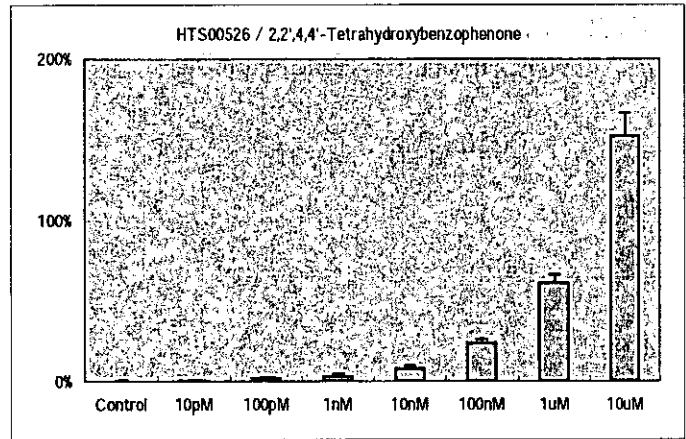


ERβ /HeLa

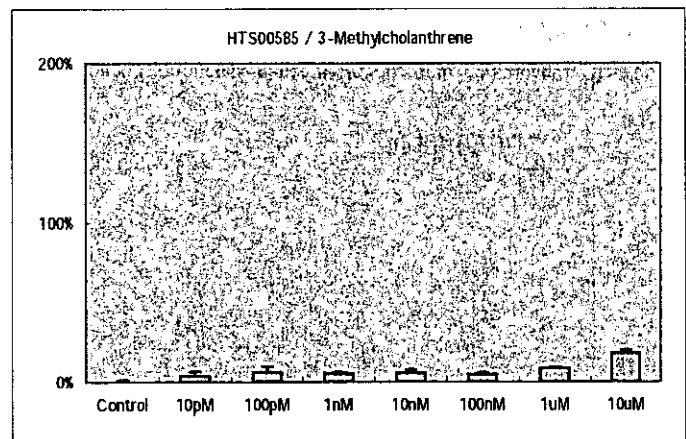
HTS00526
2,2',4,4'-Tetrahydroxybenzophenone

PC50 (pM): 5.06E+05



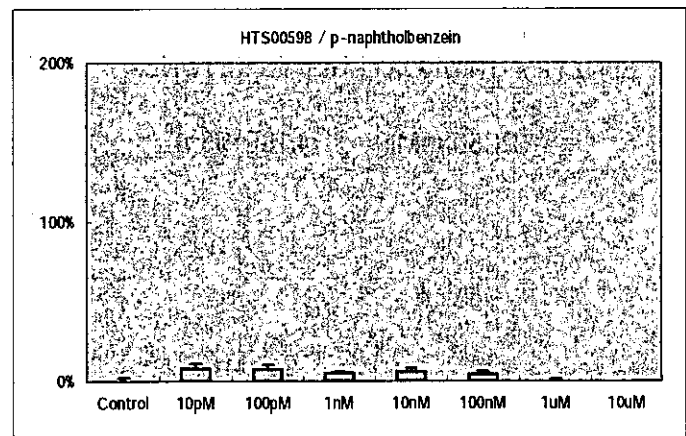
HTS00585
3-Methylcholanthrene

PC50 (pM): -



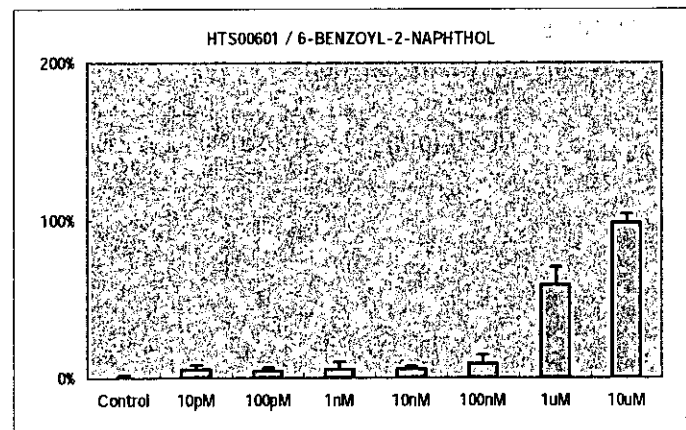
HTS00598
p-naphtholbenzein

PC50 (pM): -



HTS00601
6-BENZOYL-2-NAPHTHOL

PC50 (pM): 6.60E+05

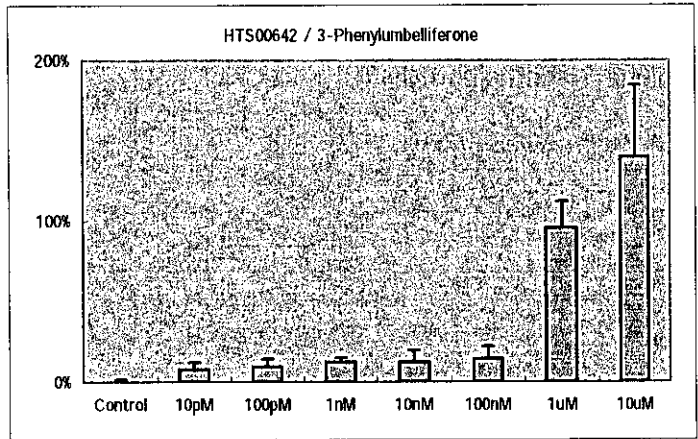


ER β / HeLa

HTS00642

3-Phenylumbelliferone

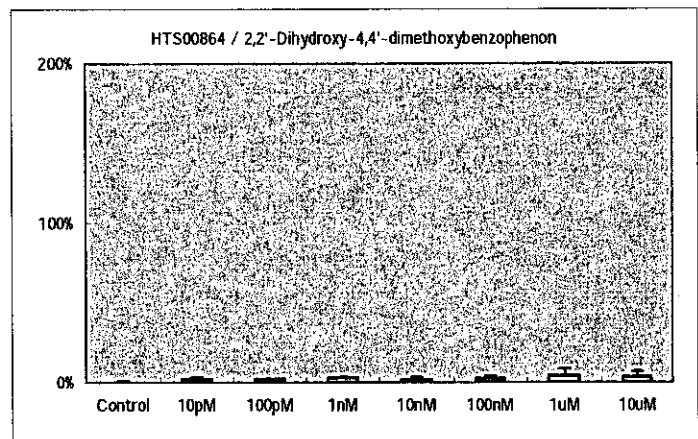
PC50 (pM): 2.75E+05



HTS00864

2,2'-Dihydroxy-4,4'-dimethoxybenzophenon

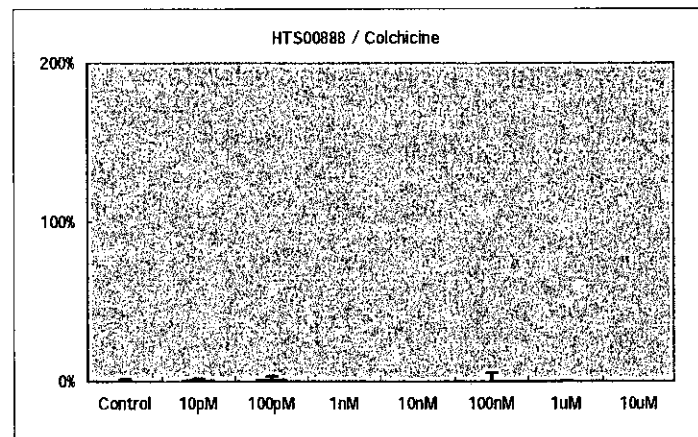
PC50 (pM): -



HTS00888

Colchicine

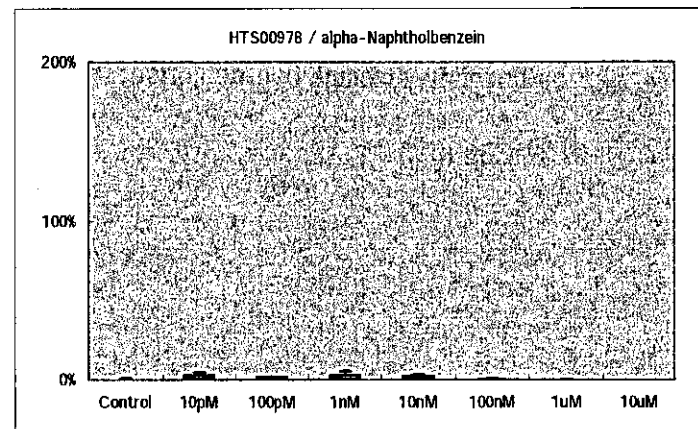
PC50 (pM): -



HTS00978

alpha-Naphtholbenzein

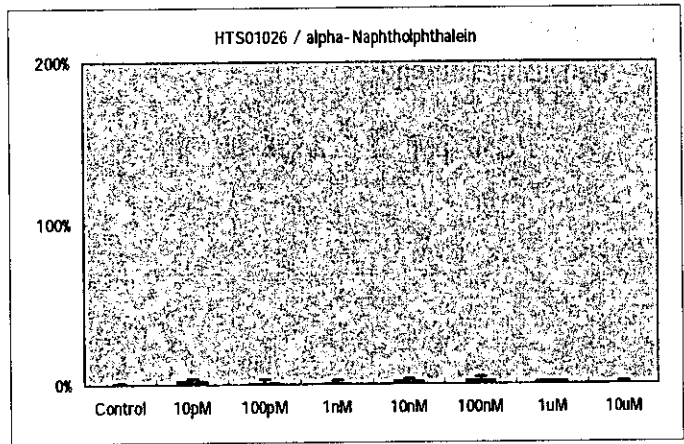
PC50 (pM): -



ER β /HeLa

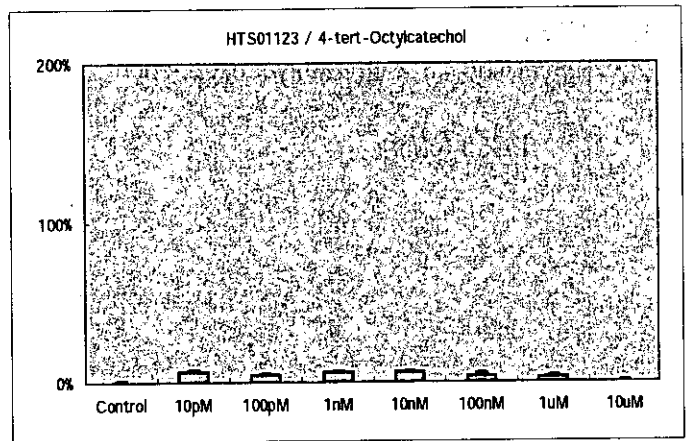
HTS01026
alpha-Naphtholphthalein

PC50 (pM): -



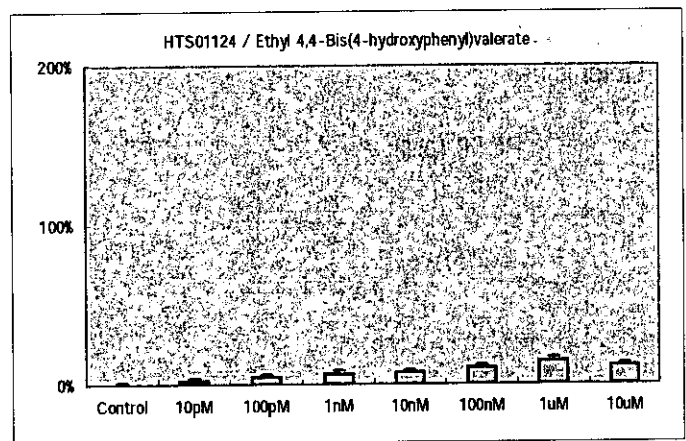
HTS01123
4-tert-Octylcatechol

PC50 (pM): -



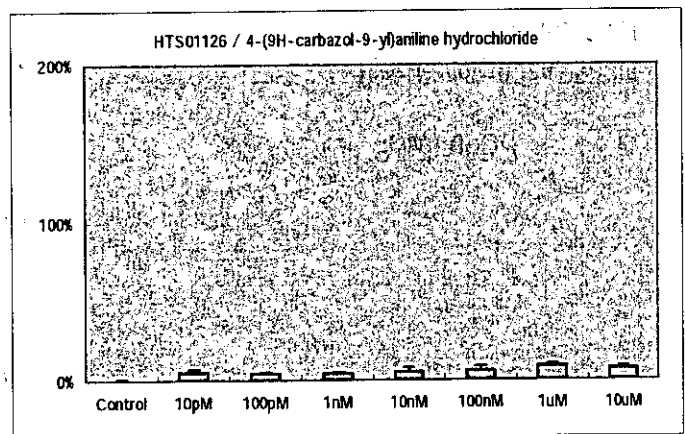
HTS01124
Ethyl 4,4-Bis(4-hydroxyphenyl)valerate

PC50 (pM): -



HTS01126
4-(9H-carbazol-9-yl)aniline hydrochloride

PC50 (pM): -

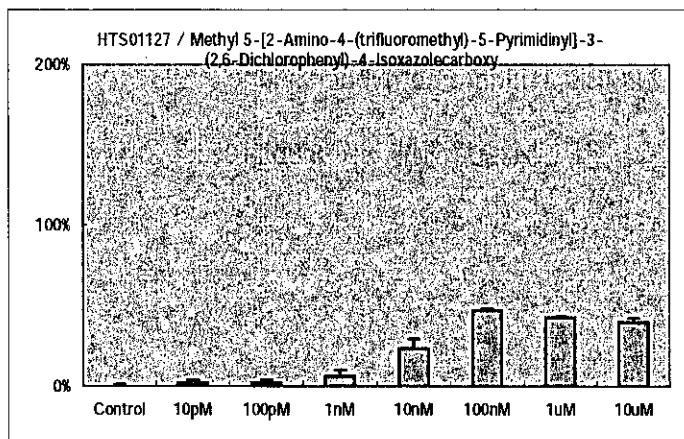


ER β / HeLa

HTS01127

Methyl 5-[2-Amino-4-(trifluoromethyl)-5-Pyrimidinyl]-3-(2,6-Dichlorophenyl)-4-Isoxazolecarboxy

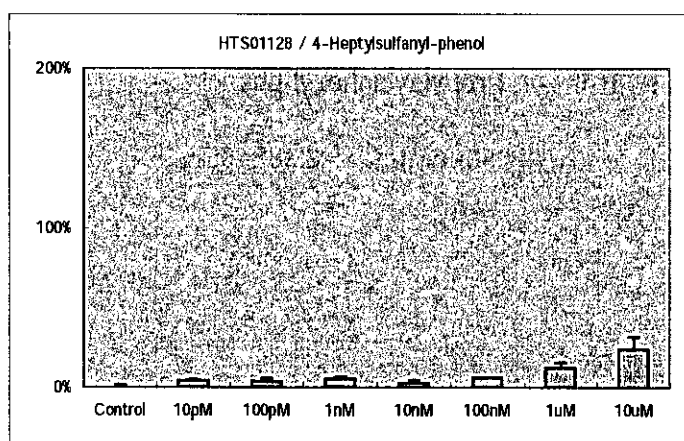
PC50 (pM): -



HTS01128

4-Heptylsulfanyl-phenol

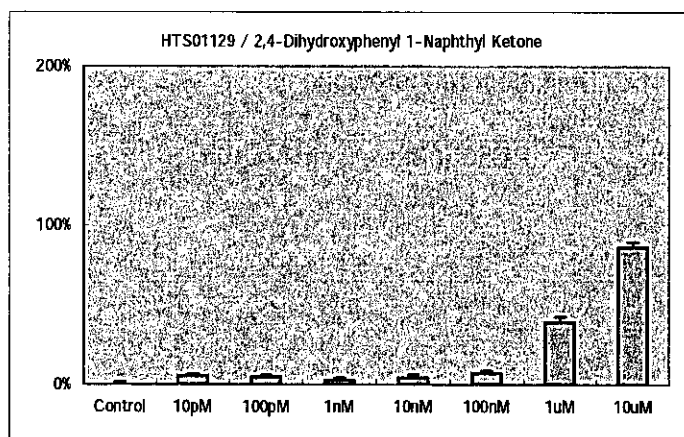
PC50 (pM): -



HTS01129

2,4-Dihydroxyphenyl 1-Naphthyl Ketone

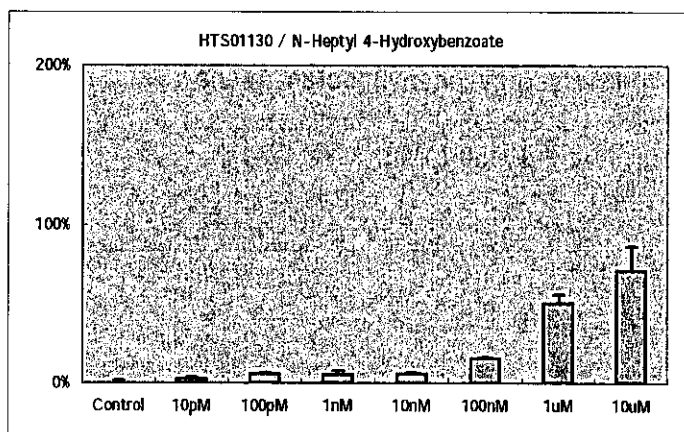
PC50 (pM): 1.73E+06



HTS01130

N-Heptyl 4-Hydroxybenzoate

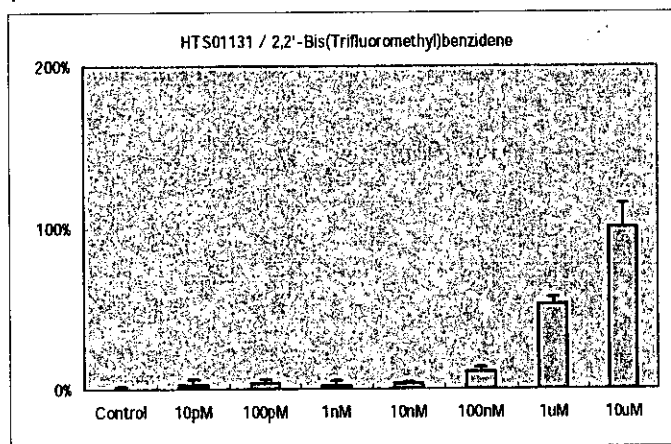
PC50 (pM): 9.55E+05



ER β / HeLa

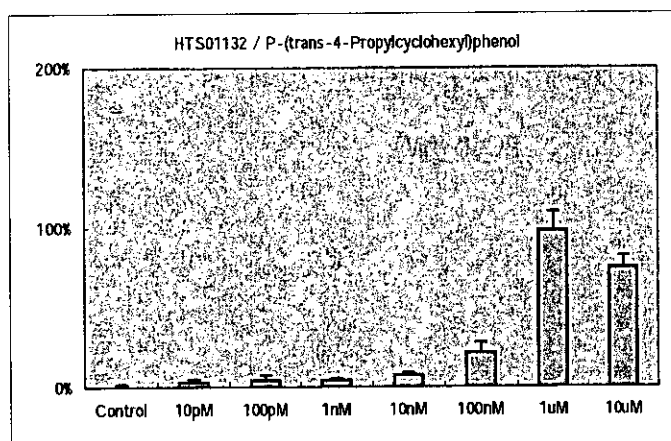
HTS01131
2,2'-Bis(Trifluoromethyl)benzidine

PC50 (pM): 8.80E+05



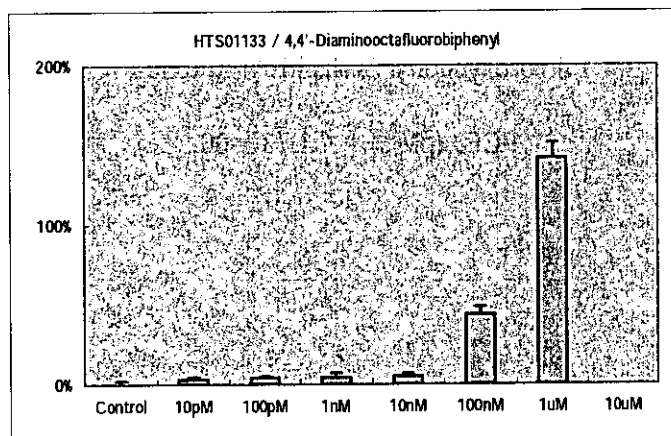
HTS01132
P-(trans-4-Propylcyclohexyl)phenol

PC50 (pM): 2.38E+05



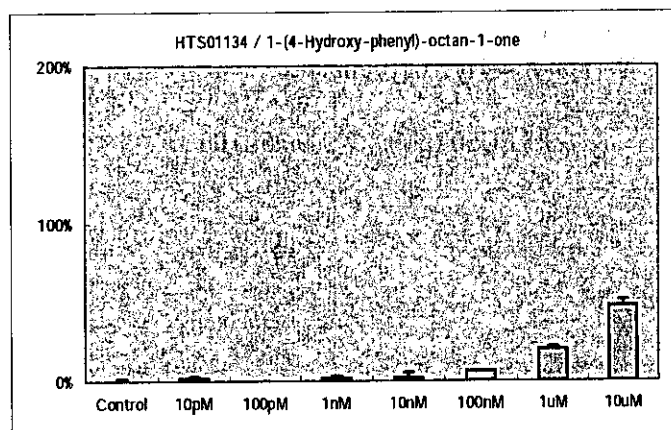
HTS01133
4,4'-Diaminooctafluorobiphenyl

PC50 (pM): 1.17E+05



HTS01134
1-(4-Hydroxy-phenyl)-octan-1-one

PC50 (pM): -

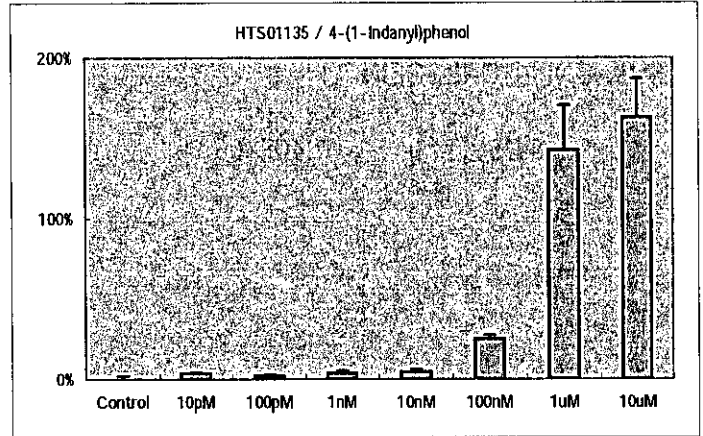


ER β /HeLa

HTS01135

4-(1-Indanyl)phenol

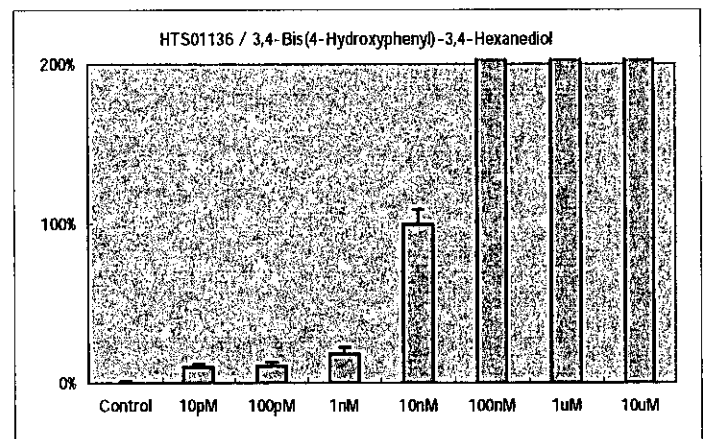
PC50 (pM): 1.63E+05



HTS01136

3,4-Bis(4-Hydroxyphenyl)-3,4-Hexanediol

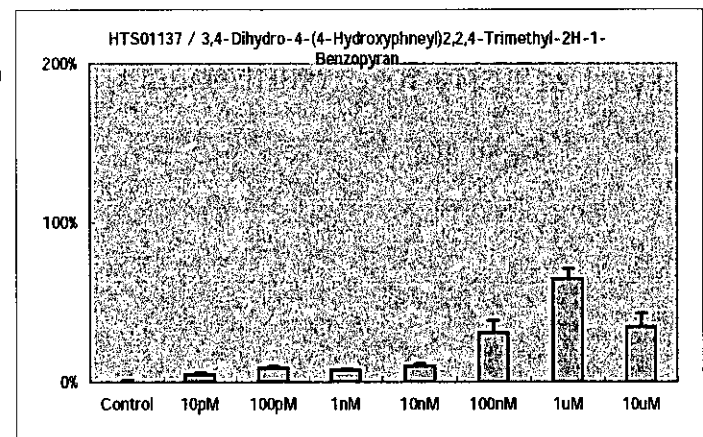
PC50 (pM): 2.47E+03



HTS01137

3,4-Dihydro-4-(4-Hydroxyphenyl)2,2,4-Trimethyl-2H-1-Benzopyran

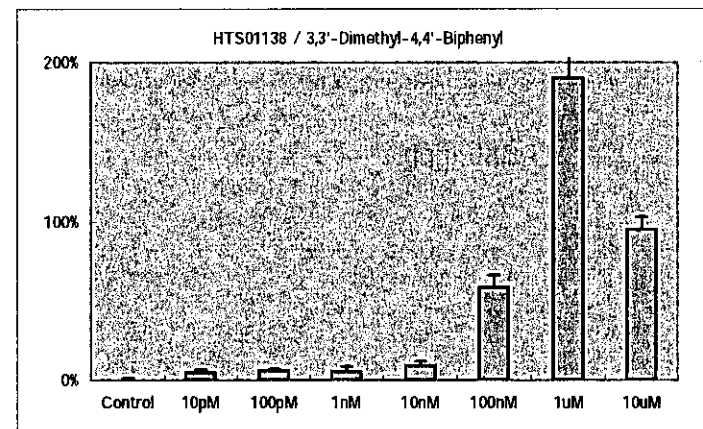
PC50 (pM): 3.76E+05



HTS01138

3,3'-Dimethyl-4,4'-Biphenyl

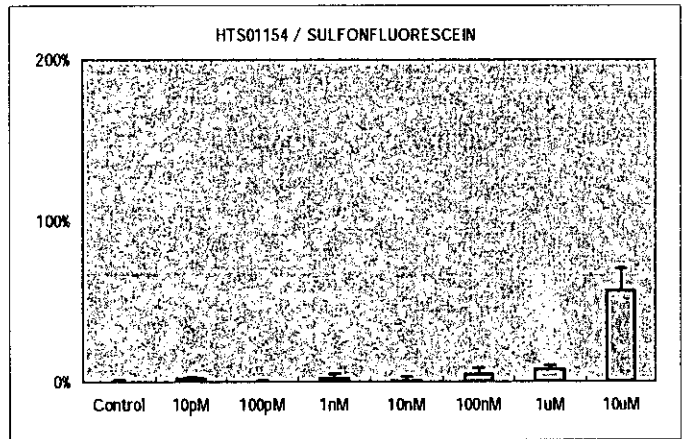
PC50 (pM): 6.69E+04



ERβ / HeLa

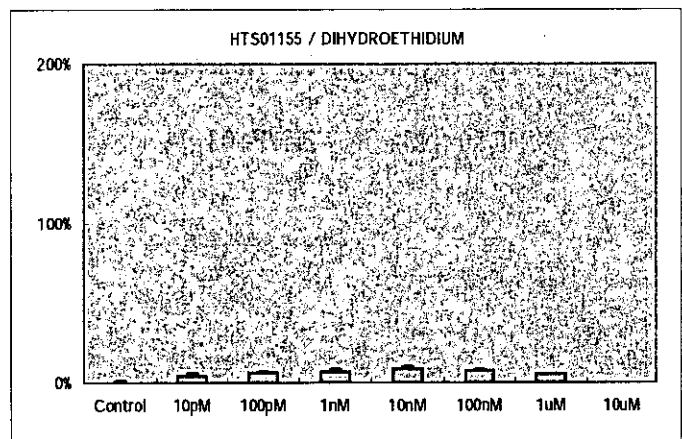
HTS01154
SULFONFLUORESCIN

PC50 (pM): 7.40E+06



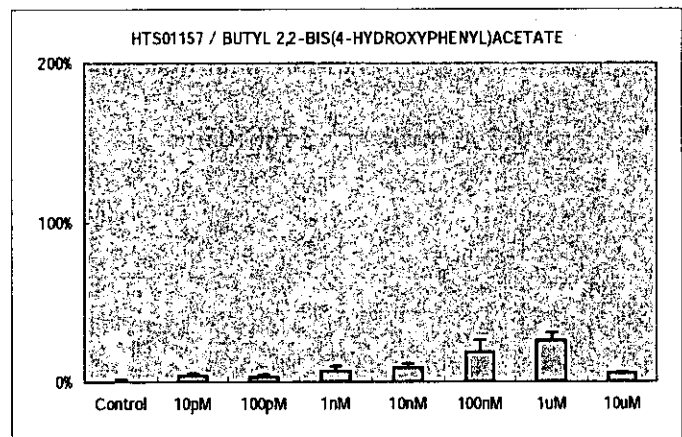
HTS01155
DIHYDROETHIDIUM

PC50 (pM): -



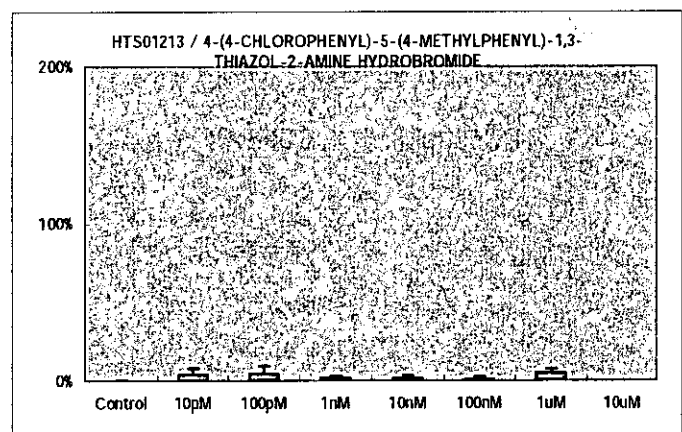
HTS01157
BUTYL 2,2-BIS(4-HYDROXYPHENYL)ACETATE

PC50 (pM): -



HTS01213
4-(4-CHLOROPHENYL)-5-(4-METHYLPHENYL)-1,3-THIAZOL-2-AMINE HYDROBROMIDE

PC50 (pM): -

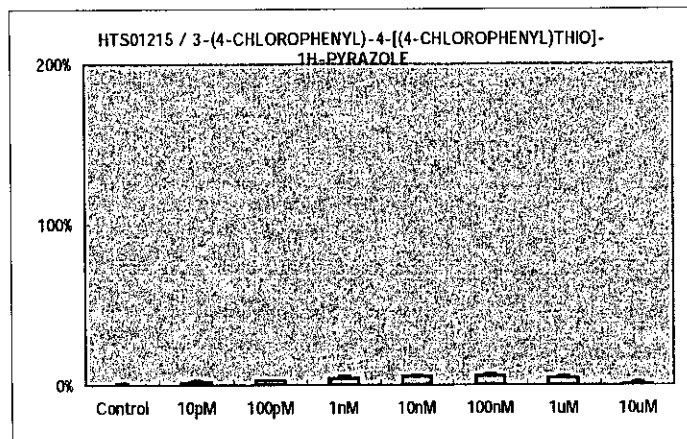


ER β /HeLa

HTS01215

3-(4-CHLOROPHENYL)-4-[(4-CHLOROPHENYL)THIO]-1H-PYRAZOLE

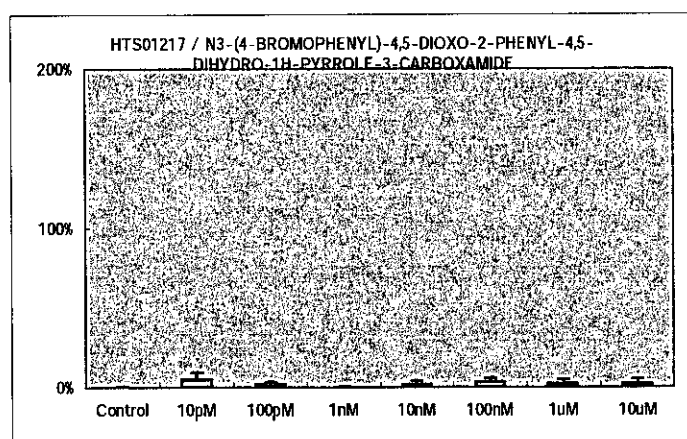
PC50 (pM): -



HTS01217

N3-(4-BROMOPHENYL)-4,5-DIOXO-2-PHENYL-4,5-DIHYDRO-1H-PYRROLE-3-CARBOXAMIDE

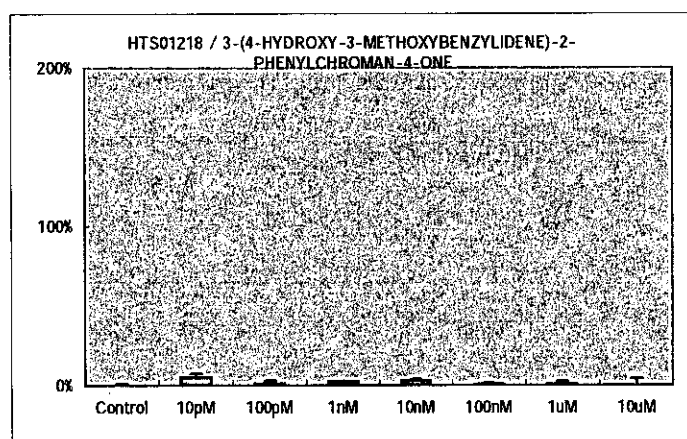
PC50 (pM): -



HTS01218

3-(4-HYDROXY-3-METHOXYBENZYLIDENE)-2-PHENYLCHROMAN-4-ONE

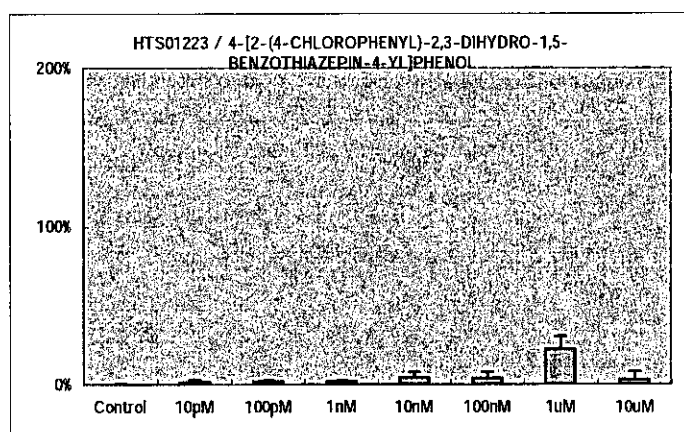
PC50 (pM): -



HTS01223

4-[2-(4-CHLOROPHENYL)-2,3-DIHYDRO-1,5-BENZOTHAZEPIN-4-YL]PHENOL

PC50 (pM): -

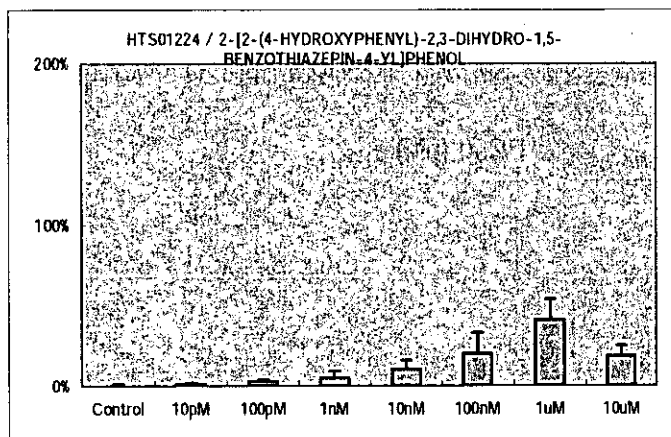


ER β / HeLa

HTS01224

2-[2-(4-HYDROXYPHENYL)-2,3-DIHYDRO-1,5-BENZOTHAZEPIN-4-YL]PHENOL

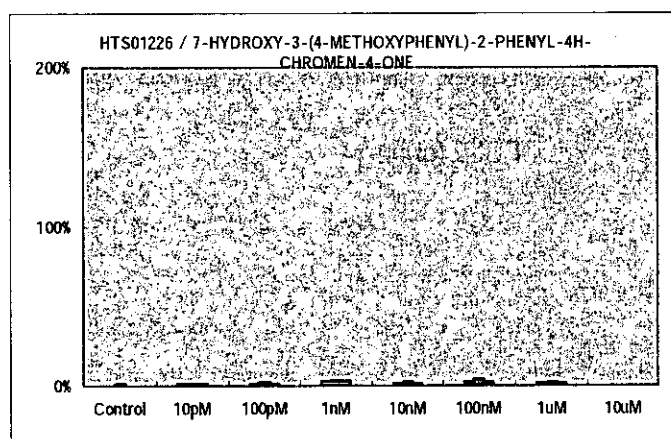
PC50 (pM): -



HTS01226

7-HYDROXY-3-(4-METHOXYPHENYL)-2-PHENYL-4H-CHROMEN-4-ONE

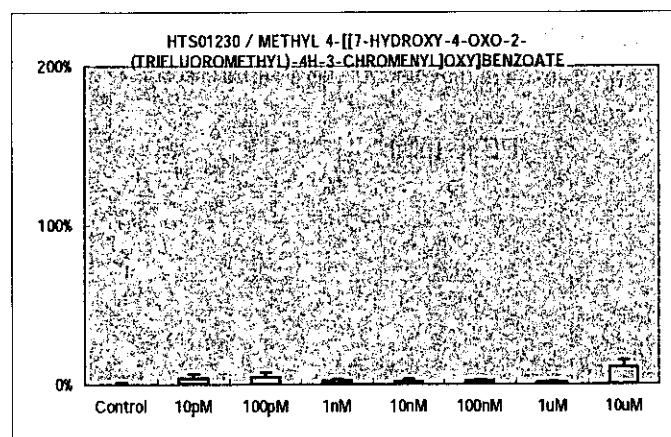
PC50 (pM): -



HTS01230

METHYL 4-[[[7-HYDROXY-4-OXO-2-(TRIFLUOROMETHYL)-4H-3-CHROMENYL]OXY]BENZOATE

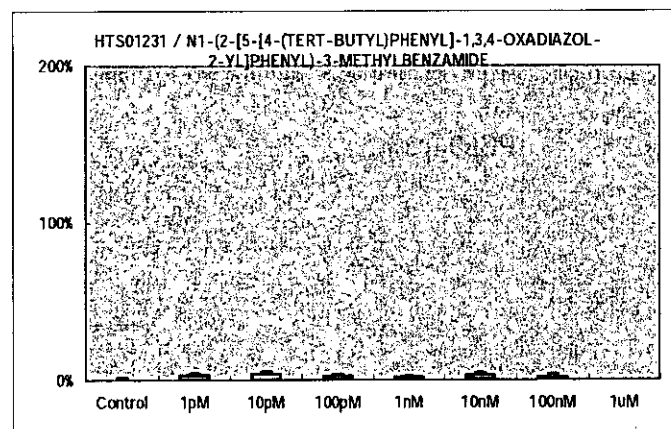
PC50 (pM): -



HTS01231

N1-(2-[5-[4-(TERT-BUTYL)PHENYL]-1,3,4-OXADIAZOL-2-YL]PHENYL)-3-METHYLBENZAMIDE

PC50 (pM): -

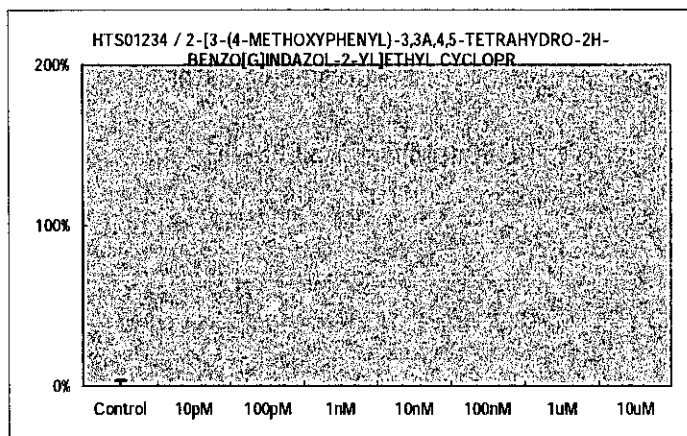


ER β / HeLa

HTS01234

2-[3-(4-METHOXYPHENYL)-3,3A,4,5-TETRAHYDRO-2H-BENZO[G]INDAZOL-2-YL]ETHYL CYCLOPR

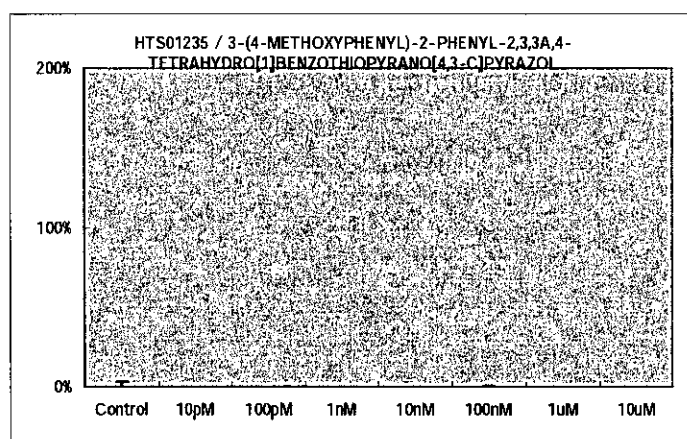
PC50 (pM): -



HTS01235

3-(4-METHOXYPHENYL)-2-PHENYL-2,3,3A,4-TETRAHYDRO[1]BENZOTHIOPYRANO[4,3-C]PYRAZOL

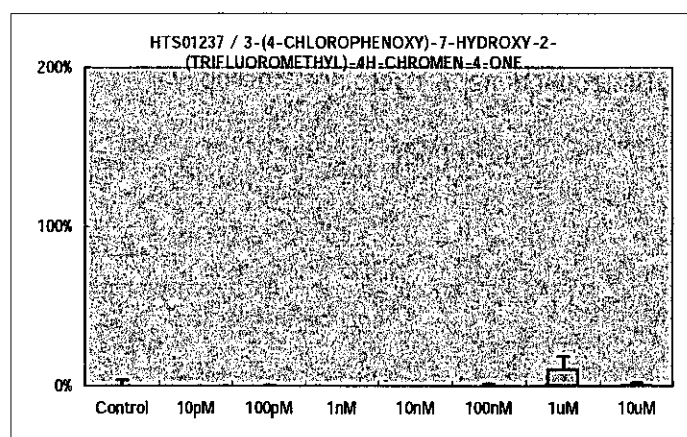
PC50 (pM): -



HTS01237

3-(4-CHLOROPHENOXY)-7-HYDROXY-2-(TRIFLUOROMETHYL)-4H-CHROMEN-4-ONE

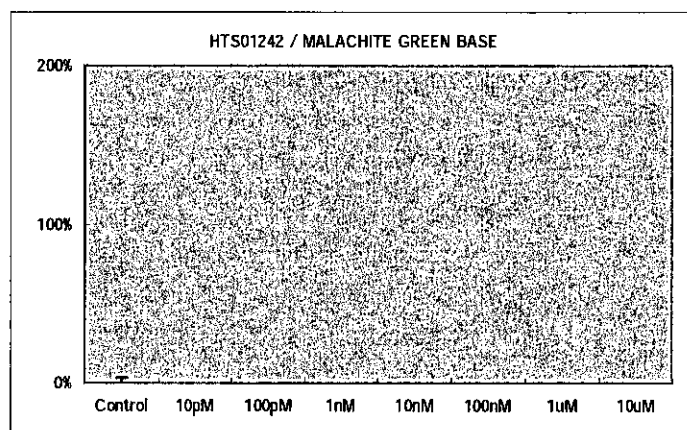
PC50 (pM): -



HTS01242

MALACHITE GREEN BASE

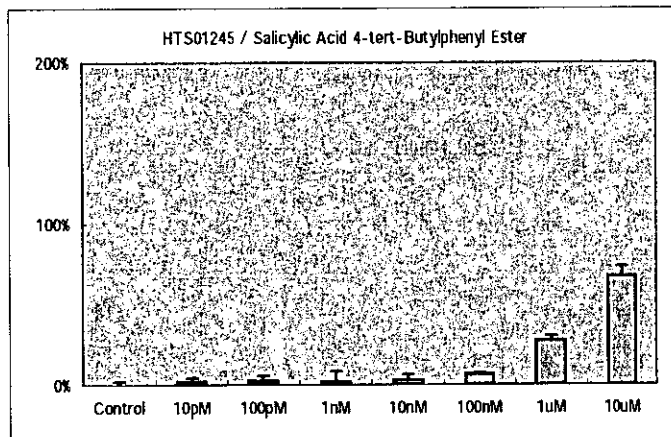
PC50 (pM): -



ER β /HeLa

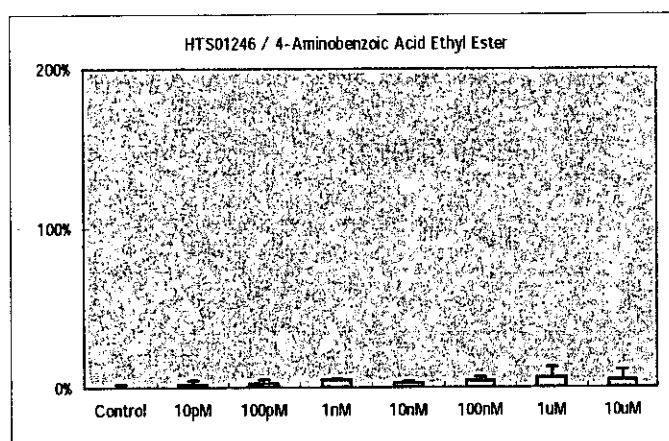
HTS01245
Salicylic Acid 4-tert-Butylphenyl Ester

PC50 (pM): 3.68E+06



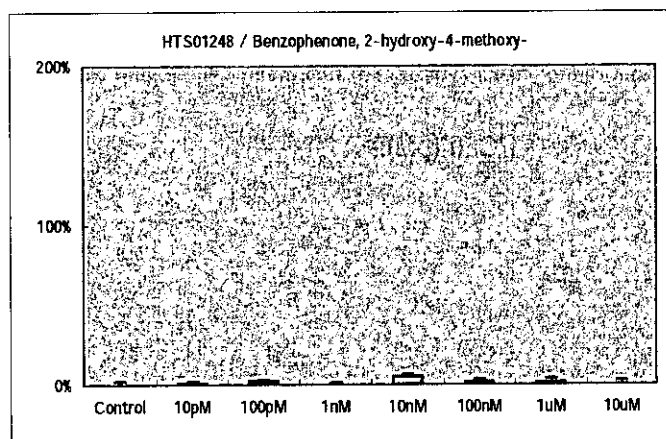
HTS01246
4-Aminobenzoic Acid Ethyl Ester

PC50 (pM): -



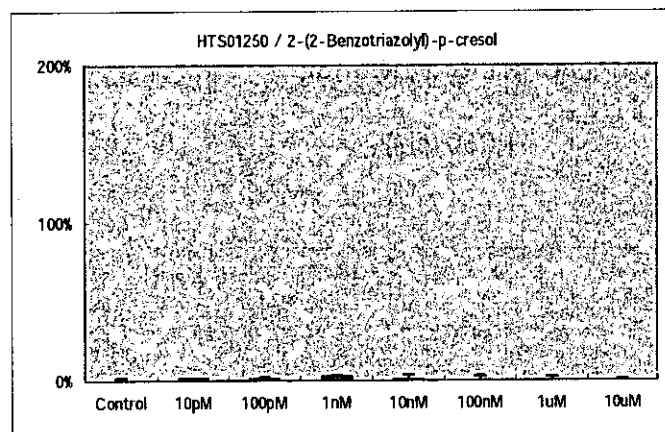
HTS01248
Benzophenone, 2-hydroxy-4-methoxy-

PC50 (pM): -



HTS01250
2-(2-Benzotriazolyl)-p-cresol

PC50 (pM): -

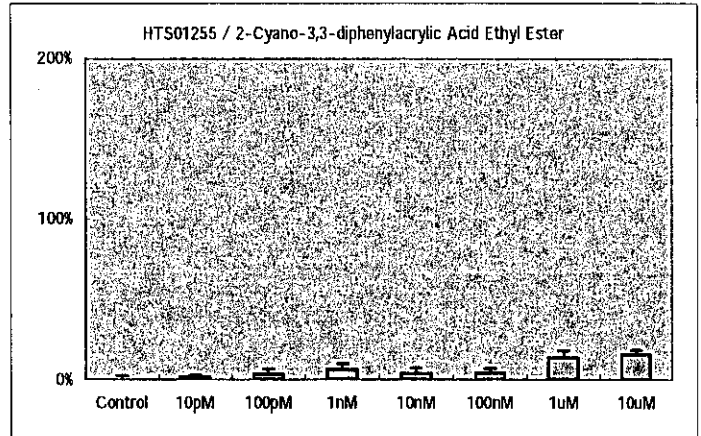


ER β / HeLa

HTS01255

2-Cyano-3,3-diphenylacrylic Acid Ethyl Ester

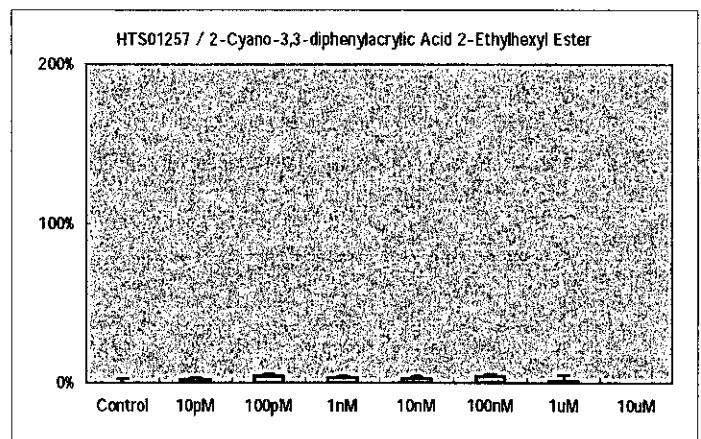
PC50 (pM): -



HTS01257

2-Cyano-3,3-diphenylacrylic Acid 2-Ethylhexyl Ester

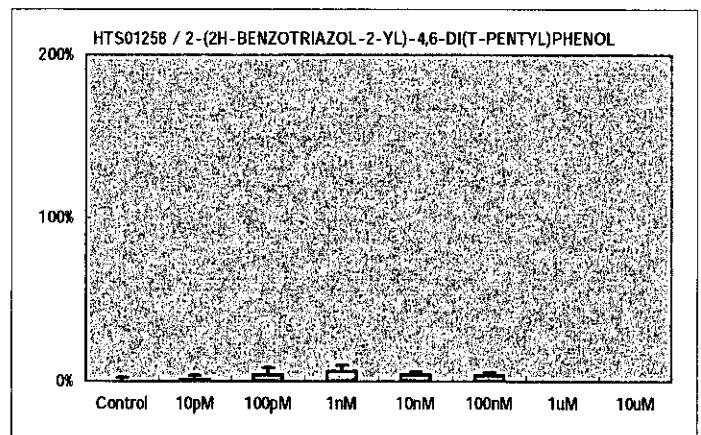
PC50 (pM): -



HTS01258

2-(2H-BENZOTRIAZOL-2-YL)-4,6-DI(T-PENTYL)PHENOL

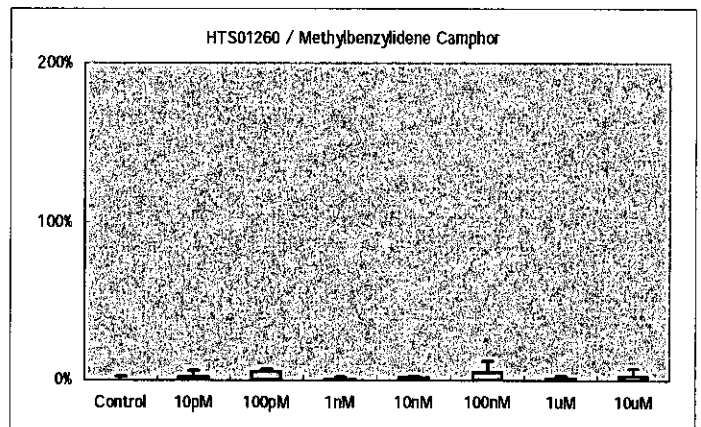
PC50 (pM): -



HTS01260

Methylbenzylidene Camphor

PC50 (pM): -



厚生労働科学研究費補助金(化学物質リスク研究事業)

総括研究報告書 図表

レポーター遺伝子導入培養細胞株を用いたTR、AR作用物質超高速分析法に関する
試験研究

(主任研究者:大塚製薬ライフサイエンス事業部EDC分析センター委託業務)

Table 1 AR アンタゴニストアッセイの検出能力

samples	fold	PC value	p value	b + Xsd	PC10
AT01-2	1.1	1.3	0.0331	1.7	1.77f
AR13-1	1.1	1.5	0.0555	1.4	1.64f
AR27-1	1.11	1.5	0.0399	1.6	1.75f
AR25-1	1.12	1.5	0.0418	1.6	1.75f
AR12-1	1.15	1.6	0.033	1.8	1.65f
AR26	1.13	1.7	0.084	1.5	1.75f
AR15	1.12	1.8	0.0285	1.7	1.64f
AR28-1	1.15	1.9	0.0204	2.1	1.75f
AR07	1.13	2.0	0.012	2.4	1.64f
AR14-1	1.14	2.0	0.0258	2.1	1.64f
AR27	1.15	2.0	0.0106	2.2	1.75f
AR11-1	1.2	2.0	0.0016	3	1.65f
AR15-1	1.13	2.1	0.0132	2	1.64f
AR28	1.18	2.3	0.0054	2.6	1.75f
AR16	1.16	2.4	0.0073	2.3	1.64f
AR25	1.2	2.7	0.0054	2.9	1.75f
AT01-1	1.3	3.8	0.0001	4.9	1.77f
AR12	1.3	4	0.0002	5.3	1.65f
AT07	1.3	4	0.0048	7.5	1.74f
AR09	1.3	5	0.008	5	1.65f
AR13	1.3	5	0.0002	5	1.64f
AR10-1	1.35	6	p<0.0001	6	1.65f
AR14	1.4	6	p<0.0001	6.4	1.64f
AT08	1.35	7	p<0.0001	8.8	1.74f
AR08-1	1.5	7	p<0.0001	8.7	1.64f
AR11	1.5	8	p<0.0001	9	1.65f
AT09	1.65	8	p<0.0001	15.7	1.74f
AR10	1.8	12	p<0.0001	14	1.65f
AT01	2.2	15	p<0.0001	19.6	1.77f
AR08	2.2	17	p<0.0001	20	1.64f

not significant
 0.05<p
 P<0.01

Table 5b Results of TR antagonist assay

ID	antagonist assay		
	IC50	IC40	IC20
TR24	-	-	1.80X10-6
			4.61X10-7

Table 2 コントロールと有意差のある転写阻害活性

Chemical	% activity	p value	cont-X SD
AR02	95	0.0605	1.4SD
AT13-1	95	0.0706	1.2SD
AR10	94	0.108	1.1SD
AR13-1	94	0.0945	1.2SD
AR02-2	94	0.132	1.0SD
AR01	92	0.0107	2.2SD
AR15	92	0.0117	1.8SD
AR28	92	0.0098	1.8SD
AR15	92	0.0117	1.8SD
AR23	91	0.0055	2.0SD
AR01-1	91	0.0368	1.4SD
AR04	89	0.0003	3.0SD
AT13	89	0.0045	2.6SD
AR04-1	88	0.0031	2.0SD
AT05	88	0.0097	2.1SD
AT07	88	0.0021	2.6SD
AR11	87	0.0004	3.0SD
AR11	86	0.0004	3.0SD
AT04	86	0.002	2.5SD
AR05	84	P<0.0001	4.1SD
AT06	83	0.0006	3.3SD
AR24	75	P<0.0001	5.8SD
AT09	74	P<0.0001	5.5SD
AR13	71	p<0.0001	6.0SD

not significant
 0.05<p
 P<0.01

Figure 1 コントロールと有意差のある転写阻害活性

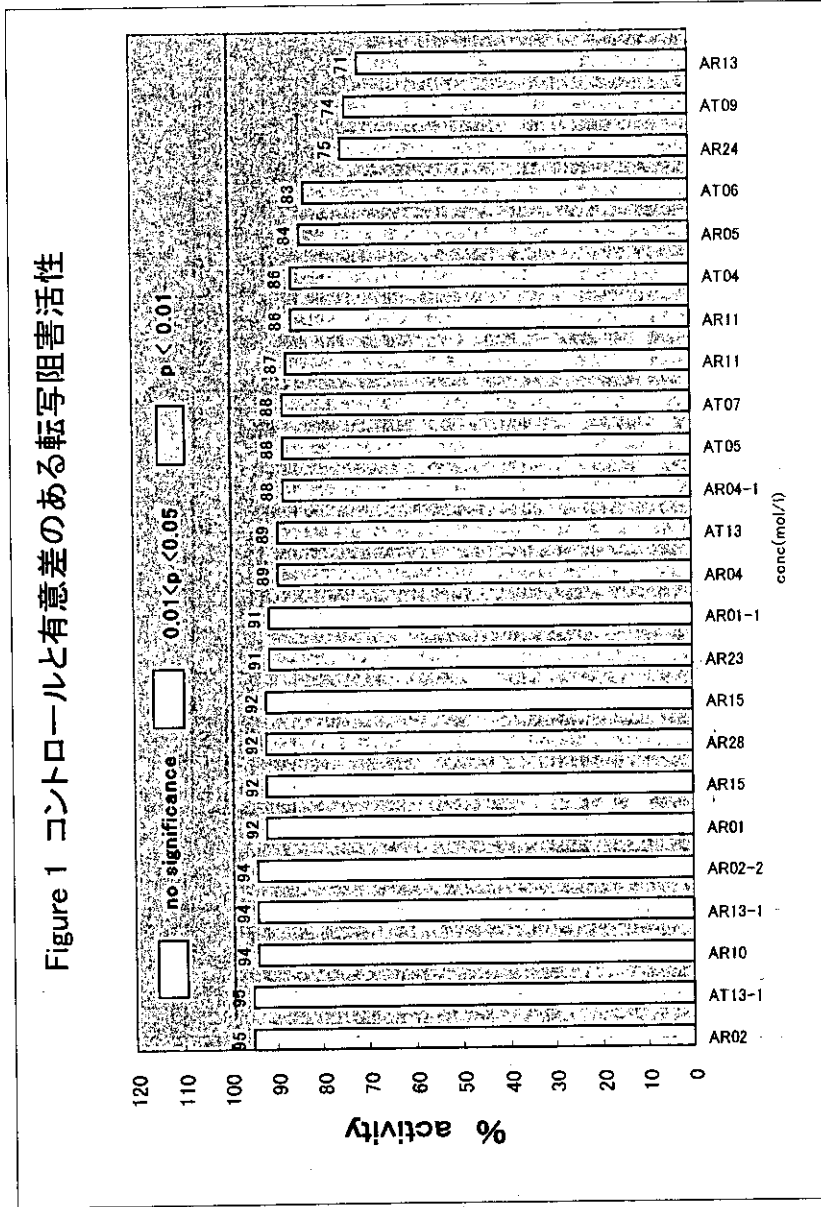


Table 3a TRアゴニストアッセイにおける蛍光Luciferase
転写活性性の検出能力

chemicals	fold	PC-value	p value	b ₊₊ Xsd	PC10(fold)
TR4	1.1	0.7	0.0650	1.6	2.59
TR2	1.1	0.6	0.1097	1.5	2.59
TR1	1.1	0.8	0.0658	1.9	2.59
TR3	1.2	1.0	0.0081	2.3	2.59
TR17	1.2	1.2	0.0020	3.8	2.67
TR28-1	1.2	1.2	0.0037	3.2	2.61
AT1-2	1.2	1.0	0.0016	3.6	2.56
AT1-3	1.2	1.5	0.0001	4.9	2.56
TR20-1	1.3	1.6	0.0007	5.1	2.67
TR26	1.3	1.7	0.0002	4.7	2.61
TR29	1.3	1.9	0.0003	5.1	2.61
TR5	1.4	2.4	0.0070	4.2	2.65
AR30	1.4	2.3	0.0001	7.4	2.56
AT1-4	1.5	3.1	P<0.0001	10.1	2.56
TR28-2	1.6	4.0	0.0004	10.8	2.61
TR27	1.7	4.2	P<0.0001	11.4	2.61
TR20-2	2.0	5.8	P<0.0001	18.6	2.6
AT1-5	2.0	6.7	P<0.0001	21.6	2.56
TR17-2	2.1	6.2	P<0.0001	20.0	2.67

Table 3b TR アントゴニストアッセイにおける
転写活性低下の検出能力

chemical	% activity	p value	cont-X SD
100-1	95	0.2063	1.0
TR24-1	95	0.21	0.8
TR14	95	0.0841	1.1
99-2	94	0.0985	1.5
100-2	94	0.0795	1.2
TR5	92	0.0005	3.1
99-1	89	0.0011	2.8
AT14	89	0.007	2.1
TR7	89	p<0.0001	4.5
AT2	85	0.0004	3.6
AT2	83	p<0.0001	4.0
TR15	83	0.0003	3.1
TR23	73	p<0.0001	5.0
101	71	p<0.0001	3.1
TR24	71	p<0.0001	5.4

not significant
0.01<p
p<0.01

Table 3c TRアノタゴニストアッセイにお
ける細胞毒性の指標となるRenil
Luciferaseの活性低下の検

chemical	% activity	p value	cont-X SD
TR14	96	0.2145	0.8
TR4	94	0.0426	1.5
TR7-1	94	0.0546	1.3
TR13	93	0.0219	1.7
TR14-1	93	0.0451	1.4
TR6-1	93	0.0298	1.5
TR16-1	92	0.0117	1.9
TR25-1	91	0.0164	1.4
TR28-1	91	0.0200	1.6
TR26-1	89	0.0047	2.2
TR16-2	89	0.0012	2.5
TR25	87	0.0018	2.4
TR3	87	p<0.0001	3.4
TR16	82	p<0.0001	4.0
TR26	81	p<0.0001	3.4
TR1	81	p<0.0001	4.7
TR28	80	p<0.0001	3.8
TR15	77	p<0.0001	5.0
TR8	77	p<0.0001	4.8
TR5	76	p<0.0001	5.0

Table 4a Results of AR agonist assay

ID	agonist assay			
	PC50	PC20	PC10	EC50
AR08	-	-	1.67x10 ⁻⁶	2.88x10 ⁻⁶
AR10	-	-	4.30x10 ⁻⁶	1.61x10 ⁻⁶
AR19	-	-	2.73x10 ⁻⁶	-
AR21	-	-	1.78x10 ⁻⁶	1.32x10 ⁻⁶
AT01	-	-	3.44x10 ⁻⁶	-
AT09	-	-	1.48x10 ⁻⁶	-
AT10	-	-	5.86x10 ⁻⁶	-
AT11	-	9.7x10 ⁻⁸	5.67x10 ⁻⁷	6.66x10 ⁻⁸
AT17	-	-	5.82x10 ⁻⁷	1.08x10 ⁻⁷

Table 4b Results of AR antagonist assay

ID	antagonist assay			
	IC50	IC40	IC30	IC20
AR04	4.88x10 ⁻⁶	-	-	-
AR05	3.13x10 ⁻⁶	-	-	-
AR06	-	-	-	6.17x10 ⁻⁶
AR08	-	-	8.97x10 ⁻⁶	-
AR12	-	9.2x10 ⁻⁶	-	-
AR14	2.07x10 ⁻⁶	-	-	-
AR17	-	8.91x10 ⁻⁶	-	-
AR24	-	-	-	4.59x10 ⁻⁶
AR30	5.02x10 ⁻⁶	-	-	-
AT02	-	9.16x10 ⁻⁶	-	-
AT03	-	-	-	6.79x10 ⁻⁶
AT07	8.22x10 ⁻⁶	-	-	-
AT09	8.11x10 ⁻⁶	-	-	-
AT10	-	-	-	5.97x10 ⁻⁶
AT13	3.40x10 ⁻⁷	-	-	-
AT15	-	6.89x10 ⁻⁶	-	-
AT16	4.86x10 ⁻⁶	-	-	-
AT19	4.63x10 ⁻⁶	-	-	-

Table 5a Results of TR agonist assay

ID	agonist assay			
	PC50	PC10	PC10	EC50
TR12	1.97x10 ⁻⁷	2.05x10 ⁻⁸	2.31x10 ⁻⁷	-
TR17	5.03x10 ⁻⁹	1.15x10 ⁻⁹	6.65x10 ⁻⁹	-
TR18	3.85x10 ⁻⁸	1.16x10 ⁻⁸	5.61x10 ⁻⁸	-
TR20	4.68x10 ⁻⁹	1.15x10 ⁻⁹	6.39x10 ⁻⁹	-
TR25	4.54x10 ⁻¹²	2.45x10 ⁻¹³	7.26x10 ⁻¹²	-
AT11	-	-	2.7x10 ⁻⁷	-
AT12	-	-	2.45x10 ⁻⁶	-

Table 5b Results of TR antagonist assay

ID	antagonist assay			
	IC50	IC40	IC30	IC20
TR24	-	-	1.80x10 ⁻⁶	4.61x10 ⁻⁷

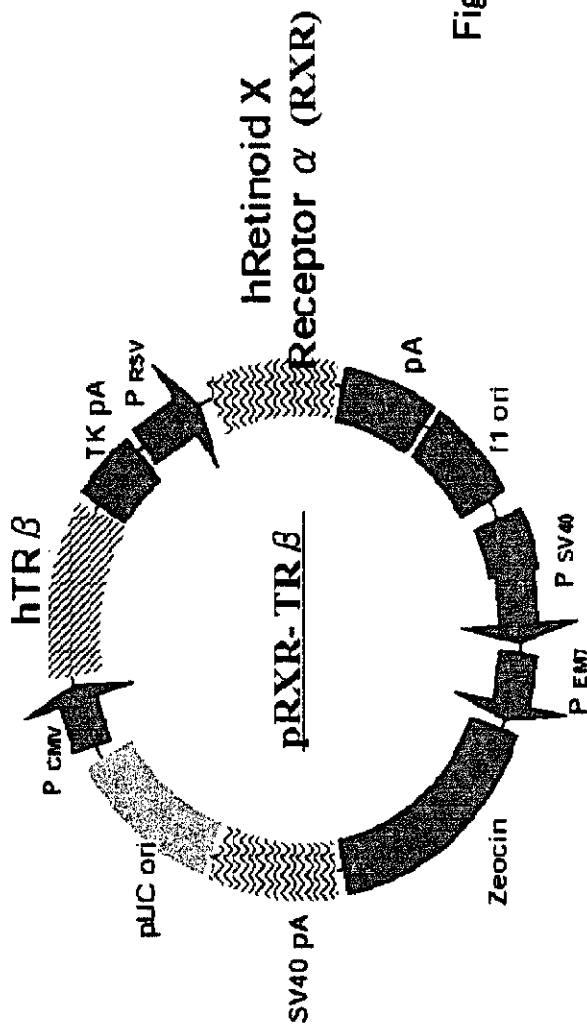


Figure 1 pRXR-TR β のマップ

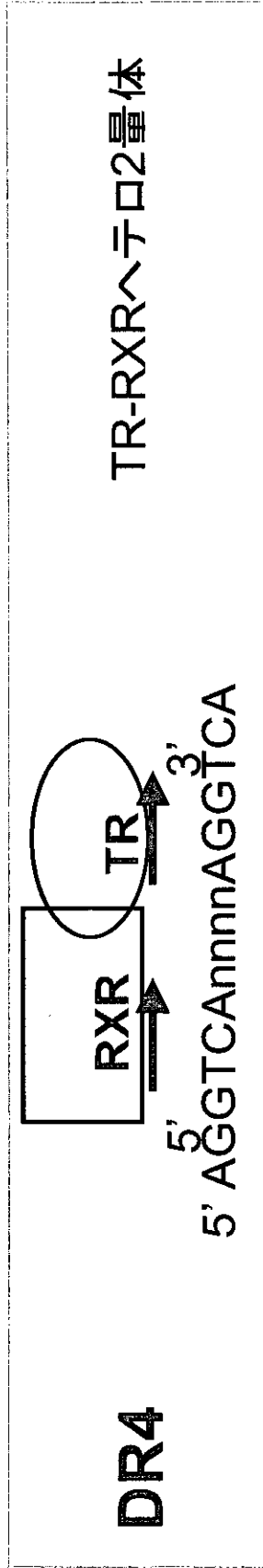


Figure 2 TRE 配列と TR, RXR 受容体の結合様式

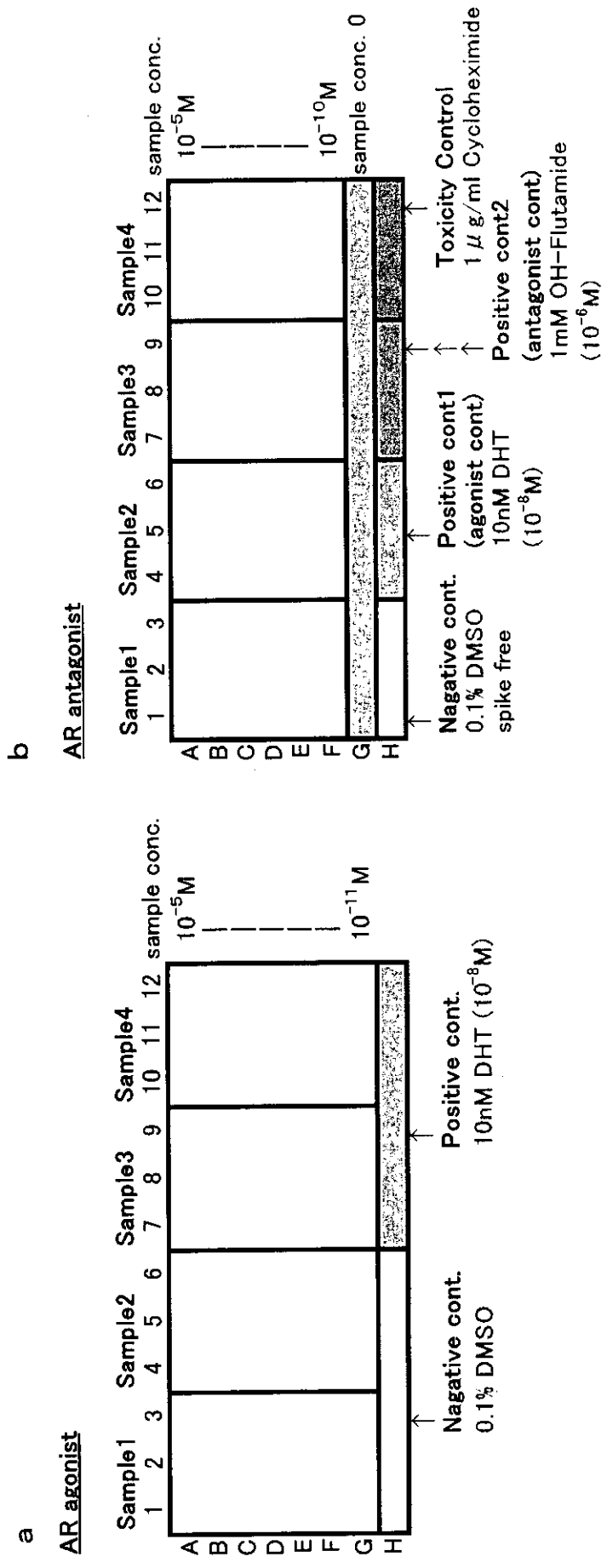


Figure 3 AR reporter assay の Plate Format

a:アゴニストアッセイ b:アンタゴニストアッセイ

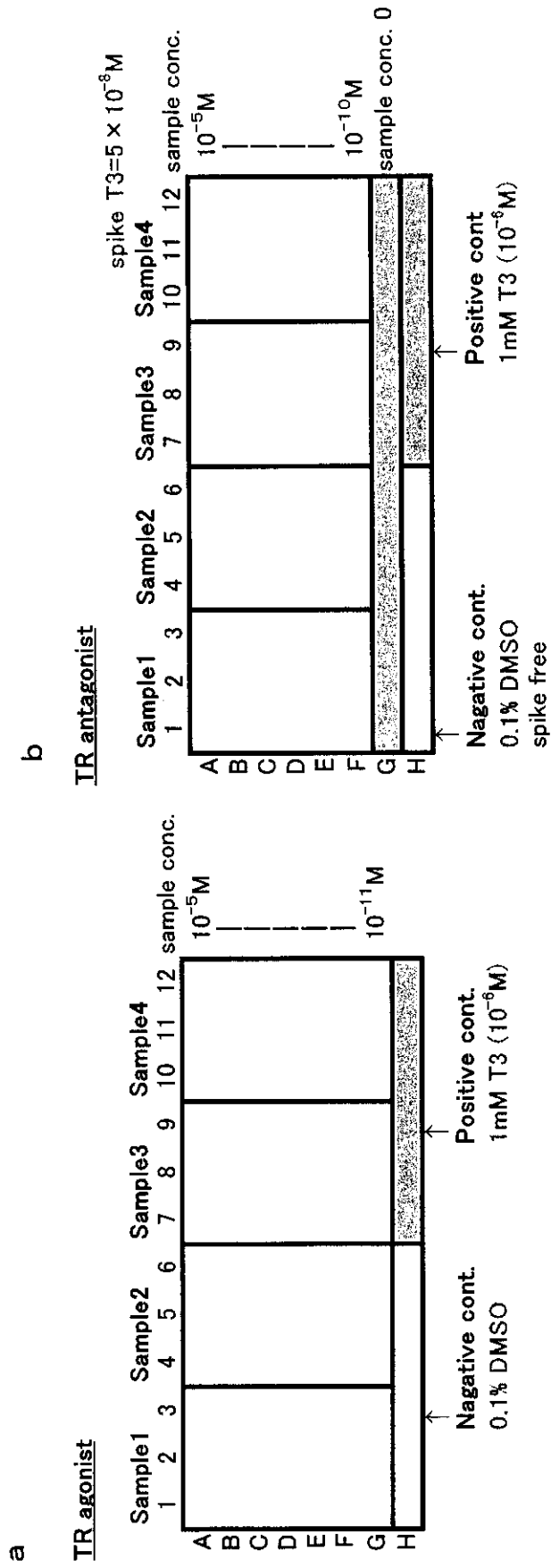


Figure 4 TR reporter assay の Plate Format

a; アゴニストアッセイ b; アンタゴニストアッセイ