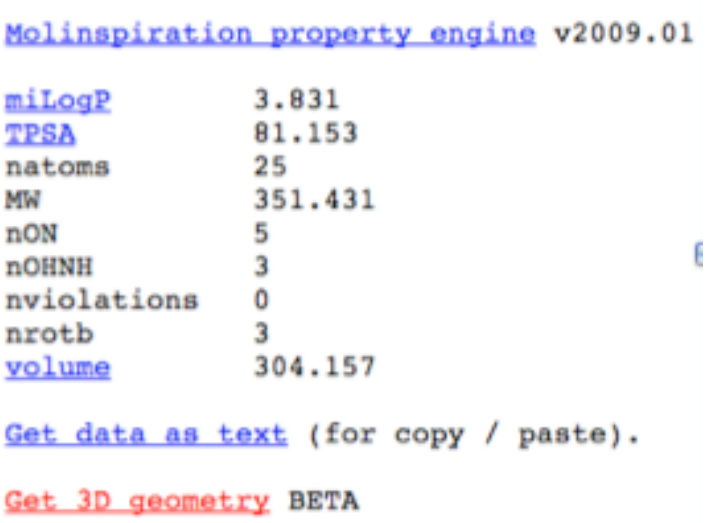
Lipinski's rule of 5 says that, in general, an orally active drug has no more than one violation of the following criteria:

- Not more than 5 hydrogen bond donors (nitrogen or oxygen atoms with one or more hydrogen atoms)
- Not more than 10 hydrogen bond acceptors (nitrogen or oxygen atoms)
- A molecular weight under 500 daltons
- An octanol-water partition coefficient log P of less than 5

More recent “improvements” to Lipinski's rule suggest…

- Partition coefficient log P in -0.4 to +5.6 range
- Molar refractivity from 40 to 130
- Molecular weight from 160 to 480
- Number of atoms from 20 to 70

www.molinspiration.com/



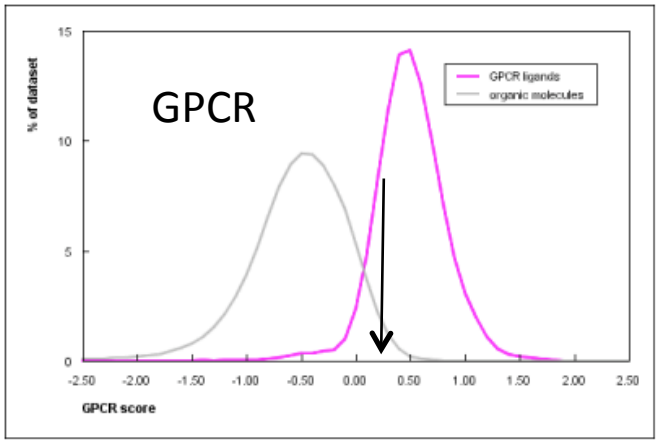
Molinspiration property engine v2009.01

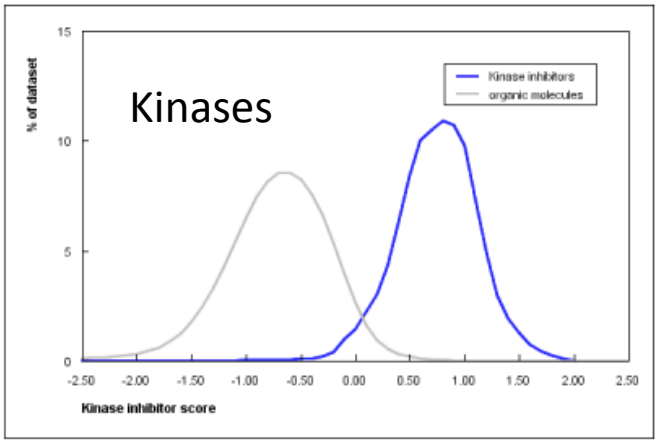
miLogP	3.831
TPSA	81.153
natoms	25
MW	351.431
nON	5
nOHNH	3
nviolations	0
nrotb	3
volume	304.157

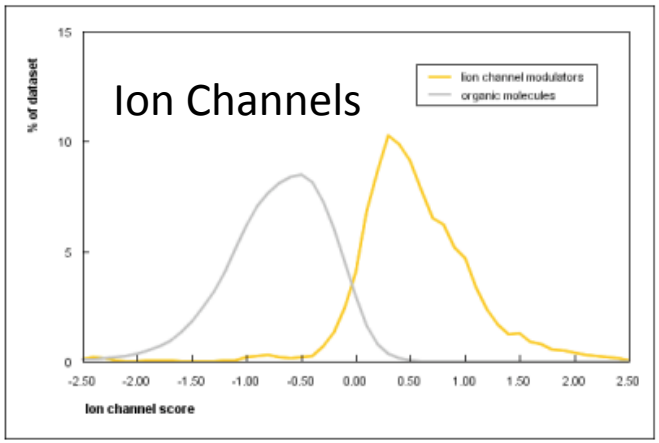
Get data as text (for copy / paste).

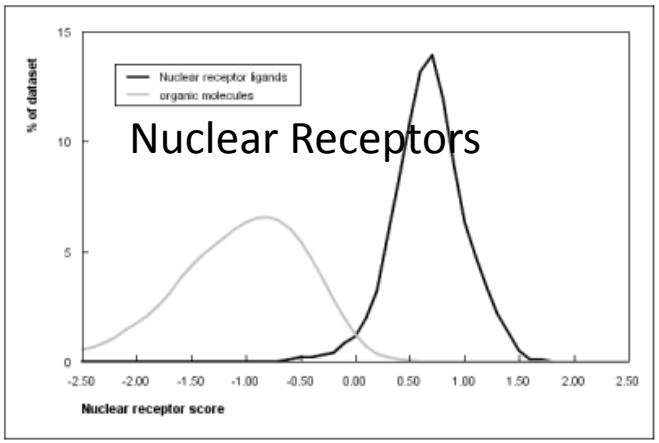
Get 3D geometry BETA

miLogP = hydrophobicity
TPSA = polar surface area
natoms = # atoms except H
nON = # hydrogen bond acceptors
nOHNH = # hydrogen bond donors
nViolations = # Lipinski rule violations
nrotb = # rotatable bonds
Volume = molecular volume

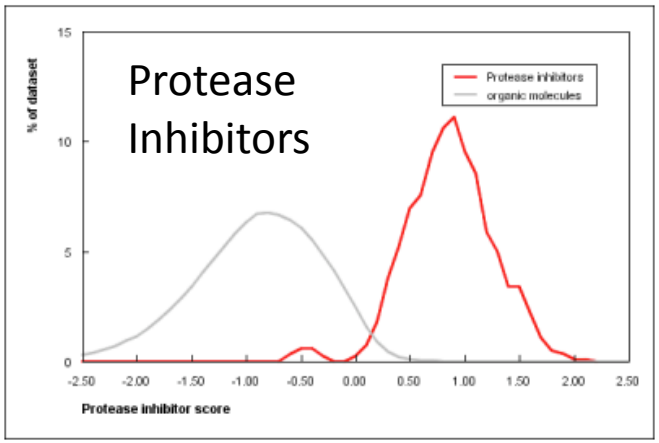








Based on 100,000 compounds



LogPS

Liu et al., Drug Metabolism and Disposition 32:132-139, 2004

LogPS

BBB permeability is often expressed as the BBB permeability-surface area product PS (quantified as logPS)

Earlier estimates relied upon LogBB. LogPS is a direct measure of permeability and theoretically is not confounded by the plasma and brain tissue binding.

$$\mathrm{logPS} = -2.19 + 0.262\ \mathrm{logD} + 0.0583\ \mathrm{vas_{base}} - 0.00897\ \mathrm{TPSA}$$

LogD= dissociative partition coefficient
Vas_base = surface area of the basic atoms
TPSA = surface area

LogP and logD (at pH 7.4) were calculated by ACD/LogP 4.56 and ACD/LogD 4.56, respectively

LogBB

Fu et al., Predicting blood brain barrier penetration of drugs by polar molecular surface area and molecular volume. Acta pharmacol Sin 22(7):663-8, 2001

$$\log BB = -1.037 \times 10^{-5} V^2 + 6.755 \times 10^{-3} V - 0.01808PSA - 0.1581$$

V = Molecular volume
PSA = polar surface area

For ASN 05544420

$LogBB=-1.037x10^{-5}xV^2 + 6.755x10^{-3}xV – 0.01808xPSA – 0.1581$
$LogBB=-1.037x10^{-5}x(304.15)^2 + 6.755x10^{-3}x304.15 – 0.01808x81.153 – 0.1581$
LobBB= -0.53

The Asinex web site posted LogBB = -0.8

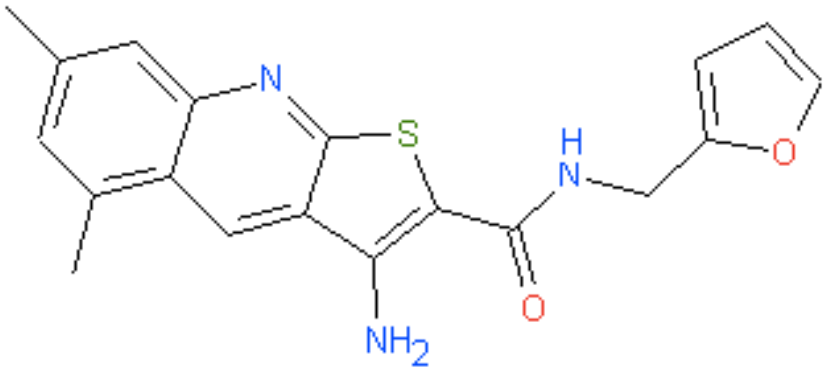
The molecules and correponding Firefly luciferase and Renilla luciferase data

and Lipinski data….

ASN 05544420

DL39-B6

Master plate E13

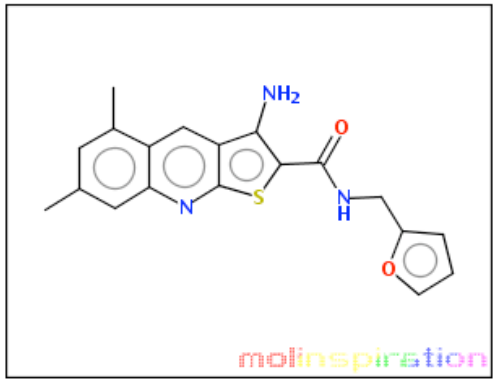


ID number: **ASN 05544420**

Molecular Formula: C_{19} H_{17} N_3 O_2 S
Molecular Weight: 351.4283
Calculated LogP: 4.7070
Number of Freely Rotational Bonds: 4
Number of Hydrogen Bond Acceptors: 4
Number of Hydrogen Bond Donors: 3
Number of Atoms of Nitrogens and Oxygens: 5
Number of Condenced Rings: 3
Fraction of Single Bonds: 0.80
The Predicted Logarithm of the Aqueous Solubility (mol/l): -5.4120
Solubility in Water (mg/l): 1.3609
The Predicted Central Nervous System Activity: -1
The Predicted Apparent Caco-2 Cell Permeability in nm/sec: 142.2680
The Predicted Logarithm of the Brain/Blood Partition Coefficient: -0.8060
Fraction Absorbed: 0.80
Topological Polar Surface Area: 81.15
Acid-base Ionization Constant: 4.72
Purity: 97
The Source of Data: Platinum
Cluster Number: 4348
Cluster Size: 7
Cluster Variation: 0.0014

Name	Value
STRUCTURE NAME	
Molweight	351.42218
TPSA	68.05
HBa	4
HBd	3
IDNUMBER	ASN 05544420
PLATE	39
CELL	B006
WEIGHT	0.2
MOL_WEIGHT	351.43
STRUCT_FORMULA	C19H17N3O2S
VOLUME_DMSO	50_MICRO_L
CONCENTRATION	10_MICROMOL
VENDOR_LOT	442182

ASN 05544420



Molinspiration property engine v2009.01

miLogP	3.831
TPSA	81.153
natoms	25
MW	351.431
nON	5
nOHNH	3
nviolations	0
nrotb	3
volume	304.157

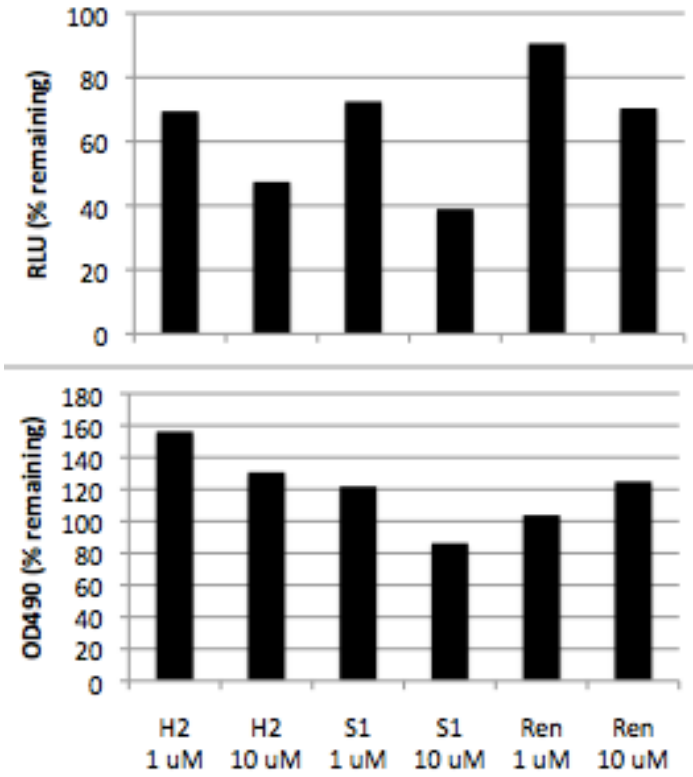
Get data as text (for copy / paste).

Get 3D geometry BETA

Molinspiration drug-likeness score v2008.12

GPCR ligand	-0.56
Ion channel modulator	-0.85
Kinase inhibitor	-0.76
Nuclear receptor ligand	-2.16

Master Plate Assays

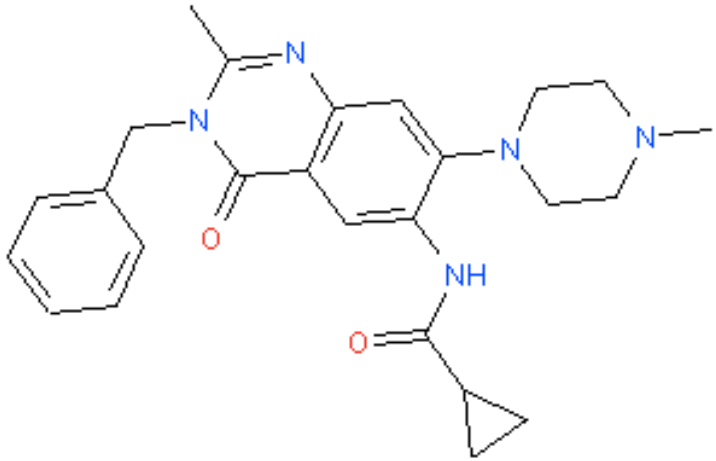


Cyclopropanecarboxylic acid [3-benzyl-2-methyl-7-(4-methyl-piperazin-1-yl)-4-oxo-3,4-dihydro-quinazolin-6-yl]-amide

ASN 05819045

Master plate F11

DL55-A13

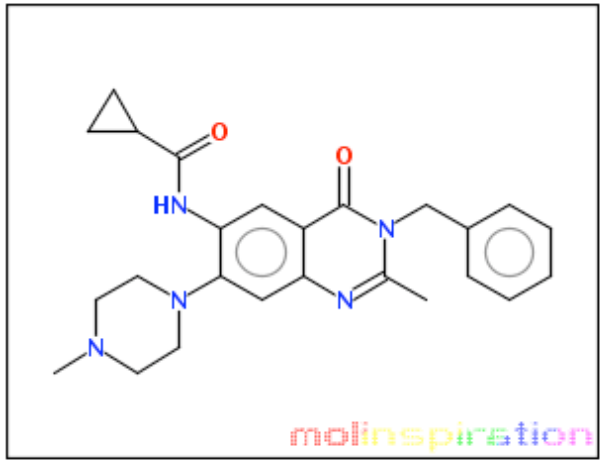


ID number: ASN 05819045

Molecular Formula: C_{25} H_{29} N_5 O_2
Molecular Weight: 431.5371
Calculated LogP: 3.1090
Number of Freely Rotational Bonds: 6
Number of Hydrogen Bond Acceptors: 4
Number of Hydrogen Bond Donors: 1
Number of Atoms of Nitrogens and Oxygens: 7
Number of Condenced Rings: 2
Fraction of Single Bonds: 58.3333
The Predicted Logarithm of the Aqueous Solubility (mol/l): -3.6160
Solubility in Water (mg/l): 104.4764
The Predicted Central Nervous System Activity: -1
The Predicted Apparent Caco-2 Cell Permeability in nm/sec: 59.4160
The Predicted Logarithm of the Brain/Blood Partition Coefficient: 0.0130
Fraction Absorbed: 0.57
Topological Polar Surface Area: 70.47
Acid-base Ionization Constant: 3.75
Purity: 99
The Source of Data: Platinum
Cluster Number: 1368
Cluster Size: 17
Cluster Variation: 0.0182

Name	Value
STRUCTURE NAME	
Molweight	431.53006
TPSA	70.47
HBa	5
HBd	1
IDNUMBER	ASN 05819045
PLATE	55
CELL	A013
WEIGHT	0.2
MOL_WEIGHT	431.54
STRUCT_FORMULA	C25H29N5O2
VOLUME_DMSO	50_MICRO_L
CONCENTRATION	10_MICROMOL
VENDOR_LOT	531087

ASN 05819045



Molinspiration property engine v2009.01

miLogP	2.681
TPSA	70.471
natoms	32
MW	431.54
nON	7
nOHNH	1
nviolations	0
nrotb	5
volume	402.47

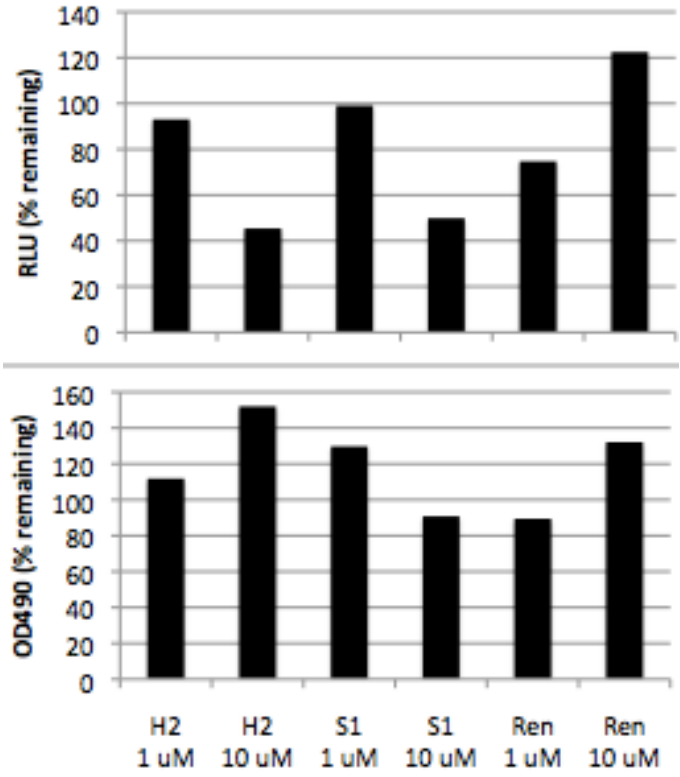
Get data as text (for copy / paste).

Get 3D geometry BETA

Molinspiration drug-likeness score v2008.12

GPCR ligand	0.20
Ion channel modulator	-0.38
Kinase inhibitor	-0.04
Nuclear receptor ligand	-0.91

Master Plate Assays

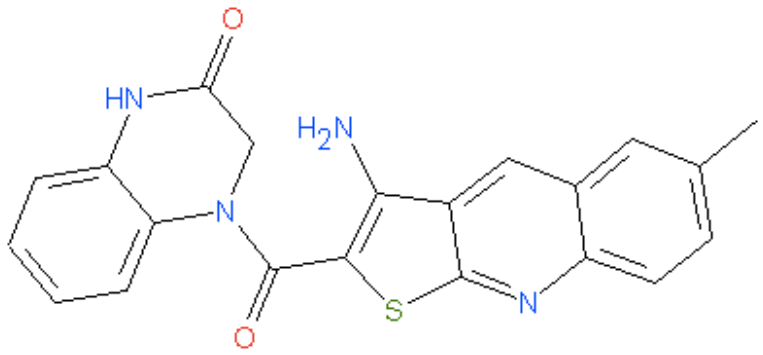


4-(3-Amino-6-methyl-thieno[2,3-b]quinoline-2-carbonyl)-3,4-dihydro-1H-quinoxalin-2-one

ASN 05543441

DL34-L20

Master plate E7

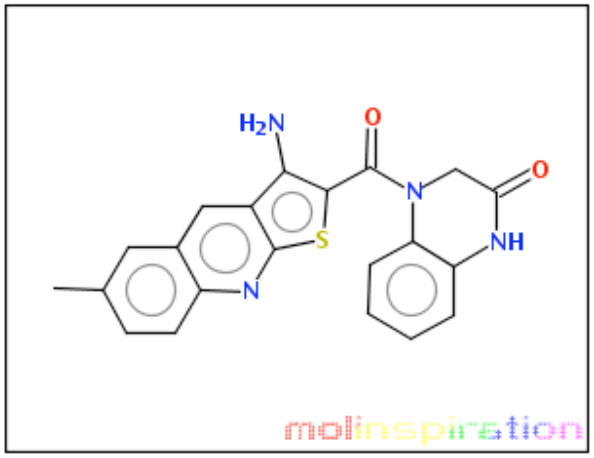


ID number: ASN 05543441

Molecular Formula: C_{21} H_{16} N_4 O_2 S
Molecular Weight: 388.4494
Calculated LogP: 3.1780
Number of Freely Rotational Bonds: 2
Number of Hydrogen Bond Acceptors: 4
Number of Hydrogen Bond Donors: 3
Number of Atoms of Nitrogens and Oxygens: 6
Number of Condenced Rings: 3
Fraction of Single Bonds: 28.1250
The Predicted Logarithm of the Aqueous Solubility (mol/l): -5.2710
Solubility in Water (mg/l): 2.0813
The Predicted Central Nervous System Activity: -2
The Predicted Apparent Caco-2 Cell Permeability in nm/sec: 43.1890
The Predicted Logarithm of the Brain/Blood Partition Coefficient: -1.2370
Fraction Absorbed: 0.62
Topological Polar Surface Area: 88.32
Acid-base Ionization Constant: 4.72
Purity: 98
The Source of Data: Platinum
Cluster Number: 27860
Cluster Size: 1
Cluster Variation: 0

Name	Value
STRUCTURE NAME	
Molweight	388.44234
TPSA	88.36
HBa	5
HBd	3
IDNUMBER	ASN 05543441
PLATE	34
CELL	L020
WEIGHT	0.2
MOL_WEIGHT	388.45
STRUCT_FORMULA	C21H16N4O2S
VOLUME_DMSO	50_MICRO_L
CONCENTRATION	10_MICROMOL
VENDOR_LOT	422669

ASN 05543441



Molinspiration property engine v2009.01

miLogP	3.797
TPSA	88.322
natoms	28
MW	388.452
nON	6
nOHNH	3
nviolations	0
nrotb	1
volume	326.954

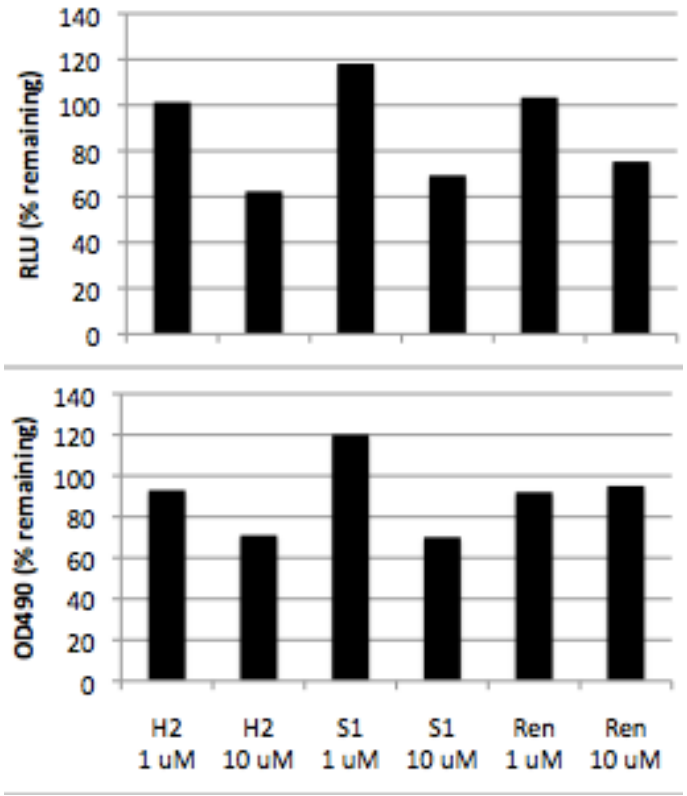
Get data as text (for copy / paste).

Get 3D geometry BETA

Molinspiration drug-likeness score v2008.12

GPCR ligand	-0.62
Ion channel modulator	-1.12
Kinase inhibitor	-0.74
Nuclear receptor ligand	-1.96

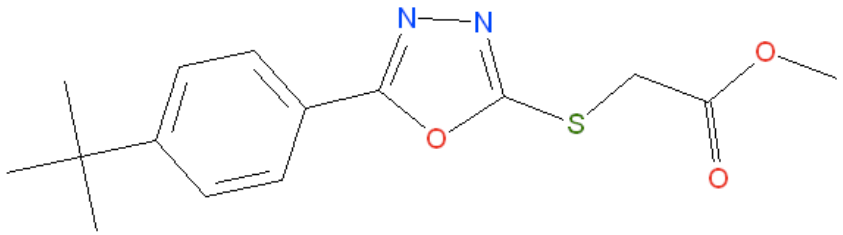
Master Plate Assays



[5-(4-tert-Butyl-phenyl)-[1,3,4]oxadiazol-2-ylsulfanyl]-acetic acid methyl ester

ASN 03574739 Master plate D1

DL5-M5

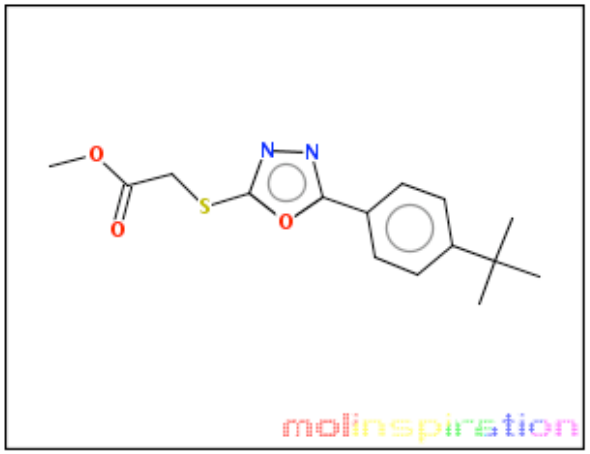


ID number: ASN 03574739

Molecular Formula: $C_{15}H_{18}N_2O_3S$
Molecular Weight: 306.3842
Calculated LogP: 3.1480
Number of Freely Rotational Bonds: 6
Number of Hydrogen Bond Acceptors: 6
Number of Hydrogen Bond Donors: 0
Number of Atoms of Nitrogens and Oxygens: 5
Number of Condenced Rings: 0
Fraction of Single Bonds: 45.4545
The Predicted Logarithm of the Aqueous Solubility (mol/l): -3.6380
Solubility in Water (mg/l): 70.5125
The Predicted Central Nervous System Activity: -1
The Predicted Apparent Caco-2 Cell Permeability in nm/sec: 106.0490
The Predicted Logarithm of the Brain/Blood Partition Coefficient: -0.8720
Fraction Absorbed: 0.94
Topological Polar Surface Area: 65.22
Acid-base Ionization Constant:
Purity: 95
The Source of Data: Platinum
Cluster Number: 3904
Cluster Size: 8
Cluster Variation: 0.0122

Name	Value
STRUCTURE NAME	
Molweight	306.38002
TPSA	52.08
HBa	7
HBd	0
IDNUMBER	ASN 03574739
PLATE	5
CELL	M005
WEIGHT	0.2
MOL_WEIGHT	306.38
STRUCT_FORMULA	C15H18N2O3S
VOLUME_DMSO	50_MICRO_L
CONCENTRATION	10_MICROMOL
VENDOR_LOT	373610

ASN 03574739



Molinspiration property engine v2009.01

miLogP	4.097
TPSA	65.229
natoms	21
MW	306.387
nON	5
nOHNH	0
nviolations	0
nrotb	6
volume	274.353

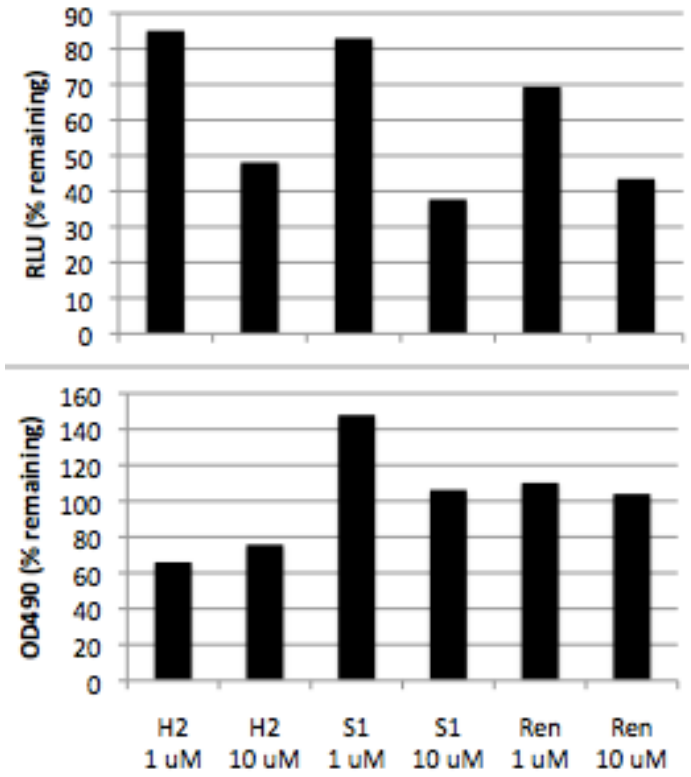
Get data as text (for copy / paste).

Get 3D geometry BETA

Molinspiration drug-likeness score v2008.12

GPCR ligand	-1.24
Ion channel modulator	-1.37
Kinase inhibitor	-1.10
Nuclear receptor ligand	-1.38

Master Plate Assays

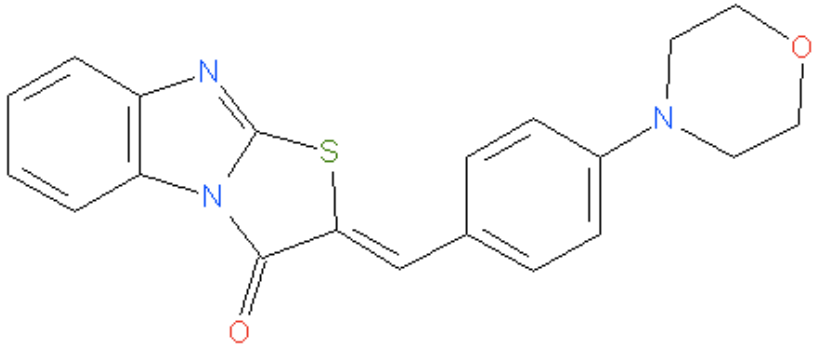


Chembridge 5378047

Plate 10101 well 11B

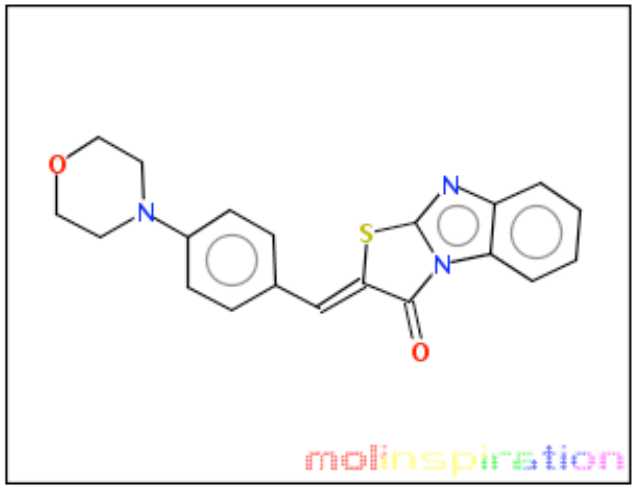
UC26-A21

Master plate G24



Name	Value
STRUCTURE NAME	
Molweight	363.43288
TPSA	47.36
HBa	5
HBd	0
ID	5378047
Plate	10101
Col	11
Row	B
Supplier	ChemBridge
Coordinates	B11
clogP	2.500000000000000e+000
RB	2
tPSA	4.683999999999999e+001
Hacc	4
Hdon	0

Chembridge 5378047



Molinspiration property engine v2009.01

miLogP	3.655
TPSA	46.85
natoms	26
MW	363.442
nON	5
nOHNH	0
nviolations	0
nrotb	2
volume	312.476

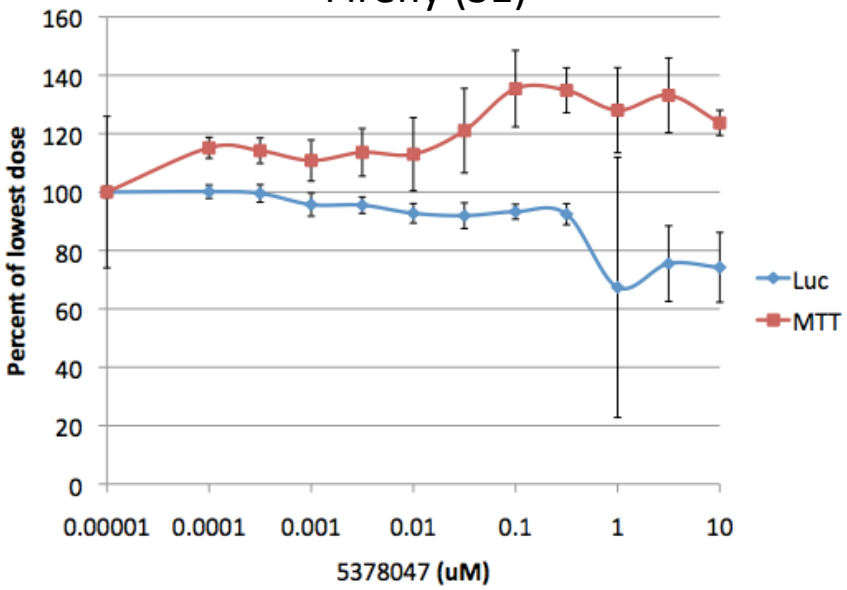
Get data as text (for copy / paste).

Get 3D geometry BETA

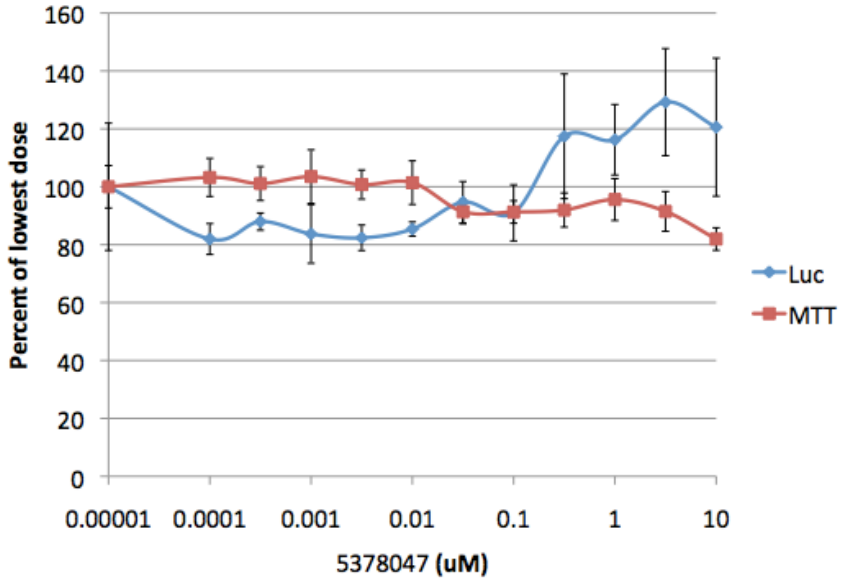
Molinspiration drug-likeness score v2008.12

GPCR ligand	-0.97
Ion channel modulator	-1.46
Kinase inhibitor	-0.78
Nuclear receptor ligand	-1.35

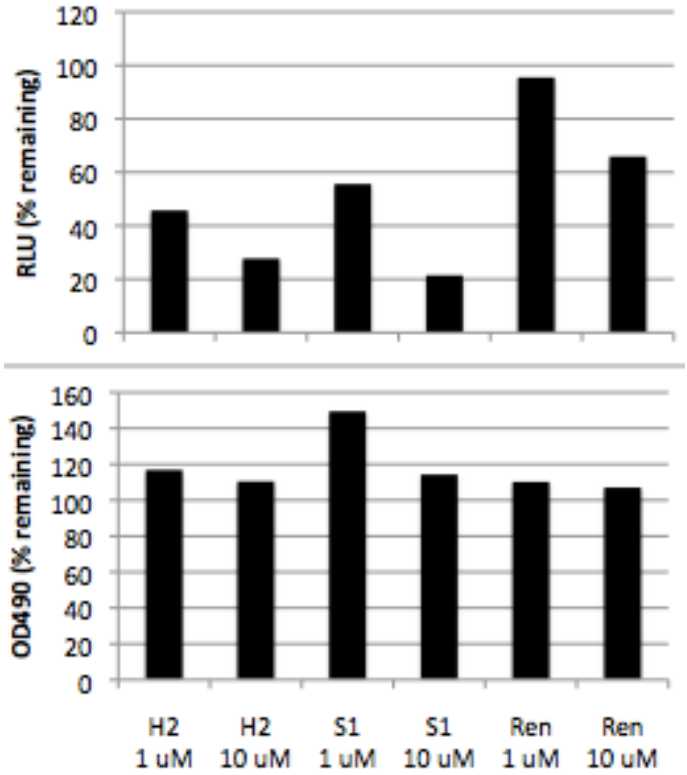
Firefly (S1)



Renilla (HR)



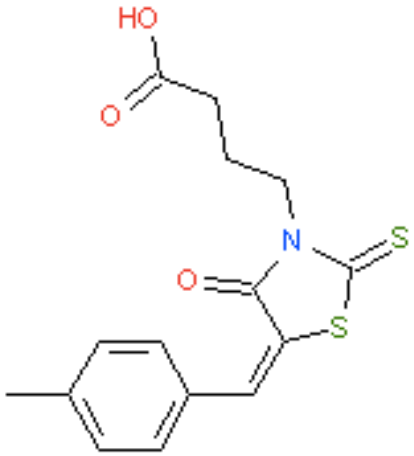
Master Plate Assays



Chembridge 5545700 UC41-F5

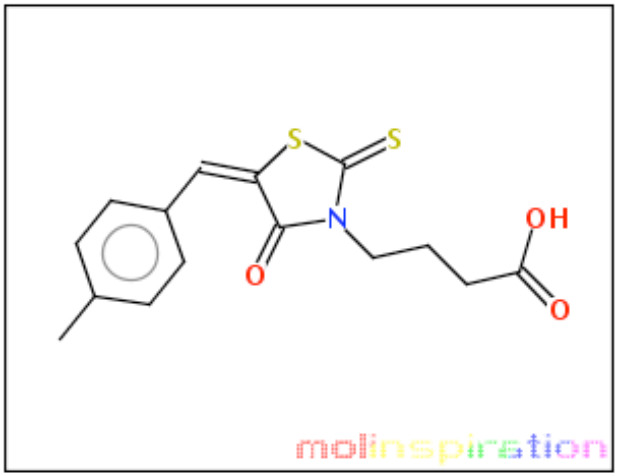
Plate 10162 well D3

Master plate H15



Name	Value
STRUCTURE NAME	
Molweight	321.4145
TPSA	57.61
HBa	4
HBd	1
ID	5545700
Plate	10162
Col	03
Row	D
Supplier	ChemBridge
Coordinates	D03
clogP	2.560000000000000e+000
RB	5
tPSA	5.761000000000000e+001
Hacc	3
Hdon	1

Chembridge 5545700



Molinspiration property engine v2009.01

miLogP	2.128
TPSA	59.304
natoms	21
MW	321.423
nON	4
nOHNH	1
nviolations	0
nrotb	5
volume	272.344

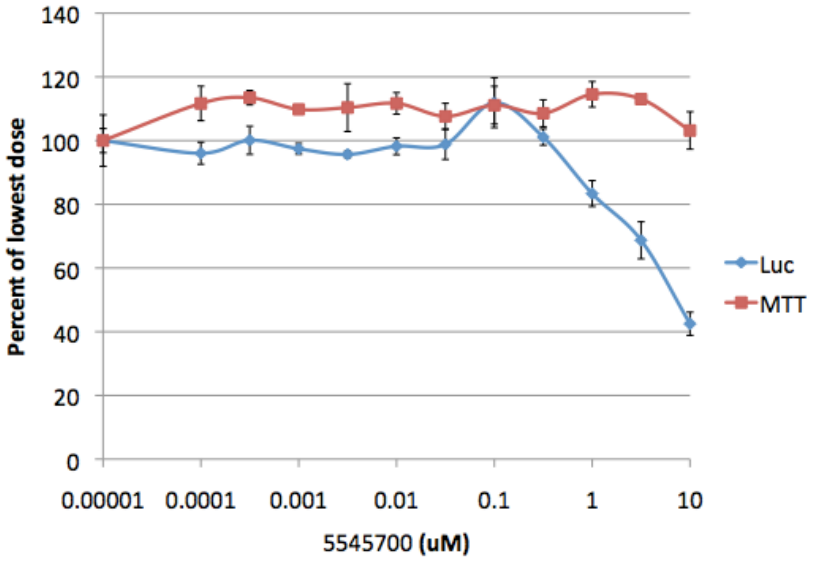
Get data as text (for copy / paste).

Get 3D geometry BETA

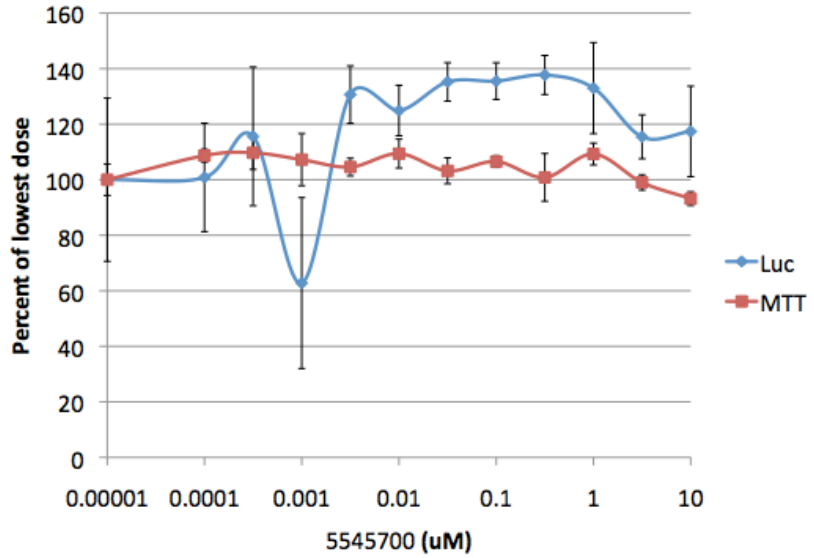
Molinspiration drug-likeness score v2008.12

GPCR ligand	-2.03
Ion channel modulator	-1.97
Kinase inhibitor	-1.09
Nuclear receptor ligand	-1.67

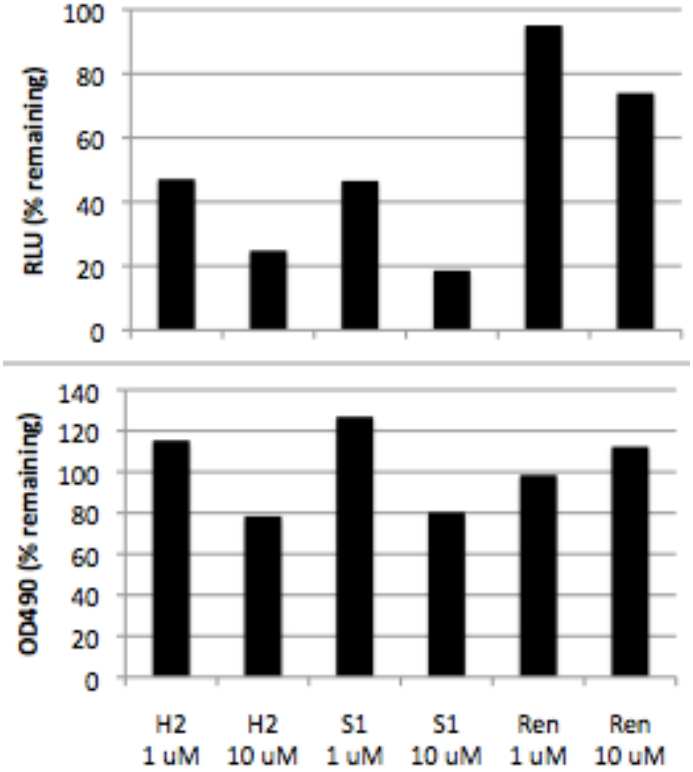
Firefly (S1)



Renilla (HR)



Master Plate Assays

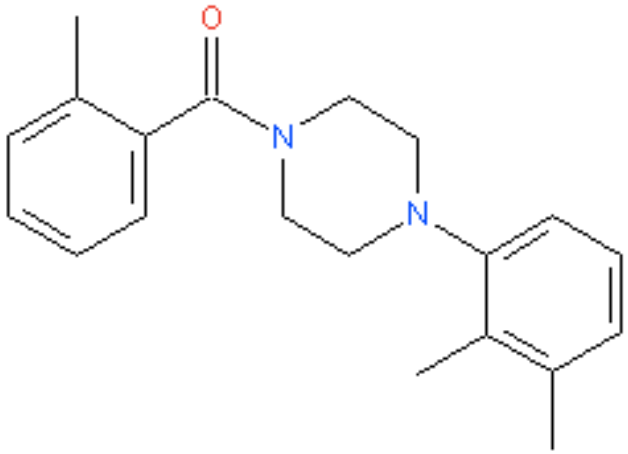


Chembridge 5686284

Plate 10218 well C7

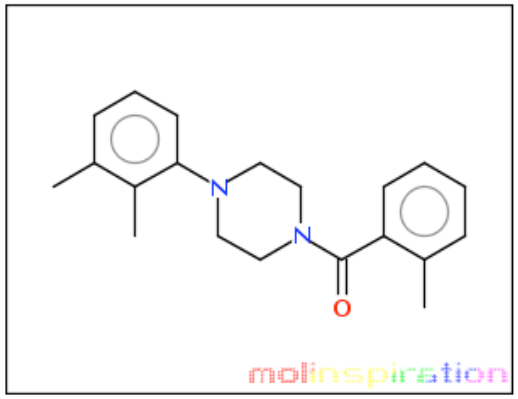
UC55-F14

Master plate H24



Name	Value
STRUCTURE NAME	
Molweight	308.41736
TPSA	23.55
HBa	2
HBd	0
ID	5686284
Plate	10218
Row	C
Col	07
Supplier	ChemBridge
Coordinates	C07
clogP	3.390000000000000e+000
RB	2
tPSA	2.355000000000000e+001
Hacc	1
Hdon	0

Chembridge 5686284



Molinspiration property engine v2009.01

miLogP	3.695
TPSA	23.547
natoms	23
MW	308.425
nON	3
nOHNH	0
nviolations	0
nrotb	2
volume	306.052

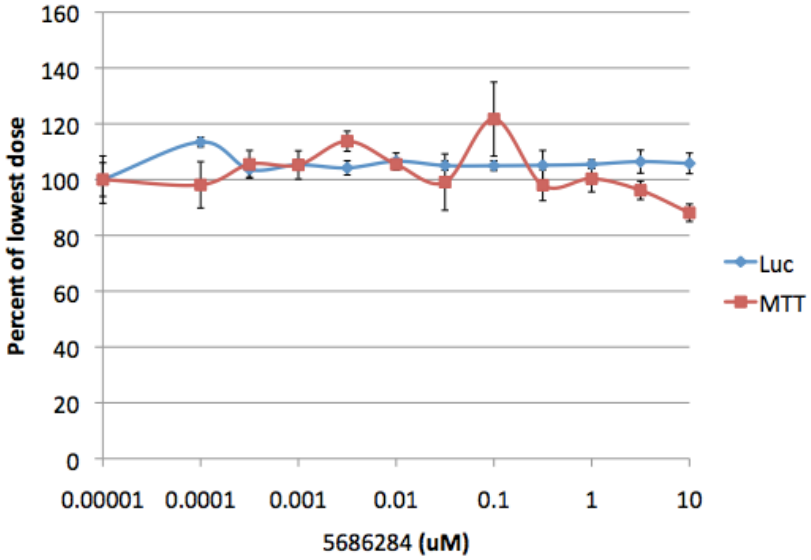
Get data as text (for copy / paste).

Get 3D geometry BETA

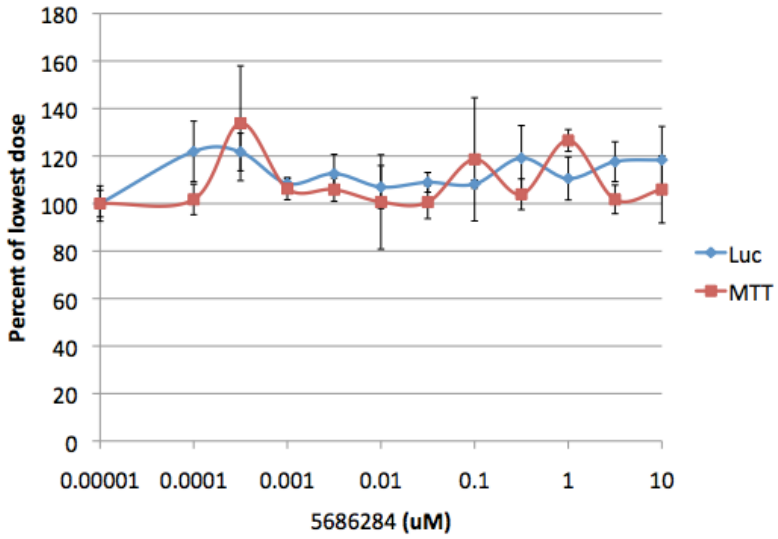
Molinspiration drug-likeness score v2008.12

GPCR ligand	0.16
Ion channel modulator	-0.10
Kinase inhibitor	-0.36
Nuclear receptor ligand	-0.51

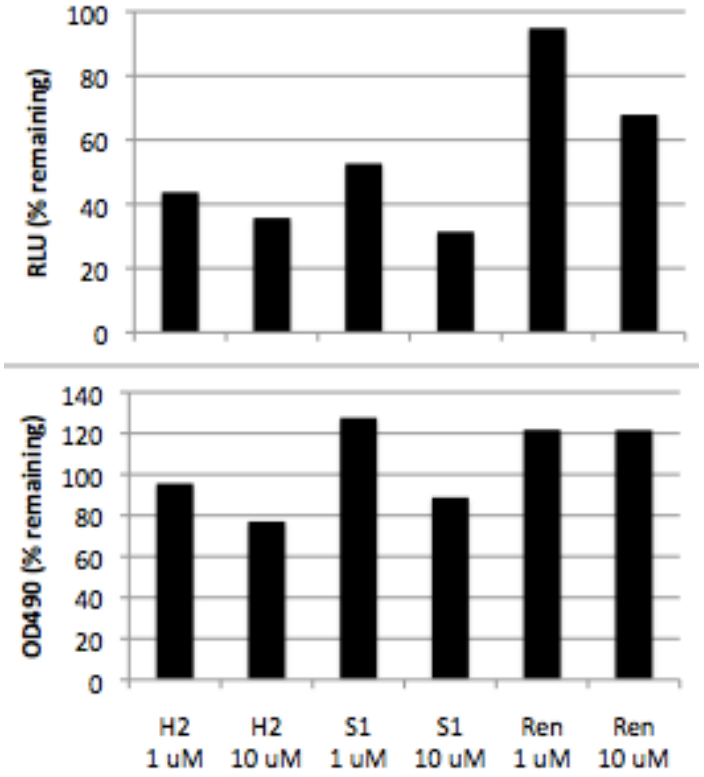
Firefly (S1)



Renilla (HR)

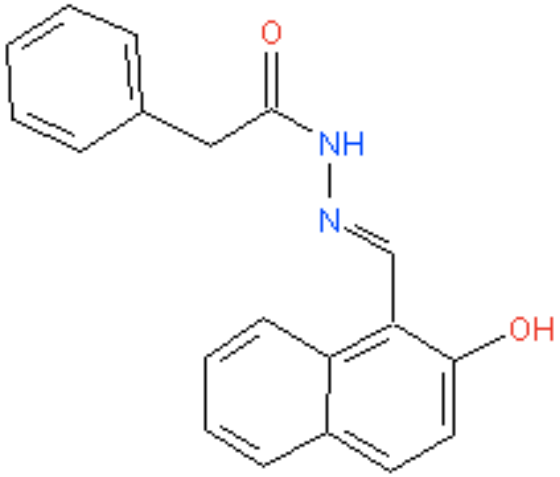


Master Plate Assays



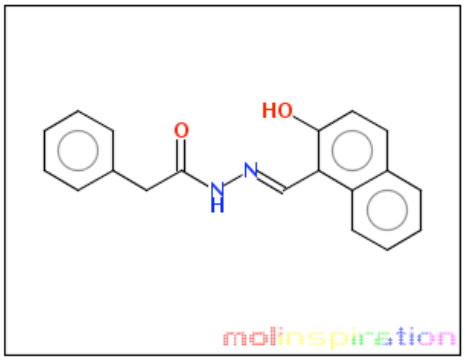
Chembridge 5113092 UC65-A15

Plate 10257 well B8 Master plate I12



Name	Value
STRUCTURE NAME	
Molweight	304.34254
TPSA	61.69
HBa	3
HBd	2
ID	5113092
Plate	10257
Col	08
Row	B
Supplier	ChemBridge
Coordinates	B08
clogP	3.440000000000000e+000
RB	4
tPSA	6.169000000000000e+001
Hacc	3
Hdon	2

Chembridge 5113092



Molinspiration property engine v2009.01

miLogP	4.29
TPSA	61.69
natoms	23
MW	304.349
nON	4
nOHNH	2
nviolations	0
nrotb	4
volume	278.91

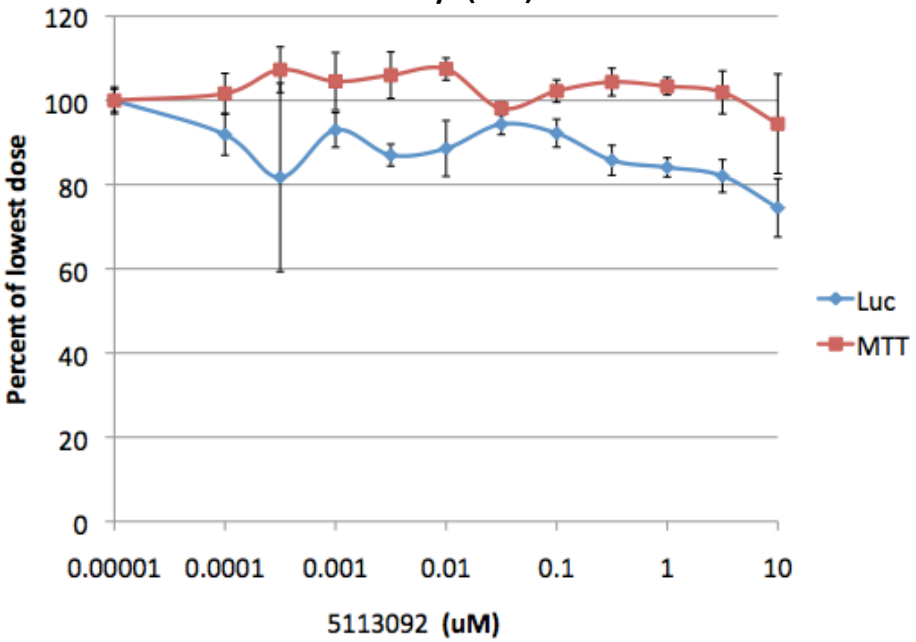
Get data as text (for copy / paste).

Get 3D geometry BETA

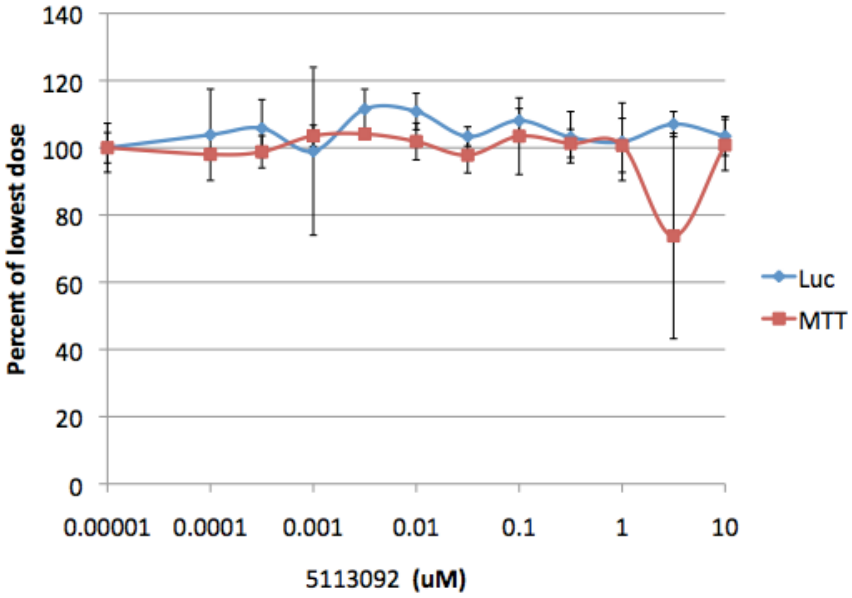
Molinspiration drug-likeness score v2008.12

GPCR ligand	-0.46
Ion channel modulator	-0.53
Kinase inhibitor	-0.73
Nuclear receptor ligand	-0.43

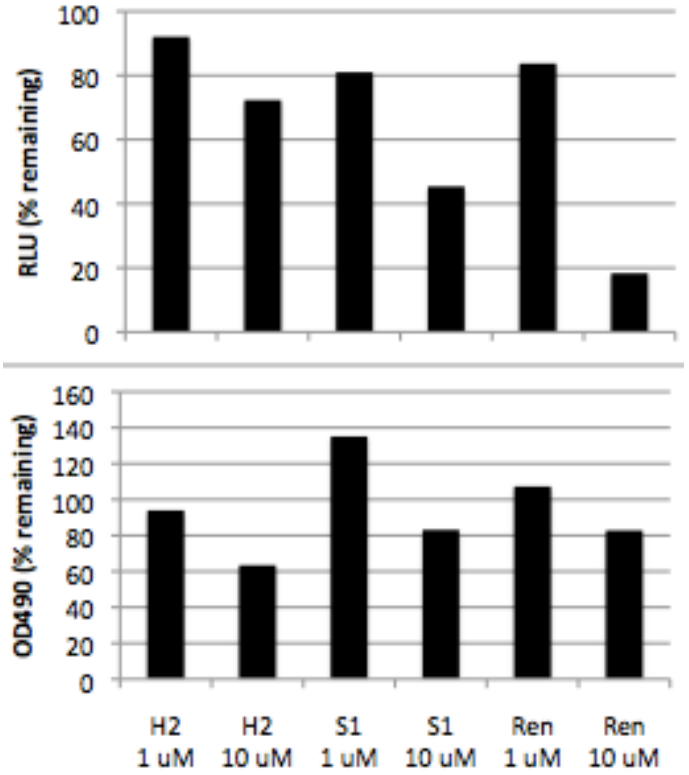
Firefly (S1)



Renilla (HR)



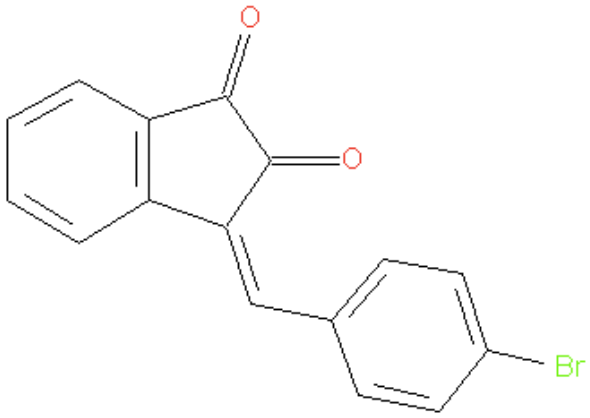
Master Plate Assays



Chembridge 5314590
Plate 10063 well D9

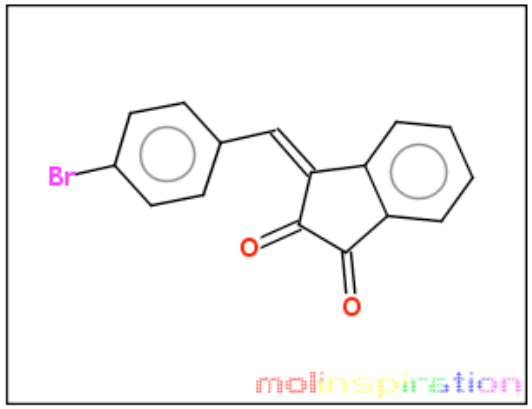
UC16-J17

Master plate G11



Name	Value
STRUCTURE NAME	
Molweight	313.14546
TPSA	34.14
HBa	4
HBd	0
ID	5314590
Plate	10063
Col	09
Row	D
Supplier	ChemBridge
Coordinates	D09
clogP	3.290000000000000e+000
RB	1
tPSA	3.414000000000000e+001
Hacc	2
Hdon	0

Chembridge 5314590



Molinspiration property engine v2009.01

miLogP	3.697
TPSA	34.142
natoms	19
MW	313.15
nON	2
nOHNH	0
nviolations	0
nrotb	1
volume	227.879

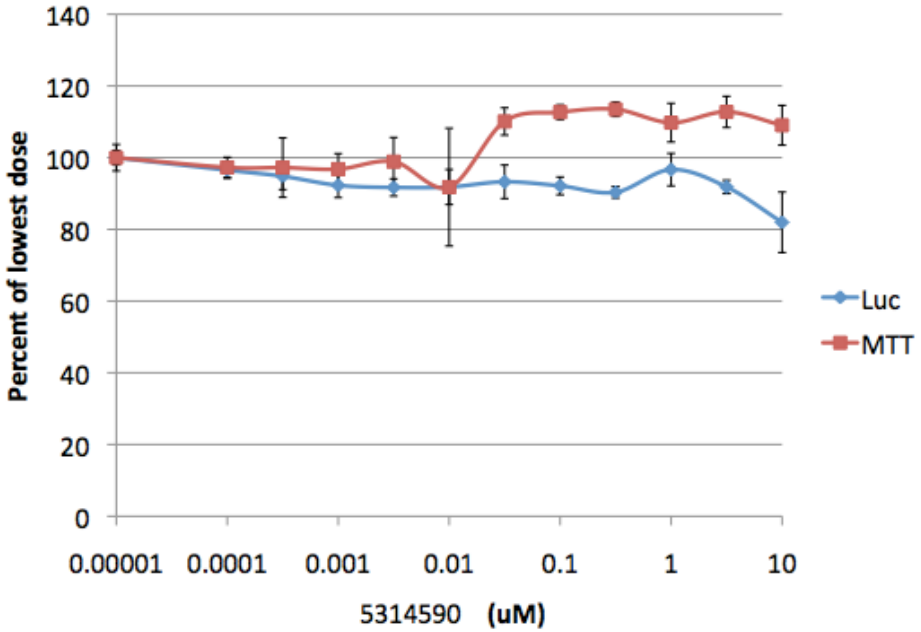
Get data as text (for copy / paste).

Get 3D geometry BETA

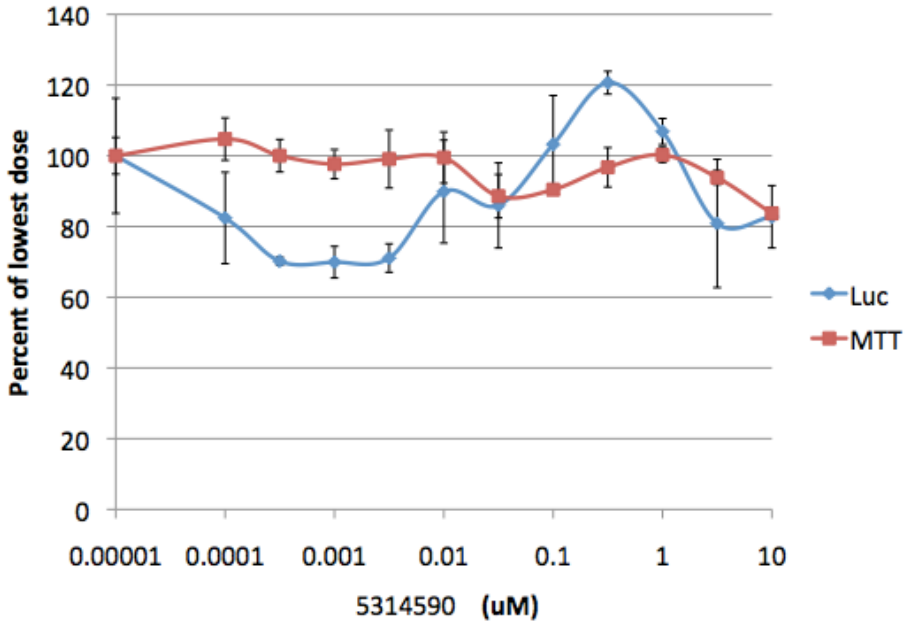
Molinspiration drug-likeness score v2008.12

GPCR ligand	-0.85
Ion channel modulator	-1.06
Kinase inhibitor	-0.03
Nuclear receptor ligand	-0.57

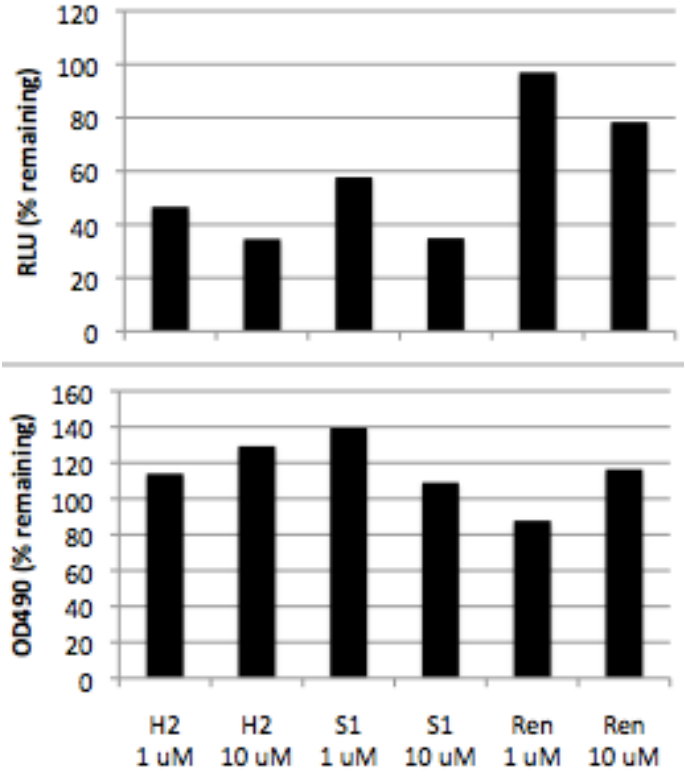
Firefly (S1)



Renilla (HR)



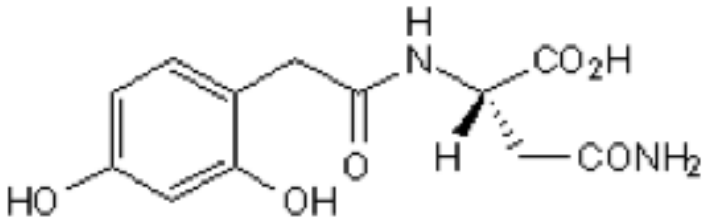
Master Plate Assays



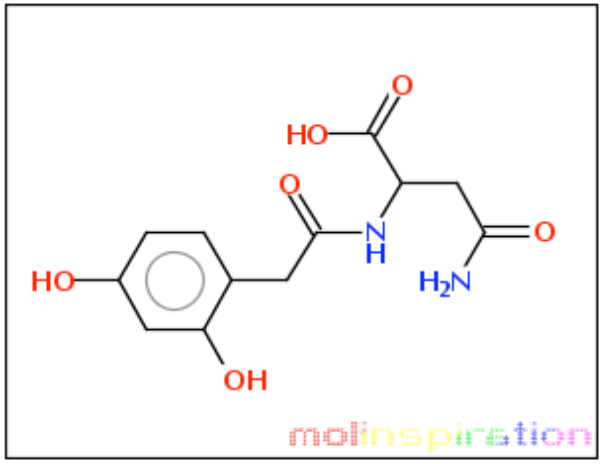
2,4-Dihydroxyphenylacetyl-L-asparagine

Master plate J15

Plate ENZ well H5



2,4-Dihydroxyphenylacetyl-L-asparagine



Molinspiration property engine v2009.01

miLogP	-1.338
TPSA	149.947
natoms	20
MW	282.252
nON	8
nOHNH	6
nviolations	1
nrotb	6
volume	239.17

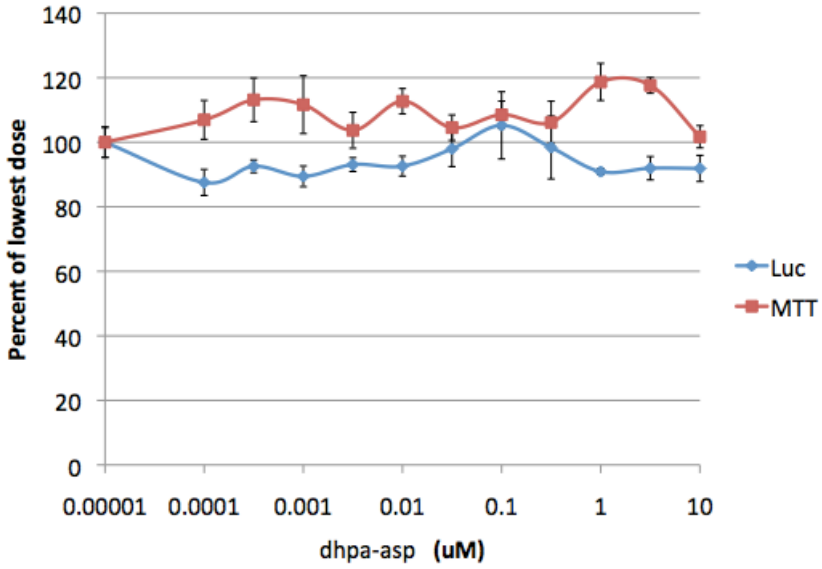
Get data as text (for copy / paste).

Get 3D geometry BETA

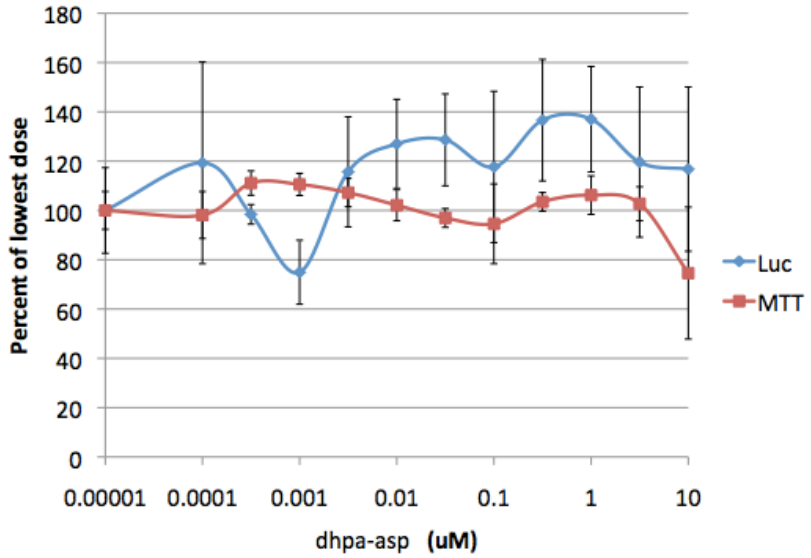
Molinspiration drug-likeness score v2008.12

GPCR ligand	0.23
Ion channel modulator	0.02
Kinase inhibitor	-0.62
Nuclear receptor ligand	-0.39

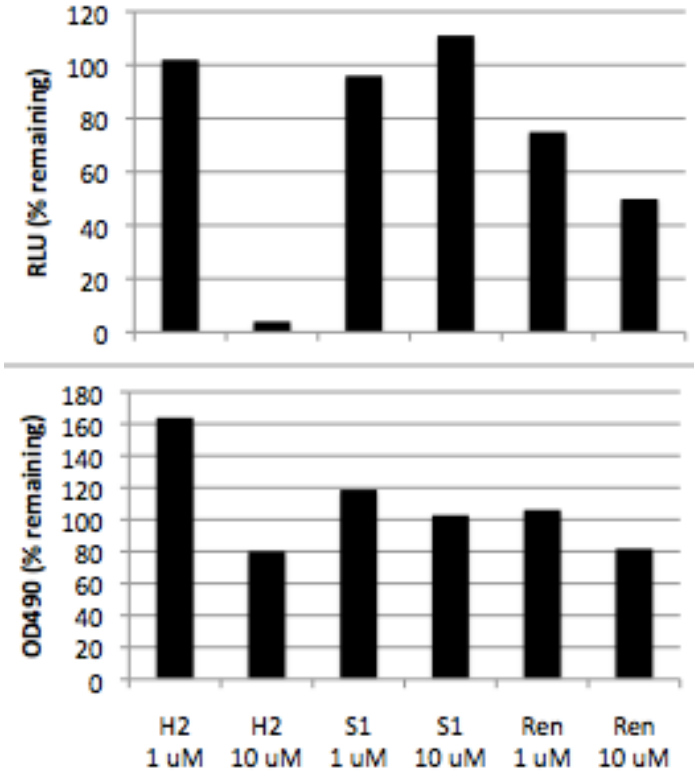
Firefly (S1)



Renilla (HR)



Master Plate Assays



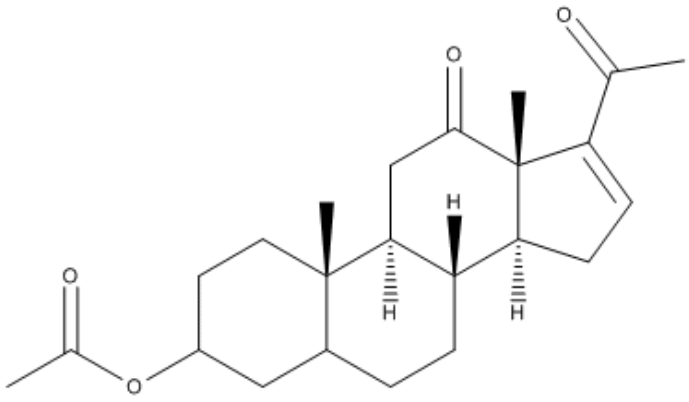
Screen results: 3 trials

51% 19% & 14% reduction in H2 cells

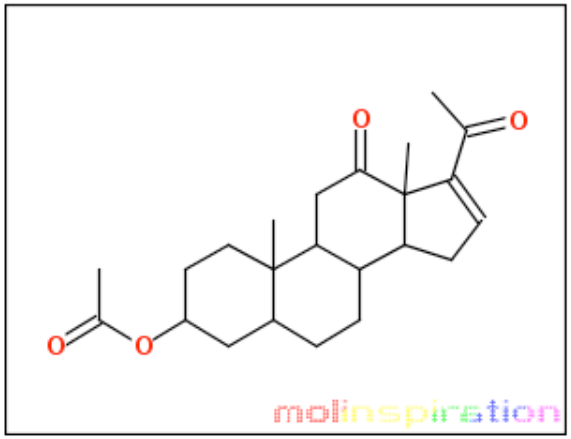
3-acetoxypregn-16-en-12,20-dione

Master plate J19

Plate MS1 well G12



3-acetoxypregn-16-en-12,20-dione



Molinspiration property engine v2009.01

miLogP	3.594
TPSA	60.447
natoms	27
MW	372.505
nON	4
nOHNH	0
nviolations	0
nrotb	3
volume	363.622

Get data as text (for copy / paste).

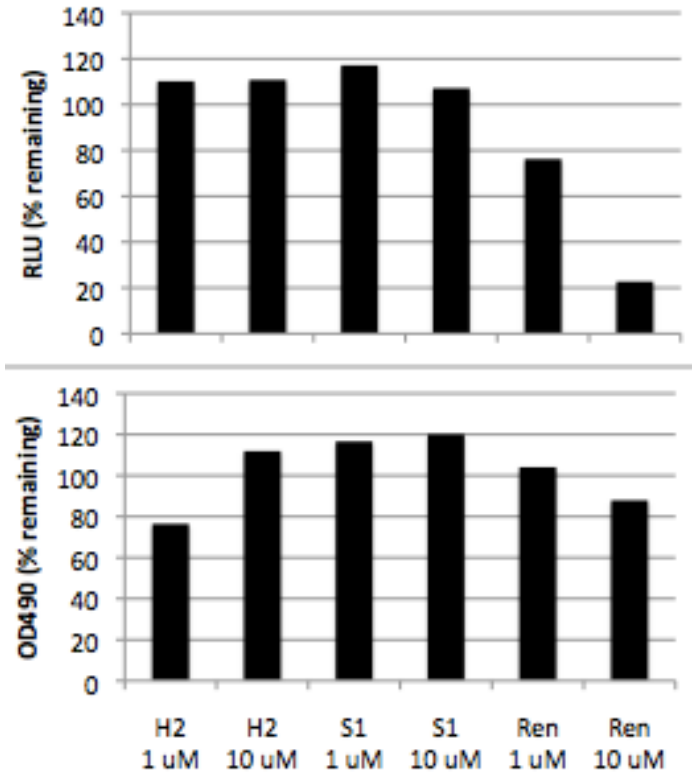
Get 3D geometry BETA

Molinspiration drug-likeness score v2008.12

GPCR ligand	-1.00
Ion channel modulator	-0.29
Kinase inhibitor	-1.23
Nuclear receptor ligand	-0.66

Don’t do this one

Master Plate Assays

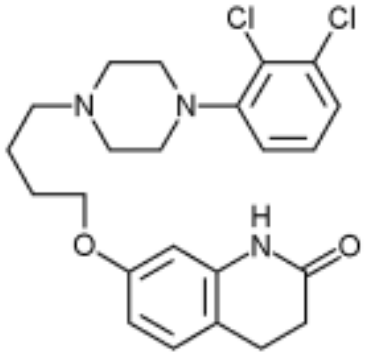


Screen results: 63% reduction in H2 cells

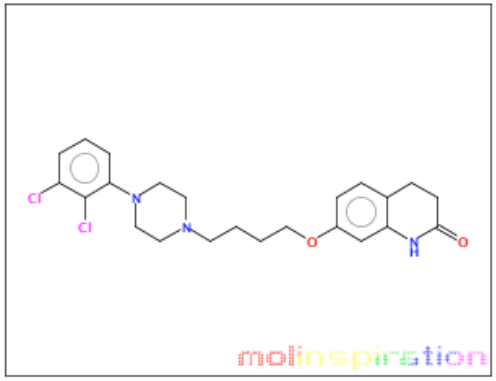
Aripiprazole

Master plate K7

Plate NIH2 well I18



Aripiprazole



Molinspiration property engine v2009.01

miLogP	5.079
TPSA	44.808
natoms	30
MW	448.394
nON	5
nOHNH	1
nviolations	1
nrotb	7
volume	394.797

Get data as text (for copy / paste).

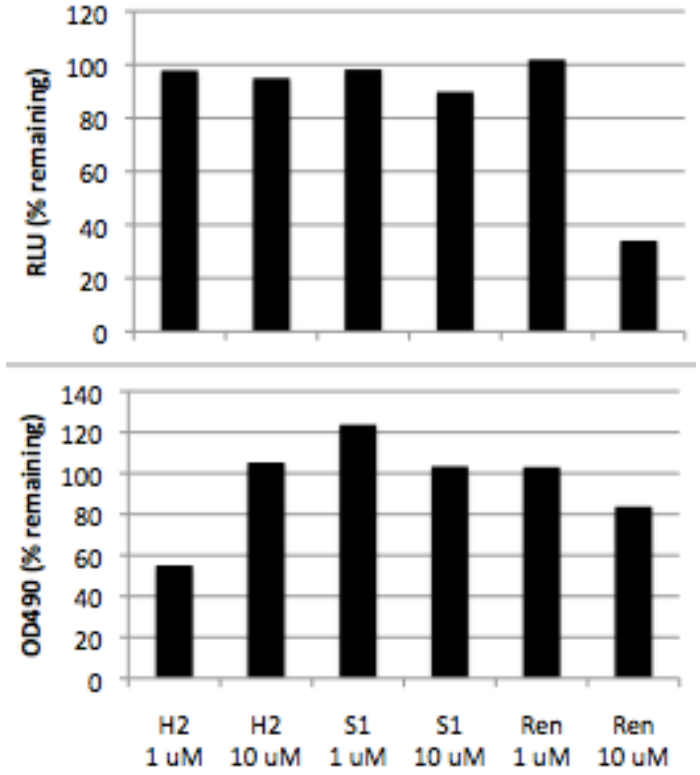
Get 3D geometry BETA

Molinspiration drug-likeness score v2008.12

GPCR ligand	0.24
Ion channel modulator	-0.15
Kinase inhibitor	-0.19
Nuclear receptor ligand	-0.34

Maybe don’t do this one

Master Plate Assays



Screen results: 51% reduction in H2 cells

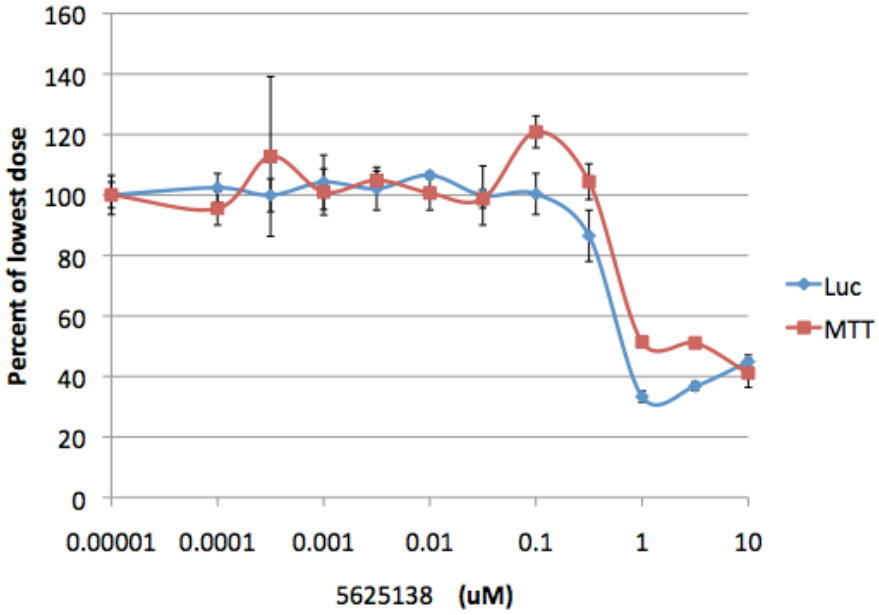
Chembridge 5625138

UC48-A14

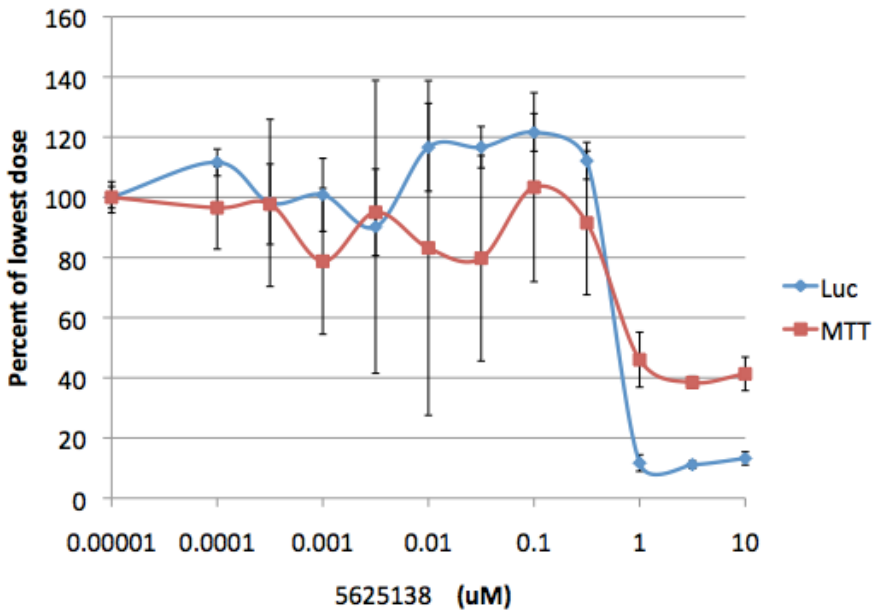
Plate 10189 well A7

Master plate H18

Firefly (S1)



Renilla (HR)



Chembridge 5331023 UC19-H7

Plate 10074 well H4

This is the wrong compound