.37 (dt of a AMX system, 1 H, *J* = 1.52, 11.15 Hz, geminal coupling of H4*E*), 5.47 (ddd of a AMX system, 1 H, *J* = 0.38, 1.73, 17.72 Hz, H4*Z*), 5.53 (dd of a AMX system, 1 H, *J* = 1.63, 17.20 Hz, H4'*Z*), 6.57 (ddd of a AMX system, 1 H, *J* = 17.24, 10.69, 0.85 Hz, H3'), 6.62 (s, 1 H, H1), 6.73 (ddd of a AMX system, 1 H, *J* = 17.76, 11.13, 0.83 Hz, H3), 6.91 (d, 2 H, *J* = 8.83 Hz, HAr3 and HAr5), 6.91 (d, 2 H, *J* = 8.41 Hz, HAr2 and HAr6). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 158.9 (CAr4), 138.1 (C3'), 136.4 (C2), 133.7 (C3), 131.1 (CAr2 and CAr6), 129.8 (CAr1), 129.2 (C1), 117.9 (C4), 115.4 (C4'), 113.6 (CAr3 and CAr5), 55.3 (OCH_3). **MS** (ESI^+) *m/z* (relative intensity): 160.69 ($[M - CHCH_2 + H]^{\cdot+}$, 100%).

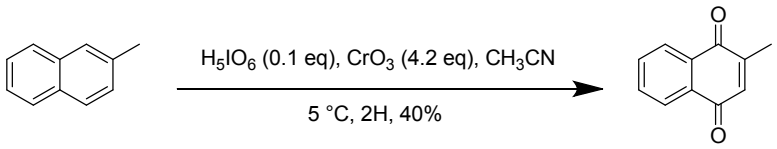
Synthesis of 1-chloro-4-(2-vinylbuta-1,3-dienyl)benzene



$C_{12}H_{11}Cl$
Mol. Wt.: 190.67

The product was isolated as clear oil (106 mg, 53%). **IR** (ATR, λ_{max}/cm^{-1}): 3091, 3008, 1486, 1422, 1091, 1013, 988, 911, 873, 825, 784. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.19 (dd of a AMX system, 1 H, *J* = 1.1, 10.6 Hz, H4′*E*), 5.34 (dt of a AMX system, 1 H, *J* = 1.1, 11.1 Hz, geminal coupling of H4*E*), 5.42 (ddd of a AMX system, 1 H, *J* = 0.8, 1.5, 17.7 Hz, H4*Z*), 5.50 (dd of a AMX system, 1 H, *J* = 1.5, 17.4 Hz, H4′*Z*), 6.50 (dd of a AMX system, 1 H, *J* = 10.7, 17.3 Hz, H3′), 6.52 (s, 1 H, H1), 6.59 (dd of a AMX system, 1 H, *J* = 11.2, 17.8 Hz, H3), 7.30 (s, 4 H, HAr2, HAr3, HAr5 and HAr6). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 138.6 (C2), 137.7 (C3′), 136.2 (CAr4), 133.1 (C3), 132.9 (CAr1), 130.9 (CAr3 and CAr5), 128.3 (CAr2 and CAr6), 128.1 (C1), 119.0 (C4), 116.5 (C4′).

General procedure for the Synthesis 2-methyl- and 2,3-dimethyl- naphthoquinone



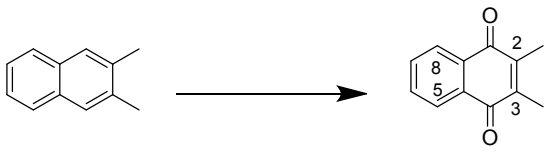
$C_{11}H_8O_2$
MW: 172.18

H_5IO_6 (3.52 mmol, 1.0 eq.) was dissolved in acetonitrile (65 ml) with vigorous stirring, and CrO_3 (0.352 mmol, 0.1 eq.) was dissolved to the solution. The resulted solution was cooled at 5 °C. 2-Methylnaphthalene (3.52 mmol, 1.0 eq.) dissolved in mlacetonitrile (5 ml) was added to the previous solution with stirring. A white precipitate formed immediately with exothermic reaction. After 2h stirring at 5°C, the supernatant liquid of the reaction mixture was decanted to a flask, and the solvent was removed by evaporation. The residues after decantation and evaporation were dissolved in H_2O and CH_2Cl_2, combined and then extracted with CH_2Cl_2 (10 ml×2). The collected organic extracts were washed with aq.NaOH. The aqueous phase was acidified with 1 M aq. HCl and extracted with CH_2Cl_2. 2-Naphthoic acid (55 mg, 9%) was obtained from acidified aqueous solution by CH_2Cl_2 extraction. The organic layer was washed with brine, and dried over $MgSO_4$. The solvent was concentrated under reduced pressure. The raw product obtained was recrystallized from ethanol to afford 2-methyl-1,4-naphthoquinone (40%) as yellow crystals.[2]

2-methyl-naphthoquinone

Y = 40%;$\boldsymbol{R_f}$ 0.24 (CH_2Cl_2/*n*-hexane 50:50);**^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.06 – 8.13 (2H,m, H^6& H^7), 7.75 (2H,dd, H^7&H^6), 6.87 (1H, s,H^3), 2.22 (3H, s,CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 195.0 (C^1& C^4), 156.0 (C^2&C^3), 138.0 (C^{4a}&C^{8a}), 135.7 (C^7), 133.7 (C^6), 126.5 (C^5), 126.1 (C^8), 18.0 (CH_3).

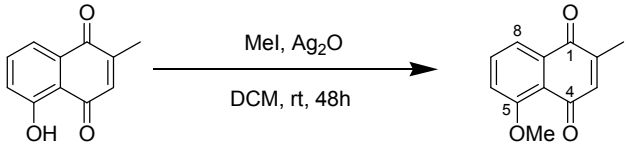
2,3-dimethyl-1,4-naphthoquinone



$C_{12}H_{10}O_2$
MW: 186.21

The product was isolated as a yellow solid. **Y** = 45%; R_f 0.25 (Silica gel, CH_2Cl_2); **IR**: 2924, 1656, 1620, 1592, 1458, 1371, 1334, 1293, 790, 695 cm^{-1}.**^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.06 – 8.13 (2H,m, $H^{6,7}$), 7.75 (2H,dd, $H^{7,6}$), 6.87 (1H, s,H^3), 2.22 (3H, s,CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 184.7 ($C^{1,4}$), 143.3 ($C^{2,3}$), 133.2 ($C^{5,6}$), 132.0 ($C^{7,8}$), 126.1 ($C^{4a,\ 8a}$), 12.8 (2 × CH_3) ; **HRMS**: found MH^+ 181.0756, $C_{12}H_{11}O_2$ requires 181.0759. Spectroscopic data in accordance with those reported in literature.[3]

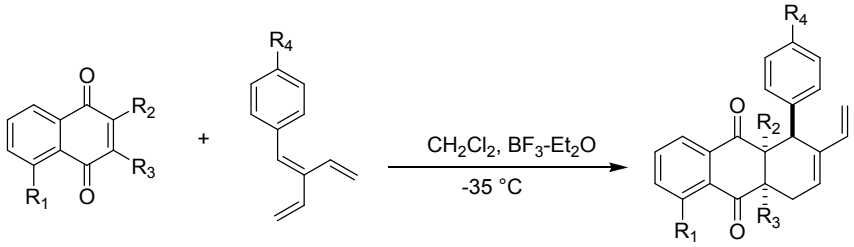
5-methoxy-2-methylnaphthoquinone



$C_{12}H_{10}O_3$
MW: 202.21

The product was isolated as yellow compound; **Y** = 99%; R_f0.27 (Silica gel, CH_2Cl_2); **IR**: 2950,1663,1583,1282,1256 cm^{-1}; **Mp.** 93-95 ˚C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.74 (d,1H, *J* = 6.9Hz, H^8), 7.65 (t, 1H, *J* = 7.8 Hz, H^7), 7.29 (d, 1H, *J* = 8.1 Hz, H^7), 6.73 (d, 1H, *J* = 1.5Hz, H^3), 4.00 (s, 3H, CH_3O), 2.13 (s, 3H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ185.7 ($C^{1/4}$), 184.4 ($C^{1/4}$), 159.3 (C^5), 145.3 (C^2), 137.8 (C^3), 134.5 (C^7), 134.3 (C^{8a}), 119.8 (C^{4a}), 119.3 (C^8), 117.6 (C^6), 56.4 (CH_3O), 15.7 (CH_3); **Elemental analysis**, Calcd for $C_{12}H_{10}O_3$: C 71.28%, H 4.98%;found C 71.01%, H 5.05%. Spectroscopic data in accordance with those reported in literature.[3]

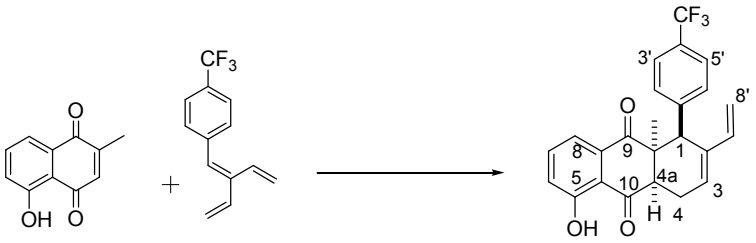
General procedure for the synthesis of the tricyclic compounds: 1st Diels-Alders reaction



The procedure employed for the preparation of the tricyclic compounds by Kormann *et al.* [3] was modified as follow. A solution of quinone (0.14 mmol, 1.0 eq.) and cross-conjugated triene (0.21 mmol, 1.5 eq.) in CH_2Cl_2 (5 ml) was cooled to −35 °C (acetonitrile in immersion cooler) under inert atmosphere. Boron trifluorideEt_2Oate (0.37 mmol, 2.5 eq.) was added dropwise within 5min. After stirring for 1 h, the reaction mixture was treated with an additional amount

of cross-conjugated triene (0.068mmol, 0.5 eq.). The solution was allowed to stir overnight at -35 ºC. After addition of H_2O (5 ml) the reaction mixture was allowed to warm to 0 °C under vigorous stirring. Treatment with *n*-hexane (5 ml) followed by cooling to −60 °C (acetone/MeOH 1:1 and dry ice) resulted in freezing of the aqueous layer. The supernatant organic phase was removed by pipetting and evaporated under reduced pressure. Purification of the resulting residue was performed by adsorption to silica gel; the un-reacted triene and nonpolar side-products were removed by washing with *n*-hexane (500 ml). Elution using CH_2Cl_2 (500 ml) and subsequent evaporation of the solvent afforded the tricyclic compound.

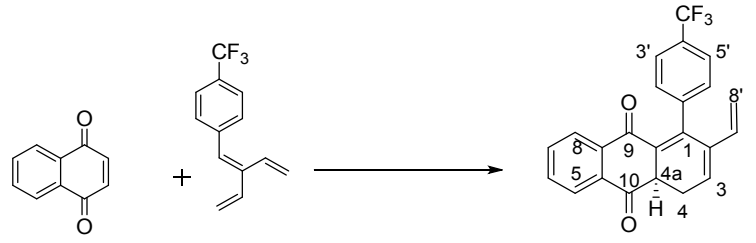
(1SR,4aRS,9aSR)-5-hydroxy-9a-methyl-1-(4-(trifluoromethyl)phenyl)-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{24}H_{19}F_3O_3$
MW: 412.40

The product is a yellow solid; **Y** = 65%; $\boldsymbol{R_f}$ 0.51 (Silica gel, CH_2Cl_2), **Mp** = 114-118 ºC; **IR** 2917, 2873, 1690, 1642, 1453, 1418, 1320, 1264, 1162, 1063, 902, 816, 725 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ11.59 (1H, s, OH), 7.34 (2H, dd, *J*=7.6, 1.6 Hz, $H^{6/8}$), 7.30 (1H, t, *J* = 7.6Hz, H^7), 7.06 (2H, d, *J*= 8.2Hz, $H^{5',3'}$), 6.94 (2H, d, *J* = 8.3Hz, $H^{6',2'}$), 6.89 (1H, dd, *J*= 7.8, 1.6Hz, H^8), 6.27 (1H, dd, *J*= 17.6, 10.9Hz, $H^{7'}$), 6.16 (1H, t, *J*= 3.9Hz, H^3), 4.81 (1H, d, J = 10.9Hz, $H^{8'cis}$), 4.65 (1H, d, J = 17.6Hz, $H^{8'trans}$), 4.21 (1H, d, J = 6.1Hz, H^4), 3.78 (1H,s, H^1), 3.14 (1H, d, *J*= 7.9Hz, H^{4a}), 2.43 (1H, dd,*J*= 20.16, 7.9Hz, H^4), 1.65 (3H, s, CH_3);**^{13}C NMR** (100MHz, $CDCl_3$): δ 202.1 ($C^{9/10}$), 199.5 ($C^{9/10}$), 159.8 (0), 142.3 (0), 137.5 (C^6), 135.8 (C^8), 134.2 (0), 134.1 (0), 129.5 ($C^{6',2'}$), 128.2 (C^3), 124.5 (q, *J*= 4Hz, $C^{5'/3'}$), 123.8 (q, *J*= 270Hz, CF_3), 123.1 (C^7), 118.2 ($C^{7'}$), 117.5 (0), 113.3 ($C^{8'}$), 52.1 (0), 49.5 (C^1), 48.1 (C^{4a}), 23.9 (CH_3), 20.3 (C^4); **MS** (EI): *m/z* 411.53 ($M-H^+$) (100); **HRMS**: Found MH^+ 413.1356, $C_{24}H_{19}F_3O_3$ requires *MH*, 413.1364.

(RS)-4-(4-(trifluoromethyl)phenyl)-3-vinyl-1,9a-dihydroanthracene-9,10-dione

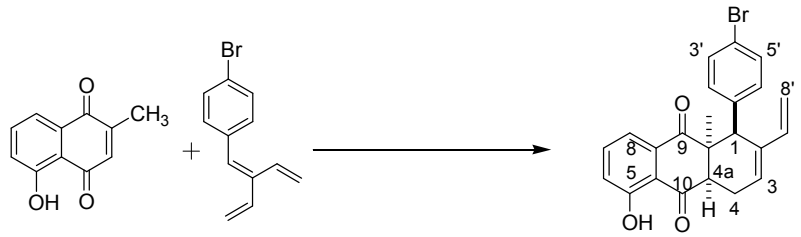


$C_{23}H_{15}F_3O_2$
MW: 380.36

The product is a yellow solid; **Y** = 56%; $\boldsymbol{R_f}$ 0.52 (Silica gel, CH_2Cl_2); **Mp** = 127-130 ºC; **IR** 2359, 2330, 1661, 1594, 1416, 1290, 1163, 1121, 1017, 840 cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ 8.07 (1H, m, $H^{5/8}$), 8.03 (1H, m, $H^{5/8}$), 7.69 (2H, m, $H^{7,6}$), 7.50 (4H, dd, *J*= 11.96, 8.8Hz, $H^{6',2',5',3'}$), 6.34 (1H, dd, *J*= 17.6, 10.9Hz, $H^{7'}$), 6.21 (1H, t, *J*= 2.5Hz, H^3), 5.30 (1H, t, H^{4a}), 5.26 (1H, d, J = 17.6Hz, $H^{8'}$), 5.04 (1H, d, *J*= 10.9Hz, $H^{8'}$), 3.7 (1H, dt, *J*= 24.8, 4.6Hz, H^4), 3.46 (1H, ddd, *J*= 22.8, 4.6, 2.5, H^4); **MS** (EI): *m/z* 381.25 ($M+H^+$) (100); **HRMS**: Found

MNa^+ 403.0928, $C_{23}H_{15}F_3O_2$ requires *MNa*, 403.0922; **Purity** 95 %. Spectroscopic data in accordance with those reported in literature.[3]

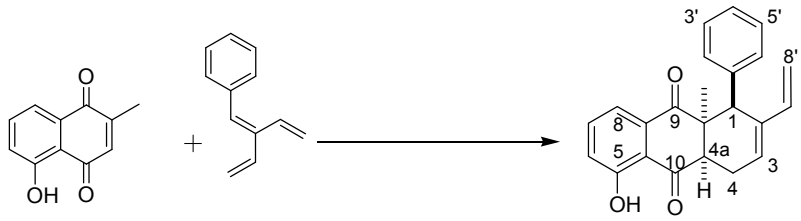
(1S,4aR,9aS)-1-(4-bromophenyl)-5-hydroxy-9a-methyl-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{23}H_{19}BrO_3$
423.29

The product is a dark yellow solid; **Y** = 92%; $\boldsymbol{R_f}$ 0.26 (Silica gel, CH_2Cl_2/*n*-hexane 5:5); **IR** 2975, 2923, 1688, 1639, 1452, 750 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ11.60 (1H, s, OH), 7.60 (2H, m, $H^{3',5'}$), 7.36 (1H, m, H^8), 7.26 (2H, d, *J*= 4.3Hz, $H^{2',6'}$), 6.94 (1H, m,H^7), 6.68 (1H, m, H^6), 6.24 (1H, m, $H^{7'}$), 6.12 (1H, d, *J* = 3.3 Hz, H^3), 4.80 (1H, dd, *J*= 10.9, 3.3 Hz, $H^{8'}$), 4.67 (1H, dd, *J*= 17.5, 3.2 Hz, $H^{8'}$), 3.70 (1H, s, H^1), 3.58 (1H,dd, *J*= 16.1, 4.1 Hz, H^4), 3.02 (1H, dd, *J*= 7.7, 3.7 Hz, H^{4a}), 2.41 (dd, 1H, *J*= 18.3, 2.5 Hz, H^4), 1.62 (3H, s, CH_3); **MS** (EI): *m/z* 424.38 ($M\text{-}H^+$) (100); **Purity** 95 %.Spectroscopic data in accordance with those reported in literature[3].

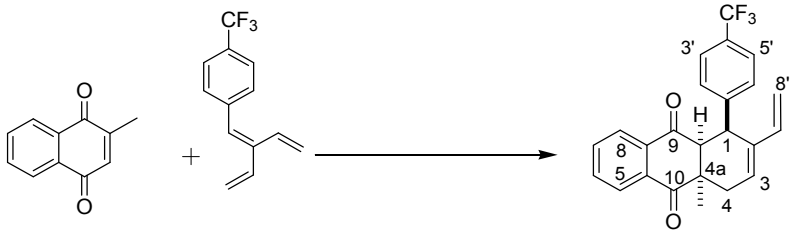
(1S,4aR,9aS)-5-hydroxy-9a-methyl-1-phenyl-2-vinyl-1,4,4a,9a-tetrahydro-anthracene-9,10-dione



$C_{23}H_{20}O_3$
MW: 344.40

The product is a yellow solid; **Y** = 62%; $\boldsymbol{R_f}$ 0.27 (Silica gel, CH_2Cl_2/*n*-hexane 5:5); **IR:** 2971, 2926, 2868, 1690, 1641, 1452, 753 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ11.67 (1H, s, OH), 7.37 (1H, dd, *J* = 8.2, 1.1 Hz, H^7), 7.30 (1H, t, *J*= 8.0Hz, H^8), 6.88 (1H, dd, *J*= 8.2, 1.1Hz, H^6), 6.81 (5H, m, $H^{2'\text{-}6'}$), 6.26 (1H, dd, *J*= 17.6, 10.9Hz, $H^{7'}$), 6.12 (1H, t, *J*= 3.9Hz , H^3), 4.73 (1H, d, *J*= 17.6 Hz, $H^{8'}$), 3.76 (1H,s, H^1), 3.61 (1H, dd, 20.1, 4.6, H^4), 3.01 (1H, d, *J*= 8.0Hz, H^{4a}), 2.43 (dd, 1H, *J*= 20.3, 7.8Hz, H^4); 1.64 (3H, s, CH_3); **MS** (EI): *m/z* 343.64 ($M\text{-}H^+$) (100); **Purity** 95 %.Spectroscopic data in accordance with those reported in literature.[3]

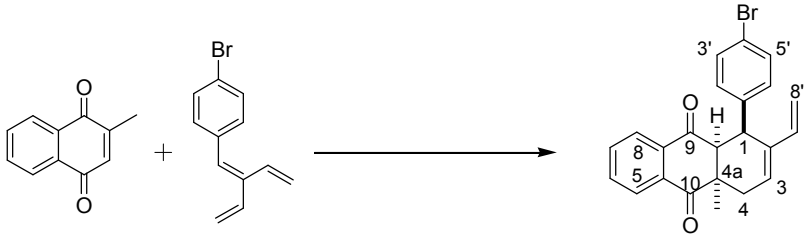
(1SR,4aRS,9aSR)-4a-methyl-1-(4-(trifluoromethyl)phenyl)-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{24}H_{19}F_3O_2$
MW: 396.40

The product was obtained as yellow solid; **Y** = 86%; R_f 0.36 (Silica gel, chloroform); **Mp** = 79.2 – 78.3 ºC; **IR** 3385, 2919, 2358, 1688, 1616, 1592, 1420, 1252, 1163, 1122, 1068, 979, 720 cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ 7.69 (1H, m, $H^{7/6}$), 7.54 (1H, m, $H^{7/6}$), 7.37 (2H, m, $H^{5,8}$), 6.97 (2H, d, *J* = 8.2Hz, H3´, $H^{5´}$), 6.87 (2H, d, *J* = 8.2Hz, $H^{2´,6´}$), 6.21 (1H, dd, *J*= 17.6, 10.9Hz, $H^{7´}$), 6.12 (1H, t, *J* = 4Hz, H^3), 4.77 (1H, d, *J*= 10.9Hz, $H^{8´cis}$), 4.63 (1H, d, *J*= 17.6Hz, $H^{8´trans}$), 4.23 (1H, d, *J*= 6.4Hz, H^{9a}), 3.67 (1H, dd, *J*= 20.1, 4.6Hz, H^4), 3.42 (1H, d, *J*= 6.5Hz, H^1), 2.08 (d, 1H, *J*= 20.1Hz, H^4),1.26 (3H, s, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 199.4 ($C^{9/10}$), 199.3 ($C^{9/10}$), 142.2, 137.2 ($C^{7´}$), 134.9, 134.6, 134.1 ($C^{5/8}$), 133.6, 133.5 ($C^{5/8}$), 130.3 (C2), 129.9 ($C^{2´,6´}$), 126.8 ($C^{7/6}$), 126.1 ($C^{7/6}$), 125.1 ($C^{3´,5´}$), 123.9 (CF_3, q, *J* = 270Hz), 113.6 ($C^{8´}$), 59.5 (C^1), 45.8 (C^{4a}), 43.9 (C^{9a}), 32.1 (C^4), 30.5 (CH_3); **MS** (EI): *m/z* 397.47 ($M+H^+$) (100). **HRMS**: Found MNa^+ 419.1254, $C_{24}H_{19}F_3O_2$ requires *MNa*, 419.1235; **Purity** 95 %.

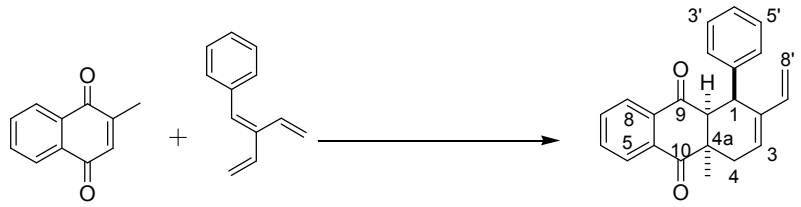
(1SR,4aRS,9aSR)-1-(4-bromophenyl)-4a-methyl-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{23}H_{19}BrO_2$
MW: 407.30

The product was obtained as yellow solid; **Y** = 83%; R_f 0.33 (Silica gel, chloroform); **Mp** = 85.2–86.4 ºC; **IR:** 2964, 2359, 2335, 1591, 1485, 1407, 1281, 1249, 1072, 1009, 800, 736 cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ 7.72 (1H, m, $H^{7/6}$), 7.58 (1H, m, $H^{7/6}$), 7.45 (2H, m, $H^{5,8}$), 6.84 (2H, d, *J* = 8.4Hz, $H^{3´,5´}$), 6.61 (2H, d, *J* = 8.4Hz, $H^{2´,6´}$), 6.19 (1H, dd, *J*= 17.6, 10.9Hz, $H^{7´}$), 6.08 (1H, t, *J* = 4Hz, H^3), 4.76 (1H, d, *J*= 10.9Hz, $H^{8´cis}$), 4.65 (1H, d, *J*= 17.6Hz, $H^{8´trans}$), 4.14 (1H, d, *J*= 6.2Hz, H^{9a}), 3.64 (1H, dd, *J*= 20.1, 4.4Hz, H^4), 3.38 (1H, d, *J*= 6.4Hz, H^1), 2.05 (1H,d, *J*= 20.0Hz, H^4),1.25 (3H, s, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 199.4 ($C^{9/10}$), 199.1 ($C^{9/10}$), 137.3 (C^3), 137.1, 135.0, 134.9, 133.9 ($C^{5/8}$), 133.7, 133.6 ($C^{5/8}$), 131.2 ($C^{2´/6´/3´/5´}$), 131.1 ($C^{2´/6´/3´/5´}$), 130.0 ($C^{7´}$), 126.9 ($C^{7/6}$), 126.1 ($C^{7/6}$), 121.2 (0), 113.5 ($C^{8´}$), 59.6 (C^1), 45.6 (C^{4a}), 43.4 (C^{9a}), 31.9 (C^4), 30.4 (CH_3); **MS** (EI): *m/z* 407.33 ($M+H^+$) (100); **HRMS**: Found MNa^+ 429.0456, $C_{23}H_{19}BrO_2$ requires *MNa*, 429.0466; **Purity** 95 % .

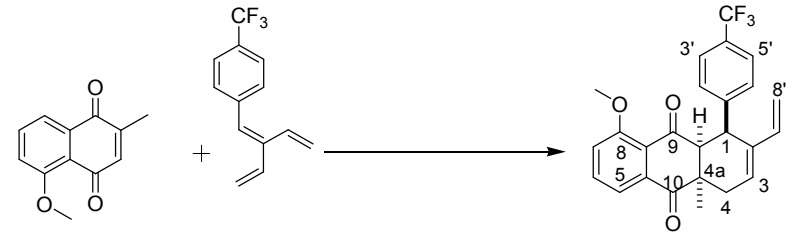
(1SR,4aRS,9aSR)-4a-methyl-1-phenyl-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{23}H_{20}O_2$
MW: 328.40

The product was obtained as yellow solid; **Y** = 78%; R_f 0.36 (Silica gel, chloroform); **Mp** = 77.4 ºC; **IR** 2926, 2359, 1592, 1492, 1453, 1282, 1251, 979, 701 cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ 7.69 (1H, m, $H^{7/6}$), 7.54 (1H, m, $H^{7/6}$), 7.35 (2H, m, $H^{5,8}$), 6.64 - 6.79 (5H, m, $H^{2'-6'}$), 6.20 (1H, dd, *J*= 17.6, 10.9Hz, $H^{7'}$), 6.06 (1H, t, *J* = 3.8Hz, H^3), 4.75 (1H, d, *J*= 10.9Hz, $H^{8'cis}$), 4.68 (1H, d, *J*= 17.6Hz, $H^{8'trans}$), 4.18 (1H, d, *J*= 6.3Hz, H^{9a}), 3.57 (1H, dd, *J*= 20.1, 4.4Hz, H^4), 3.39 (1H, d, *J*= 6.4Hz, H^1), 2.05 (1H,d, *J*= 20.0Hz, H^4),1.24 (3H, s, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 199.8 ($C^{9/10}$), 199.4 ($C^{9/10}$), 137.8 (C^3), 137.4 (0), 135.4 (0), 134.9 (0), 133.7 ($C^{5/8}$), 133.6 (0), 133.2 ($C^{5/8}$), 129.5 ($C^{2'-6'}$), 129.4 ($C^{2'-6'}$),128.1 ($C^{7'}$), 127.2 ($C^{7/6}$), 126.6 ($C^{7/6}$), 125.9 (0), 113.3 ($C^{8'}$), 59.8 (C^1), 45.8 (C^{4a}), 44.2 (C^{9a}), 32.1 (C^4), 30.7 (CH_3); **MS** (EI): *m/z* 329.39 ($M+H^+$) (100); **HRMS**: Found MNa^+, 351.1362, $C_{23}H_{20}O_2$ requires *MNa*, 351.1361; **Purity** 95 %.

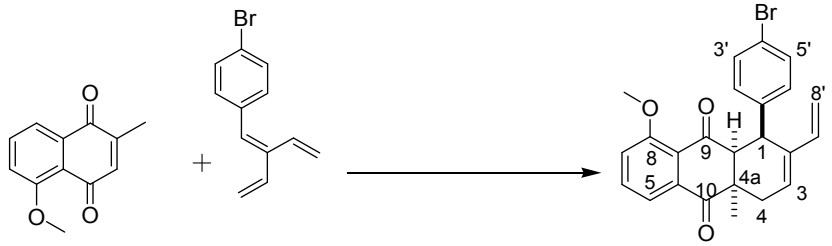
(1SR,4aRS,9aSR)-8-methoxy-4a-methyl-1-(4-(trifluoromethyl)phenyl)-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{25}H_{21}F_3O_3$
MW: 426.43

The product was obtained as yellow solid; **Y** = 76%; R_f 0.28 (Silica gel, chloroform); **Mp** = 107.9-110.3 ºC; **IR:** 3374, 2931, 2358, 1684, 1585, 1468, 1277, 1231, 1163, 1120, 1068, 993 cm^{-1};**^{1}H NMR** (500MHz, $CDCl_3$): δ 7.32 (1H, t, *J* = 8.0Hz, H^6), 7.24 (1H, m, $H^{7/5}$), 7.02 (2H, d, *J* = 8.2Hz, $H^{3',5'}$), 6.94 (2H, d, *J* = 8.3Hz, $H^{2',6'}$), 6.92 (1H, dd, *J* = 8.4, 1.0Hz, $H^{5/7}$), 6.22 (1H, dd, *J*= 17.6, 11.0Hz, $H^{7'}$), 6.13 (1H, t, *J* = 4.0Hz, H^3), 4.78 (1H, d, *J*= 10.9Hz, $H^{8'cis}$), 4.62 (1H, d, *J*= 17.6Hz, $H^{8'trans}$), 4.26 (1H, d, *J*= 6.9Hz, H^{9a}), 3.89 (s, 3H, CH_3), 3.58 (1H, dd, *J*= 19.8, 4.9Hz, H^4), 3.37 (1H, d, *J*= 6.5Hz, H^1), 2.08 (1H, d,*J*= 19.8Hz, H^4),1.31 (3H, s, CH_3); **^{13}C NMR** (125MHz, $CDCl_3$): δ 199.0 ($C^{9/10}$), 198.9 ($C^{9/10}$), 158.1 (C^8), 142.8 ($C^{1'}$), 137.2 ($C^{7'}$), 135.3 (C^{5a}), 134.5 (C^6), 134.1 (C^{8a}), 130.1 (C^3), 129.8 (C^2), 129.4 ($C^{5',6'}$), 124.6 ($C^{2'/3'}$), 124.6 ($C^{2'/3'}$), 124.0 (CF_3, q, *J* = 270Hz), 118.8 ($C^{5/7}$), 116.8 ($C^{5/7}$), 113.4 ($C^{8'}$), 61.0 (C^1), 56.3 (CH_3), 45.6 (C^{4a}), 43.1 (C^{9a}), 31.9 (C^4), 29.3 (CH_3); **MS** (EI): *m/z* 427.33 ($M+H^+$) (100); **HRMS**: Found MNa^+, 449.1351, $C_{25}H_{21}F_3O_3$ requires *MNa*, 449.1341; **Purity** 95 %.

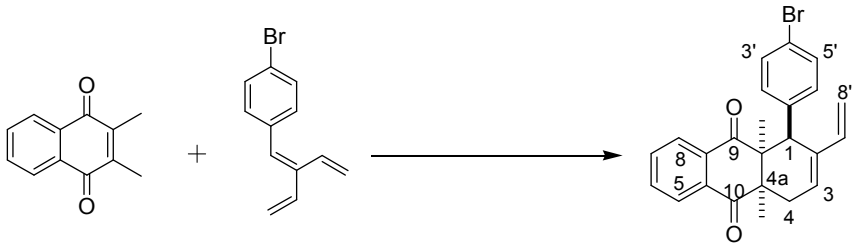
(1SR,4aRS,9aSR)-1-(4-bromophenyl)-8-methoxy-4a-methyl-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{24}H_{21}BrO_3$
MW: 437.33

The product was obtained as yellow solid; **Y** = 81%; $\boldsymbol{R_f}$ 0.29 (Silica gel, chloroform); **Mp** = 115.2 – 116.9 ºC; **IR:** 3400, 2964, 2359, 1680, 1584, 1485, 1467, 1275, 1229, 1069, 992 cm^{-1};**^{1}H NMR** (500MHz, $CDCl_3$): δ 7.32 (1H, t, *J* = 8.0Hz, H^6), 7.24 (1H, m, $H^{7/5}$), 7.02 (2H, d, *J* = 8.2Hz, $H^{3',5'}$), 6.94 (2H, d, *J* = 8.3Hz, $H^{2',6'}$), 6.92 (1H, dd, *J* = 8.4, 1.0Hz, $H^{5/7}$), 6.22 (1H, dd, *J*= 17.6, 11.0Hz, $H^{7'}$), 6.08 (1H, t, *J* = 4.0Hz, H^3), 4.77 (1H, d, *J*= 10.9Hz, $H^{8'cis}$), 4.64 (1H, d, *J*= 17.6Hz, $H^{8'trans}$), 4.16 (1H, d, *J*= 6.7Hz, H^{9a}), 3.91 (s, 3H, CH_3), 3.56 (1H, dd, *J*= 19.8, 4.8Hz, H^4), 3.33 (1H, d, *J*= 6.9Hz, H^1), 2.04 (1H, dd,*J*= 19.8, 2.0Hz, H^4),1.29 (3H, s, CH_3); **^{13}C NMR** (125MHz, $CDCl_3$): δ 199.2 ($C^{9/10}$), 198.2 ($C^{9/10}$), 158.2 (C^8), 137.6 ($C^{1'}$), 137.1 ($C^{7'}$), 135.4 (C^{5a}), 134.4 (C^{8a}), 134.3 (C^6), 130.8 ($C^{2',6'}$), 130.7 ($C^{3',5'}$), 129.8 (C^3), 123.4 (C^2), 120.8 ($C^{4'}$), 118.9 ($C^{5/7}$), 116.8 ($C^{5/7}$), 113.3 ($C^{8'}$), 61.2 (C^1), 56.4 (CH_3), 45.5 (C^{4a}), 42.8 (C^{9a}), 31.9 (C^4), 29.3 (CH_3); **MS** (EI): *m/z* 437.22 ($M+H^+$) (100); **HRMS**: Found MH^+, 437.0737, $C_{24}H_{21}BrO_3$ requires *M*, 437.0752; **Purity** 95 %.

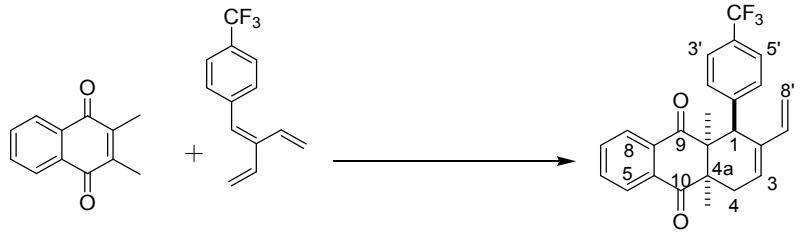
(1SR,4aRS,9aSR)-1-(4-bromophenyl)-4a,9a-dimethyl-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{24}H_{21}BrO_2$
MW: 421.33

The product was obtained as yellow solid; **Y** = 80%; $\boldsymbol{R_f}$ 0.39 (Silica gel, chloroform); **Mp** = 103.8-105.4 ºC; **IR** 3441, 2969, 2359, 2330, 1741, 1680, 1592, 1370, 1262, 1010, 980cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ 7.75 (1H, m, $H^{5/8}$), 7.57 (1H, m, $H^{8/5}$), 7.44 (2H, m, $H^{7,6}$), 6.84 (2H, d, *J* = 8.3Hz, $H^{3',5'}$), 6.63 (2H, dd, *J* = 8.7, 1.0Hz, $H^{2',6'}$), 6.22 (1H, dd, *J*= 17.6, 10.9Hz, $H^{7'}$), 6.12 (1H, t, *J* = 4.0Hz, H^3), 4.76 (1H, d, *J*= 10.9Hz, $H^{8'cis}$), 4.57 (1H, d, *J*= 17.7Hz, $H^{8'trans}$), 3.74 (1H, s, H^1), 3.55 (1H, dd, *J*= 19.8, 4.4Hz, H^4), 2.06 (1H,ddt, *J*= 19.7, 2.0, 1.0Hz, H^4), 1.57 (3H, s, CH_3),1.14 (3H, s, CH_3);**^{13}C NMR** (100MHz, $CDCl_3$): δ 201.5 ($C^{9/10}$), 199.8 ($C^{9/10}$), 137.6 ($C^{7'}$), 137.2 (C^2), 134.6 ($C^{1'/4'}$), 134.0 (C^{8a}), 133.9 (C^{9a}), 133.3 ($C^{6/7}$), 133.1 ($C^{6/7}$), 131.5 ($C^{2',6'}$), 130.8 ($C^{3',5''}$), 129.4 (C^3), 126.1 ($C^{5,8}$), 121.0 ($C^{1'/4'}$), 113.1 ($C^{8'}$), 55.8 ($C^{4a/9a}$), 52.1 (C^1), 49.3 ($C^{4a/9a}$), 30.8 (C^4), 26.7 (CH_3), 19.8 (CH_3); **MS** (EI): *m/z* 443.07 ($M+Na^+$) (100); **HRMS**: Found MNa^+ 443.0604, $C_{24}H_{21}BrO_2$ requires *MNa*, 443.0623; **Purity** 95%.

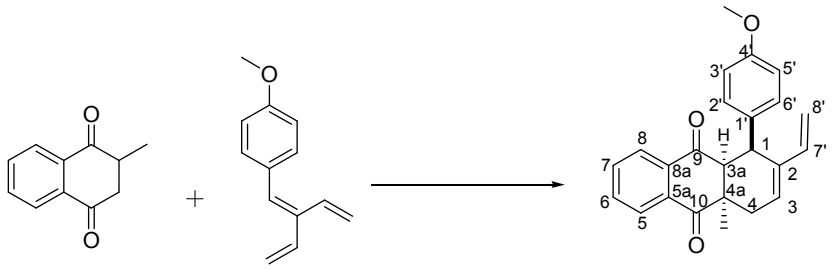
(1S,4aR,9aS)-4a,9a-dimethyl-1-(4-(trifluoromethyl)phenyl)-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{25}H_{21}F_3O_2$
MW: 410.43

The product was obtained as yellow solid; **Y** = 77%; R_f 0.37 (Silica gel, chloroform); **Mp** = 122.7–124.3 ºC; **IR** 2985, 2873, 2358, 1681, 1615, 1594, 1419, 1262, 1111, 980cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ 7.71 (1H, m, $H^{8/5}$), 7.50 (1H, m, $H^{8/5}$), 7.34 (2H, m, $H^{7,6}$), 6.94 (2H, d, *J* = 8.1Hz, $H^{3',5'}$), 6.87 (2H, dd, *J* = 8.2Hz, $H^{2',6'}$), 6.21 (1H, dd, *J*= 17.6, 11.0Hz, $H^{7'}$), 6.14 (1H, t, *J* = 3.9Hz, H^3), 4.72 (1H, d, *J*= 11.0Hz, $H^{8'cis}$), 4.53 (1H, d, *J*= 17.6Hz, $H^{8'trans}$), 3.81 (1H, s, H^1), 3.55 (1H, dd, *J*= 19.8, 4.9Hz, H^4), 2.05 (1H,dt, *J*= 19.8, 0.9Hz, H^4), 1.57 (3H, s, CH_3),1.11 (3H, s, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 201.2 ($C^{9/10}$), 199.6 ($C^{9/10}$), 142.4 (C^2), 137.6 ($C^{7'}$), 134.6 ($C^{1',4'}$), 133.8 (C^{8a}), 133.7 (C^{9a}), 133.5 ($C^{6/7}$), 133.2 ($C^{6/7}$), 130.2 ($C^{3',5'}$), 129.7 ($C^{2',6''}$), 129.4 (C^3), 126.1 ($C^{5,8}$), 124.6 (C^8), 124.0 (q, *J* = 270Hz, CF_3), 113.3 ($C^{8'}$), 55.8 ($C^{4a/9a}$), 52.4 (C^1), 49.3 ($C^{4a/9a}$), 30.8 (C^4), 26.7 (CH_3), 19.9 (CH_3); **MS** (EI): *m/z* 410.52 ($M+H^+$) (100); **HRMS**: Found MH^+, 411.1552, $C_{25}H_{21}F_3O_2$ requires *M*, 411.1572; **Purity** 97%.

Synthesis of (1*S*,4a*R*,9a*S*)-1-(4-methoxyphenyl)-4a-methyl-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione

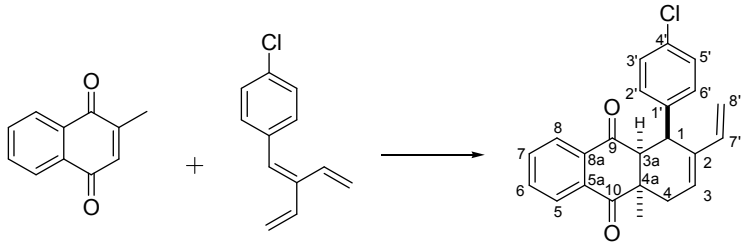


$C_{24}H_{22}O_3$
Mol. Wt.: 358.43

Boron trifluoride (0.42 mL, 3.35 mmol, 2.7 equiv.) was slowly added (dropwise over 10 mim) to a solution of 1-methoxy-4-(2-vinylbuta-1,3-dienyl)benzene (300 mg, 1.61 mmol, 1.3 equiv.) and 2-methyl-2,3-dihydronaphthalene-1,4-dione (213 mg, 1.24 mmol, 1.0 equiv.) in anhydrous DCM (5 mL) under nitrogen atmosphere in a sealed tube at -40 ºC under magnetically stirring. The mixture was kept under the same conditions for 1 d and then allowed to warm to room temperature. Water (4 mL) was then poured into the tube and the mixture was transferred to a separating funnel. The organic layer was washed with an additional aliquot of water, dried over MgSO4, filtrated and concentrated under reduced pressure. The remaining crude material was subjected to flash chromatography (hexane/EtOAc 10:0 → hexane/EtOAc 6:4) to isolate the product as a colourless solid (130 mg, 22%). **IR** (ATR, λ_{max}/cm^{-1}): 2966, 2908, 2834, 1695, 1681, 1608, 1591, 1509, 1284, 1249, 1222, 1030, 978, 913, 827, 716. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 1.29 (s, 3 H, CH_3), 2.09 (d, 1 H, *J* = 20.0 Hz, H4), 3.40 (d, 1 H, *J* = 6.2 Hz, H3a), 3.54 (s, 3 H, OCH_3), 3.69 (dd, 1 H, *J* = 4.5, 20.0 Hz, H4, 4.19 (d, 1 H, *J* = 6.1 Hz, H1), 4.75 (d, 1 H, *J* = 17.6 Hz, H8'*Z*), 4.81 (d, 1 H, *J* = 10.9 Hz, H8'*E*), 6.09 (t, 1 H, *J* = 4.0 Hz, H3), 6.25 (dd of a AMX system, 1 H, *J* = 10.9, 17.6 Hz, H7'), 6.31 (d, 2 H, *J* = 8.7 Hz, H3' and H5'), 6.68 (d, 2 H, *J* = 8.7 Hz, H2' and H6'), 7.41-7.47 (m, 2 H, H7 and H6), 7.62-7.64 (m, 1 H, H5), 7.77-7.79

(m, 1 H, H8). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 200.0 (C9), 199.4 (C10), 158.5 (C4'), 137.2 (C7'), 135.4 (C8a), 134.7 (C2), 133.6 (C5a), 133.3 (C7 or C6), 132.9 (C7 or C6), 130.3 (C2' and C6'), 129.7 (C1'), 129.1 (C3), 126.4 (C5), 125.8 (C8), 113.3 (C3' and C5'), 113.0 (C8'), 60.0 (C3a), 55.1 (OCH_3), 45.6 (C4a), 43.2 (C1), 31.8 (C4), 30.4 (CH_3). **MS** (ESI^+) *m/z* (relative intensity): 359.9 ($[M + H]^{\cdot+}$, 5 %). **HRMS**: Theoretical mass $[M + H]^{\cdot+}$, 359.1647; Measured mass $[M + H]^{\cdot+}$, 359.1638 (2 ppm).

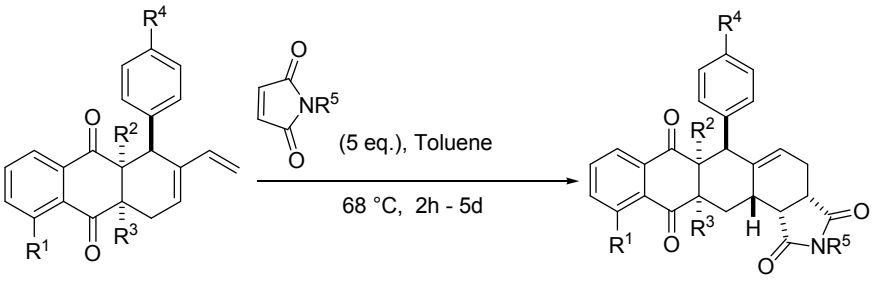
Synthesis of (1*S*,4a*R*,9a*S*)-1-(4-chlorophenyl)-4a-methyl-2-vinyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione



$C_{23}H_{19}ClO_2$
Mol. Wt.: 362.85

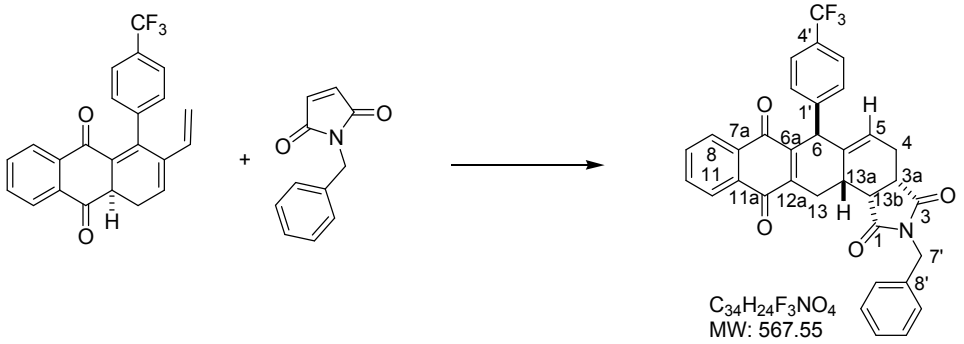
Boron trifluoride (0.13 mL, 1.11 mmol, 2.7 equiv.) was slowly added (dropwise over 10 mim) to a solution of 1-chloro-4-(2-vinylbuta-1,3-dienyl)benzene (100 mg, 0.53 mmol, 1.3 equiv.) and 2-methyl-2,3-dihydronaphthalene-1,4-dione (71.0 mg, 0.41 mmol, 1.0 equiv.) in anhydrous DCM (3 mL) under nitrogen atmosphere in a sealed tube at -40 ºC under magnetically stirring. The mixture was kept under the same conditions for 1 d and then allowed to warm to room temperature. Water (4 mL) was then poured into the tube and the mixture was transferred to a separating funnel. The organic layer was washed with an additional aliquot of water, dried over MgSO4, filtrated and concentrated under reduced pressure. The remaining crude material was subjected to flash chromatography (hexane/EtOAc 10:0 → hexane/EtOAc 6:4) to furnish the product as clear oil (70 mg, 47 %). **IR** (ATR, λ_{max}/cm^{-1}): 3024, 2967, 1687, 1593, 1489, 1416, 1282, 1249, 1226, 1090, 1015, 980, 902, 821, 802, 743. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 1.28 (s, 3 H, CH_3), 2.08 (d, 1 H, *J* = 19.9 Hz, H4), 3.40 (d, 1 H, *J* = 6.5 Hz, H3a), 3.67 (dd, 1 H, *J* = 4.6, 20.0 Hz, H4, 4.17 (d, 1 H, *J* = 6.4 Hz, H1), 4.67 (d, 1 H, *J* = 17.6 Hz, H8'*Z*), 4.79 (d, 1 H, *J* = 10.9 Hz, H8'*E*), 6.10 (t, 1 H, *J* = 4.0 Hz, H3), 6.22 (dd of a AMX system, 1 H, *J* = 10.9, 17.6 Hz, H7'), 6.70 (q, 4 H, *J* = 7.6 Hz, H2', H3', H4' and H5'), 7.45-7.49 (m, 2 H, H7 and H6), 7.60-7.65 (m, 1 H, H5), 7.77-7.78 (m, 1 H, H8). **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 199.4 (C9), 199.1 (C10), 137.0 (C7'), 136.2 (C8a), 134.8 (C2), 134.7 (C5a), 133.6 (C7 or C6), 133.5 (C1'), 133.2 (C7 or C6), 132.9 (C4'), 130.7 (C2' and C6'), 129.5 (C3), 128.0 (C3' and C5'), 126.5 (C5), 125.8 (C8), 113.1 (C8'), 59.5 (C3a), 45.6 (C4a), 43.4 (C1), 31.8 (C4), 30.2 (CH_3). **MS** (ESI^+) *m/z* (relative intensity): 359.9 ($[M + H]^{\cdot+}$, 5 %). **HRMS**: Theoretical mass $[M + H]^{\cdot+}$, 359.1647; Measured mass $[M + H]^{\cdot+}$, 359.1638 (2 ppm).

General procedure for the synthesis of the pentacyclic compounds: 2nd Diels-Alders reaction



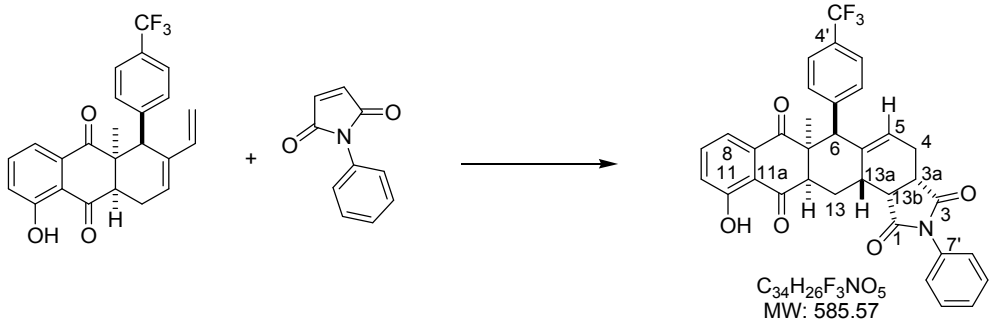
The preparation of the tetracyclic compounds was carried out as reported by Kormann *et. al*.[3].

(3aSR,6SR,13aSR,13bRS)-2-benzyl-6-(4-(trifluoromethyl)phenyl)-3a,4,13,13a-tetrahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,6H,13bH)-tetraone (YB021)



YB021 was obtained as a clear yellow solid; **Y** = 85%; ***R_f*** 0.09 (Silica gel, CH_2Cl_2); **Mp** = 145-150 ºC; **IR**: 2363, 2339, 1707, 1325, 1165, 668 cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ 8.20 (m, 1H, $H^{8/11}$), 8.08 (m, 1H, $H^{8/11}$), 7.73 (m, 2H, $H^{9,10}$), 7.47 (d, 2H, *J*= 8.3Hz, $H^{5',3'}$), 7.22 (d, 2H, *J*= 8.4Hz, $H^{2',6'}$), 7.14 (t, 1H, *J*= 7.4Hz, $H^{11'}$), 7.04 (t, 2H, *J*= 7.3Hz, $H^{10',12'}$), 6.89 (d, 2H, *J*= 7.2Hz, $H^{9',13'}$), 6.00 (m, 1H, H^5), 5.08 (s, 1H, H^6), 4.41 (d, 1H, *J*= 14.2Hz, $H^{7'}$), 4.30 (d, 1H, *J*= 14.2Hz, $H^{7'}$), 3.71 (d, 1H, *J*= 17.4Hz, H^{13}), 3.20 (m, 1H, H^{13b}), 3.17 (dt, 1H, *J*= 8.7, 1.1Hz, H^{3a}), 3.01 (m, 1H, H^{13a}), 2.91 (ddd, 1H, *J*= 14.9, 7.2, 1.4Hz, H^4), 2.44 (dd, 1H, *J*= 17.4, 9.3Hz, H^{13}), 2.30 (ddd, 1H, *J* 15.4, 6.6, 2.9 Hz, H^4);**^{13}C NMR** (100MHz, $CDCl_3$): δ 183.3 (C^{12}), 182.9 (C^7), 178.8 (C^3), 177.2 (C^1), 146.4 (0), 144.2 (0), 141.7 (0), 139.2 (0), 135.5 (0), 133.7 ($C^{9/10}$), 133.4 ($C^{9/10}$), 132.1 ($C^{6a/12a}$), 131.8 ($C^{6a/12a}$), 128.4 ($C^{10',12'}$), 127.7 ($C^{11'}$), 127.6 ($C^{9',3'}$), 127.4 ($C^{2',6'}$), 126.7 ($C^{8/11}$), 126.5 ($C^{8/11}$), 125.5 ($C^{5',3'}$), 124.1 (C^5), 124.0 (q, CF3, *J*= 270Hz), 44.1 (C^{13b}), 43.1 (C^6), 42.2 ($C^{7'}$), 39.2 (C^{3a}), 32.8 (C^{13a}), 24.9 (C^4), 23.6 (C^{13}); **MS** (EI): *m/z* 568.41 ($M+H^+$) (100); **HRMS** (ESI): Found 568.1752 $[M+H]^+$, calculated for $C_{34}H_{25}F_3NO_4$ 568.1736; **Elemental analysis** calculated for $C_{34}H_{24}F_3NO_4$: C, 71.95; H, 4.26; N, 2.47. Found: C, 72.02; H, 4.20; N, 2.56.

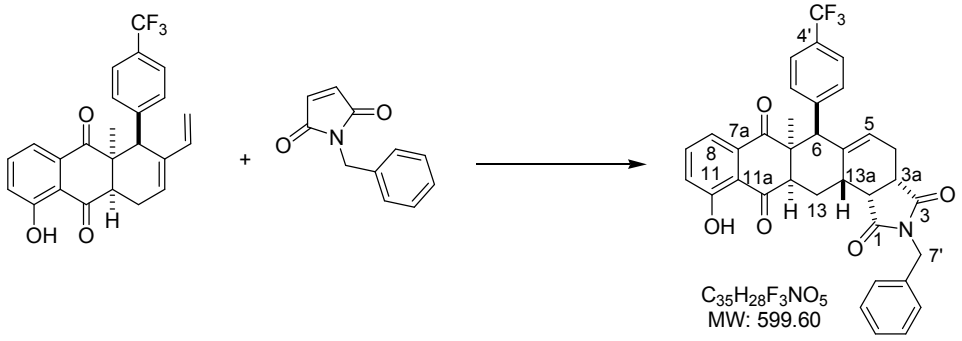
(3aSR,6SR,6aSR,13aSR,13bRS)-11-hydroxy-6a-methyl-2-phenyl-6-(4-(trifluoromethyl)phenyl)-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB022)



YB022 was obtained as a yellow solid; **Y** = 86%; ***Rf*** 0.08 (Silica gel, CH_2Cl_2); **Mp** = 125-127 ºC; **IR**: 2909, 1976, 1707, 1325, 1165 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 11.91 (s, 1H, OH), 7.53 (t, 1H, *J*= 7.9Hz, H^9), 7.5 (dd, 2H, *J*= 5.6, 1.4Hz, $H^{8',12'}$), 7.45 (m, 3H, $H^{9',10',11'}$), 7.41 (d, 2H, *J*= 8.4, $H^{5',H3'}$), 7.32 (dd, 1H, *J*= 7.5, 0.8Hz, H^{10}), 7.25 (d, 2H, *J*= 8.0 Hz, $H^{2',6'}$), 7.13 (d, 1H, *J*= 5.3Hz, H^8), 5.41 (dt, 1H, *J* = 5.9, 2.7Hz, H^5), 3.51 (s, 1H, H^6), 3.35 (dd, 1H, *J*= 11.6, 5.8Hz, H^{12a}), 3.33 (dd, 1H, *J*= 9.4, 5.8Hz, H^{13b}), 3.28 (dd, 1H, *J* = 8.3, 1.7Hz, H^{3a}), 3.03 (ddd, 1H, *J*= 14.5, 8.6, 6.3 Hz, H^{13}), 2.86 (m, 1H, H^{13a}), 2.72 (ddd, 1H, *J*= 15.7, 7.0, 1.3Hz, H^4), 2.60 (ddd, 1H, *J* = 14.9, 8.4, 6.8 Hz, H^{13}), 2.21 (m, 1H, H^4),1.36 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 204.3 (C^{12}), 199.3 (C^7), 178.3 (C^3), 177.5 (C^1), 161.1 (C^{11}), 142.8 ($C^{1'/7a}$), 140.5

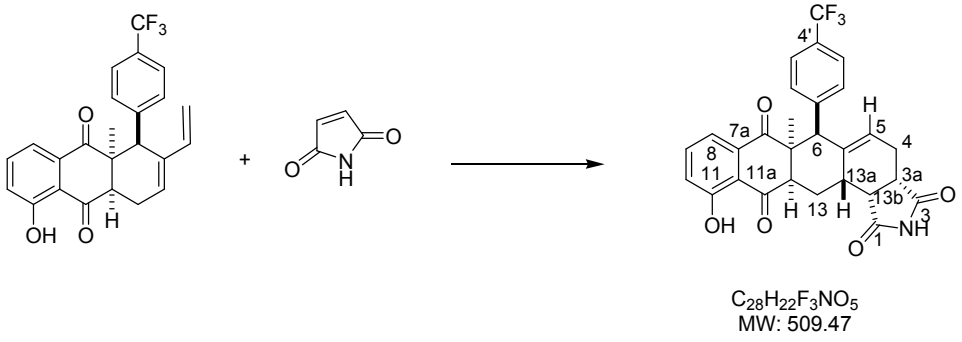
(C^{5a}), 136.9 (C^{9}), 135.6 ($C^{7'}$), 131.7 ($C^{4'}$), 131.3 ($C^{2',6'}$), 129.2 ($C^{9',C11'}$), 128.8 ($C^{10'}$), 126.4 ($C^{8',12'}$), 124.9 ($C^{5',3'}$), 124.0 (q, CF_3, *J*= 270Hz), 123.9 (C^{5}), 123.4 (C^{8}), 118.6 (C^{10}), 116.6 (C^{11a}), 56.2 (C^{6}), 53.9 (C^{12a}), 52.7 (C^{6a}), 44.7 (C^{13b}), 40.2 (C^{3a}), 32.8 (C^{13a}), 25.6 (C^{4}), 25.1 (CH_3), 24.2 (C^{13}); **MS** (EI): *m/z* = 584.74 ($M-H^+$) (100); **HRMS**: Found 586.1816 $[M+H]^+$, calculated for $C_{34}H_{27}F_3NO_5$ 586.1841; **Elemental analysis** calculated for $C_{34}H_{26}F_3NO_5$: C, 69.74; H, 4.48; N, 2.39. Found: C, 69.75; H, 4.23; N, 2.36.

(3aSR,6SR,6aSR,13aSR,13bRS)-2-benzyl-11-hydroxy-6a-methyl-6-(4-(trifluoromethyl)phenyl)-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB023)



YB023 was obtained as a clear, yellow solid; **Y** = 82%; ***Rf*** 0.09 (Silica gel, CH_2Cl_2); **Mp** = 120-122 ºC; **IR**: 2032, 1695, 1396, 1163, 1111, 1068, 699 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 11.87 (s, 1H, OH),7.49 (t, 1H, *J*= 8.0Hz, H^{9}), 7.33 (d, 2H, *J*= 8.2Hz, $H^{3',5'}$), 7.28 (d, 1H, *J*= 8.7Hz, H^{10}), 7.25 (m, 5H, $H^{8'-13'}$), 7.12 (d, 1H, *J*= 8.3Hz, H^{8}), 7.03 (d, 2H, *J*= 8.2Hz, $H^{2',H6'}$), 5.21 (dt, 1H, *J*= 5.8, 2.7Hz, H^{5}), 4.61 (d, 1H, *J*= 14.1Hz, $H^{7'}$), 4.54 (d, 1H, *J*= 14.1Hz, $H^{7'}$), 3.25 (t, 1H, *J*= 6.5Hz, H^{12a}),3.18 (s, 1H, H^{6}), 3.14 (m, 2H, $H^{3a,13b}$), 2.95 (ddd, 1H, *J*= 14.6, 8.2, 6.4Hz, H^{13}), 2.74 (m, 1H, H^{13a}), 2.63 (dd, 1H, *J*= 15.4, 7.6, H^{4}), 2.50 (ddd, 1H, *J*= 15.0, 8.5, 7.0Hz, H^{13}), 2.12 (tdd, 1H, *J* = 17.65, 6.31, 3.27 Hz, H^{4}),1.22 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 204.4 (C^{12}), 199.3 (C^{7}), 178.9 (C^{3}), 178.0 (C^{1}), 161.1 (C^{11}), 142.8 ($C^{1',4'}$), 140.3 (C^{5a}), 136.9 (C^{9}), 135.8 ($C^{8'}$), 135.6 (C^{7a}), 131.6 ($C^{2',6'}$), 128.7 (C $C^{9'/10'/12'/13'}$), 128.4 ($C^{9'/10'/12'/13'}$), 127.8 ($C^{11'}$), 124.7 ($C^{5',3'}$), 124.0(q, CF_3, *J*= 270Hz), 123.9 (C^{5}), 123.3 (C^{8}), 118.6 (C^{10}), 116.5 (C^{11a}), 56.8 (C^{6}), 54.1 (C^{12a}), 52.6 (C^{6a}), 44.6 (C^{13b}), 42.4 ($C^{7'}$), 40.1 (C^{3a}), 32.6 (C^{13a}), 25.2 (C^{4}), 25.1 (CH_3), 24.2 (C^{13}); **MS** (EI): *m/z* 600.64 ($M+H^+$) (100); **HRMS** (EI): Found 600.2014 $[M+H]^+$, calculated for $C_{35}H_{29}F_3NO_5$ 600.1998 $[M+H]^+$; **Elemental alalysis** calculated for $C_{35}H_{28}F_3NO_5$: C, 70.11; H, 4.71; N, 2.34. Found: C, 70.09; H, 4.51; N, 2.29.

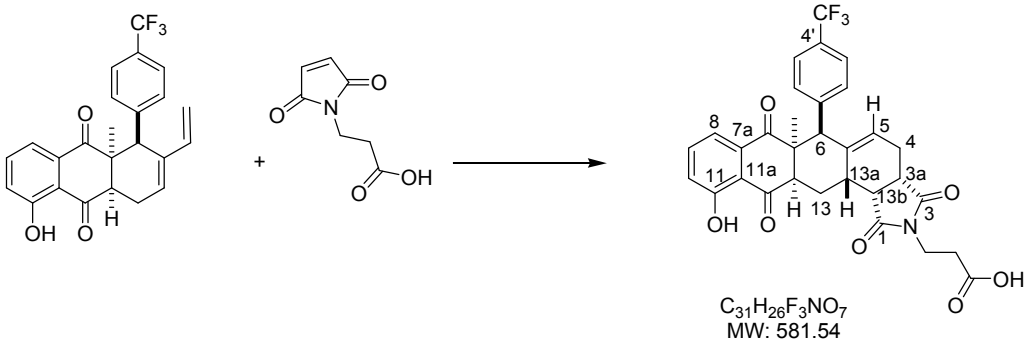
(3aSR,6SR,6aSR,13aSR,13bRS)-11-hydroxy-6a-methyl-6-(4-(trifluoromethyl)phenyl)-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB024) (5a)



YB024 was obtained as a yellow solid; **Y** = 90%; ***R$_f$*** 0.08 (Silica gel, CH_2Cl_2); **Mp** = 273-280 º C; **IR**: 3356, 2364, 2355, 2174, 2049, 1641 cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ11.85 (s, 1H,

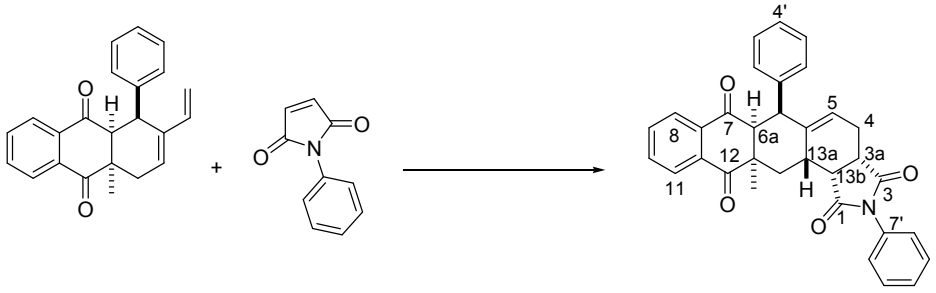
OH),8.8 (br s, 1H, NH), 7.49 (t, 1H, *J*= 7.9Hz, H^9), 7.34 (d, 2H, *J*= 8.3Hz, $H^{3',5'}$), 7.28 (dd, 1H, *J*= 7.55, 0.97Hz, H^{10}), 7.22 (d, 2H, *J*= 8.2Hz, $H^{2',6'}$), 7.11 (dd, 1H, *J*= 8.3, 0.95Hz, H^8), 5.37 (m, 1H, H^5), 3.54 (s, 1H, H^6),3.28 (t, 1H, *J*= 6.22Hz, H^{12a}), 3.22 (dd, 1H, *J*= 8.7, 5.5Hz, H^{13b}), 3.15 (td, 1H, *J*= 8.3, 1.4Hz, H^{3a}), 2.97 (ddd, 1H, *J*= 15.5, 9.2, 6.5Hz, H^{13}), 2.78 (m, 1H, H^{13a}), 2.57 (m, 1H, H^4), 2.50 (m, 1H, H^{13}), 2.13 (m, 1H, H^4),1.25 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 204.5 (C^{12}), 199.3 (C^7), 179.8 (C^3), 178.9 (C^1), 160.7 (C^{11}), 143.3 ($C^{1',4'}$), 140.1 (C^{5a}), 136.9 (C^9), 135.8 (C^{7a}), 131.4 ($C^{2',6'}$), 124.7 ($C^{5',3'}$), 124.2 (C^5), 124.0 (q, CF_3, *J*= 270Hz), 123.3 (C^8), 118.6 (C^{10}), 116.9 (C^{11a}), 55.8 (C^6), 53.4 (C^{12a}), 52.8 (C^{6a}), 44.5 (C^{13b}), 41.1 (C^{3a}), 32.3 (C^{13a}), 25.1 (CH_3), 24.9 (C^4), 23.6 (C^{13});**MS (EI):** *m/z* 510.41 ($M+H^+$) (100); **HRMS**: Found 532.1348 $[M+Na]^+$, $C_{28}H_{22}F_3NNaO_5$, calculated 532.1348 $[M+Na]^+$; **Elemental analysis** calculated for $C_{28}H_{22}F_3NO_5$: C, 66.01; H, 4.35; N, 2.75. Found: C, 66.67; H, 4.27; N, 2.66.

3-((3aSR,6SR,6aSR,13aSR,13bRS)-11-hydroxy-6a-methyl-1,3,7,12-tetraoxo-6-(4-(trifluoromethyl)phenyl)-3a,4,6a,7,12,12a,13,13a-octahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,13bH)-yl)propanoic acid (YB025)



YB025 was obtained as an orange solid; **Y** = 95%; R_f 0.14 (Silicagel, EtOAc); **Mp** = 129-132 ºC; **IR**: 2919, 2360, 2335, 2167, 2140, 1990, 1699 cm^{-1}. **^{1}H NMR** (400MHz, $CDCl_3$): δ 11.82 (s, 1H, OH), 10.43 (br s, 1H, COOH),7.46 (t, 1H, *J*= 7.9Hz, H^9), 7.32 (d, 2H, *J*= 8.3Hz, $H^{3',5'}$), 7.23 (dd, 1H, *J*= 7.4, 0.8Hz, H^{10}), 7.22 (d, 2H, *J*= 8.2Hz, $H^{2',6'}$), 7.07 (dd, 1H, *J*= 8.4, 0.9Hz, H^8), 5.25 (m, 1H, H^5), 3.78 (t, 2H, *J*= 7.1Hz, $H^{7'}$), 3.45 (s, 1H, H^6), 3.27 (t, 1H, *J*= 6.3Hz, H^{12a}), 3.16 (t, 1H, *J*= 9.5Hz, C^{13b}), 3.13 (m, 1H, H^{3a}), 2.94 (m, 1H, H^{13}), 2.74 (m, 1H, H^{13a}), 2.64 (t, 2H, *J*= 7.1Hz, $H^{8'}$), 2.56 (m, 1H, H^4), 2.51 (dt, 1H, *J*= 16.0, 9.0 Hz, H^{13}), 2.10 (m, 1H, H^4),1.31 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 204.5 (C^{12}), 199.3 (C^7), 179.3 (C^3), 178.7 (C^1), 176.0 ($C^{9'}$), 160.7 (C^{11}), 143.3 ($C^{1',4'}$), 140.1 (C^{5a}), 136.9 (C^9), 135.5 (C^{7a}), 131.4 ($C^{2',C6'}$), 124.7 ($C^{5',3'}$), 124.0 (C^5), 124.0 (q, CF_3, *J*= 270Hz), 123.3 (C^8), 118.6 (C^{10}), 116.6 (C^{11a}), 55.7 (C^6), 53.5 (C^{12a}), 52.8 (C^{6a}), 44.3 (C^{3a}), 39.8 (C^{13b}), 33.3 ($C^{7'}$), 32.4 (C^{13a}), 32.5 ($C^{8'}$), 25.1 (C^4) , 25.0 (CH_3), 23.6 (C^{13}). **MS (EI):** *m/z* 604.49 ($M+Na^+$) (100); **HRMS**: Found 604.0683 $[M+Na]^+$, calculated for $C_{31}H_{26}F_3NNaO_7$ 604.1559 $[M+Na]^+$; **Elemental analysis** calculated for $C_{31}H_{26}F_3NO_7$: C, 64.03; H, 4.51; N, 2.41. Found: C, 64.03; H, 4.24; N, 2.61.

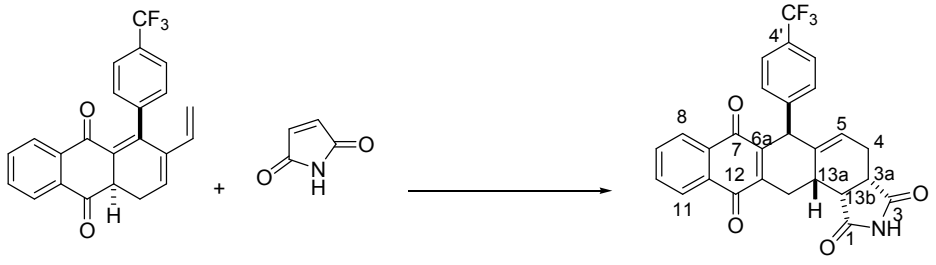
(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-12a-methyl-2,6-diphenyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB026)



$C_{33}H_{27}NO_4$
MW: 501.57

YB026 was obtained as a white solid; **Y** = 82%; R_f 0.07 (Silicagel, CH_2Cl_2); **Mp** = 127-130 ºC; **IR**: 2922, 2359, 2165, 2011, 1958, 1683, 694 cm^{-1}.**^{1}H NMR** (400MHz, $CDCl_3$): δ7.93 (d, 1H, *J* = 7.6Hz, $H^{8/11}$), 7.58 (m, 3H, $H^{8/11,9,10}$), 7.35–7.48 (m, 3H, $H^{3'-5'}$), 7.14 (m, 2H, $H^{2',6'}$), 6.97 (dd, 3H, *J* = 5.1, 1.8Hz, $H^{9'-11'}$), 6.68 (dd, 2H, *J* = 7.9, 2.4Hz, $H^{8',12'}$), 5.48 (dt, 1H, *J* = 5.8, 2.5 Hz, H^5), 4.15 (d, 1H, *J* = 8.9Hz, H^6), 3.45 (d, 1H, *J* = 10.3Hz, H^{6a}), 3.38 (dd, 1H, *J* = 8.5, 5.1Hz, H^{13b}), 3.28 (td, *J* = 8.3, 1.9Hz, 1H, H^{3a}), 3.06 (dtd, 1H, *J* = 8.1, 6.0, 2.3 Hz, H^{13a}), 2.78 (dd, 1H, *J* = 13.8, 6.4, H^{13}), 2.67 (ddd, 1H, *J* = 15.7, 6.7, 1.6Hz, H^4), 2.50 (dd, 1H, *J* = 13.5, 0.9Hz, H^{13}), 2.0 (dddd, 1H, *J* = 15.4, 7.5, 5.7, 3.6 Hz, 1H, H^4),1.35 (s, 3H, CH_3);**^{13}C NMR** (100MHz, $CDCl_3$): δ 200.3 (C^{12}), 198.4 (C^7), 178.5 (C^3), 177.4 (C^1), 140.3 (C^{5a}), 139.0 ($C^{7'}$), 135.9 ($C^{7a/11a}$), 134.0 (C^{10}), 133.8 (C^9), 133.6 ($C^{7a/11a}$), 132.1 ($C^{1'}$), 129.9 ($C^{8',12'}$), 129.2 ($C^{3',5'}$), 128.7 ($C^{4'}$), 127.9 ($C^{9',11'}$), 127.0 ($C^{2',6'}$), 126.5 ($C^{10'}$), 126.5 ($C^{8,11}$), 124.2 (C^5), 61.1 (C^{6a}), 48.5 (C^{12a}), 47.8 (C^6), 43.6 (C^{13b}), 40.2 (C^{3a}), 34.3 (C^{13a}), 33.1 (C^{13}), 29.7 (CH_3), 25.4 (C^4).**MS (EI):** *m/z*500.58 ($M-H^+$) (100); **HRMS**: Found 502.2031 $[M+H]^+$, calculated for $C_{33}H_{28}NO_4$ 502.2018 $[M+H]^+$; **Elemental analysis** calculated for $C_{33}H_{27}NO_4$: C, 79.02; H, 5.43; N, 2.79. Found: C, 79.03; H, 5.24; N, 2.79.

(3aSR,6SR,13aSR,13bRS)-6-(4-(trifluoromethyl)phenyl)-3a,4,13,13a-tetrahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,6H,13bH)-tetraone (YB027)

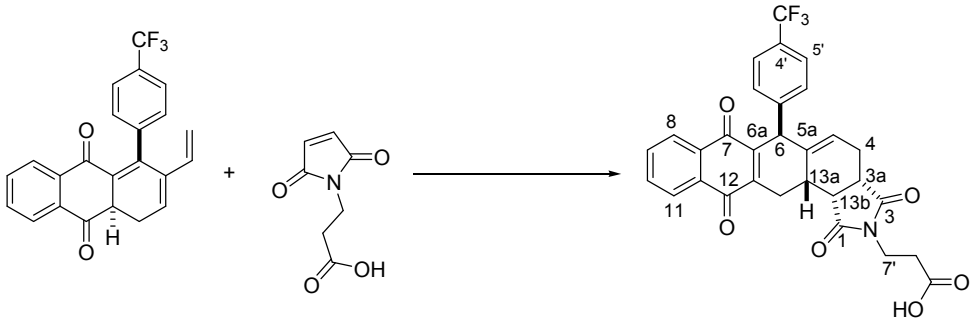


$C_{27}H_{18}F_3NO_4$
MW: 477.43

YB027 was obtained as a yellow solid; **Y** = 95%; R_f 0.29 (Silica gel, Et_2O); **Mp** = 310-315 ºC; **IR**: 2914, 2171, 2098, 2152, 2009, 1986 cm^{-1}, **^{1}H NMR** (400MHz, DMSO): δ 10.10 (s, 1H, NH), 8.20 (m, 1H, $H^{8/11}$), 8.12 (m, 1H, $H^{8/11}$), 7.74 (m, 1H, $H^{9,10}$), 7.51 (d, 2H, *J* = 8.3Hz, $H^{5',3'}$), 7.27 (d, 2H, *J* = 8.3Hz, $H^{2',6'}$), 6.15 (dd, 1H, *J* = 6.5, 3.0Hz, H^5), 5.29 (s, 1H, H^6), 3.61 (dd, 1H, *J* = 17.5, 1.6Hz, H^{13}), 3.25 (dt, 2H, *J* = 13.5, 10.5Hz, $H^{3a,13b}$), 3.00 (m, 1H, H^{13a}), 2.88 (dd, 1H, *J* = 7.0, 5.0Hz, H^4), 2.52 (dd, 1H, *J* = 17.5, 9.1Hz, H^{13}),2.34 (m, 1H, H^4); **^{13}C NMR** (100MHz, CD_2Cl_2):δ 204.9 (C^{12}), 199.6 (C^7), 179.2 (C^3), 178.5 (C^1), 161.3 ($C^{6a/11a}$), 161.1 ($C^{6a/11a}$), 143.9 ($C^{7a,5a}$), 140.4 (C^{11a}), 136.8 ($C^{9/10}$), 136.1 ($C^{9/10}$), 133.1 ($C^{4'}$), 131.9 ($C^{2',6'}$), 129.4 ($C^{3',5'}$), 129.1 ($C^{1'}$), 125.6 ($C^{8/11}$), 124.5 (CF_3), 123.4 ($C^{8/11}$), 117.2 (C^5), 51.4 (C^6), 44.7 (C^{13b}), 40.3 (C^{3a}), 34.5 (C^{13a}), 32.9 (C^{13}), 24.1 (C^4); **MS (EI):** *m/z*478.39 (M+H+) (100). **HRMS**:

Found 478.1277 $[M+H]^+$, calculated for $C_{27}H_{19}F_3NO_4$ 478.1266. **Elemental analysis** calculated for $C_{27}H_{18}F_3NO_4$: C, 67.92; H, 3.80; N, 2.93. Found: C, 67.12; H, 3.98; N, 2.49.

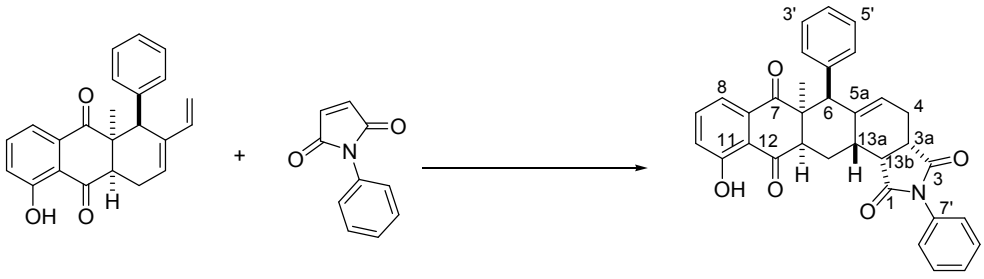
3-((3aS,6S,13aS,13bR)-1,3,7,12-tetraoxo-6-(4-(trifluoromethyl)phenyl)-3a,4,13,13a-tetrahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,7H,12H,13bH)-yl)propanoic acid (YB028)



$C_{30}H_{22}F_3NO_6$
MW: 549.49

YB028 was obtained as an orange solid; **Y** = 82%; R_f 0.37 (Silica gel, CH_2Cl_2/methanol 85:15); **Mp** = 160-162 ºC; **IR**: 2355, 2181, 2157, 2030, 1697, 1323, 1112, 1066, 646 cm^{-1}; **^{1}H NMR** (400MHz, DMSO): δ 9.88 (s, 1H, COOH), 8.07-8.28 (m, 2H, $H^{9,10}$), 7.88-8.00 (m, 2H, $H^{3',5'}$), 7.78-7.88 (m, 2H, $H^{8,11}$), 7.56-7.65 (m, 2H, $H^{2',6'}$), 7.27 (d, 2H, J = 8.3Hz, $H^{2',6'}$), 6.14 (m, 1H, H^5), 5.45 (s, 1H, H^6), 3.59 (m, 2H, $H^{7'}$), 3.31 (m, 1H, H^{13}), 2.51(m, 2H, $H^{8'}$), 2.19 (m, 2H, $H^{3a,13b}$), 2.13 (m, 1H, H^{13a}), 2.02 (m, 1H, H^4), 1.93 (m, 1H, H^{13}),1.74 (m, 1H, H^4); **^{13}C NMR** (100MHz, CD_2Cl_2) δ 204.9 (C^{12}), 199.6 (C^7), 179.3 (C^3), 178.4 (C^1), 161.2 ($C^{6a/11a}$), 160.1 ($C^{6a/11a}$), 144.2 ($C^{7a,5a}$), 140.3 (C^{11a}), 136.5 ($C^{9/10}$), 136.2 ($C^{9/10}$), 133.1 ($C^{4'}$), 131.2 ($C^{2',6'}$), 129.5 ($C^{3',5'}$), 129.0 ($C^{1'}$), 125.2 ($C^{8/11}$), 124.0 (CF_3), 123.5 ($C^{8/11}$), 117.2 (C^5), 51.3 (C^6), 44.8 (C^{13b}), 40.2 (C^{3a}), 35.1 (C^{13a}), 34.2 ($C^{7'}$), 31.9 (C^{13}), 31.5 ($C^{8'}$), 24.1 (C^4); **MS (EI):** *m/z*548.42 ($M-H^+$) (100); **HRMS** (EI): Found 550.1501 $[M+H]^+$, calculated for $C_{30}H_{23}F_3NO_6$ 550.1477 $[M+H]^+$; **Elemental analysis** calculated for $C_{30}H_{22}F_3NO_6$: C, 65.57; H, 4.04; N, 2.55. Found: C, 65.63; H, 4.06; N, 2.50.

(3aSR,6SR,6aSR,13aSR,13bRS)-11-hydroxy-6a-methyl-2,6-diphenyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB029)

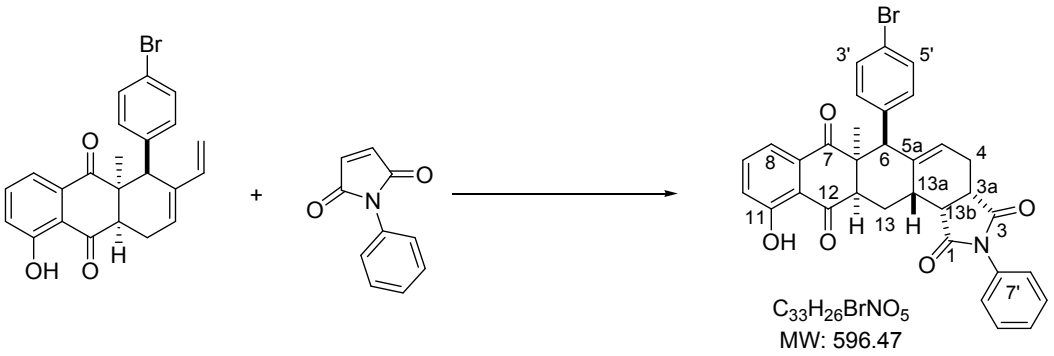


$C_{33}H_{27}NO_5$
MW: 517.57

YB029 was obtained as a yellow solid; **Y** = 84%; R_f 0.67 (Silica gel, EtOAc); **Mp** = 150-152 ºC; **IR**: 2914, 2363, 2192, 2164, 1708, 615 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 1.25 (s, 3H, CH_3), 1.80 (dd, 1H, J= 24.6, 13.0, H^4), 2.53 (td, 1H, J = 19.0Hz, H^{13}), 2.59 (m, 2H, $H^{4,13}$), 2.95 (d, 1H, J= 19.0Hz, H^{13a}), 3.21 (t, 1H, J = 8.4Hz, H^{3a}), 3.27 (m, 1H, H^{13b}), 3.97 (dd, 1H, J = 11.3, 3.8 Hz, H^{12a}), 4.13 (s, 1H, H^6), 5.91 (t, 1H, J = 3.30 Hz, H^5), 7.13 (d, 2H, J= 7.5 Hz, Ar^C), 7.17 (t, 1H, J= 7.2 Hz, Ar^C), 7.24 (dd, 2H, J= 6.3, 1.3 Hz, Ar^C), 7.28 (dd, 1H, J= 9.1, 4.2 Hz, C^{10}), 7.38-7.34 (m, 2H, Ar^B), 7.46-7.41 (m, 1H, Ar^B), 7.53 (t, J= 7.66 Hz, 2H, Ar^B), 7.68-7.64 (m, 2H, $C^{8,9}$), 11.68 (s, 1H, OH).; **^{13}C NMR** (100MHz, $CDCl_3$): δ 204.5 (C^{12}), 199.4 (C^7),

178.5 (C^{3}), 177.6 (C^{1}), 160.8 (C^{11}), 140.6 (C^{5a}), 138.8 (C^{7a}), 136.0 ($C^{7'}$), 130.7 ($C^{1'}$), 129.3 (Ar^{B}), 128.8 (Ar^{B}), 128.7 (Ar^{C}), 128.4 (Ar^{C}), 126.5 (Ar^{B}), 125.5 (Ar^{C}), 124.5 (C^{10}), 122.4 (C^{5}), 119.6 ($C^{8,9}$), 117.1 (C^{11a}), 56.5 (C^{6}), 53.5 (C^{12a}), 52.9 (C^{6a}), 44.4 (C^{13b}), 40.3 (C^{3a}), 33.1 (C^{13a}), 25.5 (C^{4}), 25.2 (CH_3), 23.5 (C^{13}); **MS (EI):** *m/z* 519.49 ($M+H^+$) (100); **HRMS** (EI): Found 518.1976 $[M+H]^+$, calculated for $C_{33}H_{27}NO_5$ 518.1967 $[M+H]^+$; **Elemental analysis** calculated for $C_{33}H_{27}NO_5$: C, 76.58; H, 5.26; N, 2.71. Found: C, 76.25; H, 5.32; N, 2.71. Spectroscopic data in accordance with those reported in literature.[3]

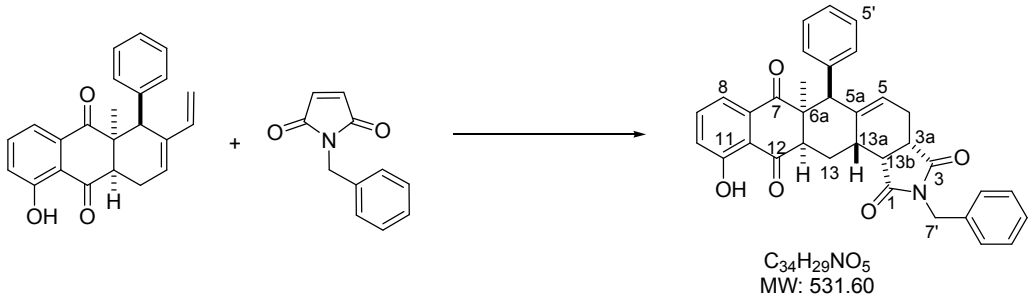
(3aSR,6SR,6aSR,13aSR,13bRS)-6-(4-bromophenyl)-11-hydroxy-6a-methyl-2-phenyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB030)



$C_{33}H_{26}BrNO_5$
MW: 596.47

YB030 was obtained as a yellow solid; **Y** = 95%; R_f 0.67 (Silica gel, EtOAc); **Mp** = 167-169 ºC; **IR**: 3738, 2361, 2173, 2033, 1987, 1958, 1541 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ11.90 (s, 1H, OH), 7.55 (t, 1H, *J* = 8.0Hz, H^{9}), 7.39-7.49 (3H, m, $H^{9'-11'}$), 7.33 (dd, 1H, *J* = 7.6, 1.2Hz, H^{8}), 7.29 (d, 2H, *J* = 8.45Hz, $H^{3',5'}$), 7.17 (dd, 1H, *J* = 8.4, 1.0Hz, H^{10}), 7.12 (dd, 2H, *J* = 7.1, 1.5Hz, $H^{8',12'}$), 6.99 (dd, 2H, *J* = 6.8, 1.8Hz, $H^{2',6'}$), 5.42 (m, 1H, H^{5}), 3.9 (s, 1H, H^{6}), 3.33 (dd, 1H, *J* = 8.6, 5.3, H^{12a}), 3.28 (m, 2H, $H^{3a,13b}$), 2.82 (m, 1H, H^{13a}), 2.82 (ddd, 1H, *J* = 14.7, 9.1, 6.1Hz, H^{13}), 2.71 (ddd, 1H, *J* = 16.6, 7.1, 1.4Hz, H^{4}), 2.59 (ddd, 1H, *J* = 14.7, 8.3, 6.6Hz, H^{13}), 2.21 (m, 1H, H^{4}), 1.35 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 204.5 (C^{12}), 199.4 (C^{7}), 178.3 (C^{3}), 177.5 (C^{1}), 161.0 (C^{11}), 140.7 ($C^{1'}$), 137.5 (C^{5a}), 136.9 (C^{9}), 135.7 ($C^{7'}$), 132.7 ($C^{2'/6'}$), 131.7 ($C^{4'}$), 131.2 ($C^{3',5'}$), 129.2 ($C^{9'}$), 128.8 ($C^{11'}$), 126.4 ($C^{8',12'}$), 123.6 (C^{10}), 123.2 (C^{5}), 121.3 (C^{7a}), 118.6 (C^{8}), 116.7 (C^{11a}), 55.9 (C^{6}), 53.9 (C^{12a}), 52.7 (C^{6a}), 44.7 (C^{13b}), 40.2 (C^{3a}), 33.0 (C^{13a}), 25.6 (C^{4}), 25.1 (CH_3), 24.3 (C^{13}); **MS (EI):** *m/z* 595.50 ($M-H^+$) (100); **HRMS**: Found 596.1064 $[M+H]^+$, calculated for $C_{33}H_{27}BrNO_5$ 596.1073 $[M+H]^+$; **Elemental analysis** calculated for $C_{33}H_{26}BrNO_5$: C, 66.45; H, 4.39; N, 2.35. Found: C, 66.65; H, 4.18; N, 2.15.

(3aSR,6SR,6aSR,13aSR,13bRS)-2-benzyl-11-hydroxy-6a-methyl-6-phenyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB031)

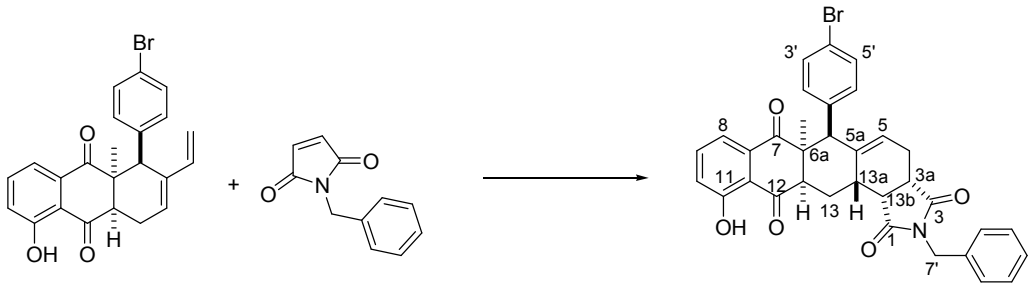


$C_{34}H_{29}NO_5$
MW: 531.60

YB031 was obtained as a yellow solid, **Y** = 92%; R_f 0.67 (Silica gel, EtOAc); **Mp** = 187-188 ºC; **IR**: 3338, 2924, 2364, 2330, 2150, 2032, 1959 cm^{-1}.**^{1}H NMR** (400MHz, $CDCl_3$): δ 11.84

(s, 1H, OH), 7.48 (t, 1H, *J*= 7.9Hz, H^{9}), 7.26-7.28 (2H, m, H^{8}), 7.22-7.27 (m, 5H, $H^{2'-6'}$), 7.09 (dd, 1H, *J*= 8.3, 1.0Hz, H^{10}), 7.06 (m, 3H, $H^{10'-12'}$), 6.88 (m, 2H, $H^{9',13'}$), 5.32 (m, 1H, H^{5}), 4.60 (d, 2H, *J*= 12.2Hz, $H^{7'}$), 3.25 (s, 1H, H6), 3.20 (t, 1H, *J*= 5.9Hz, H^{12a}),3.16 (dd, 1H, *J*= 8.4, 3.14Hz, H^{13b}), 3.12 (td, 1H, *J*= 8.6, 1.4Hz, H^{3a}), 2.94 (ddd, 1H, *J*= 15.3, 9.4, 6.0Hz, H^{13}), 2.79 (m, 1H, H^{13a}), 2.61 (ddd, 1H, *J*= 16.7, 7.2, 1.34Hz, H^{4}), 2.55 (ddd, 1H, *J*= 14.1, 8.0, 5.8Hz, H^{13}), 2.11 (m, 1H, H^{4}),1.28 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 204.5 (C^{12}), 199.5 (C^{7}), 179.1 (C^{3}), 178.0 (C^{1}), 160.7 (C^{11}), 140.5 (C^{5a}), 138.9 ($C^{1'}$), 136.7 (C^{9}), 135.9 (C^{7a}), 135.7 ($C^{8'}$), 130.8 ($C^{9',13'}$), 128.7 ($C^{2'-6'}$), 128.3 ($C^{2'-6'}$), 127.8 ($C^{2'-6'}$), 127.0 ($C^{2'-6'}$), 123.9 (C^{5}), 122.8 (C^{10}), 118.5 (C^{8}), 117.0 (C^{11a}), 56.0 (C^{6}), 53.5 (C^{12a}), 52.7 (C^{6a}), 44.3 (C^{13b}), 42.4 ($C^{7'}$), 40.1 (C^{3a}), 32.7 (C^{13a}), 25.2 (CH_3), 25.1 (C^{4}), 23.4 (C^{13});**MS (EI):** *m/z* 530.55 ($M-H^{+}$) (100); **HRMS**: Found 532.2097 $[M+H]^{+}$, calculated for $C_{34}H_{30}NO_5$ 532.2119 $[M+H]^{+}$; **Elemental analysis** calculated for $C_{34}H_{29}NO_5$: C, 76.82; H, 5.50; N, 2.63. Found: C, 76.39; H, 5.55; N, 2.54.

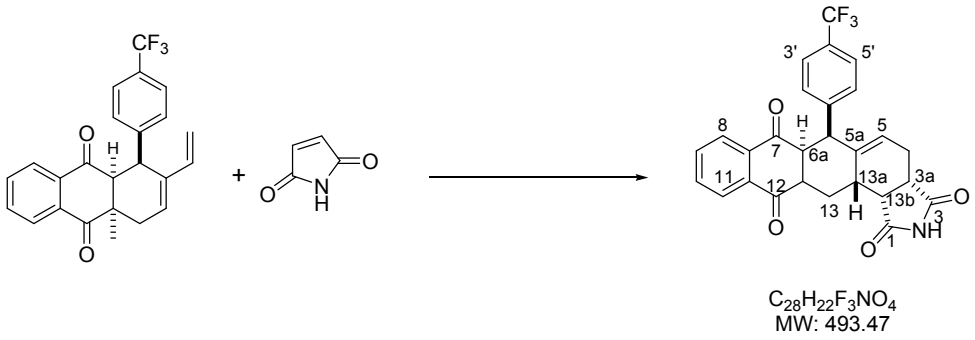
(3aSR,6SR,6aSR,13aSR,13bRS)-2-benzyl-6-(4-bromophenyl)-11-hydroxy-6a-methyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB032)



$C_{34}H_{28}BrNO_5$
MW: 610.49

YB032 was obtained as a yellow solid; **Y** = 87%; R_f 0.67 (Silica gel, EtOAc); **Mp** = 210-211 ºC; **IR**: 2361, 2196, 2047, 2015, 1960, 1940 cm^{-1};**^{1}H NMR** (400MHz, $CDCl_3$): δ11.84 (s, 1H, OH), 7.53 (t, 1H, *J*= 8.0Hz, H^{9}), 7.25 (d, 1H, H^{8}), 7.22-7.30 (5H, m, $H^{9'-13'}$), 7.22 (d, 2H, *J*= 6.7Hz, $H^{3',5'}$), 7.15 (dd, 1H, *J*= 8.4, 0.9Hz, H^{10}), 6.80 (d, 2H, *J*= 8.5Hz, $H^{2',6'}$), 5.24 (m, 1H, H^{5}), 4.58 (d, 2H, *J*= 9.2Hz, $H^{7'}$), 3.22 (t, 1H, *J*= 6.0, H^{12a}),3.11 (m, 2H, $H^{3a,13b}$), 3.07 (br s, 1H, H^{6}), 2.94 (ddd, 1H, *J*= 14.6, 8.3, 6.3Hz, H^{13}), 2.70 (m, 1H, H^{13a}), 2.62 (dd, 1H, *J*= 15.0, 7.3Hz, H^{4}), 2.48 (ddd, 1H, *J*= 15.0, 8.4, 7.0Hz, H^{13}), 2.09 (m, 1H, H^{4}),1.22 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 204.5 (C^{12}), 199.5 (C^{7}), 178.9 (C^{3}), 178.0 (C^{1}), 161.0 (C^{11}), 140.5 (C^{5a}), 137.5 ($C^{1'}$), 136.9 (C^{9}), 135.8 (C^{7a}), 135.7 ($C^{8'}$), 132.9 ($C^{3'/5'}$), 128.7 ($C^{9',13'}$), 128.3 ($C^{10',12'}$), 127.8 ($C^{11'}$), 123.7 (C^{10}), 123.2 (C^{5}), 121.1 ($C^{4'}$), 118.5 (C^{8}), 116.5 (C^{11a}), 55.6 (C^{6}), 54.1 (C^{12a}), 52.6 (C^{6a}), 44.6 (C^{13b}), 42.4 ($C^{7'}$), 40.1 (C^{3a}), 32.7 (C^{13a}), 25.2 (C^{4}), 25.1 (CH_3), 23.4 (C^{13}); **MS (EI):** *m/z* 608.55 ($M-H^{+}$) (100) **HRMS(EI):** Found 610.1218 $[M+H]^{+}$, calculated for $C_{34}H_{29}BrNO_5$ 610.1229 $[M+H]^{+}$; **Elemental analysis** calculated for $C_{34}H_{28}BrNO_5$: C, 66.89; H, 4.62; N, 2.29. Found: C, 66.85; H, 4.52; N, 2.12.

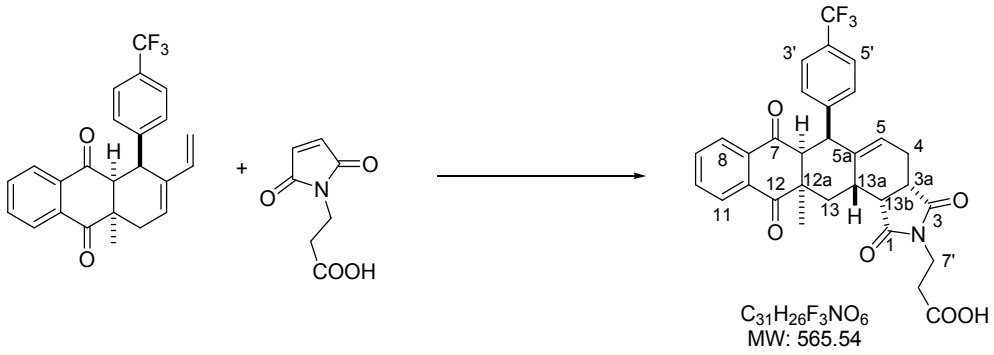
(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-12a-methyl-6-(4'-(trifluoromethyl)phenyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB036) (5b)



$C_{28}H_{22}F_3NO_4$
MW: 493.47

YB036 was obtained as a white solid; **Y** = 92%; $\boldsymbol{R_f}$ 0.39 (Silicag el, Et_2O); **Mp** = 204-207 ºC; **IR**: 2362, 2335, 1705, 1325 cm^{-1}. **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.90 (br s, 1H, -NH), 7.89 (d, 1H, *J* =7.7Hz, H^9), 7.59 (m, 1H, H^{11}), 7.51 (m, 2H, $H^{8,10}$), 7.15 (d, 2H, *J*= 8.1Hz, $H^{3',5'}$), 6.78 (d, 2H, *J*= 8.1Hz $H^{2',6'}$), 5.48 (dd, 1H, *J*= 6.1, 3.0Hz, H^5), 4.25 (d, 1H, *J*= 8.0Hz, H^6), 3.47 (d, 1H, *J*= 10.2Hz, H^{6a}), 3.28 (dd, 1H, *J*= 8.6, 5.7Hz, H^{13b}), 3.18 (td, 1H, *J*= 8.5, 1.8Hz, H^{3a}), 3.01 (m, 1H, H^{13a}), 2.73 (dd, 1H, *J*= 13.9, 6.6Hz, H^{13}), 2.58 (ddd, 1H, *J*= 15.9, 6.8, 1.6Hz, H^4), 2.45 (dd, 1H, *J*= 13.7, 12.5Hz, H^{13}), 2.15 (m, 1H, H^4), 1.35 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.0 (C^{12}), 198.1 (C^7), 178.9 (C^3), 178.1 (C^1), 144.0 ($C^{4'}$), 139.6 (C^{5a}), 135.6 (C^{7a}), 134.1 ($C^{10/11}$), 134.0 ($C^{10/11}$), 133.6 (C^{11a}), 130.3 ($C^{2',6'}$), 128.9 ($C^{1'}$), 126.5 ($C^{8/9}$), 126.4 ($C^{8/9}$), 125.1 (C^5), 124.6 ($C^{3'/5'}$), , 124.0 (q, CF_3, *J*= 270Hz), 60.5 (C^{6a}), 48.2 (C^{12a}), 46.9 (C^6), 44.7 (C^{13b}), 41.2 (C^{3a}), 33.6 (C^{13a}), 32.7 (C^{13}), 29.7 (CH_3), 24.9 (C^4); **HRMS**: Found 494.1593 $[M+H]^+$, calculated for $C_{28}H_{23}F_3NO_4$ 494.1574 $[M+H]^+$.**Elemental analysis** calculated for $C_{28}H_{22}F_3NO_4$: C, 68.15; H, 4.49; N, 2.84. Found: C, 67.98; H, 4.25; N, 2.72.

3-((3aS,6S,6aS,12aR,13aS,13bR)-12a-methyl-1,3,7,12-tetraoxo-6-(4'-(trifluoromethyl)phenyl)-3a,4,6a,7,12,12a,13,13a-octahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,13bH)-yl)propanoicacid (YB037)

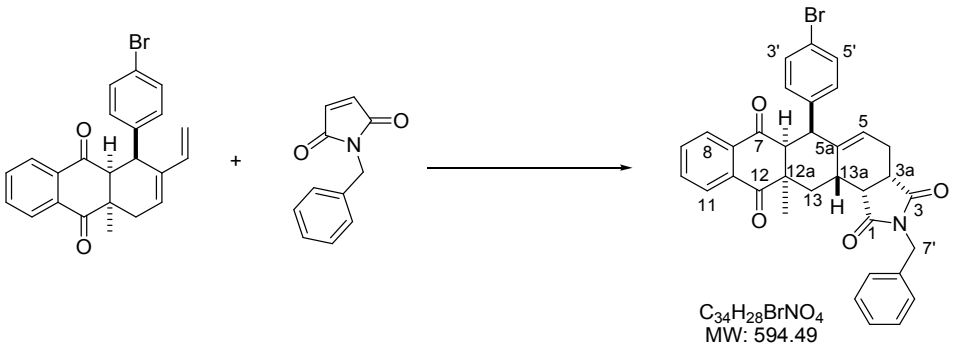


$C_{31}H_{26}F_3NO_6$
MW: 565.54

YB037 was obtained as a white solid; **Y** = 79%**;** $\boldsymbol{R_f}$ 0.43 (Silicagel, AcOH/EtOAc1:99); **Mp** = 140.8 – 142.1 °C; **IR**: 2890, 2366, 1692, 1325, 1163 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.87 (d, 1H, *J* = 7.7Hz, H^9), 7.58 (m, 1H, H^{11}), 7.51 (m, 2H, $H^{8,10}$), 7.15 (d, 2H, *J*= 8.1Hz, $H^{3',5'}$), 6.75 (d, 2H, *J*= 8.1Hz $H^{2',6'}$), 5.38 (dd, 1H, *J*= 6.1, 2.9Hz, H^5), 4.22 (d, 1H, *J*= 8.8Hz, H^6), 3.76 (m, 2H, *J*= 6.8Hz, $H^{7'}$), 3.46 (d, 1H, *J*= 10.0Hz, H^{6a}), 3.22 (dd, 1H, *J*= 8.5, 5.7Hz, H^{13b}), 3.14 (td, 1H, *J*= 8.6, 1.4Hz, H^{3a}), 3.02 (m, 1H, H^{13a}), 2.78 (dd, 1H, *J*= 14.0, 6.9Hz, H^{13}), 2.60 (t, 2H, *J* = 6.8, $H^{8'}$), 2.58 (m, 1H, H^4), 2.48 (dd, 1H, *J*= 13.9, 12.0Hz, H^{13}), 2.12 (m, 1H, H^4),1.37 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.0 (C^{12}), 198.7 (C^7), 179.0 (C^3), 177.1 (C^1), 174.9 (COOH), 144.4 ($C^{4'}$), 139.6 (C^{5a}), 135.5 (C^{7a}), 134.1 ($C^{10,11}$), 133.6 (C^{11a}), 130.3 ($C^{2',6'}$), 128.9 ($C^{1'}$), 126.5 ($C^{8/9}$), 126.4 ($C^{8/9}$), 125.2 (C^5), 124.6 ($C^{3',5'}$), 124.0 (q, CF_3, *J*= 270Hz), 60.2

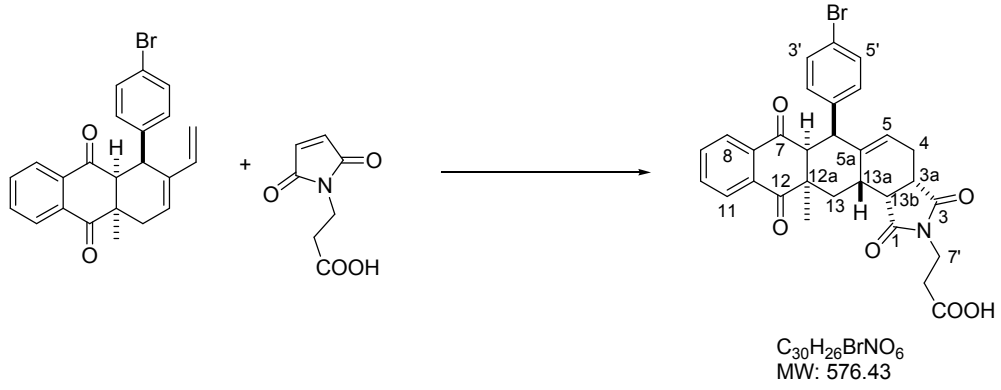
(C^{6a}), 48.1 (C^{12a}), 46.7 (C^{6}), 43.7 (C^{13b}), 39.9 (C^{3a}), 34.3 ($C^{7'}$), 33.7 (C^{13a}), 32.4 (C^{13}), 31.8 ($C^{8'}$) 29.7 (CH_3), 25.1 (C^{4}); **HRMS**: Found 566.1805 $[M+H]^+$, calculated for $C_{31}H_{27}F_3NO_6$ 566.1785 $[M+H]^+$; **Elemental analysis** calculated for $C_{31}H_{26}F_3NO_6$: C, 68.84; H, 4.63; N, 2.48. Found: C, 65.73; H, 4.58; N, 2.54.

(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-2-benzyl-6-(4-bromophenyl)-12a-methyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB038)



YB038 was obtained as a white solid; **Y** = 72%; R_f 0.67 (Silica gel, EtOAc); **Mp** = 177.5–179.1 ºC; **IR**: 2935, 2354, 1693, 1397, 701 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.93 (dd, 1H, *J*= 7.6, 1.2 Hz, H^8), 7.64 (dt, 1H, *J*= 7.5, 1.4Hz, H^{10}), 7.58 (dt, 1H, *J*= 7.3, 1.0Hz, H^9), 7.52 (dd, 1H, *J*= 7.7, 1.4Hz, H^{11}), 7.25 (m, 5H, $H^{9'\text{-}13'}$), 7.04 (d, 2H, *J*= 8.4Hz, $H^{3',5'}$), 6.35 (d, 2H, *J*= 8.4Hz $H^{2',6'}$), 5.25 (dd, 1H, *J*= 6.6, 3.2Hz, H^5), 4.58 (d, 2H, *J*= 8.2Hz, $C^{7'}$), 3.80 (dt, 1H, *J*= 10.6, 1.5Hz, H^6), 3.34 (d, 1H, *J*= 10.7Hz, H^{6a}), 3.18 (dd, 1H, *J*= 8.5, 5.5Hz, H^{13b}), 3.14 (td, 1H, *J*= 8.6, 1.3Hz, H^{3a}), 2.90 (m, 1H, H^{13a}), 2.65 (dd, 1H, *J*= 13.8, 6.5Hz, H^{13}), 2.56 (ddd, *J*= 15.7, 7.2, 1.3Hz, 1H, H^4), 2.41 (dd, 1H, *J*= 13.5, 12.6Hz, H^{13}), 2.08 (m, 1H, H^4),1.32 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.0 (C^{12}), 198.2 (C^7), 179.0 (C^3), 178.0 (C^1), 139.9 (C^{5a}), 138.0 ($C^{4'}$), 135.8 (C^{7a}), 134.2 (C^9), 134.0 (C^{10}), 133.5 (C^{11a}), 131.7 ($C^{2',6'}$), 130.8 ($C^{3',5'}$), 128.7 ($C^{10',11'}$), 128.2 ($C^{9',13'}$), 127.8 ($C^{11'}$), 126.6 ($C^{8/11}$), 126.5 ($C^{8/11}$), 124.6 (C^5), 120.8 ($C^{8',1'}$), 60.7 (C^{6a}), 48.3 (C^{12a}), 46.3 (C^6), 43.7 (C^{13b}), 42.3($C^{7'}$), 40.2 (C^{3a}), 34.2 (C^{13a}), 32.6 (C^{13}), 29.7 (CH_3), 25.2 (C^4); **HRMS**: Found 594.1251 $[M+H]^+$, calculated for $C_{34}H_{29}BrNO_4$ 594.1280 $[M+H]^+$; **Elementalanalysis** calculated for $C_{34}H_{28}BrNO_4$: C, 68.69; H, 4.75; N, 2.36. Found: C, 68.68; H, 4.63; N, 2.45.

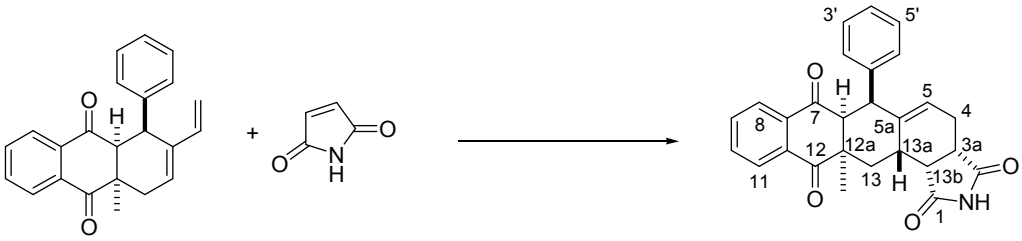
3-((3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-6-(4-bromophenyl)-12a-methyl-1,3,7,12-tetraoxo-3a,4,6a,7,12,12a,13,13a-octahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,13bH)-yl)propanoic acid (YB039) (5c)



YB039 was obtained as a white solid; **Y** = 72%; R_f 0.43 (Silica gel, AcOH/EtOAc1:99); **Mp** = 160.7–161.2 ºC; **IR**: 2940, 2356, 2160,1688 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.89 (d, 1H, *J*

= 7.3Hz, H^{8}), 7.63 (td, 1H, H^{10}), 7.56 (m, 2H, $H^{11,9}$), 7.20 (d, 2H, *J*= 8.4Hz, $H^{3',5'}$), 6.5 (d, 2H, *J*= 8.5Hz $H^{2',6'}$), 5.35 (dd, 1H, *J*= 6.3, 2.9Hz, H^{5}), 4.09 (d, 1H, *J*= 9.5Hz, H^{6}), 3.75 (m, 2H, $H^{7'}$), 3.43 (d, 1H, *J*= 10.1Hz, H^{6a}), 3.20 (dd, 1H, *J*= 8.6, 5.7Hz, H^{13b}), 3.12 (td, 1H, *J*= 8.6, 1.3Hz, H^{3a}), 2.95 (m, 1H, H^{13a}), 2.74 (dd, 1H, *J*= 13.9, 6.7Hz, H^{13}), 2.59 (t, 2H, *J* = 7.0, $H^{8'}$), 2.57 (m, 1H, H^{4}), 2.46 (dd, 1H, *J*= 13.9, 12.1Hz, H^{13}), 2.10 (m, 1H, H^{4}),1.36 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.1 (C^{12}), 198.8 (C^{7}), 179.0 (C^{3}), 177.0 (C^{1}), 174.8 (COOH), 139.8 (C^{5a}), 138.7 ($C^{4'}$), 135.7 (C^{7a}), 134.1 ($C^{10,9}$), 134.0 ($C^{10,9}$), 133.6 (C^{11a}), 131.6 ($C^{2',6'}$), 130.8 ($C^{3',5'}$), 126.6 ($C^{8/11}$), 126.5 ($C^{8/11}$), 124.8 (C^{5}), 120.9 ($C^{1'}$), 60.4 (C^{6a}), 48.1 (C^{12a}), 46.5 (C^{6}), 43.7 (C^{13b}), 40.0 (C^{3a}), 34.2 ($C^{7'}$), 33.9 (C^{13a}), 32.5 (C^{13}), 31.8 ($C^{8'}$) 29.7 (CH_3), 25.1 (C^{4}); **HRMS**: Found 576.1041 $[M+H]^+$, calculated for $C_{30}H_{27}BrNO_6$ 576.1016 $[M+H]^+$; **Elemental analysis** calculated for $C_{30}H_{26}BrNO_6$: C, 62.51; H, 4.55; N, 2.43. Found: C, 62.60; H, 4.56; N, 2.43.

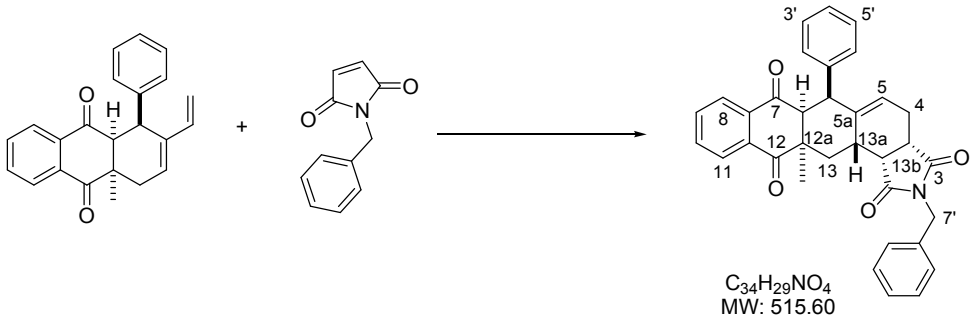
(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-12a-methyl-6-phenyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB040)



$C_{27}H_{23}NO_4$
MW: 425.48

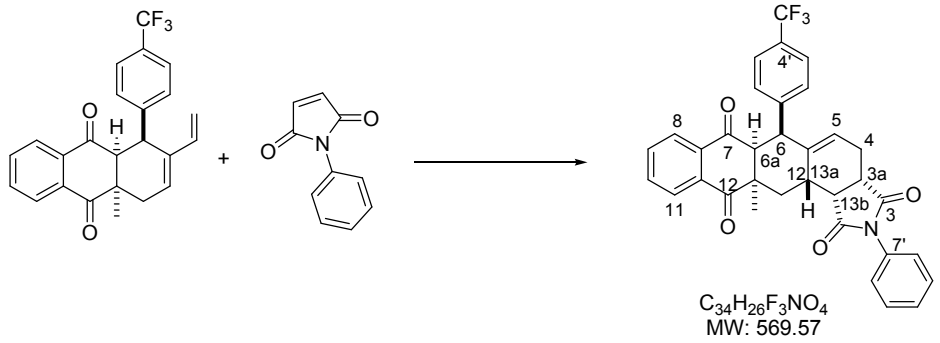
YB040 was obtained as a white solid; **Y** = 75%; R_f 0.35 (Silica gel, Et_2O); **Mp** = 223.4–225.1 ºC; **IR**: 3230, 2356, 1706, 1682, 701 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): 7.90 (ddd, 1H, *J* = 7.5, 1.1, 0.7Hz, H^{11}), 7.58 (ddd, 1H, *J*= 7.7, 6.1, 2.6Hz, H^{9}), 7.53 (m, 2H, $H^{8,10}$), 6.93 (m, 1H, $H^{4'}$), 6.93 (dd, 2H, *J*= 4.9, 2.1Hz, $H^{3',5'}$), 6.66 (dd, 2H, *J*= 7.2, 2.1Hz $H^{2',6'}$), 5.46 (dt, 1H, *J*= 6.0, 2.7Hz, H^{5}), 4.17 (dd, 1H, *J*= 10.2, 3.1Hz, H^{6}), 3.47 (t, 1H, *J*= 10.2Hz, H^{6a}), 3.28 (dd, 1H, *J*= 8.6, 5.8Hz, H^{13b}), 3.15 (td, 1H, *J*= 8.4, 2.0Hz, H^{3a}), 2.99 (m, 1H, H^{13a}), 2.72 (dd, 1H, *J*= 13.7, 6.4Hz, H^{13}), 2.56 (ddd, 1H, *J*= 15.9, 6.8, 1.9Hz, H^{4}), 2.42 (dd, 1H, *J*= 13.7, 12.4Hz, H^{13}), 2.13 (m, 1H, H^{4}),1.35 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.3 (C^{12}), 198.5 (C^{7}), 179.1 (C^{3}), 178.1 (C^{1}), 140.1 (C^{5a}), 139.4 (C^{7a}), 135.9 (C^{11a}), 133.9 ($C^{9/10}$), 133.7 ($C^{9/10}$), 133.6 ($C^{1'}$), 129.9 ($C^{2',6'}$), 127.8 ($C^{3',5'}$), 126.5 ($C^{8/11}$), 126.9 ($C^{4'}$), 126.4 ($C^{8/11}$), 124.2 (C^{5}),60.9 (C^{6a}), 48.4 (C^{12a}), 46.5 (C^{6}), 44.7 (C^{13b}), 41.2 (C^{3a}), 33.8 (C^{13a}), 33.0 (C^{13}), 29.7 (CH_3), 24.9 (C^{4}); **HRMS**: Found 426.1722 $[M+H]^+$, calculated for $C_{27}H_{24}NO_4$ 426.1700 $[M+H]^+$; **Elemental analysis** calculatedfor $C_{27}H_{23}NO_4$: C, 76.22; H, 5.45; N, 3.29. Found: C, 75.98; H, 5.28; N, 3.38.

(3aS,6S,6aS,12aR,13aS,13bR)-2-benzyl-12a-methyl-6-phenyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone(YB041)



YB041 was obtained as a white solid; **Y** = 77%; R_f 0.67 (Silic agel, EtOAc); **Mp** = 190.5-193.1 ºC; **IR**: 2914, 2362, 1694, 1398 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.92 (dt, 1H, *J*= 7.2, H^8);), 7.60 (ddd, 1H, *J*= 7.7, 6.6, 2.1Hz, H^{10}), 7.52 (m, 2H, $H^{11,9}$), 7.25 (m, 5H, $H^{9'-13'}$), 6.93 (m, 3H, $H^{3',4',5'}$), 6.52 (dd, 2H, *J*= 7.9, 1.4Hz $H^{2',6'}$), 5.32 (dt, 1H, *J*= 6.1, 2.8Hz, H^5), 4.58 (s, 2H, $C^{7'}$), 3.89 (dd, 1H, *J*= 10.5, 3.4Hz, H^6), 3.36 (d, 1H, *J*= 10.6Hz, H^{6a}), 3.20 (dd, 1H, *J*= 8.5, 5.6Hz, H^{13b}), 3.12 (td, 1H, *J*= 8.4, 1.6Hz, H^{3a}), 2.93 (m, 1H, H^{13a}), 2.65 (dd, 1H, *J*= 13.8, 6.5Hz, H^{13}), 2.57 (ddd, 1H, *J*= 15.6, 7.0, 1.6Hz, H^4), 2.40 (dd, 1H, *J*= 13.6, 12.5Hz, H^{13}), 2.10 (m, 1H, H^4),1.31 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.3 (C^{12}), 198.4 (C^7), 179.1 (C^3), 178.0 (C^1), 140.1 (C^{5a}), 138.9 ($C^{1'}$), 136.1 (C^{7a}), 135.8 ($C^{8'}$), 134.0 (C^9), 133.7 (C^{10}), 133.6 (C^{11a}), 130.1 ($C^{2',6'}$), 128.7 ($C^{10'11'}$), 128.1 ($C^{9',13'}$), 127.8 ($C^{11'}$), 127.7 ($C^{3',5'}$), 126.9 ($C^{4'}$), 126.6 ($C^{8/11}$), 126.5 ($C^{8/11}$), 124.3 (C^5), 60.9 (C^{6a}), 48.4 (C^{12a}), 47.2 (C^6), 43.6 (C^{13b}), 42.3($C^{7'}$), 40.2 (C^{3a}), 34.1 (C^{13a}), 33.0 (C^{13}), 29.6 (CH_3), 25.1 (C^4); **HRMS**: Found 596.2159 $[M+H]^+$, calculatedfor$C_{34}H_{30}NO_4$ 596.2175 $[M+H]^+$; **Elemental analysis** calculated for $C_{34}H_{29}NO_4$: C, 79.20; H, 5.67; N, 2.72. Found: C, 78.99; H, 5.72; N, 2.85.

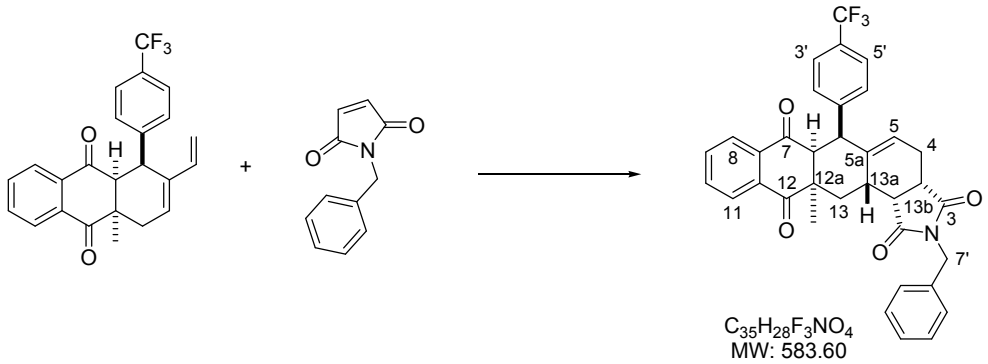
(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-12a-methyl-2-phenyl-6-(4(trifluoromethyl)phenyl)-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB063a)



YB063a was obtained as a white solid; **Y** = 83%; R_f 0.69 (Silica gel, EtOAc); **Mp** = 250.1 ºC; **IR**: 3749, 2197, 1749, 1594, 1498, 1383, 1111, 981, 743 cm^{-1}; **^{1}H NMR** (500MHz, $CDCl_3$): δ 7.92 (d, 1H, *J* = 7.7Hz, H^9);), 7.62 (m, 1H, H^{11}), 7.55 (m, 2H, $H^{8,10}$), 7.46 (t, 2H, *J*= 7.3Hz, $H^{8',12'}$), 7.39 (t, 1H, *J*= 7.5Hz, $H^{10'}$), 7.19 (d, 2H, *J*= 8.2Hz, $H^{3',5'}$), 7.15 (d, 2H, *J*= 7.3Hz, $H^{9',11'}$), 6.79 (d, 2H, *J*= 8.1Hz $H^{2',6'}$), 5.47 (dd, 1H, *J*= 6.2, 3.1Hz, H^5), 4.23 (dd, 1H, *J*= 10.2, 2.6Hz, H^6), 3.47 (d, 1H, *J*= 10.7Hz, H^{6a}), 3.41 (dd, 1H, *J*= 8.6, 5.6Hz, H^{13b}), 3.31 (td, 1H, *J*= 8.4, 1.8Hz, H^{3a}), 3.01 (m, 1H, H^{13a}), 2.79 (dd, 1H, *J* = 13.9, 6.6Hz, H^{13}), 2.69 (ddd, 1H, *J*= 15.9, 6.9, 1.8Hz, H^4), 2.54 (dd, 1H, *J*= 13.8, 12.3Hz, H^{13}), 2.25 (m, 1H, H^4),1.36 (s, 3H, CH_3);**^{13}C NMR** (125MHz, $CDCl_3$): δ 200.0 (C^{12}), 198.1 (C^7), 178.3 (C^3), 177.4 (C^1), 143.7 (C^{5a}), 139.9 ($C^{7'}$), 135.7 ($C^{7a/11a}$), 134.2 (C^{11}), 134.1 ($C^{8/10}$), 133.6 ($C^{7a/11a}$), 132.1 ($C^{1'}$), 130.3 ($C^{2',6'}$), 129.2 ($C^{8',12'}$), 128.8 ($C^{10'}$), 126.6 ($C^{9',11'}$), 126.5 (C^9), 126.4 ($C^{8/10}$), 125.0 (C^5), 124.7 ($C^{3',5'}$),124.0 (q, CF_3, *J* 270Hz), 122.7 ($C^{4'}$), 60.6 (C^{6a}), 48.3 (C^{12a}), 47.2 (C^6), 43.6 (C^{13b}), 40.2 (C^{3a}), 34.1 (C^{13a}), 32.8 (C^{13}), 29.7 (CH_3), 25.5 (C^4); **HRMS:** Found 570.1867 $[M+H]^+$,

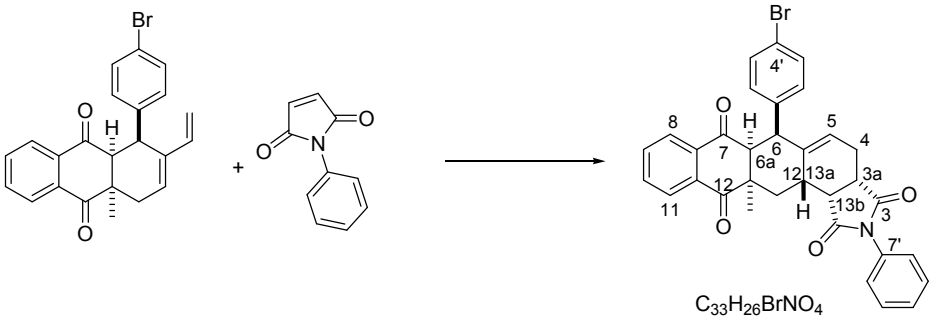
calculated for $C_{34}H_{27}F_3NO_4$ 570.1892 $[M+H]^+$; **Elemental analysis** calculated for $C_{34}H_{26}F_3NO_4$: C, 71.70; H, 4.60; N, 2.46. Found: C, 71.58; H, 5.61; N, 2.41.

(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-2-benzyl-12a-methyl-6-(4-(trifluoromethyl)phenyl)-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB063B)



YB063b was obtained as a white solid; **Y** = 77%; R_f 0.64 (Silica gel, EtOAc); **Mp** = 109.1-111.6 ºC; **IR**: 3749, 2489, 1690, 1594, 1397, 1321, 1163, 1121, 1067, 707 cm^{-1}; **^{1}H NMR** (500MHz, $CDCl_3$): δ 7.91 (dd, 1H, *J* = 7.7, 0.6Hz, H^9), 7.61 (td, 1H, *J* = 7.7, 1.4Hz, H^{11}), 7.53 (td, 1H, *J* = 7.3, 1.2Hz, H^{10}), 7.47 (dd, 1H, *J* = 7.4, 0.9Hz, H^8), 7.27 (m, 3H, *J*= 7.3Hz, $H^{10'-12'}$), 7.24 (m, 2H, $H^{9',13''}$), 7.14 (d, 2H, *J*= 8.1Hz, $H^{3',5'}$), 6.60 (d, 2H, *J*= 8.1Hz, $H^{2',6'}$), 5.61 (d, 1H, *J* = 14.0Hz, $H^{7'}$), 5.25 (dd, 1H, *J*= 6.5, 3.1Hz, H^5), 4.55 (d, 1H, *J* = 14.0Hz, $H^{7'}$), 3.91 (dd, 1H, *J*= 10.5, 2.9Hz, H^6), 3.36 (d, 1H, *J*= 10.6Hz, H^{6a}), 3.21 (dd, 1H, *J*= 8.5, 5.6Hz, H^{13b}), 3.15 (td, 1H, *J*= 8.0, 1.4Hz, H^{3a}), 2.94 (m, 1H, H^{13a}), 2.67 (dd, 1H, *J* = 13.8, 6.6Hz, H^{13}), 2.59 (ddd, 1H, *J*= 15.6, 7.1, 1.4Hz, H^4), 2.43 (dd, 1H, *J*= 13.7, 12.4Hz, H^{13}), 2.11 (m, 1H, H^4),1.32 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.0 (C^{12}), 198.1 (C^7), 178.9 (C^3), 178.0 (C^1), 143.4 (C^{5a}), 139.6 (C^{5a}), 135.9 ($C^{4'}$), 135.7 (C^{7a}), 134.2 (C^{11}), 134.1 (C^{10}), 133.5 (C^{11a}), 130.5 ($C^{2',6'}$), 128.7 ($C^{9'-11'}$), 128.4 ($C^{8'.12'}$), 127.9 ($C^{8'}$), 126.6 (C^8), 126.4 (C^9), 125.0 (C^5), 124.5 ($C^{3',5'}$),124.0 (q, CF_3, *J*= 270Hz), 60.5 (C^{6a}), 48.3 (C^{12a}), 46.6 (C^6), 43.5 (C^{13b}), 42.4 ($C^{7'}$), 40.2 (C^{3a}), 34.1 (C^{13a}), 32.7 (C^{13}), 29.6 (CH_3), 25.2 (C^4); **HRMS**: Found 584.2014 $[M+H]^+$, calculated for $C_{35}H_{29}F_3NO_4$ 584.2049 $[M+H]^+$; **Elemental analysis** calculated for $C_{35}H_{28}F_3NO_4$: C, 72.03; H, 4.84; N, 2.40. Found: C, 72.09; H, 4.88; N, 2.42.

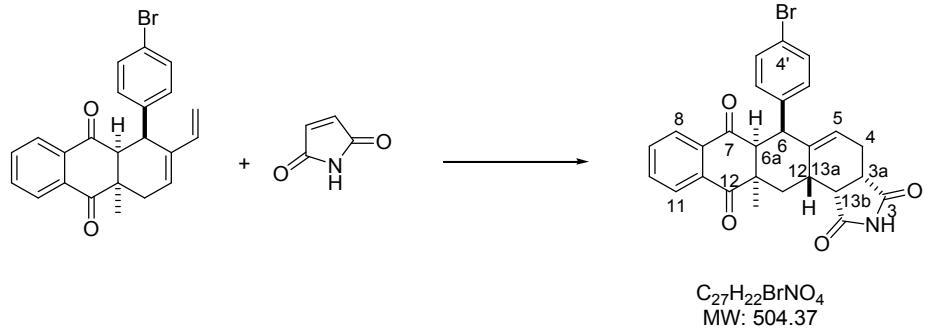
(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-6-(4-bromophenyl)-12a-methyl-2-phenyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB064a)



$C_{33}H_{26}BrNO_4$
MW: 580.47

YB064a was obtained as a white solid; **Y** = 67%; R_f 0.72 (Silica gel, EtOAc); **Mp** = 141.7-145.4 ºC; **IR**: 2197, 1700, 1593, 1488, 1383, 1293, 1199, 1150, 981, 693 cm^{-1}; **^{1}H NMR** (500MHz, $CDCl_3$): δ 7.94 (d, 1H, *J* = 7.6Hz, H^9);), 7.66 (m, 1H, H^{11}), 7.60 (m, 2H, $H^{8,10}$), 7.46 (t, 2H, *J*= 6.9Hz, $H^{9',11'}$), 7.39 (t, 1H, *J*= 7.4Hz, $H^{10'}$), 7.12 (d, 2H, *J*= 7.2Hz, $H^{8',12'}$), 7.09 (d, 2H, *J*= 8.5Hz, $H^{3',5'}$), 6.53 (d, 2H, *J*= 8.5Hz $H^{2',6'}$), 5.45 (dd, 1H, *J*= 6.3, 3.2Hz, H^5), 4.12 (dd, 1H, *J*= 7.9, 2.4Hz, H^6), 3.44 (d, 1H, *J*= 10.4Hz, H^{6a}), 3.39 (dd, 1H, *J*= 8.6, 5.6Hz, H^{13b}), 3.29 (td, 1H, *J*= 8.4, 1.8Hz, H^{3a}), 3.03 (m, 1H, H^{13a}), 2.76 (dd, 1H, *J* = 13.8, 6.5Hz, H^{13}), 2.68 (ddd, 1H, *J*= 15.7, 6.9, 1.7Hz, H^4), 2.52 (dd, 1H, *J*= 13.7, 12.4Hz, H^{13}), 2.20 (m, 1H, H^4),1.36 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.1 (C^{12}), 198.2 (C^7), 178.4 (C^3), 177.4 (C^1), 140.1 (C^{5a}), 138.2 ($C^{7'}$), 135.8 ($C^{7a/11a}$), 134.2 (C^{11}), 134.1 ($C^{8/10}$), 133.6 ($C^{7a/11a}$), 131.7 ($C^{1'}$), 131.6 ($C^{2',6'}$), 131.0 ($C^{3',5'}$), 129.2 ($C^{9',11'}$), 128.8 ($C^{10'}$), 126.6 (C^9), 126.5 ($C^{8/10}$), 126.4 ($C^{8',12'}$), 124.6 (C^5), 121.1 ($C^{4'}$), 60.8 (C^{6a}), 48.4 (C^{12a}), 46.9 (C^6), 43.6 (C^{13b}), 40.3 (C^{3a}), 34.3 (C^{13a}), 32.9 (C^{13}), 29.7 (CH_3), 25.5 (C^4); **HRMS**: Found 580.1088 $[M+H]^+$, calculated for $C_{33}H_{27}BrNO_4$ 580.1123 $[M+H]^+$; **Elemental analysis** calculated for $C_{33}H_{26}BrNO_4$: C, 68.28; H, 4.51; N, 2.41. Found: C, 67.89, H, 4.41, N, 2.33.

(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-6-(4-bromophenyl)-12a-methyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB064b)

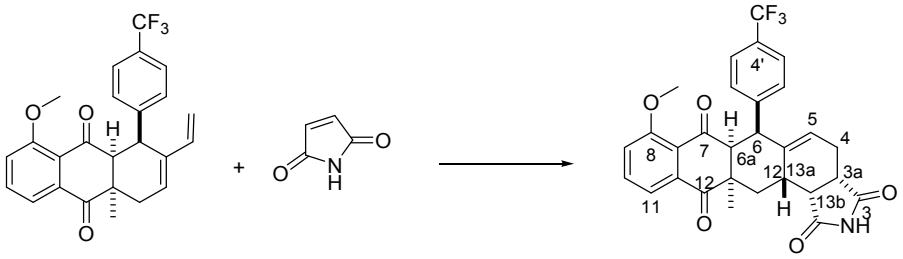


$C_{27}H_{22}BrNO_4$
MW: 504.37

YB064b was obtained as a white solid; **Y** = 81%; R_f 0.33 (Silicagel, Et_2O); **Mp** = 254.9 ºC; **IR**: 1681, 1592, 1487, 1360, 1253, 1009, 981, 712 cm^{-1};**^{1}H NMR** (500MHz, $CDCl_3$): δ 8.09 (br s, 1H, -NH);), 7.91 (d, 1H, *J* = 7.7Hz, H^9), 7.64 (t, 1H, *J* = 7.3Hz, H^{11}), 7.56 (m, 2H, $H^{8,10}$), 7.04 (d, 2H, *J*= 8.2Hz, $H^{3',5'}$), 6.52 (d, 2H, *J*= 8.3Hz $H^{2',6'}$), 5.41 (dd, 1H, *J*= 6.0, 3.0Hz, H^5), 4.12 (d, 1H, *J*= 7.9Hz, H^6), 3.45 (d, 1H, *J*= 10.3Hz, H^{6a}), 3.26 (dd, 1H, *J*= 8.6, 5.8Hz, H^{13b}), 3.16 (td, 1H, *J*= 8.4, 7.3Hz, H^{3a}), 2.95 (m, 1H, H^{13a}), 2.70 (dd, 1H, *J*= 13.8, 6.5Hz, H^{13}), 2.57 (dd, 1H, *J*= 15.3, 6.5Hz, H^4), 2.44 (dd, 1H, *J*= 13.2, 12.9Hz, H^{13}), 2.12 (m, 1H, H^4), 1.36 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.2 (C^{12}), 198.4 (C^7), 179.2 (C^3), 178.3 (C^1), 139.9 ($C^{4'}$),

138.6 (C^{5a}), 135.7 (C^{7a}), 134.2 ($C^{8/11}$), 134.0 ($C^{8/11}$), 133.6 (C^{11a}), 131.6 ($C^{2',6'}$), 130.9 ($C^{3',5'}$), 126.6 ($C^{10/9}$), 126.5 ($C^{10/9}$), 124.7 (C^{5}), 120.9 ($C^{1'}$), 60.7 (C^{6a}), 48.3 (C^{12a}), 46.6 (C^{6}), 44.7 (C^{13b}), 41.3 (C^{3a}), 33.8 (C^{13a}), 32.8 (C^{13}), 29.7 (CH_3), 24.9 (C^{4}); **HRMS**: Found 504.0807 $[M+H]^+$, calculated for $C_{27}H_{23}BrNO_4$ 504.0810 $[M+H]^+$; **Elemental analysis** calculated for $C_{27}H_{22}BrNO_4$: C, 64.30; H, 4.40; N, 2.78. Found: C, 64.08; H, 4.38; N, 2.81.

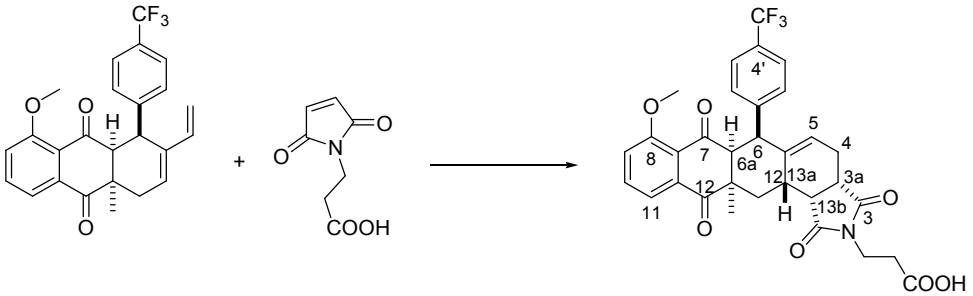
(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-8-methoxy-12a-methyl-6-(4-(trifluoromethyl)phenyl)-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB071) (5d)



$C_{29}H_{24}F_3NO_5$
MW: 523.50

YB071 was obtained as a white solid; **Y** = 78%; R_f 0.42 (Silica gel, Et_2O); **Mp** = 90.6 ºC; **IR**: 3244, 2328, 1674, 1586, 1467, 1278, 1156, 1104, 1065, 998, 730 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 8.35 (br s, 1H, -NH), 7.51 (m, 2H, $H^{11,9}$), 7.20 (d, 2H, *J*= 8.1Hz, $H^{3',5'}$), 7.02 (d, 1H, *J*= 8.2Hz, H^{10}), 6.85 (d, 2H, *J*= 8.1Hz, $H^{2',6'}$), 5.42 (dd, 1H, *J* = 6.6, 3.5Hz, H^{5}), 4.22 (m, 1H, H^{6}), 3.72 (s, 1H, -OCH_3),3.38 (d, 1H, *J*= 10.4Hz, H^{6a}), 3.21 (dd, 1H, *J*= 8.8, 5.6Hz, H^{13b}), 3.14 (td, 1H, *J*= 8.6, 1.6Hz, H^{3a}), 2.82 (m, 1H, H^{13}), 2.60 (dd, 1H, *J* = 13.7, 6.4Hz, H^{13a}), 2.55 (dd, 1H, *J* = 8.6, 1.4Hz, H^{4}), 2.50 (d, 1H, *J* = 12.2Hz, H^{13}), 2.07 (m, 1H, H^{4}), 1.37 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.2 (C^{12}), 196.7 (C^{7}), 179.4 (C^{3}), 178.4 (C^{1}), 157.9 (C^{8}), 143.7 ($C^{1',4'}$), 139.6 (C^{5a}), 135.7 (C^{7a}), 134.5 ($C^{11/9}$), 130.4 ($C^{2',6'}$), 125.1 (C^{11a}), 124.6 ($C^{5',3'}$), 124.6 (C^{5}), 124.0 (q, CF_3, *J*= 270Hz), 118.5 ($C^{11/9}$), 117.2 (C^{10}), 62.4 (C^{6a}), 55.9 (C^{OMe}), 48.4 (C^{12a}), 45.8 (C^{6}), 44.8 (C^{13b}), 41.4 (C^{3a}), 34.0 (C^{13a}), 33.2 (C^{13}), 28.6 (CH_3), 25.0 (C^{4}); **HRMS** (EI): Found 524.1683 $[M+H]^+$, $C_{29}H_{25}F_3NO_5$, calculated 524.1685 $[M+H]^+$; **Elemental analysis** calculated for $C_{29}H_{24}F_3NO_5$: C, 66.53; H, 4.62; N, 2.68. Found: C, 66.43; H, 4.77, N, 2.62.

3-((3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-8-methoxy-12a-methyl-1,3,7,12-tetraoxo-6-(4-(trifluoromethyl)phenyl)-3a,4,6a,7,12,12a,13,13a-octahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,13bH)-yl)propanoic acid (YB072)

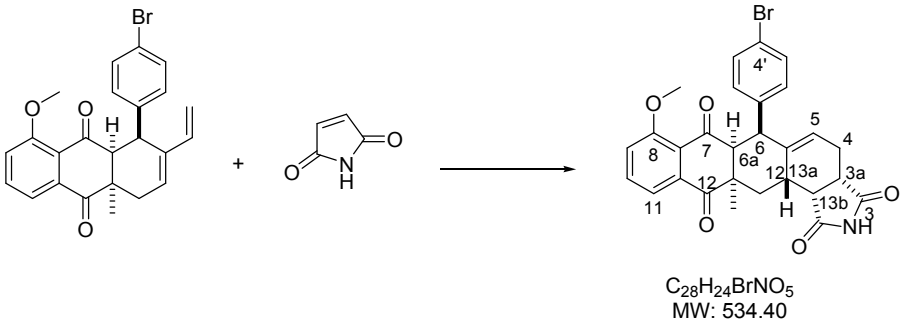


$C_{32}H_{28}F_3NO_7$
MW: 595.56

YB072 was obtained asa white solid; **Y** = 92%; R_f 0.45 (Silica gel, AcOH/EtOAc 1:99); **Mp** = 144.1–147.5 ºC; **IR**: 3749, 2359, 1993, 1740, 1671, 1398, 1316, 1216, 1156, 1105, 990, 853 cm^{-1}; **^{1}H NMR** (500MHz, $CDCl_3$): δ 7.52 (m, 2H, $H^{11,9}$), 7.18 (d, 1H, *J*= 8.2Hz, $H^{3',5'}$), 7.02

(dd, 1H, *J*= 6.3, 3.0Hz, H^{10}), 6.83 (d, 2H, *J*= 8.1, $H^{2',6'}$), 5.37 (dd, 1H, *J* = 6.6, 3.0Hz, H^5), 4.19 (d, 1H, *J* = 7.7Hz, H_6), 3.74 (s, 3H, -OCH_3), 3.72 (m, 2H, $H^{7'}$), 3.38 (d, 1H, *J*= 10.2Hz, H^{6a}), 3.17 (dd, 1H, *J*= 8.6, 5.6Hz, C^{13b}), 3.11 (t, 1H, *J* = 7.7Hz, H^{3a}), 2.85 (m, 1H, H^{13}), 2.66 (dd, 1H, *J* = 14.0, 6.7Hz, H^{13a}), 2.58 (dd, 1H, *J*= 16.1, 6.8Hz, H^4), 2.57 (t, 2H, *J* = 7.0Hz, $H^{8'}$), 2.50 (dd, 1H, *J*= 13.6, 12.6 Hz, H^{13}), 2.07 (m, 1H, H^4), 1.39 (s, 3H, CH_3);**^{13}C NMR** (125MHz, $CDCl_3$): δ 200.2 (C^{12}), 197.2 (C^7), 179.0 (C^3), 177.8 (C^1), 174.5 ($C^{9'}$), 157.9 (C^8), 144.0 ($C^{1',4'}$), 139.5 (C^{5a}), 135.7 (C^{7a}), 134.6 ($C^{11/9}$), 130.3 ($C^{2',6'}$), 128.9 (C^{11a}), 125.0 (C^5), 124.5 ($C^{3',5'}$), 124.0 (q, CF_3, *J*= 270Hz), 118.5 ($C^{11/9}$), 117.2 (C^{10}), 62.2 (C^{6a}), 55.9 (OCH_3), 48.2 (C^{12a}), 45.7 (C^6), 43.7 (C^{3a}), 40.1 (C^{13b}), 34.3 ($C^{7'}$), 34.1 (C^{13a}), 32.9 (C^{13}), 31.7 ($C^{8'}$) , 28.7 (CH_3), 25.2 (C^4); **HRMS** (EI): Found: 596.1920 $[M+H]^+$, $C_{32}H_{29}F_3NO_7$, calculated 596.1896 $[M+H]^+$; **Elemental analysis** calculated for $C_{32}H_{28}F_3NO_{7:}$ C, 64.53; H, 4.72; N, 2.35. Found: C, 64.48; H; 4.69, N, 2.08.

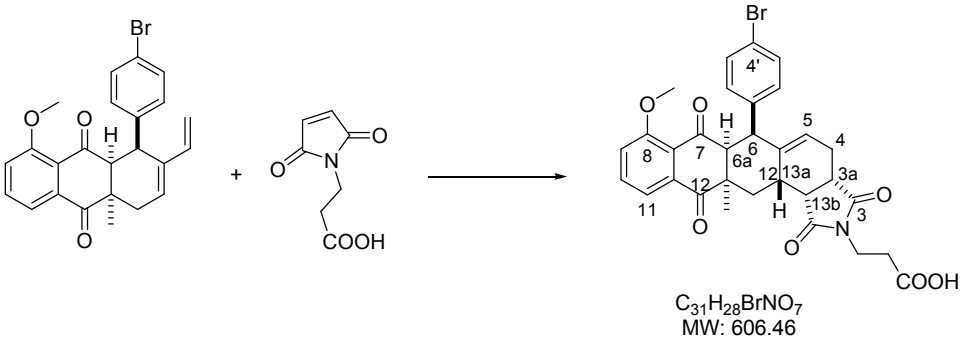
(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-6-(4-bromophenyl)-8-methoxy-12a-methyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB073)



$C_{28}H_{24}BrNO_5$
MW: 534.40

YB073 was obtained as a white solid; **Y** = 73%; R_f 0.35 (Silicagel, Et_2O); **Mp** = 170.0-173.1 ºC; **IR**: 2927, 1692, 1583, 1434, 1362, 1273, 1231, 1183, 1148, 1076 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.77 (br s, 1H, -NH), 7.55 (m, 2H, $H^{11,9}$), 7.10 (d, 2H, *J*= 8.4Hz, $H^{3',5'}$), 7.02 (m, 1H, H^{10}), 6.62 (d, 2H, *J*= 8.4Hz, $H^{2',6'}$), 5.43 (dd, 1H, *J* = 6.7, 3.2Hz, H^5), 4.11 (m, 1H, H^6), 3.80 (s, 1H, -OCH_3),3.35 (d, 1H, *J*= 10.4Hz, H^{6a}), 3.20 (dd, 1H, *J*= 8.7, 5.4Hz, H^{13b}), 3.13 (td, 1H, *J*= 8.4, 1.5Hz, H^{3a}), 2.77 (m, 1H, H^{13}), 2.58 (M, 1H, H^{13a}), 2.55 (dd, 1H, *J* = 7.2, 1.3Hz, H^4), 2.50 (d, 1H, *J* = 12.8Hz, H^{13}), 2.04 (m, 1H, H^4),1.38 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 200.4 (C^{12}), 196.9 (C^7), 178.9 (C^3), 178.0 (C^1), 157.9 (C^8), 139.8 ($C^{1'}$), 138.2 (C^{5a}), 135.7 (C^{7a}), 134.4 ($C^{11/9}$), 131.7 ($C^{2',6'}$), 130.9 ($C^{5',3'}$), 125.4 (C^{11a}), 124.2 (C^5), 120.7 ($C^{4'}$), 118.5 ($C^{11/9}$), 117.2 (C^{10}), 62.6 (C^{6a}), 56.2 (C^{OMe}), 48.5 (C^{12a}), 45.5 (C^6), 44.8 (C^{13b}), 41.4 (C^{3a}), 34.2 (C^{13a}), 33.3 (C^{13}), 28.6 (CH_3), 25.1 (C^4); **HRMS** (ESI): Found 534.0911 $[M+H]^+$, $C_{28}H_{25}BrNO_5$, calculated 534.0916 $[M+H]^+$; **Elemental analysis** calculated for $C_{28}H_{24}BrNO_{5:}$ C, 62.93; H, 4.52; N, 2.62. Found: C, 63.03; H, 4.36; N, 2.61.

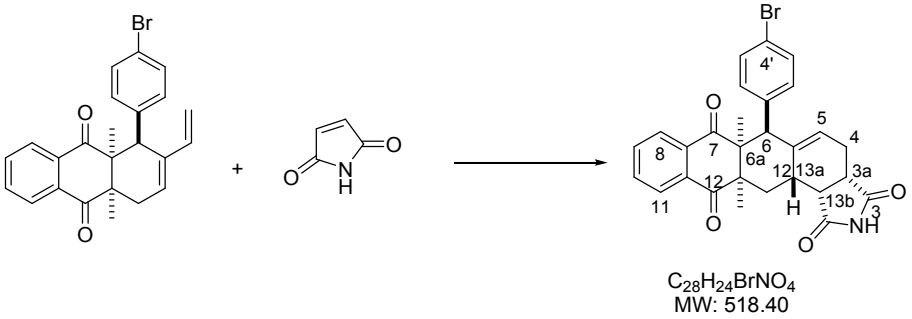
3-((3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-6-(4-bromophenyl)-8-methoxy-12a-methyl-1,3,7,12-tetraoxo-3a,4,6a,7,12,12a,13,13a-octahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,13bH)-yl)propanoic acid (YB074) (5e)



$C_{31}H_{28}BrNO_7$
MW: 606.46

YB074 was obtained as a white solid; **Y** = 93%; R_f 0.49 (Silica gel, AcOH/EtOAc 1:99); **Mp** = 151.3–154.2 ºC **IR**: 3853, 2173, 1740, 1666, 1561, 1293, 1029, 983, 710 cm^{-1}; **^{1}H NMR** (500MHz, $CDCl_3$): δ 7.53 (m, 2H, $H^{11,9}$), 7.08 (dd, 1H, *J*= 6.6, 2.8Hz, H^{10}), 7.06 (d, 1H, *J*= 8.4Hz, $H^{3',5'}$), 6.58 (d, 2H, *J*= 8.4, $H^{2',6'}$), 5.37 (dd, 1H, *J* = 6.7, 3.1Hz, H^5), 4.06 (dt, 1H, *J* = 8.6, 1.5Hz, H_6), 3.80 (s, 3H, -OCH_3),3.72 (dd, 1H, *J* = 7.1, 6.6Hz, $H^{7'}$), 3.68 (dd, 1H, *J* = 7.0, 6.8Hz, $H^{7'}$), 3.34 (d, 1H, *J*= 10.3Hz, H^{6a}), 3.14 (dd, 1H, *J*= 8.6, 5.5Hz, C^{13b}), 3.09 (dt, 1H, *J* = 8.6, 1.1Hz, H^{3a}), 2.78 (m, 1H, H^{13}), 2.61 (dd, 1H, *J* = 13.8, 6.5Hz, H^{13a}), 2.58 (dd, 1H, *J*= 7.4, 1.1Hz, H^4), 2.54 (t, 2H, *J* = 7.0Hz, $H^{8'}$), 2.50 (dd, 1H, *J*= 13.6, 12.7 Hz, H^{13}), 2.07 (m, 1H, H^4),1.38 (s, 3H, CH_3); **^{13}C NMR** (125MHz, $CDCl_3$): δ 200.4 (C^{12}), 197.4 (C^7), 179.1 (C^3), 177.9 (C^1), 174.7 ($C^{9'}$), 157.9 (C^8), 139.7 ($C^{1'}$), 138.4 (C^{5a}), 135.7 ($C^{4'}$), 134.5 ($C^{11/9}$), 131.7 ($C^{2',7'}$) 130.3 ($C^{3',5'}$), 125.2 (C^{7a}), 124.4 (C^5), 120.6 (C^{11a}), 118.5 ($C^{11/9}$), 117.2 (C^{10}), 62.4 (C^{6a}), 56.2 (OCH_3), 48.3 (C^{12a}), 45.4 (C^6), 43.6 (C^{3a}), 40.1 (C^{13b}), 34.3 (C^{13a}), 34.2 ($C^{7'}$), 33.1 (C^{13}), 31.7 ($C^{8'}$) , 28.7 (CH_3), 25.2 (C^4); **HRMS** (EI): Found 606.1133 $[M+H]^+$, $C_{31}H_{29}BrNO_7$, calculated 606.1127 $[M+H]^+$; **Elemental analysis** calculated for $C_{31}H_{28}BrNO_7$: C, 61.39; H, 4.65; N, 2.31. Found: C, 61.21; H, 4.48; N, 2.05.

(3aS,6S,6aS,12aR,13aS,13bR)-6-(4-bromophenyl)-6a,12a-dimethyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB077)

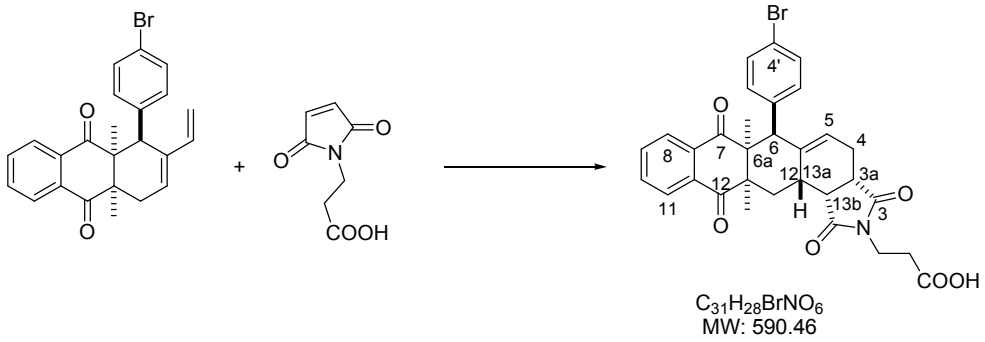


$C_{28}H_{24}BrNO_4$
MW: 518.40

YB077 was obtained as a white solid; **Y** = 67%; R_f 0.37 (Silica gel, Et_2O); **Mp** = 90.8–95.2 ºC; **IR**: 2981, 1702, 1682, 1594, 1486, 1361, 1262, 1198, 1076, 1009, 980, 788 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 8.23 (br s, 1H, -NH), 7.80 (d, 1H, *J* = 8.2Hz, $H^{9/10}$), 7.58 (dd, 1H, *J* = 7.2, 1.7Hz, $H^{9/10}$), 7.54 (dd,1H, *J* = 7.3, 1.7Hz, $H^{8/11}$), 7.51 (td, 1H, *J*= 5.9, 1.5Hz, $H^{8/11}$), 6.92 (d, 2H, *J*= 8.5Hz, $H^{3',5'}$), 6.47 (d, 2H, *J*= 8.5Hz $H^{2',6'}$), 5.41 (dd, 1H, *J*= 5.9, 2.8Hz, H^5), 3.68 (s, 1H, H^6), 3.28 (dd, 1H, *J*= 8.4, 5.6Hz, H^{13b}), 3.18 (td, 1H, *J*= 8.4, 2.0Hz, H^{3a}), 3.12 (m, 1H, H^{13a}), 2.76 (dd, 1H, *J*= 14.1, 12.0Hz, H^{13}), 2.56 (ddd, 1H, *J*= 16.1, 6.7, 1.8Hz, H^4), 2.53 (dd, 1H, *J*= 14.0, 7.5Hz, H^{13}), 2.14 (m, 1H, H^4), 1.55 (s, 1H, CH_3),1.19 (s, 3H, CH_3); **^{13}C NMR**

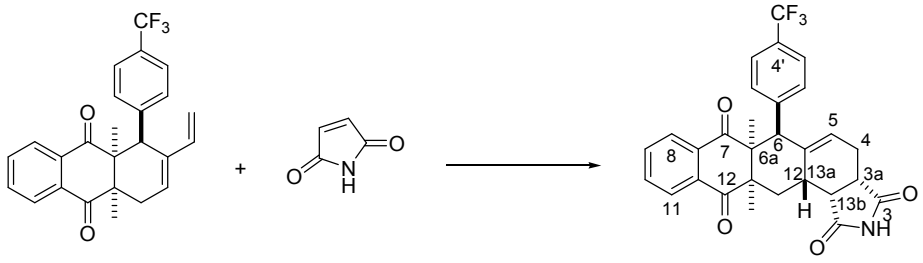
(100MHz, $CDCl_3$): δ 201.0 (C^{12}), 200.3 (C^{7}), 179.4 (C^{3}), 178.6 (C^{1}), 140.3 ($C^{1'/4'}$), 139.5 (C^{5a}), 135.6 ($C^{7a/11a}$), 133.8 ($C^{8/11}$), 133.7 ($C^{7a/11a}$), 133.6 ($C^{9/10}$), 131.7 ($C^{2',6'}$), 130.7 ($C^{3',5'}$), 126.8 ($C^{8/11}$), 126.0 (C^{5}), 125.8 ($C^{9/10}$), 120.8 ($C^{1'/4'}$), 56.8 (C^{6a}), 56.4 (C^{6}), 51.6 (C^{12a}), 44.4 (C^{13b}), 41.2 (C^{3a}), 33.7 (C^{13a}), 29.2 (C^{13}), 26.7 (C^{6a}-$\mathbf{C}H_3$), 25.1 (C^{4}), 20.8 (C^{12a}-$\mathbf{C}H_3$); **HRMS**: Found 518.0961 $[M+H]^+$, calculated for $C_{28}H_{25}BrNO_4$ 518.0967 $[M+H]^+$; **Elemental analysis** calculated for $C_{28}H_{24}BrNO_4$: C, 64.87; H, 4.67; N, 2.70. Found: C, 65.03; H, 4.48; N, 2.61.

3-((3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-6-(4-bromophenyl)-6a,12a-dimethyl-1,3,7,12-tetraoxo-3a,4,6a,7,12,12a,13,13a-octahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,13bH)-yl)propanoic acid (YB078)



YB078 was obtained as a white solid; **Y** = 76%;$\boldsymbol{R_f}$ 0.40 (Silica gel, AcOH/EtOAc 1:99);**Mp** = 137.5 – 141.4ºC; **IR**: 2981, 2356, 1738, 1692, 1594, 1486, 1364, 1262, 1219, 1009, 980, 631 cm^{-1}; **^{1}H NMR** (500MHz, $CDCl_3$): δ 7.80 (dt, 1H, *J* = 7.6, 0.7Hz, $H^{9/10}$), 7.58 (m, 1H, $H^{9/10}$), 7.56 (dd, 1H, *J* = 7.4, 1.1Hz, $H^{8/11}$), 7.52 (td, 1H, *J* = 7.3, 0.9Hz, $H^{8/11}$), 6.95 (d, 2H, *J*= 8.3Hz, $H^{3',5'}$), 6.45 (d, 2H, *J*= 8.5Hz $H^{2',6'}$), 5.32 (dd, 1H, *J*= 6.0, 2.8Hz, H^{5}), 3.77 (dd, 1H, *J* = 13.7, 7.2Hz, $H^{7'}$), 3.72 (dd, 1H, *J* = 13.8, 6.8Hz, $H^{7'}$), 3.61 (s, 1H, H^{6}), 3.20 (dd, 1H, *J*= 8.6, 5.6Hz, H^{13b}), 3.14 (td, 1H, *J*= 8.2, 1.4Hz, H^{3a}), 3.09 (m, 1H, H^{13a}), 2.82 (dd, 1H, *J*= 14.0, 12.0Hz, H^{13}), 2.58 (m, 1H, H^{4}), 2.54 (m, 2H, $H^{8'}$), 2.53 (dd, 1H, *J*= 8.9, 4.7Hz, H^{13}), 2.12 (m, 1H, H^{4}), 1.54 (s, 1H, CH_3),1.21 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 201.0 (C^{12}), 200.3 (C^{7}), 179.1 (C^{3}), 178.2 (C^{1}), 175.2 (COOH), 140.1 ($C^{1'/4'}$), 139.5 (C^{5a}), 135.6 ($C^{7a/11a}$), 133.9 ($C^{8/11}$), 133.7 ($C^{7a/11a}$), 133.6 ($C^{9/10}$), 131.7 ($C^{2',6'}$), 130.7 ($C^{3',5'}$), 126.9 ($C^{8/11}$), 126.0 (C^{5}), 125.7 ($C^{9/10}$), 120.8 ($C^{1'/4'}$), 56.8 (C^{6a}), 56.2 (C^{6}), 51.6 (C^{12a}), 43.2 (C^{13b}), 40.0 (C^{3a}), 34.1 ($C^{7'}$), 34.0 (C^{13a}), 31.7 (C^{13}), 29.2 ($C^{8'}$), 27.2 (C^{6a}-$\mathbf{C}H_3$), 25.3 (C^{4}), 20.8 (C^{12a}-$\mathbf{C}H_3$); **HRMS**: Found 590.1172 $[M+H]^+$, calculated for $C_{31}H_{29}BrNO_6$ 590.1178 $[M+H]^+$; **Elemental analysis** calculated for $C_{31}H_{28}BrNO_6$: C, 63.06; H, 4.78; N, 2.37. Found: C, 63.04; H, 4.75; N, 2.36.

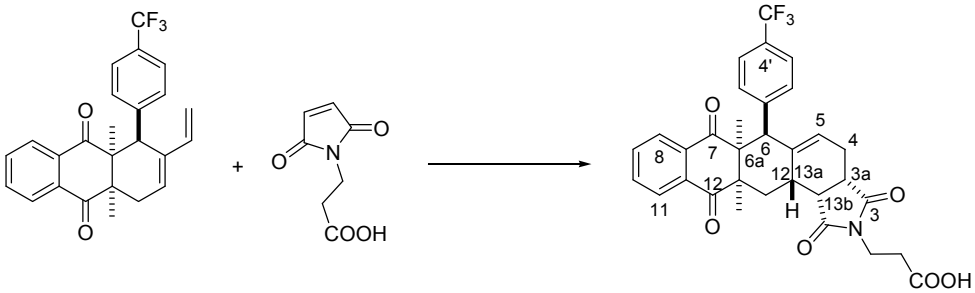
(3aSR,6SR,6aSR,12aRS,13aSR,13bRS)-6a,12a-dimethyl-6-(4-(trifluoromethyl)phenyl)-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB081) (5f)



$C_{29}H_{24}F_3NO_4$
MW: 507.50

YB081 was obtained as a white solid; **Y** = 88%; R_f 0.45 (Silica gel, Et_2O); **Mp** = 137.5–142.1 ºC; **IR**: 2909, 2165, 1596, 1558, 1416, 1361, 1323, 1263, 1122, 1067, 980, 828, 624 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.78 (dd, 1H, *J* = 7.5, 1.2Hz, $H^{9/10}$), 7.73 (br s, 1H, -NH), 7.55 (dd, 1H, *J* = 7.6, 1.3Hz, $H^{9/10}$), 7.50 (td,1H, *J* = 7.3, 1.4Hz, $H^{8/11}$), 7.45 (td, 1H, *J*= 7.5, 1.4Hz, $H^{8/11}$), 7.05 (d, 2H, *J*= 8.2Hz, $H^{3',5'}$), 6.73 (d, 2H, *J*= 8.2Hz, $H^{2',6'}$), 5.44 (dd, 1H, *J*= 6.0, 3.1Hz, H^5), 3.82 (s, 1H, H^6), 3.32 (dd, 1H, *J*= 8.6, 5.9Hz, H^{13b}), 3.21 (td, 1H, *J*= 8.5, 2.0Hz, H^{3a}), 3.20 (m, 1H, H^{13a}), 2.78 (dd, 1H, *J*= 14.1, 11.9Hz, H^{13}), 2.60 (d, 1H, *J*= 15.5Hz, H^4), 2.56 (dd, 1H, *J*= 14.3, 7.6Hz, H^{13}), 2.17 (m, 1H, H^4), 1.59 (s, 1H, CH_3),1.21 (s, 3H, CH_3);**^{13}C NMR** (100MHz, $CDCl_3$): δ 201.0 (C^{12}), 200.3 (C^7), 179.4 (C^3), 178.6 (C^1), 138.2 ($C^{1'/4'}$), 136.4 (C^{5a}), 135.4 ($C^{7a/11a}$), 133.8 ($C^{8/11}$), 133.7 ($C^{7a/11a}$), 133.6 ($C^{9/10}$), 130.4 ($C^{2',6'}$), 126.8 ($C^{8/11}$), 126.2 (C^5), 125.9 ($C^{9/10}$), 124.5 ($C^{1'/4'}$), 124.4 ($C^{3',5'}$), 124.0 (q, CF_3, *J*= 270Hz), 56.7 (C^{6a}), 56.6 (C^6), 51.5 (C^{12a}), 44.4 (C^{13b}), 41.2 (C^{3a}), 33.6 (C^{13a}), 29.1 (C^{13}), 26.8 (C^{6a}-**C**H_3), 25.1 (C^4), 20.7 (C^{12a}-**C**H_3); **HRMS**: Found 508.1731 $[M+H]^+$, calculated for $C_{29}H_{25}F_3NO_4$ 508.1736 $[M+H]^+$; **Elemental analysis** calculated for $C_{29}H_{24}F_3NO_4$: C, 68.63; H, 4.77; N, 2.76. Found: C, 66.05; H, 4.63; N, 2.37.

(3aSR,6SR,6aSR,13aSR,13bRS)-2-benzyl-6-(4-bromophenyl)-11-hydroxy-6a-methyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (YB082)

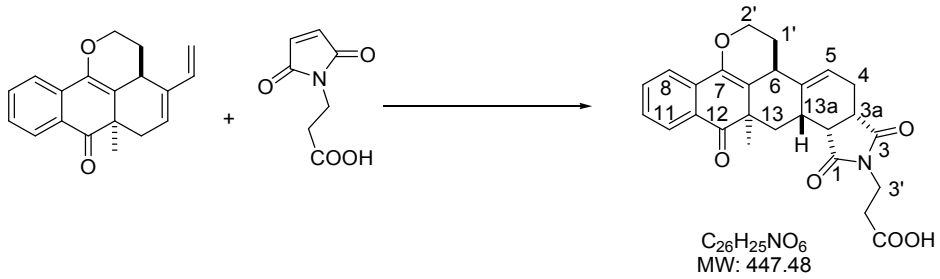


$C_{32}H_{28}F_3NO_6$
MW: 579.56

YB082 was obtained as a white solid; R_f 0.39 (Silica gel, AcOH/EtOAc 1:99); **Mp** = 202.3 207.8 ºC; **IR**: 3731, 2987,2335, 1741, 1681, 1556, 1396, 1310, 1262, 1157, 1067, 1019, 862 cm^{-1}; **^{1}H NMR** (500MHz, $CDCl_3$): δ 7.80 (dd, 1H, *J* = 7.7, 1.3Hz, $H^{8/11}$), 7.54 (dd, 1H, *J* = 7.6, 1.4Hz, $H^{8/11}$), 7.50 (td, 1H, *J* = 7.5, 1.4Hz, $H^{9/10}$), 7.44 (td, 1H, *J* = 7.5, 1.4Hz, $H^{9/10}$), 7.04 (d, 2H, *J*= 8.2Hz, $H^{3',5'}$), 6.71 (d, 2H, *J*= 8.2Hz $H^{2',6'}$), 5.35 (dq, 1H, *J*= 6.0, 2.9Hz, H^5), 3.78 (dd, 1H, *J* = 13.9, 6.7Hz, $H^{7'}$), 3.76 (s, 1H, H^6), 3.74 (dd, 1H, *J* = 13.8, 6.8Hz, $H^{7'}$), 3.23 (dd, 1H, *J*= 8.6, 5.7Hz, H^{13b}), 3.17 (td, 1H, *J* = 8.4, 1.8Hz, H^{3a}), 3.16 (m, 1H, H^{13a}), 2.85 (dd, 1H, *J*= 14.2,

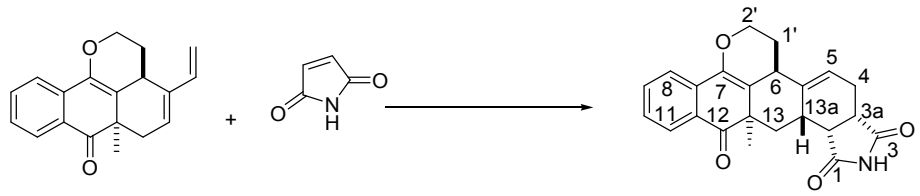
11.8Hz, H^{13}), 2.60 (td, 1H, *J* = 7.1, 1.1Hz, H^4), 2.58 (d, 2H, *J* = 7.3Hz, $H^{8'}$), 2.55 (dd, 1H, *J*= 7.3, 2.7Hz, H^{13}), 2.15 (m, 1H, H^4), 1.57 (s, 1H, $CH_{3),}$1.21 (s, 3H, CH_3),);**^{13}C NMR** (125MHz, $CDCl_3$): δ 200.9 (C^{12}), 200.2 (C^7), 179.1 (C^3), 178.2 (C^1), 175.2 (COOH), 145.8 ($C^{1'/4'}$), 139.2 (C^{5a}), 135.5 ($C^{7a/11a}$), 133.9 ($C^{9/10}$), 133.7 ($C^{7a/11a}$), 133.6 ($C^{9/10}$), 130.4 ($C^{2',6'}$), 126.8 ($C^{8/11}$), 126.2 (C^5), 125.9 ($C^{9/10}$), 124.5 ($C^{3',5'}$), 124.4 ($C^{1'/4'}$), 124.0 (q, CF_3, *J*= 270Hz), 56.8 (C^{6a}), 56.4 (C^6), 51.6 (C^{12a}), 43.2 (C^{13b}), 40.0 (C^{3a}), 34.2 ($C^{7'}$), 33.8 (C^{13a}), 31.7 (C^{13}), 29.1 ($C^{8'}$), 26.8 (C^{6a}-CH_3), 25.3 (C^4), 20.7 (C^{12a}-CH_3); **HRMS**: Found 580.1949 $[M+H]^+$, calculated for $C_{32}H_{29}F_3NO_6$ 580.1947 $[M+H]^+$; **Elemental analysis** calculated for $C_{32}H_{28}F_3NO_6$: C, 66.32; H, 4.87; N, 2.42. Found: C, 66.52; H, 4.66; N, 240.

3'-((3aSR, 6SR, 12aRS, 13bRS,13aSR,)-12a-methyl-1,3,12-trioxo-1,3,3a,5a,6,12a,13,13a,13b, -decahydro-2H-naphtho[3',2',1':8,1]isochromeno[6,5-e]isoindol-2(5H)-yl)propanoic acid (YB085)



The reaction was carried out for 48 h to afford compound **YB085** as white solid. **Y** = 65%; R_f 0.29 (Silica gel, AcOH/EtOAc 1:99); **Mp.** 207.6–210.1 ºC; **IR**: 2928, 1738, 1694, 1399 cm^{-1}; **^{1}H NMR** (400MHz, $CDCl_3$): δ 7.85 (dt, 1H, *J* = 7.7, 0.6Hz, $H^{11/8}$), 7.55 (td, 1H, *J* = 7.3, 1.3Hz, $H^{9,10}$), 7.52 (dd, 1H, *J*= 7.8, 1.6Hz, $H^{8/11}$), 7.33 (ddd, 1H, *J*= 7.6, 6.9, 1.7Hz $H^{9/10}$), 5.49 (dd, 1H, *J*= 7.0, 2.8Hz, H^5), 4.10 (ddd, 1H, *J* = 10.3, 6.4, 3.6Hz, $Hb^{2'}$), 4.03 (ddd, 1H, *J*= 10.8, 8.2, 2.8Hz, $Ha^{2'}$), 3.76 (t, 2H, *J*= 7.3Hz, $H^{3'}$), 3.16 (dd, 1H, *J*= 8.8, 6.0Hz, H^{13b}), 3.09 (td, 1H, *J*= 8.1, 1.2Hz, H^{3a}), 3.01 (m, 1H, H^{13a}), 2.99 (dd, 1H, *J*= 14.1, 4.3Hz, Hb^{13}), 2.71 (dd, 1H, *J* = 15.0, 7.2Hz, H^4), 2.61 (t, 2H, *J* = 7.1Hz, $H^{4'}$), 2.29 (q, 1H, *J*= 13.0Hz, Ha^{13}), 2.16 (m, 1H, H^6), 2.20 (m, 1H, $Hb^{1'}$), 2.02 (m, 1H, H^4), 2.11 (m, 1H, $Ha^{1'}$), 1.37 (s, 3H, CH_3); **^{13}C NMR** (100MHz, $CDCl_3$): δ 203.8 (C^{12}), 179.5 (C^3), 177.6 (C^1), 175.0 (COOH), 143.5 (C^7), 143.2 (C^{6a}), 135.0 ($C^{7a/11a}$), 133.8 ($C^{8/11}$), 129.0 ($C^{7a/11a}$), 127.9 ($C^{9/10}$), 126.7 ($C^{9/10}$), 121.6 ($C^{8/11}$), 117.8 (C^{5a}), 116.0 (C^5), 63.4 ($C^{2'}$), 49.0 (C^{12a}), 43.3 (C^{13b}), 39.8 (C^{3a}), 34.7 (C^6), 34.3 ($C^{3'}$), 31.8 ($C^{4'}$), 31.7 (C^{13a}), 29.3 (C^{13}), 29.2 (CH_3), 25.0 ($C^{1'}$), 24.5 (C^4); **MS** (EI): m/z 448.56 ($M+H^+$) (100); **HRMS**: Found M^+ 447.1584 , $C_{26}H_{25}NO_6$ requires 447.1682; **Elemental analysis** calculated for $C_{26}H_{25}NO_6$: C, 69.79; H, 5.63: N, 3.13; Found C, 69.90; H, 5.51; N, 3.02.

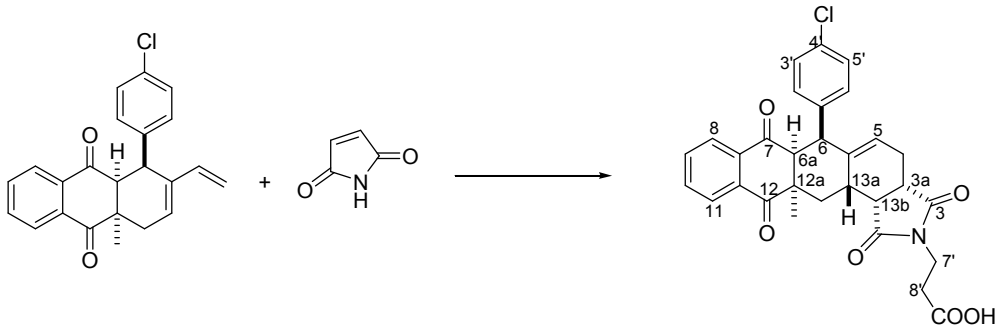
(3aSR,6SR,12aRS,13bRS,13aSR)-12a-methyl-1',3a,4,6,12a,13-hexahydro-2H-naphtho[3',2',1':8,1]isochromeno[6,5-e]isoindole-1,3,12(7H,8aH,8bH)-trione (YB086)



$C_{23}H_{21}NO_4$
MW: 375.42

As previously reported by Bendiabdellah and Zinzalla.[1]

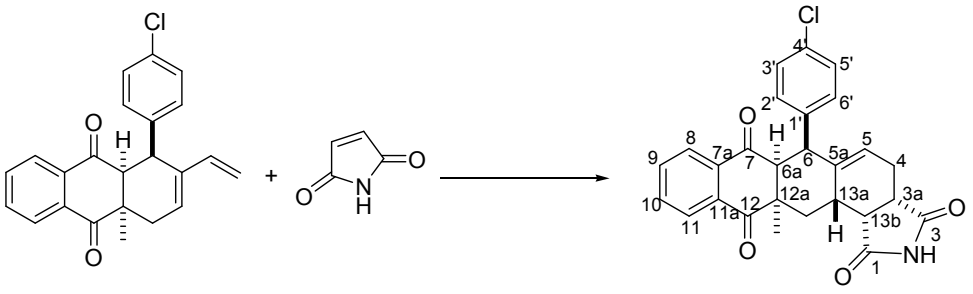
Synthesis of 3-((3aS,6S,6aS,12aR,13aS,13bR)-6-(4-chlorophenyl)-12a-methyl-1,3,7,12-tetraoxo-3a,4,6a,7,12,12a,13,13a-octahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,13bH)-yl)propanoic acid (001-DA-022-01)



$C_{30}H_{26}ClNO_6$
Mol. Wt.: 531.98

001-DA-022-01 was obtained as a colourless solid (41 mg, 28 %). **IR** (ATR, λ_{max}/cm^{-1}): 2956, 1686, 1592, 1489, 1442, 1396, 1253, 1158, 1091, 1013, 979, 871, 832, 711, 646. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 1.37 (s, 3 H, CH_3), 2.05-2.14 (m, 1 H, $H^{4)}$), 2.46 (t, 1 H, J = 12.2 Hz, H^{13}), 2.57-2.61 (m, 3 H, H^4 and $H^{8'}$), 2.76 (dd, 1 H, J = 7.2, 14.4 Hz, H13, 2.93-3.00 (m, 1 H, H^{13a}), 3.10 (t, 1 H, J = 8.0 Hz, H^{3a}), 3.19 (dd, 1 H, J = 6.2, 9.4 Hz, H^{13b}), 3.42 (d, 1 H, J = 9.9 Hz, H^{6a}), 3.68-3.82 (m, 2 H, $H^{7'}$), 4.10 (d, 1 H, J = 9.8 Hz, H^6), 5.37 (br s, 1 H, H^5), 6.55 (d, 2 H, J = 8.1 Hz, $H^{2'}$ and $H^{6'}$), 6.87 (d, 2 H, J = 8.0 Hz, H3' and H5'), 7.55-7.65 (m, 3 H, H^9, H^{10}, and H^{11}), 7.89 (d, 1 H, J = 7.5 Hz, H^8). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 200.1 (C^7), 199.0 (C^{12}), 179.0 (C^1), 177.8 (C^3), 175.0 (COOH), 140.1 (C^{5a}), 138.0 ($C^{1'}$), 135.7 (C^{7a}), 134.1 (C^9, C^{11}, and C^{11a}), 132.8 ($C^{4'}$), 131.3 ($C^{2'}$ and $C^{6'}$), 127.9 ($C^{3'}$ and $C^{5'}$), 126.5 (C^8 and C^{10}), 124.8 (C^5), 60.5 (C^{6a}), 48.1 (C^{12a}), 46.5 (C^6), 43.7 (C^{13b}), 40.1 (C^{3a}), 34.3 ($C^{7'}$), 34.0 (C^{13a}), 32.4 (C^{13}), 31.6 ($C^{8'}$), 29.7 (CH_3), 25.1 (C^4). **MS** (ESI$^+$) *m/z* (relative intensity): 532.04 ([M + H]$^{+}$, 100 %). **HRMS**: Found 532.1533 [M + H]$^+$, calculated for $C_{30}H_{26}ClNO_6$ 532.1527 [M + H]$^+$.

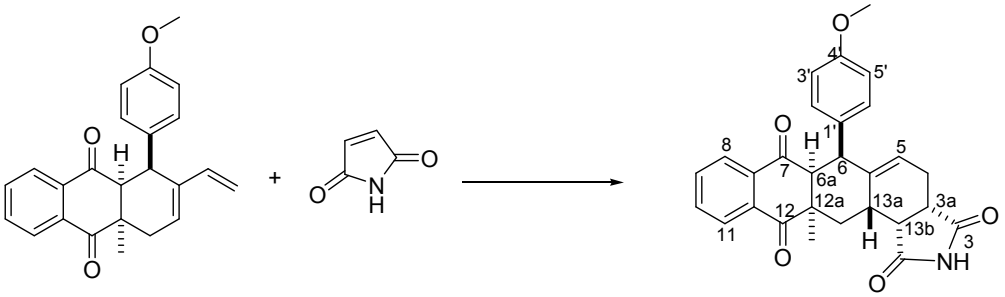
Synthesis of (3aS,6S,6aS,12aR,13aS,13bR)-6-(4-chlorophenyl)-12a-methyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (001-DA-023-01)



$C_{27}H_{22}ClNO_4$
Mol. Wt.: 459.92

001-DA-023-01 was obtained as a colourless solid (32 mg, 39 %). **IR** (ATR, λ_{max}/cm^{-1}): 3240, 3065, 2951, 1708, 1686, 1592, 1491, 1349, 1321, 1253, 1173, 1091, 1011, 981, 711, 688. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 1.36 (s, 3 H, CH_3), 2.08-2.15 (m, 1 H, ^{H4}), 2.43 (t, 1 H, J = 13.6 Hz, H^{13}), 2.56 (ddd, 1 H, J = 1.6, 6.9, 15.9 Hz, H^4), 2.70 (dd, 1 H, J = 6.5, 13.8 Hz, H^{13}, 2.95-2.97 (m, 1 H, H^{13a}), 3.16 (td, 1 H, J = 1.7, 8.5 Hz, H^{3a}), 3.26 (dd, 1 H, J = 5.7, 8.6 Hz, H13b), 3.43 (d, 1 H, J = 10.3 Hz, H^{6a}), 4.15 (d, 1 H, J = 10.2 Hz, H^6), 5.42 (br s, 1 H, H5), 6.58 (d, 2 H, J = 8.4 Hz, $H^{2'}$ and $H^{6'}$), 6.88 (d, 2 H, J = 8.4 Hz, $H^{3'}$ and $H^{5'}$), 7.53-7.59 (m, 2 H, H9 and H11), 7.62 (td, 1 H, J = 2.0, 6.7 Hz, H^{10}), 7.91 (d, 1 H, J = 7.8 Hz, H8). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 200.2 (C^7), 198.3 (C^{12}), 179.0 (C^1), 178.1 (C^3), 140.0 (C^{5a}), 138.1 ($C^{1'}$), 135.8 (C^{7a}), 134.1 and 134.0 (C^9 and C^{11}), 133.6 (C^{11a}), 132.8 ($C^{4'}$), 131.3 ($C^{2'}$ and $C^{6'}$), 127.9 ($C^{3'}$ and $C^{5'}$), 126.5 (C^8 and C^{10}), 124.6 (C^5), 60.7 (C^{6a}), 48.3 (C^{12a}), 46.6 (C^6), 44.7 (C^{13b}), 41.3 (C^{3a}), 33.8 (C^{13a}), 32.8 (C^{13}), 29.7 (CH_3), 25.0 (C4). **MS** (ESI^+) *m/z* (relative intensity): 459.95 ([M + H]$^+$, 100 %). **HRMS**: Found 460.1320 [M + H]$^+$, calculated for $C_{27}H_{22}ClNO_4$ 460.1316 [M + H]$^+$.

Synthesis of (3aS,6S,6aS,12aR,13aS,13bR)-6-(4-methoxyphenyl)-12a-methyl-3a,4,6,6a,13,13a-hexahydro-1H-anthra[2,3-e]isoindole-1,3,7,12(2H,12aH,13bH)-tetraone (001-DA-024-01)

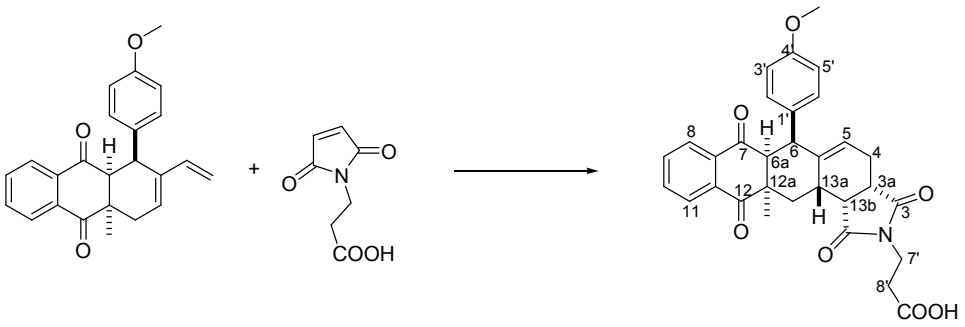


$C_{28}H_{25}NO_5$
Mol. Wt.: 455.5

001-DA-024-01 was obtained as a colourless solid (35 mg, 54 %). **IR** (ATR,λ_{max}/cm^{-1}): 2956, 1698, 1685, 1672, 1592, 1510, 1246, 1206, 1176, 1030, 988, 804, 721. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 1.34 (s, 3 H, CH_3), 2.08-2.15 (m, 1 H, H^4), 2.39 (t, 1 H, J = 13.2 Hz, H^{13}), 2.55 (dd, 1 H, J = 5.4, 14.5 Hz, H^4, 2.71 (dd, 1 H, J = 6.4, 13.7 Hz, H^{13}), 2.97 (m, 1 H, H^{13a}), 3.14 (td, 1 H, J = 1.6, 8.4 Hz, H^{3a}), 3.25 (dd, 1 H, J = 5.6, 8.5 Hz, H^{13b}), 3.42 (d, 1 H, J = 10.1 Hz, H^{6a}), 3.63 (s, 3 H, OCH_3), 4.12 (d, 1 H, J = 9.5 Hz, H^6), 5.45 (br s, 1 H, H^5), 6.44 (d, 2 H, J = 8.6 Hz, $H^{3'}$ and $H^{5'}$), 6.56 (d, 2 H, J = 8.6 Hz, $H^{2'}$ and $H^{6'}$), 7.50-7.60 (m, 3 H, H^9, H^{10}, and H^{11}), 7.90 (d, 1

H, J = 7.6 Hz, H^8), 8.04 (br s, 1 H, NH). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 200.4 (C^7), 198.6 (C^{12}), 179.2 (C^1), 178.2 (C^3), 158.3 ($C^{4'}$), 140.5 (C^{5a}), 136.0 (C^{7a}), 133.8, 133.7, 133.6 (C^{10}, C^{11}, and C^{11a}), 131.5 ($C^{1'}$), 131.0 ($C^{2'}$ and $C^{6'}$), 126.5 (C^8 and C^9), 124.0 (C^5), 113.3 ($C^{3'}$ and $C^{5'}$), 61.2 (C^{6a}), 55.1 (OCH_3), 48.3 (C^{12a}), 46.7 (C^6), 44.8 (C^{13b}), 41.3 (C^{3a}), 33.8 (C^{13a}), 33.1 (C^{13}), 29.6 (CH_3), 24.8 (C^4). **MS** (ESI^+) *m/z* (relative intensity): 456.02 ([M + H]$^+$, 25 %). **HRMS**: Found 456.1830 [M + H]$^+$, calculated for $C_{28}H_{25}NO_5$ 456.1811 [M + H]$^+$.

Synthesis of 3-((3aS,6S,6aS,12aR,13aS,13bR)-6-(4-methoxyphenyl)-12a-methyl-1,3,7,12-tetraoxo-3a,4,6a,7,12,12a,13,13a-octahydro-1H-anthra[2,3-e]isoindol-2(3H,6H,13bH)-yl)propanoic acid (001-DA-022-01)



$C_{31}H_{29}NO_7$
Mol. Wt.: 527.56

001-DA-022-01 as a colourless solid (45 mg, 48 %). **IR** (ATR, λ_{max}/cm^{-1}): 2961, 2925, 1684, 1510, 1440, 1401, 1248, 1176, 1030, 977, 949, 834, 713. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 1.35 (s, 3 H, CH_3), 2.05-2.12 (m, 1 H, H^4, 2.43 (t, 1 H, J = 13.4 Hz, H13, 2.53-2.60 (m, 3 H, H and $H^{8'}$), 2.72 (dd, 1 H, J = 6.7, 13.8 Hz, H^{13}), 2.93-2.98 (m, 1 H, H^{13a}), 3.09 (t, 1 H, J = 7.8 Hz, H), 3.18 (dd, 1 H, J = 5.8, 8.4 Hz, H), 3.40 (d, 1 H, J = 10.1 Hz, H), 3.63 (s, 3 H, OCH_3), 3.62-3.77 (m, 2 H, H), 4.06 (d, 1 H, J = 9.5 Hz, H), 5.37 (br s, 1 H, H), 6.43 (d, 2 H, J = 8.7 Hz, $H^{3'}$ and $H^{5'}$), 6.52 (d, 2 H, J = 8.7 Hz, $H^{2'}$ and $H^{6'}$), 6.70 (s, 1/2 H)*, 7.51-7.61 (m, 3 H, H^9, H^{10}, and H^{11}), 7.88 (d, 1 H, J = 7.5 Hz, H^8). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 200.4 (C^7), 199.1 (C^{12}), 179.2 (C^1), 178.0 (C^3), 174.3 (COOH), 158.3 ($C^{4'}$), 140.5 (C^{5a}), 135.9 (C^{7a}), 134.2 (C^{11a}), 133.9, 133.8 (C^{10} and C^{11}), 131.5 ($C^{1'}$), 131.0 ($C^{2'}$ and $C^{6'}$), 126.5 (C^8 and C^9), 124.1 (C^5), 113.2 ($C^{3'}$ and $C^{5'}$), 61.0 (C^{6a}), 55.1 (OCH_3), 48.2 (C^{12a}), 46.5 (C^6), 43.6 (C^{13b}), 40.1 (C^{3a}), 34.2 ($C^{7'}$), 34.1 (C^{13a}), 32.7 (C^{13}), 31.8 ($C^{8'}$), 29.7 (CH_3), 25.1 (C^4). **MS** (ESI^+) *m/z* (relative intensity): 528.13 ([M + H]$^+$, 100 %). **HRMS**: Found 528.1994 [M + H]$^+$, calculated for $C_{31}H_{29}NO_7$ 528.2022 [M + H]$^+$.

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