

# Supplementary Materials

## Computational modeling and synthesis of Pyridine variants of Benzoyl-Phenoxy-Acetamide with high glioblastoma cytotoxicity and brain tumor penetration

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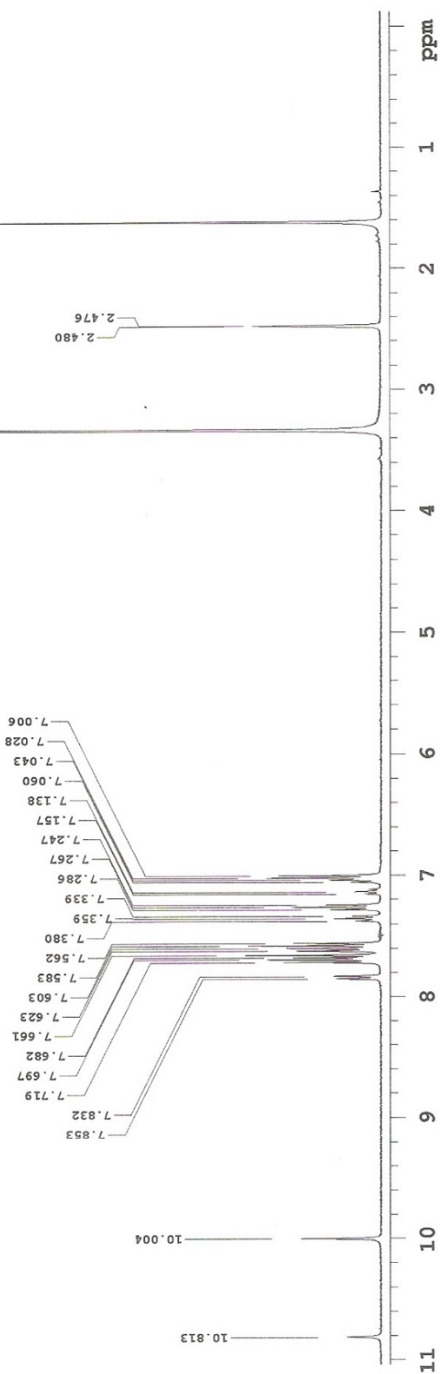
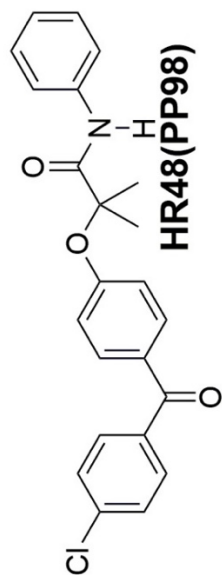
\*Corresponding authors

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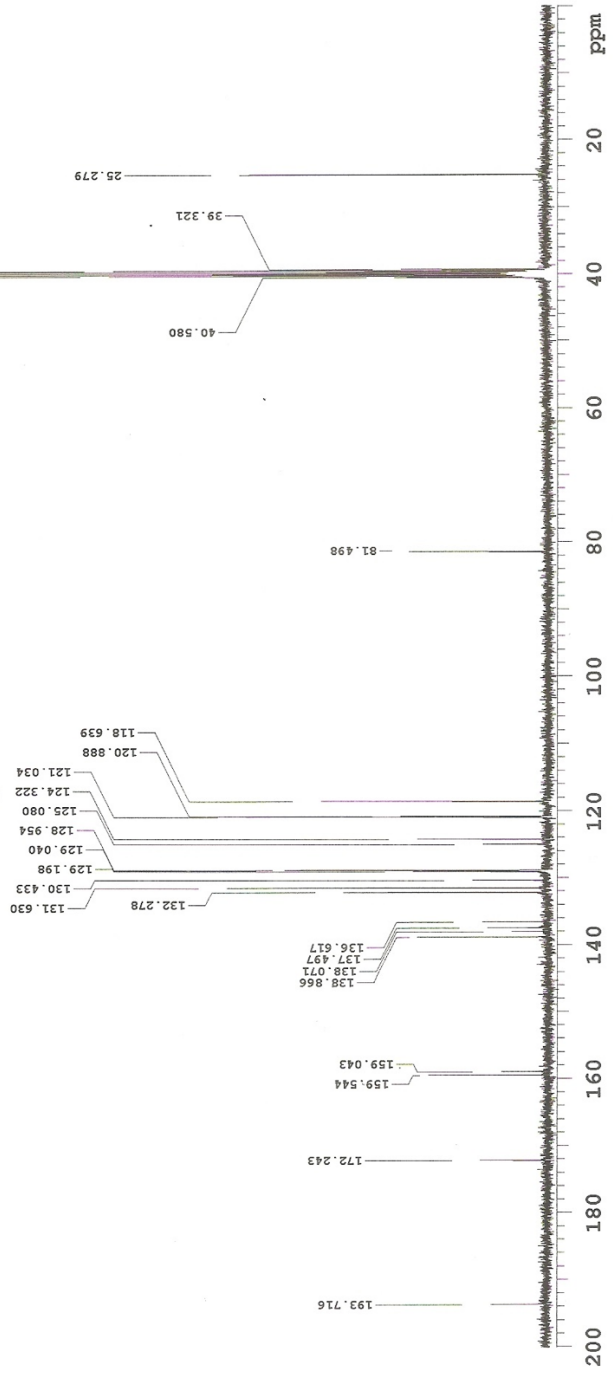
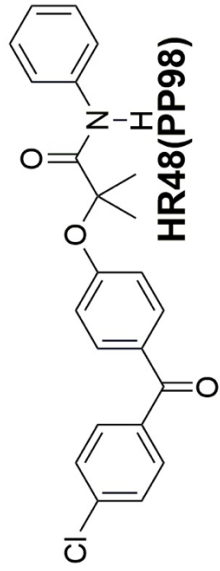
1. Nuclear Magnetic Resonance data of Pyridine-BPA variants:  
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1) Nuclear Magnetic Resonance data of Pyridine-BPA variants:  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMRs}$ .

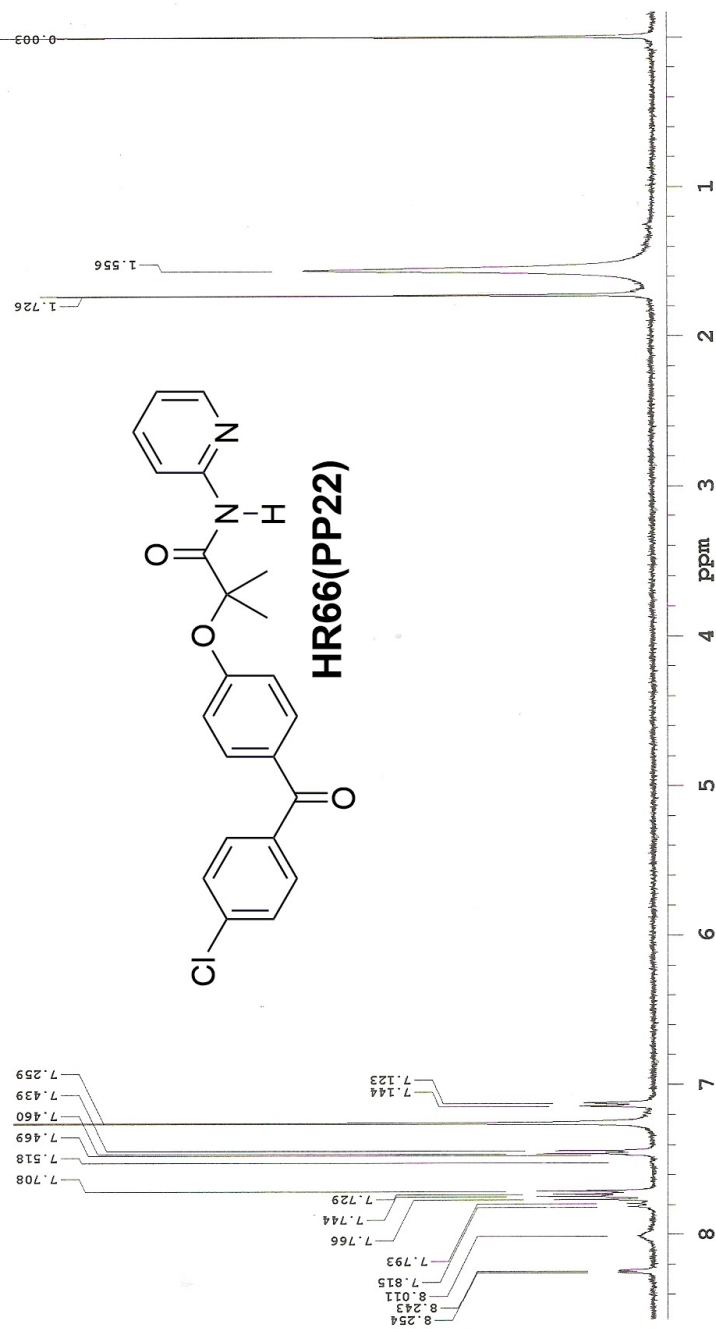
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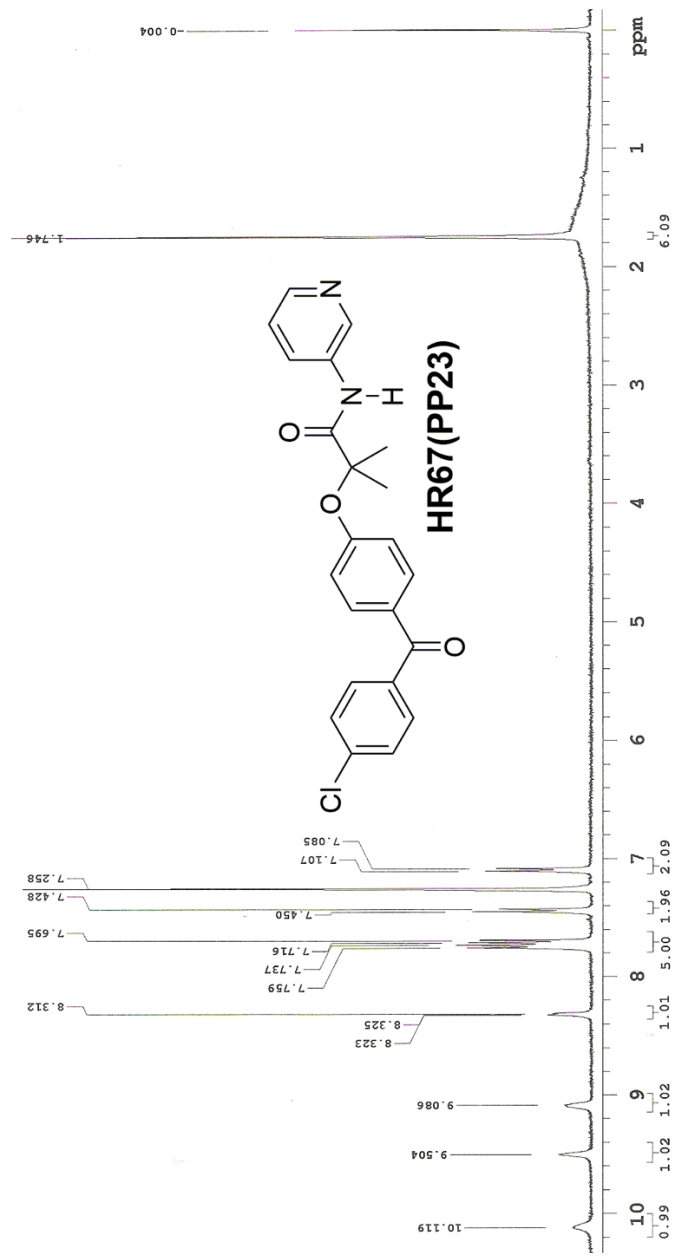
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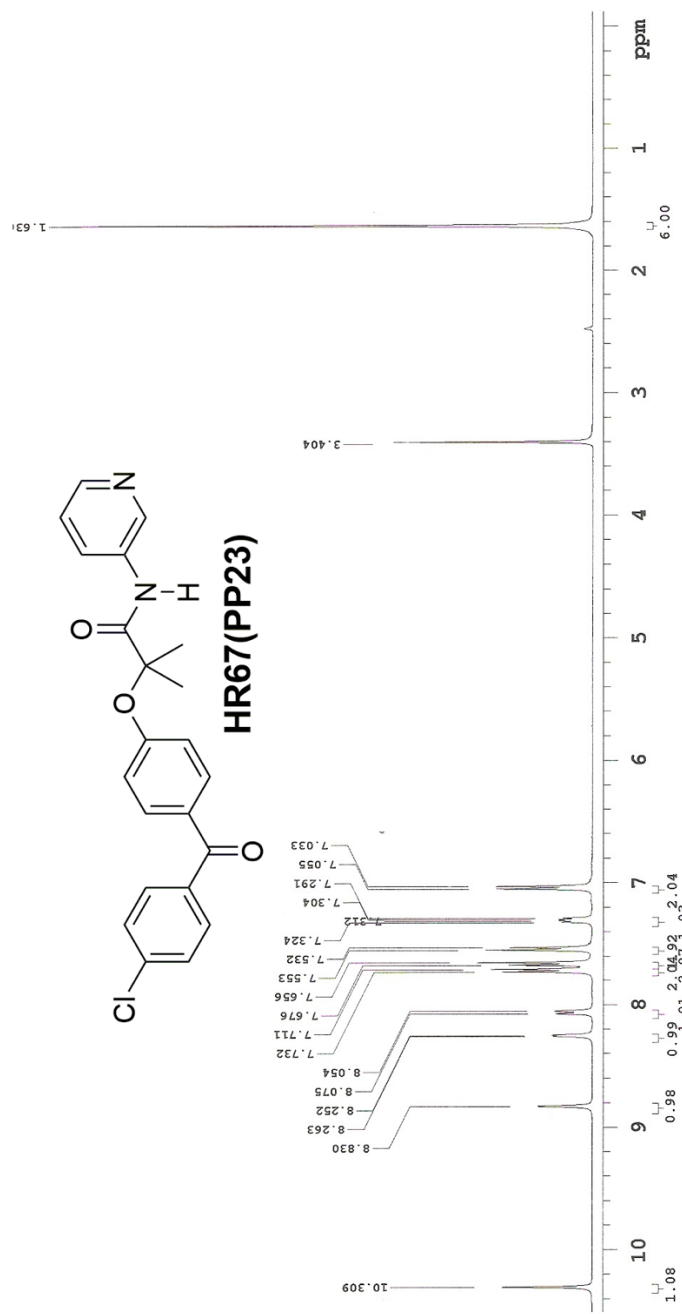
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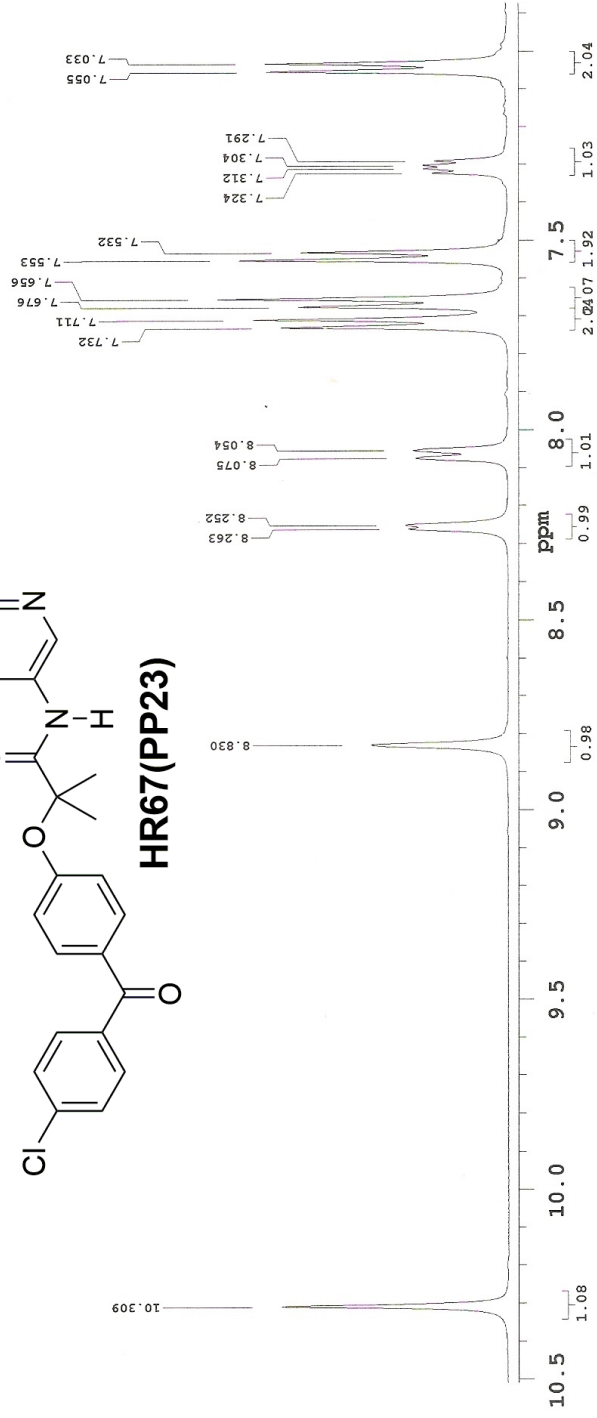
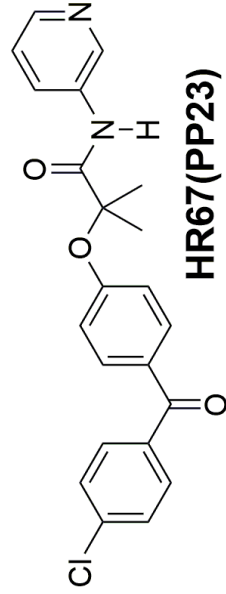
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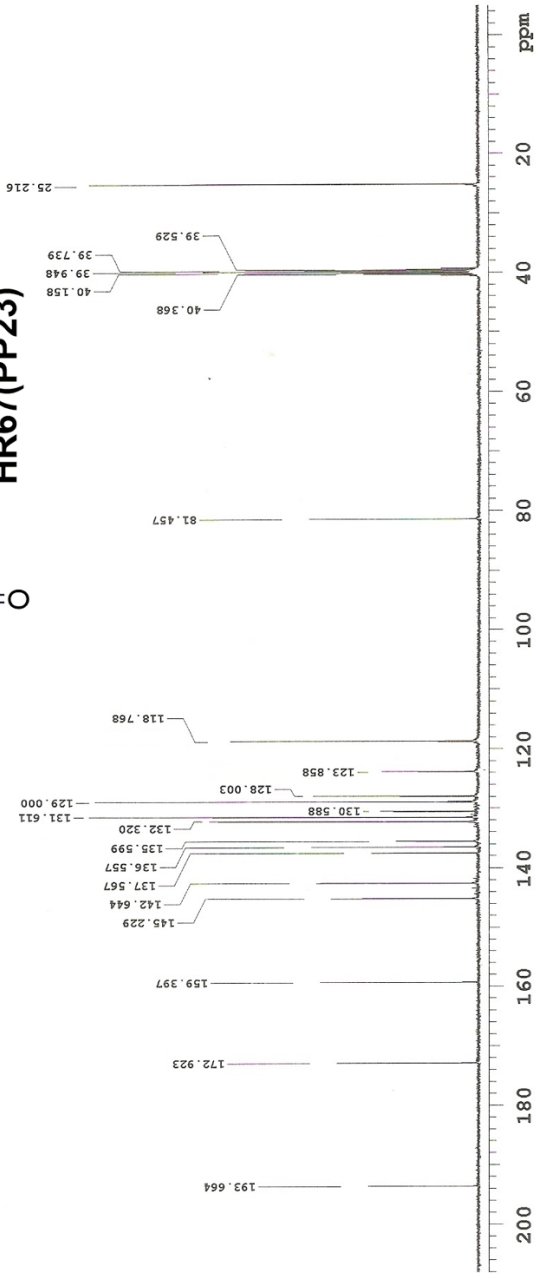
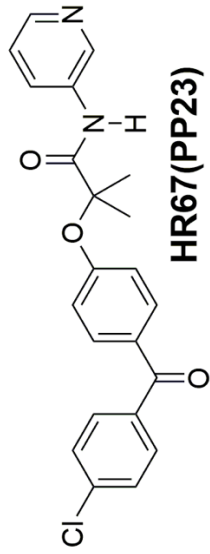
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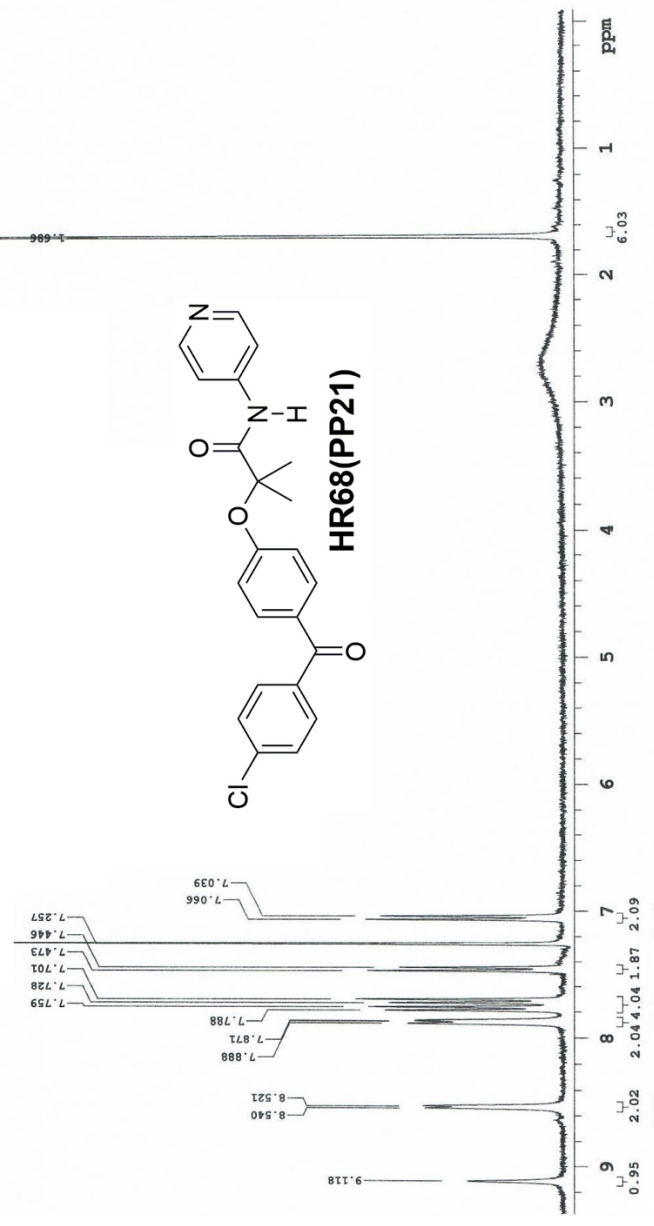
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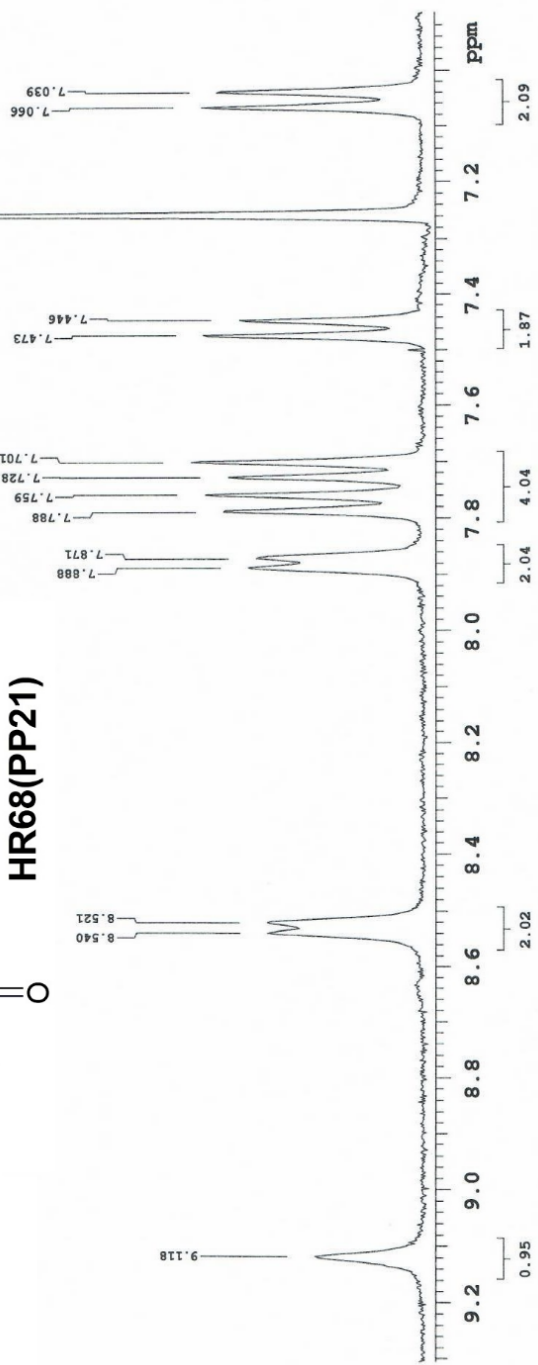
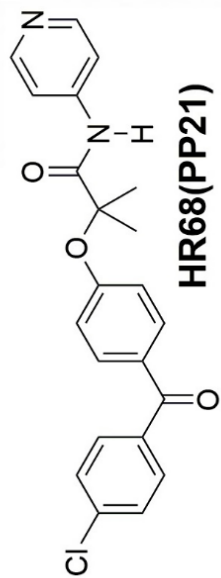
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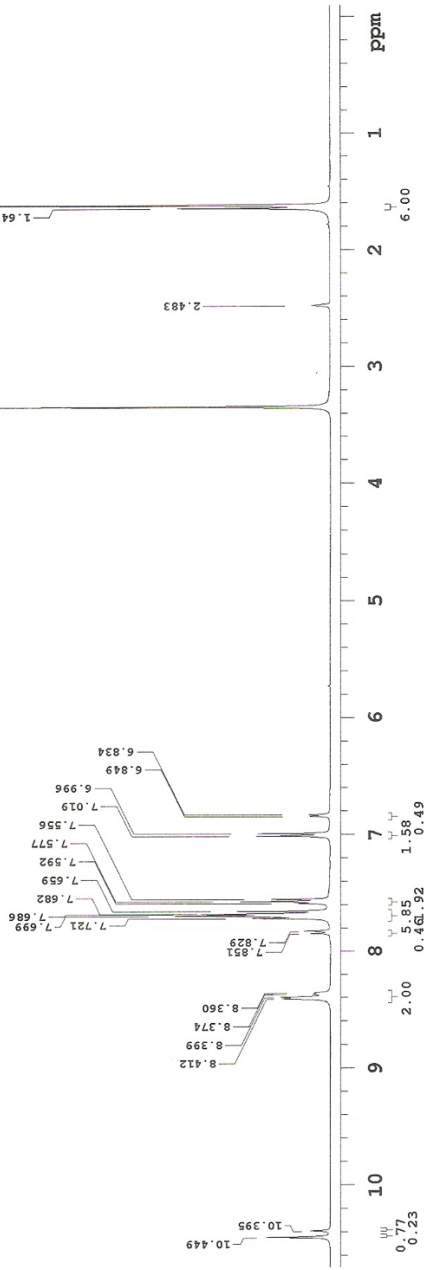
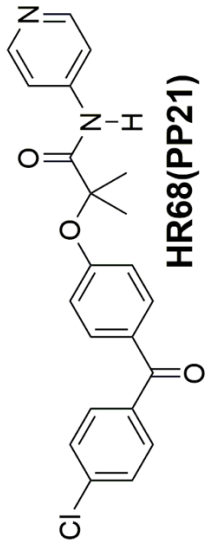
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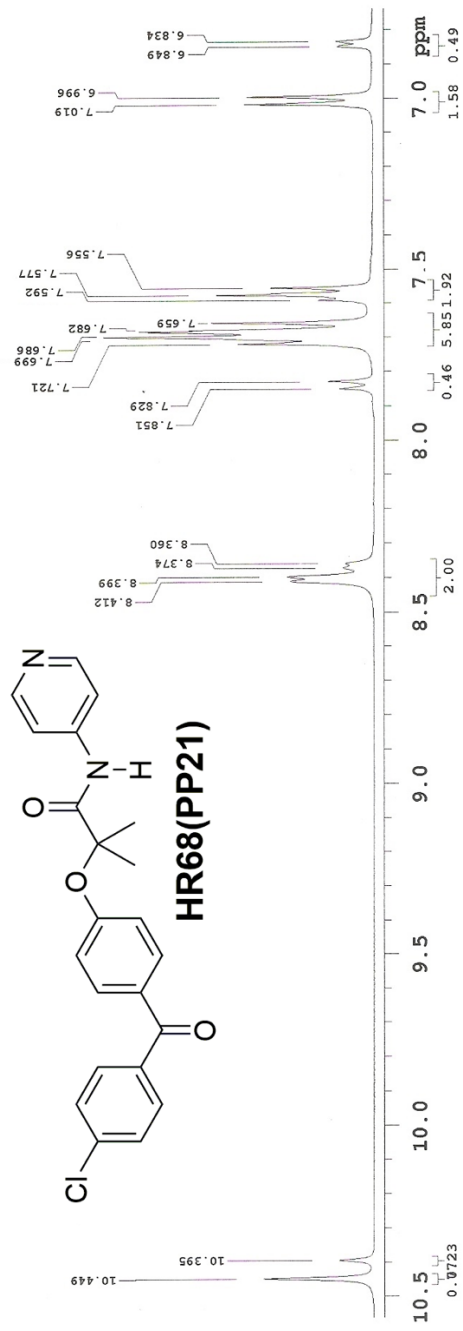
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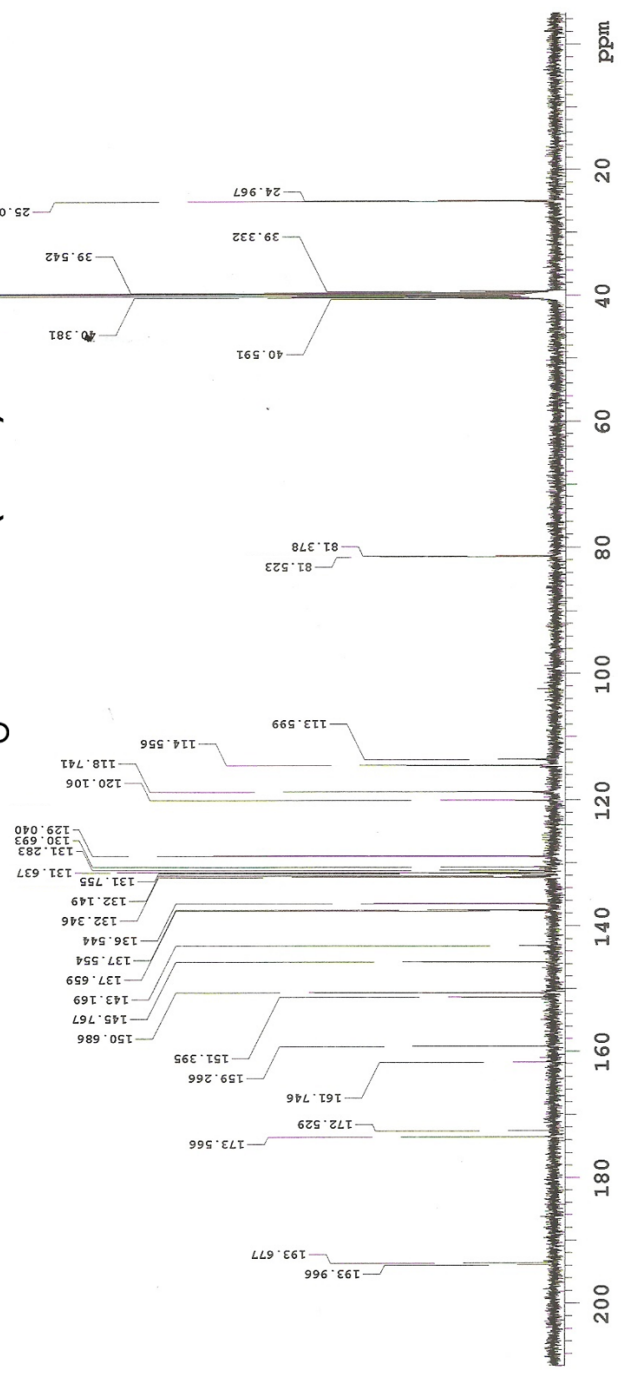
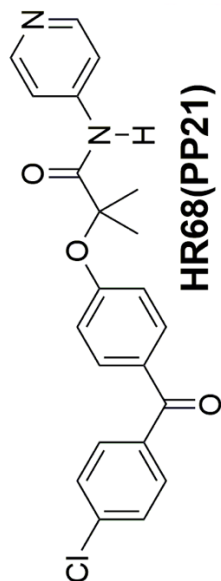
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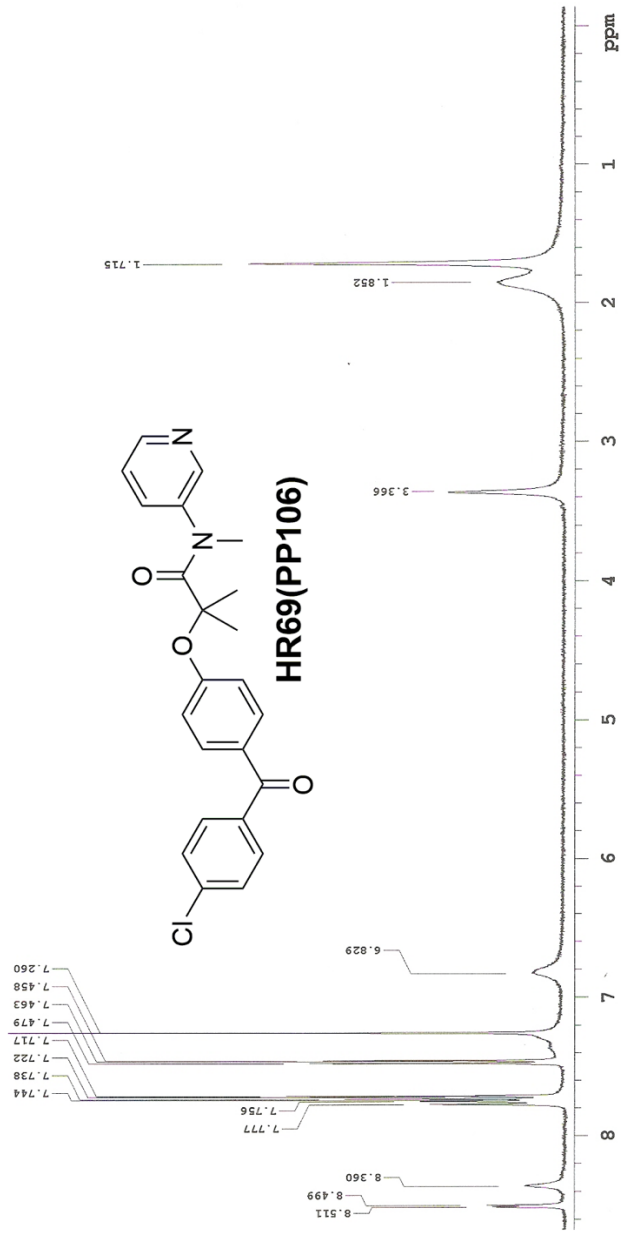
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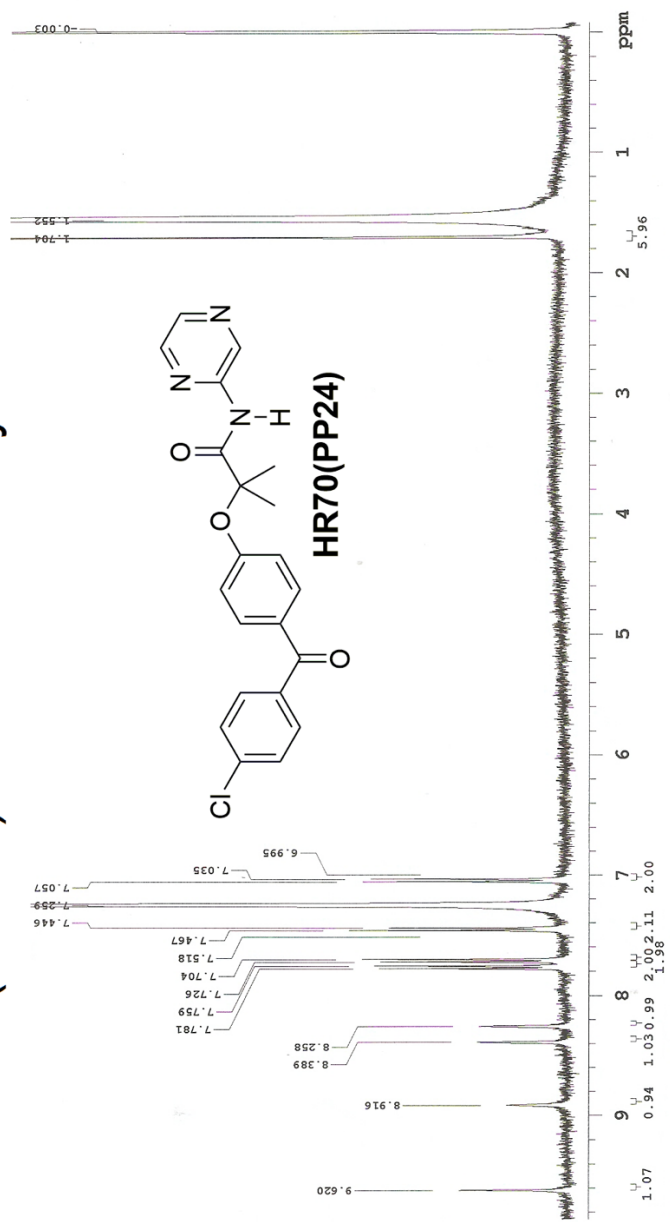
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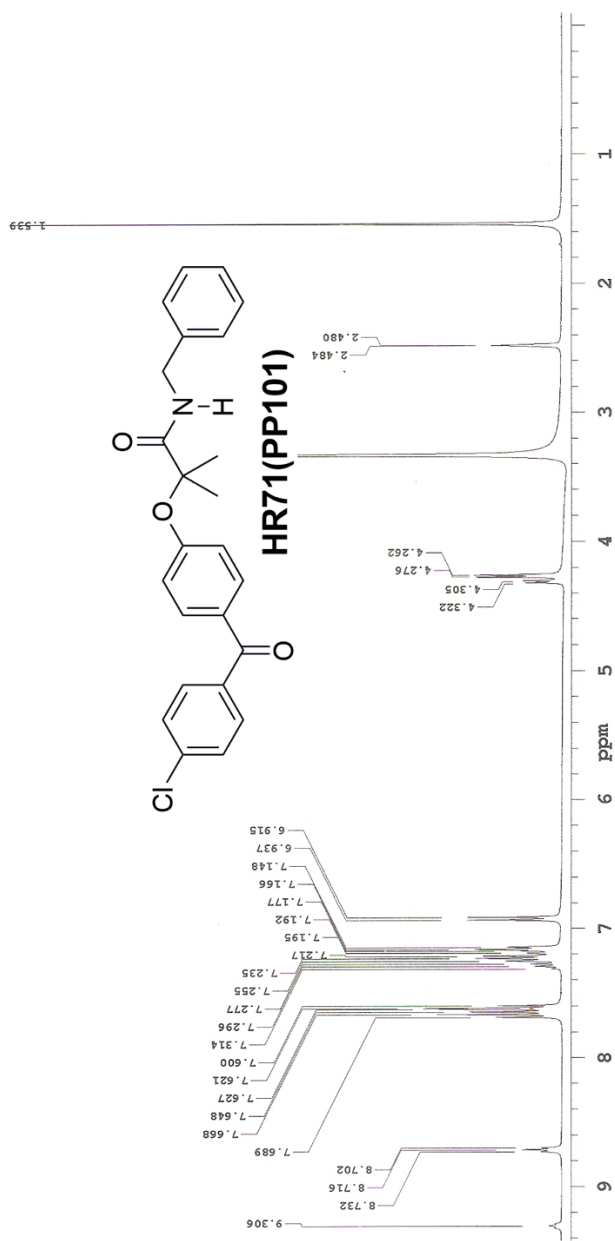
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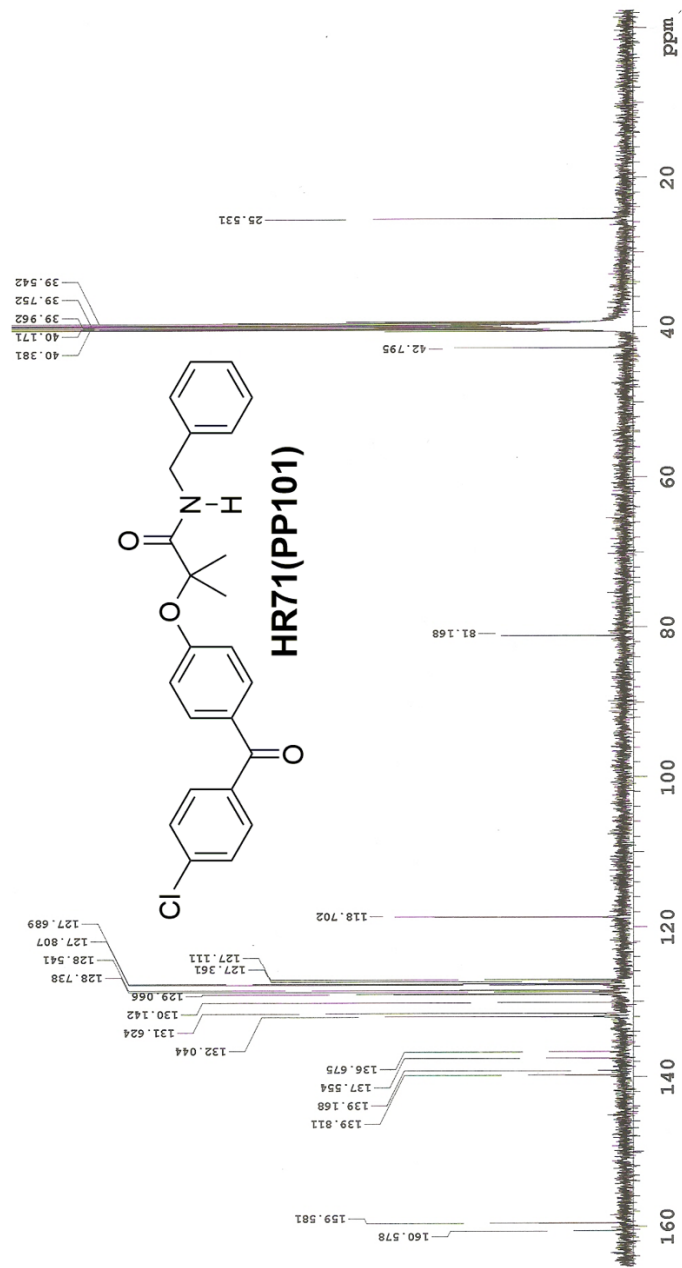
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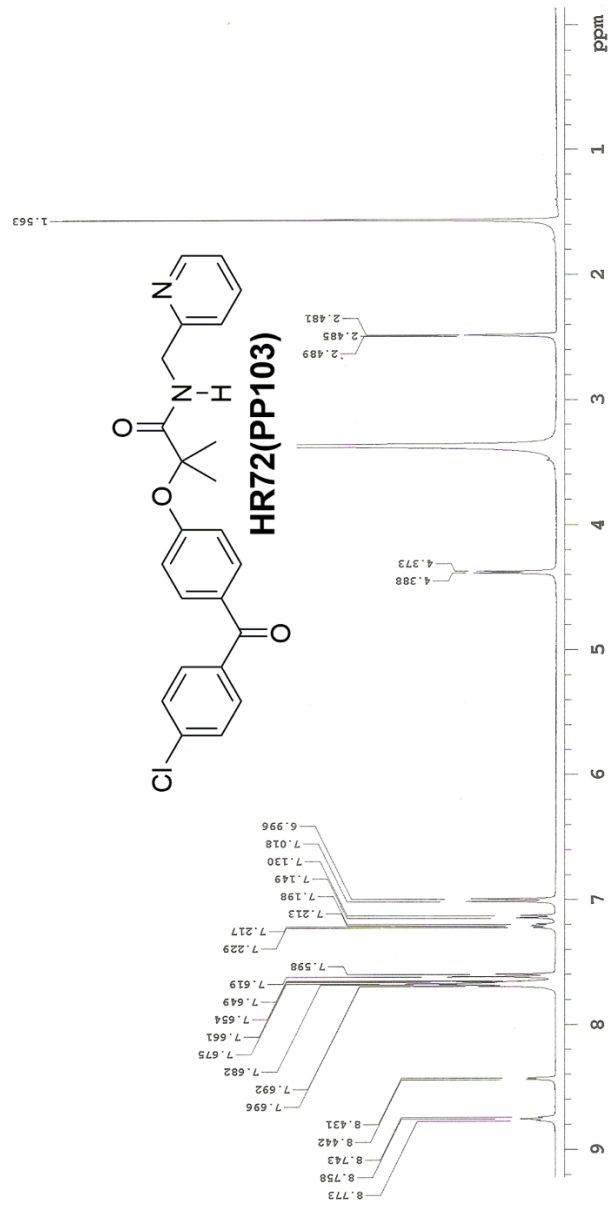
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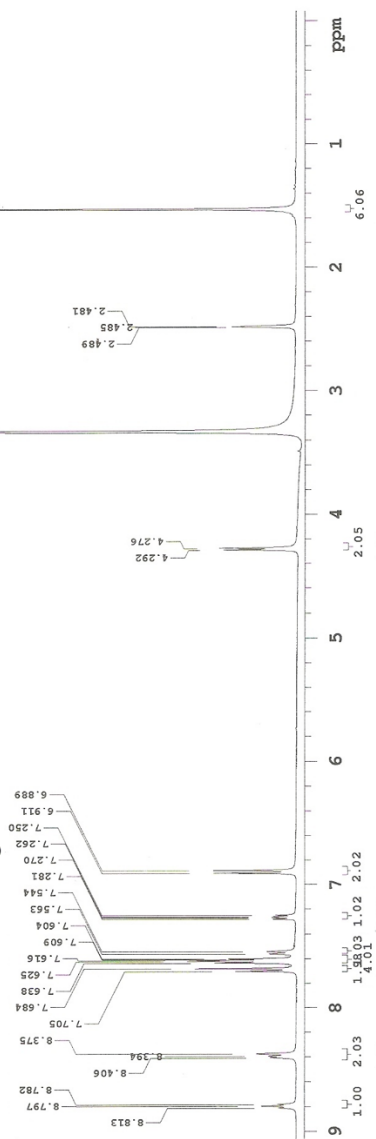
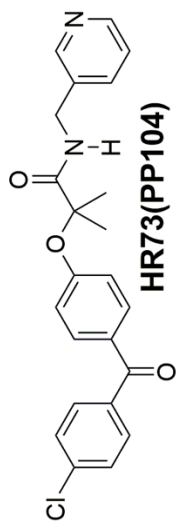
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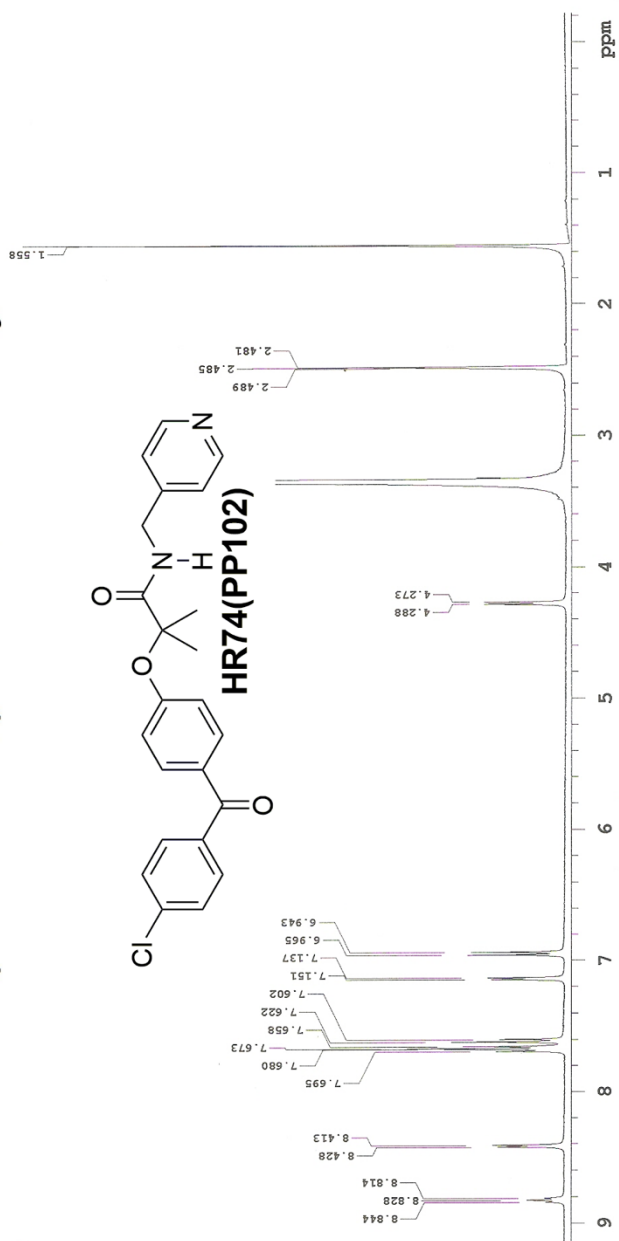


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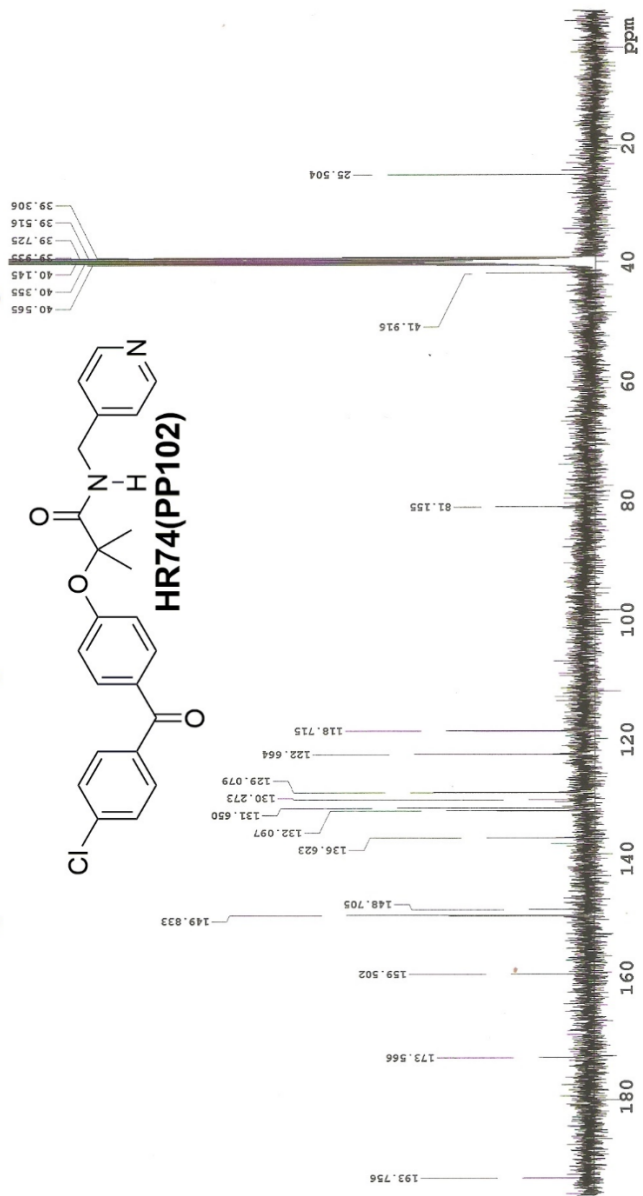




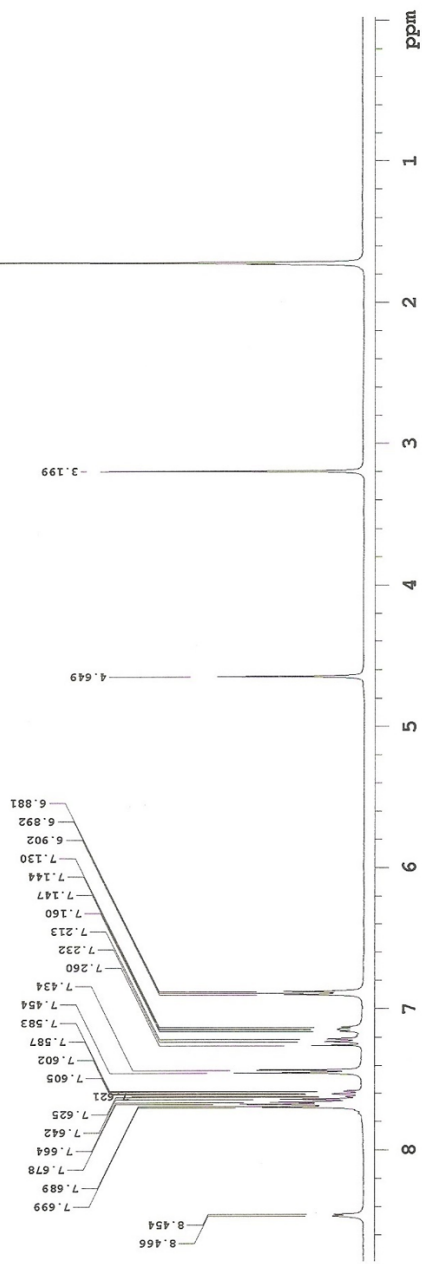
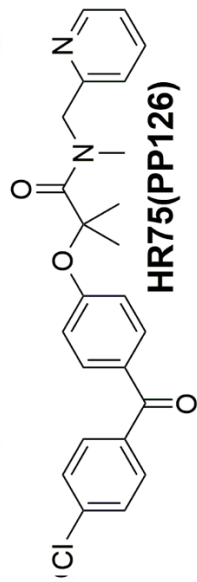
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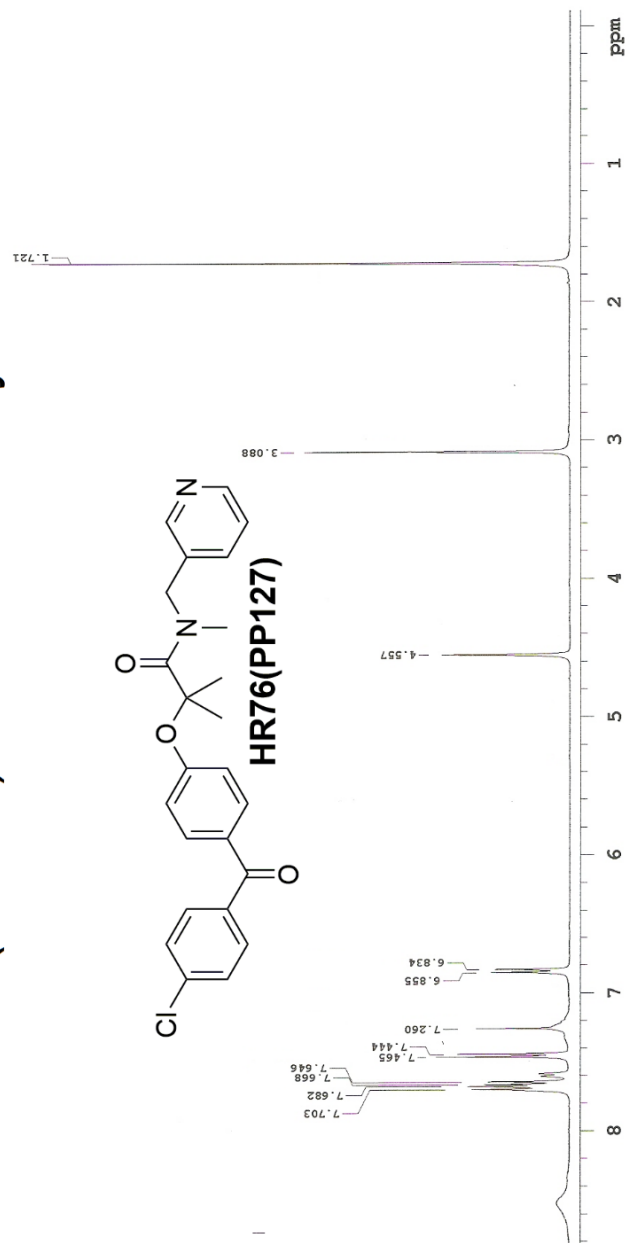
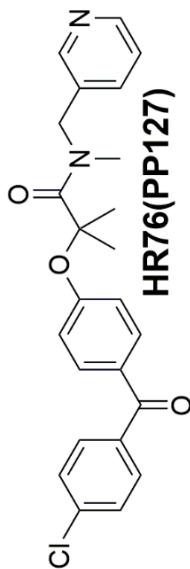
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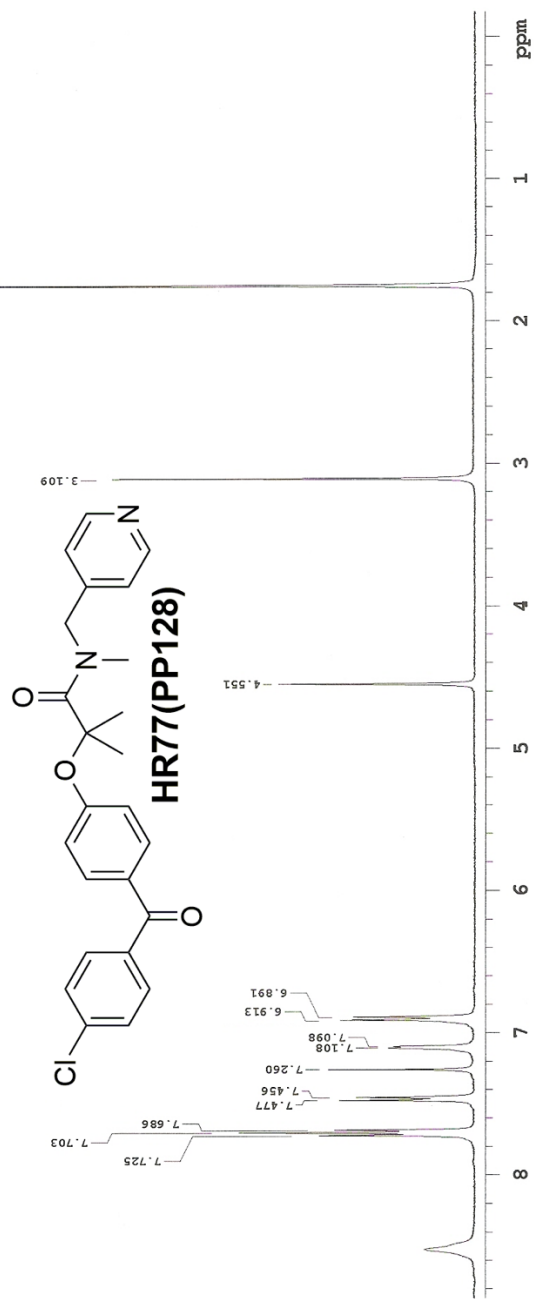
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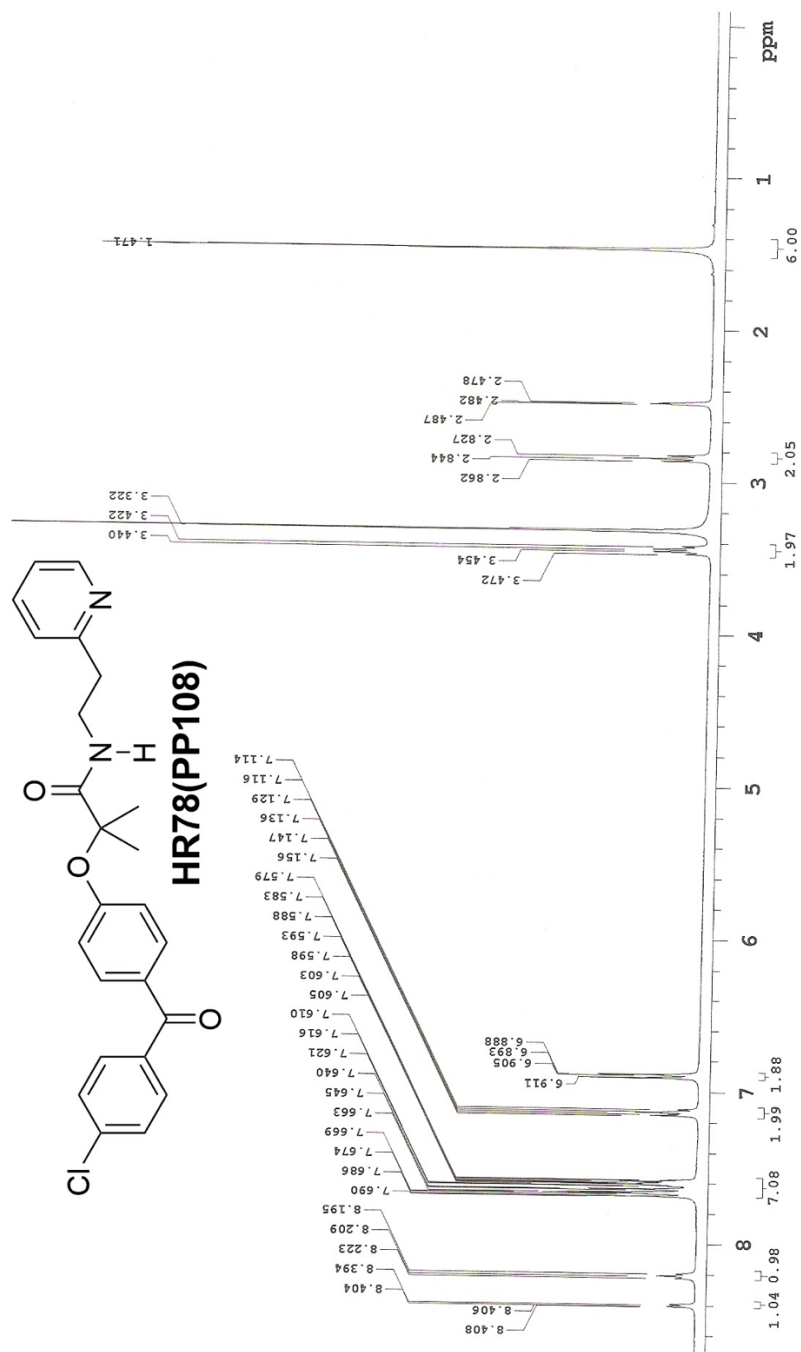
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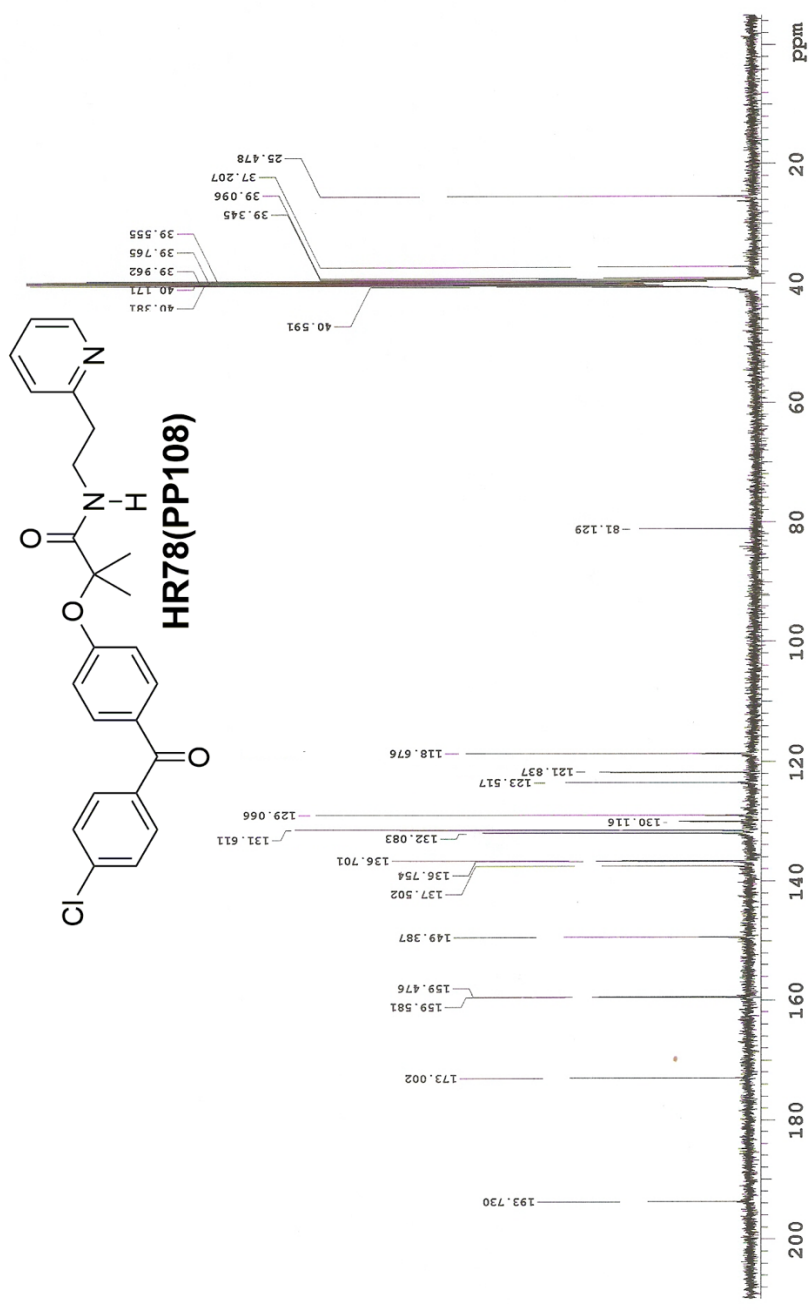
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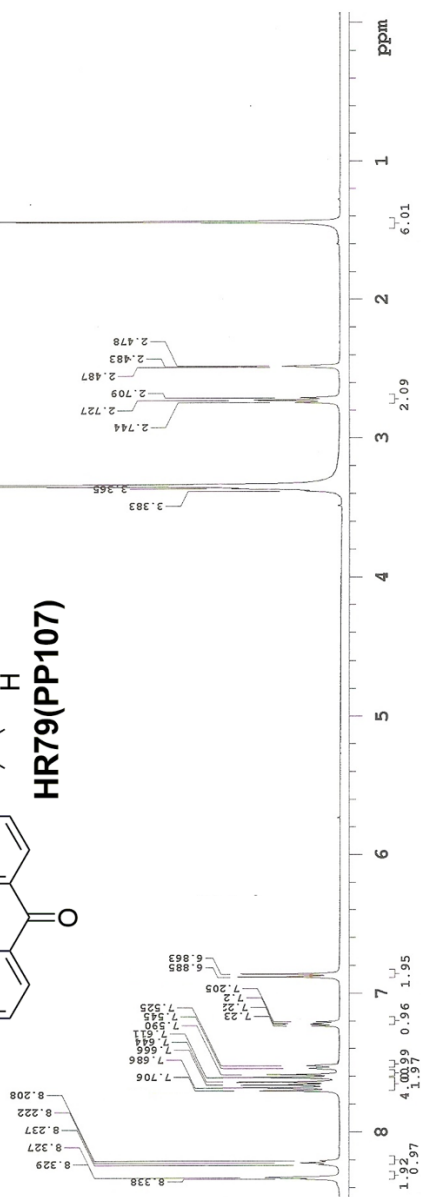
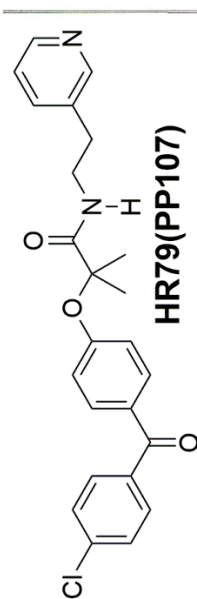
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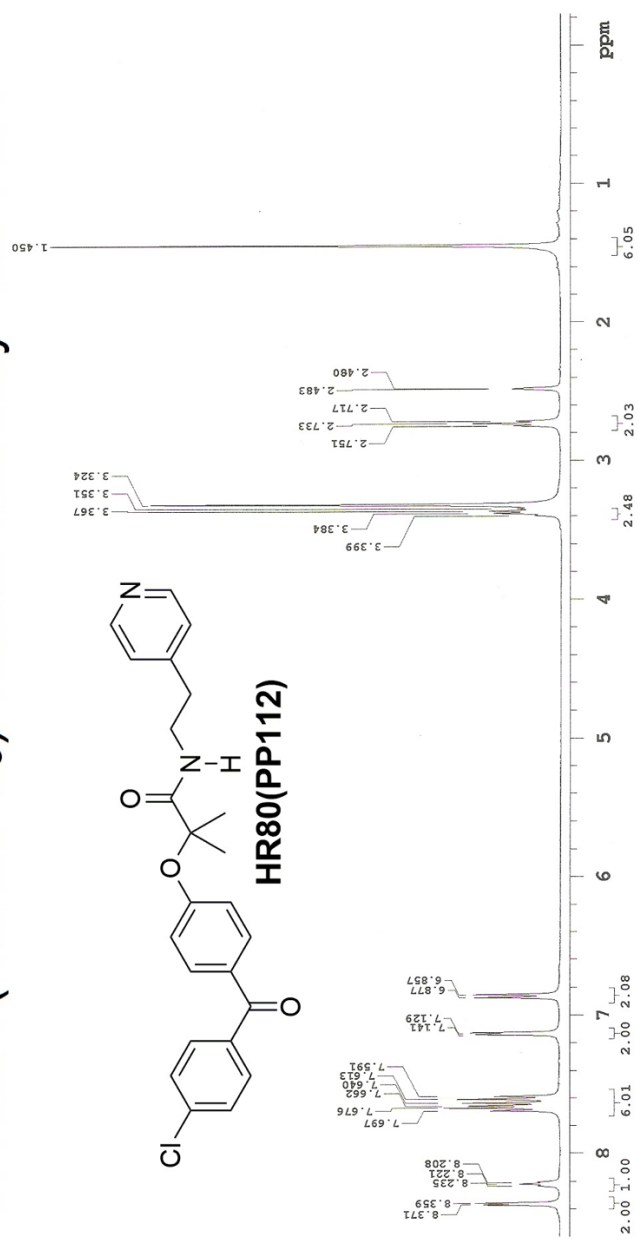
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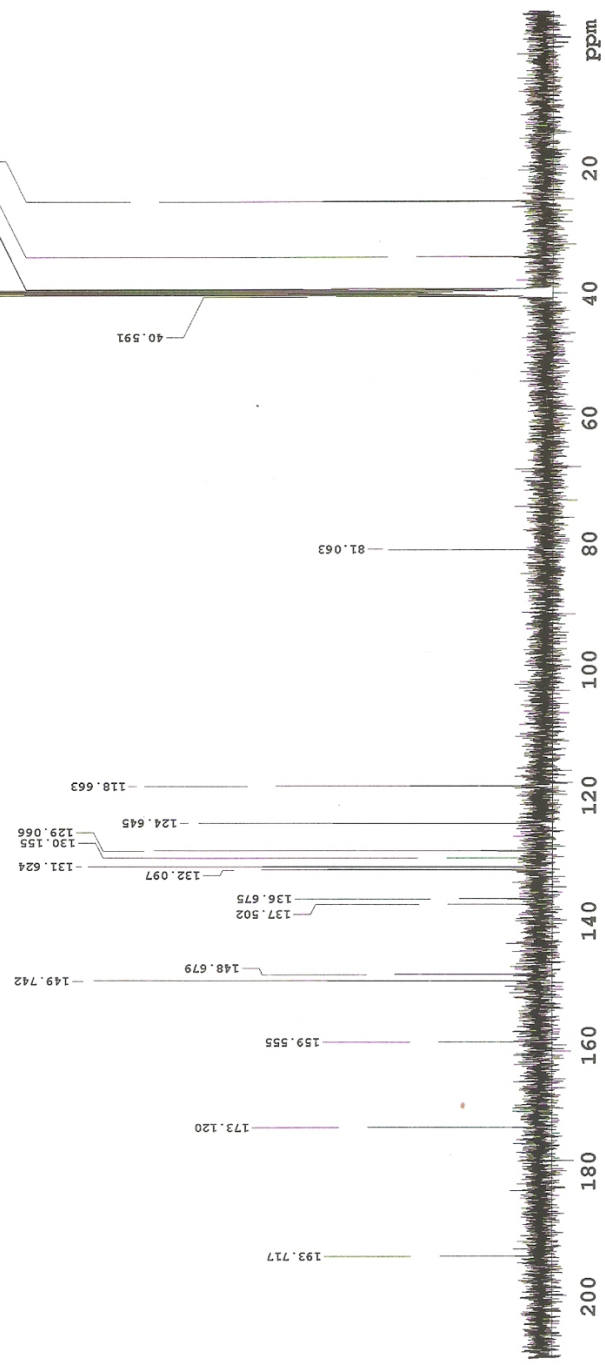
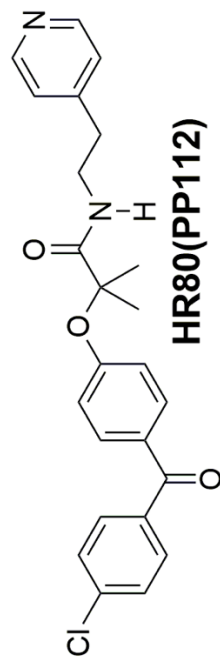
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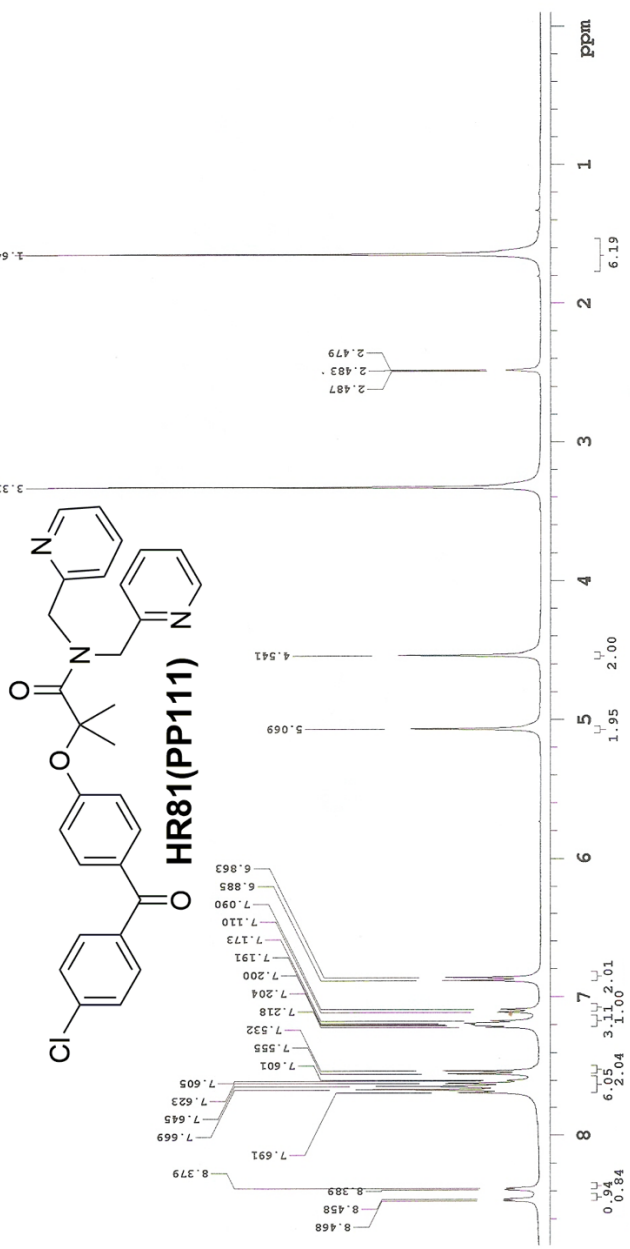
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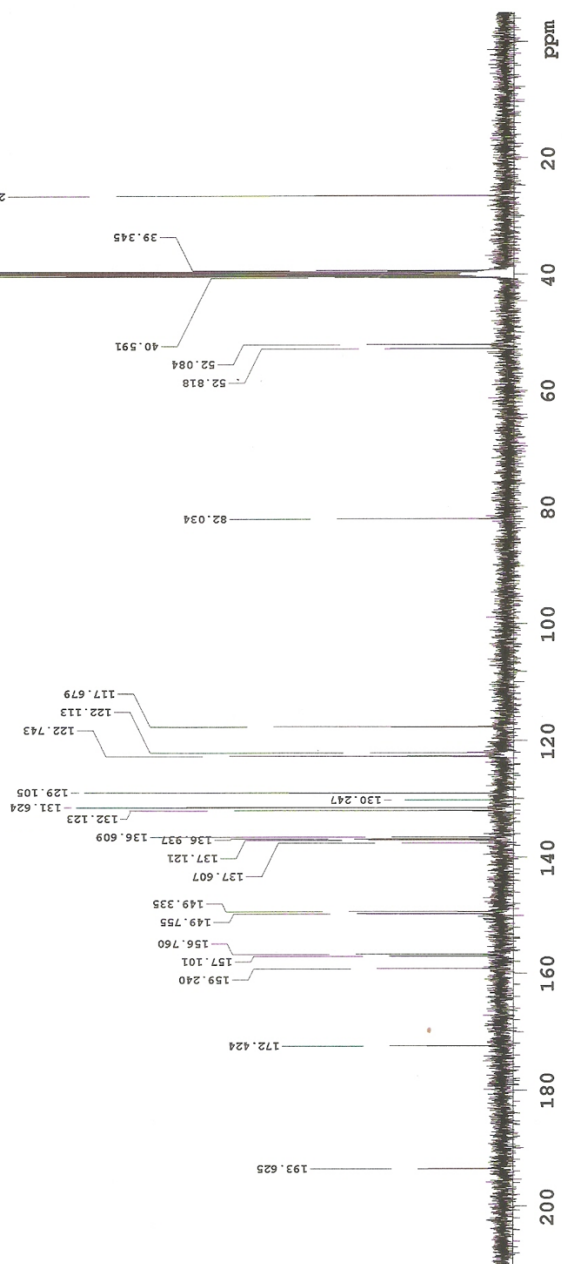
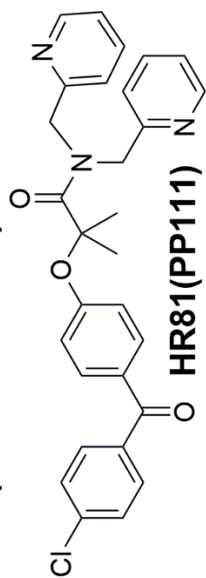
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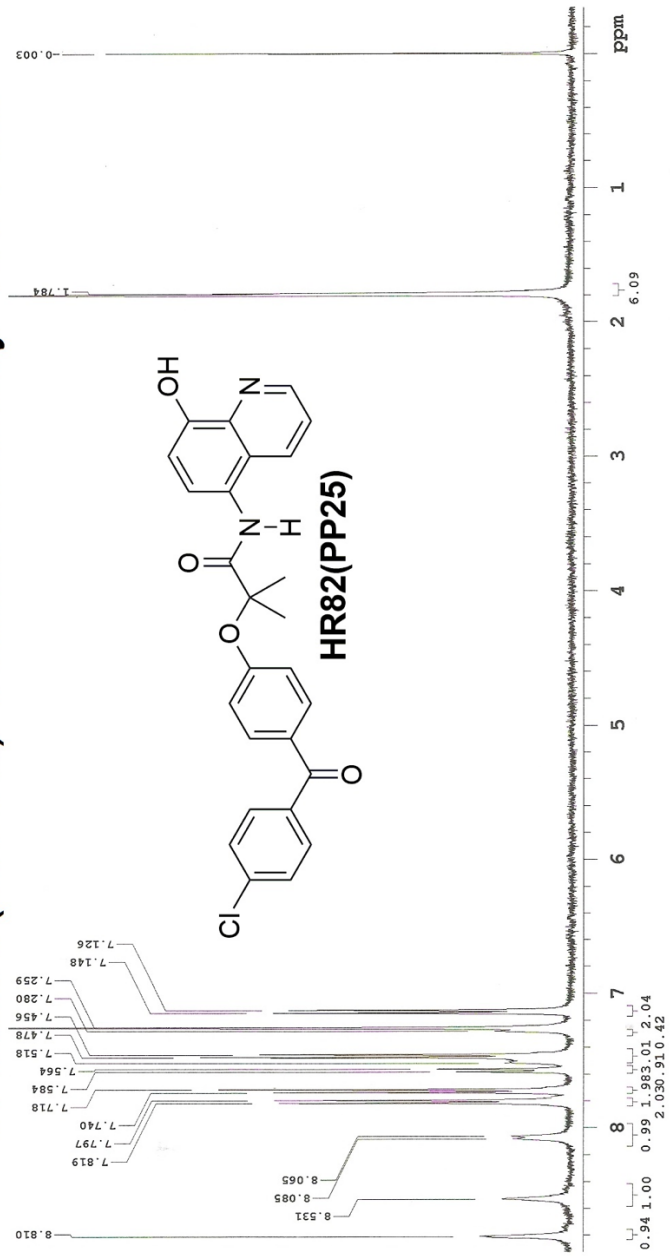
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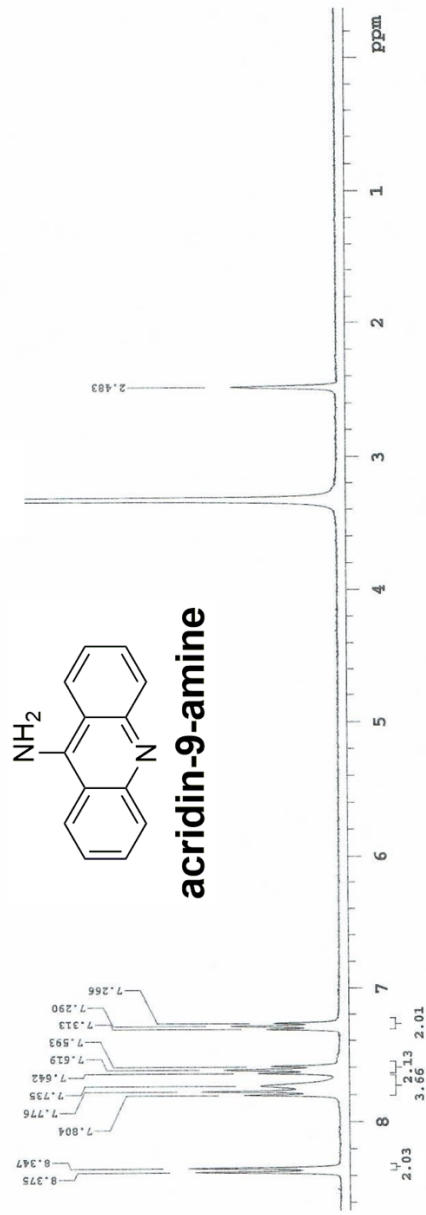
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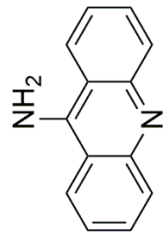
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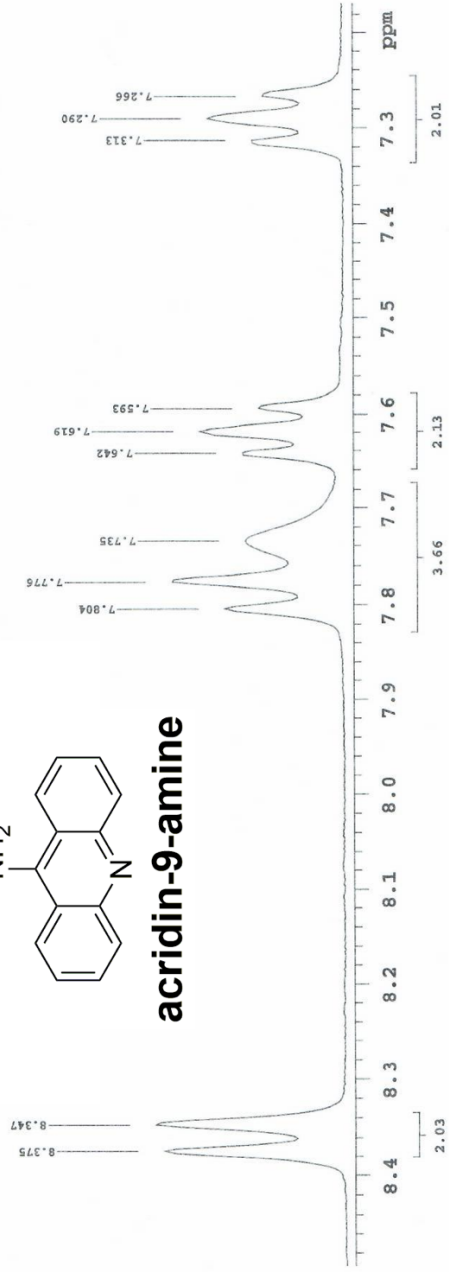
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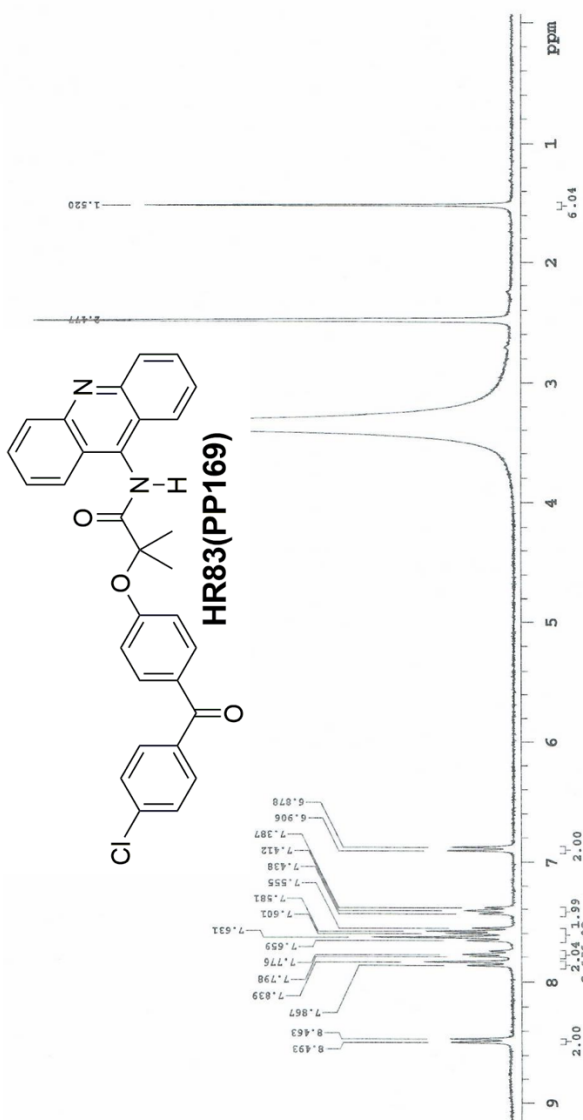
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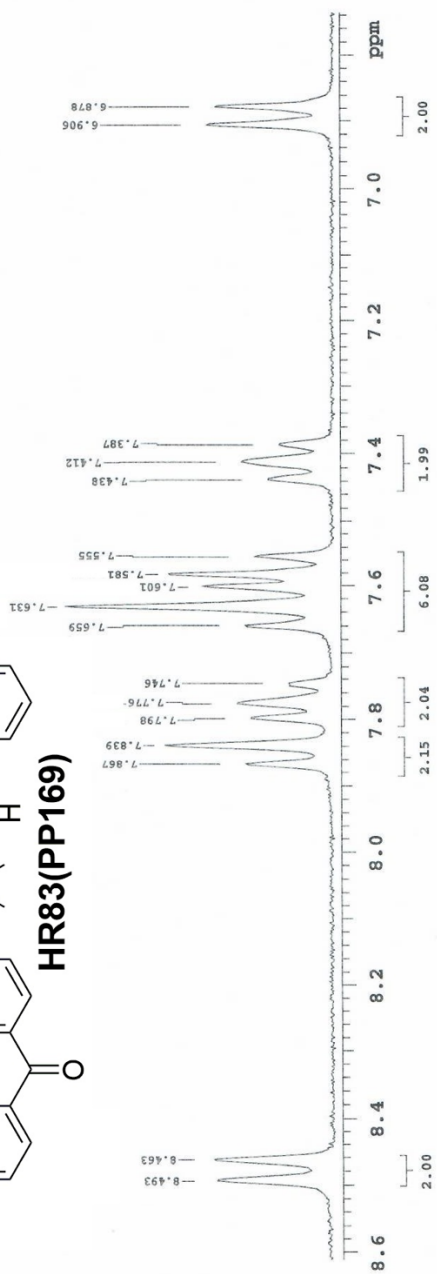
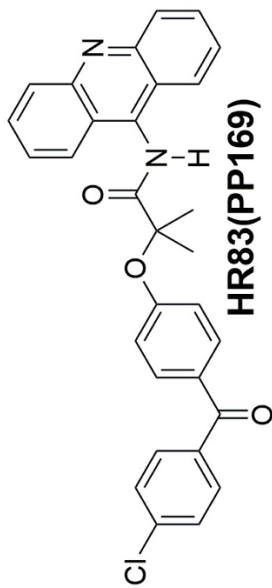
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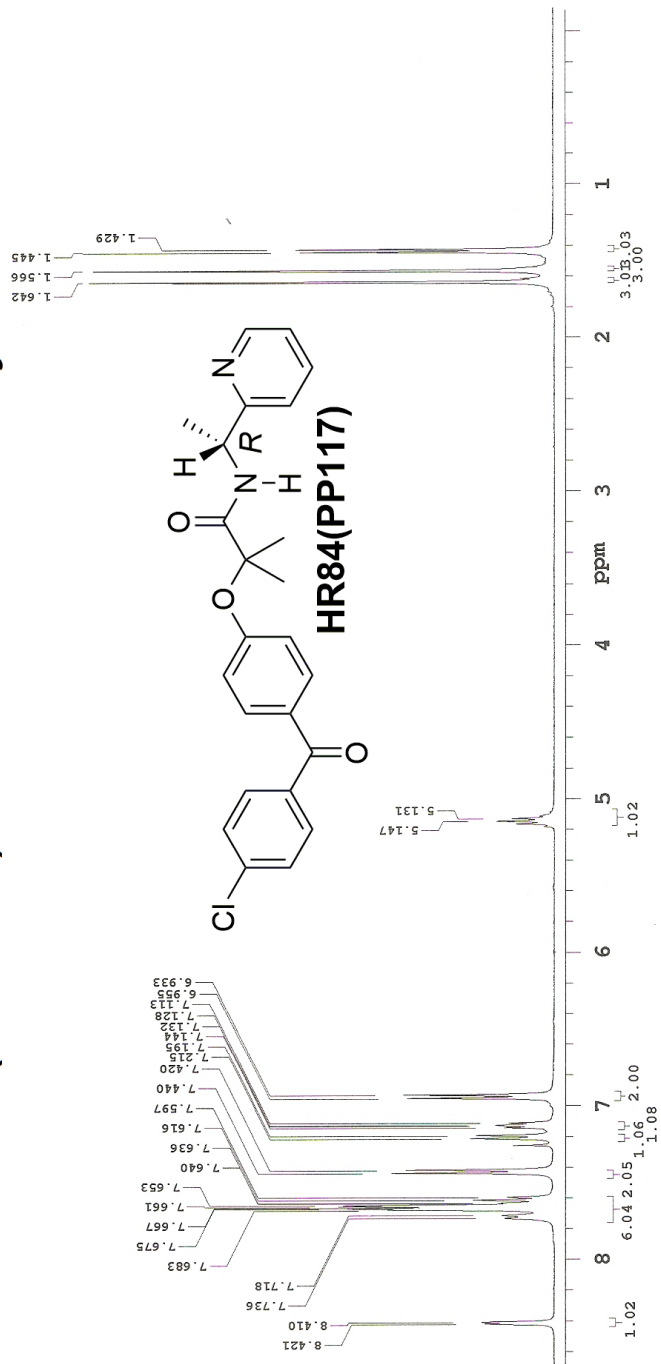
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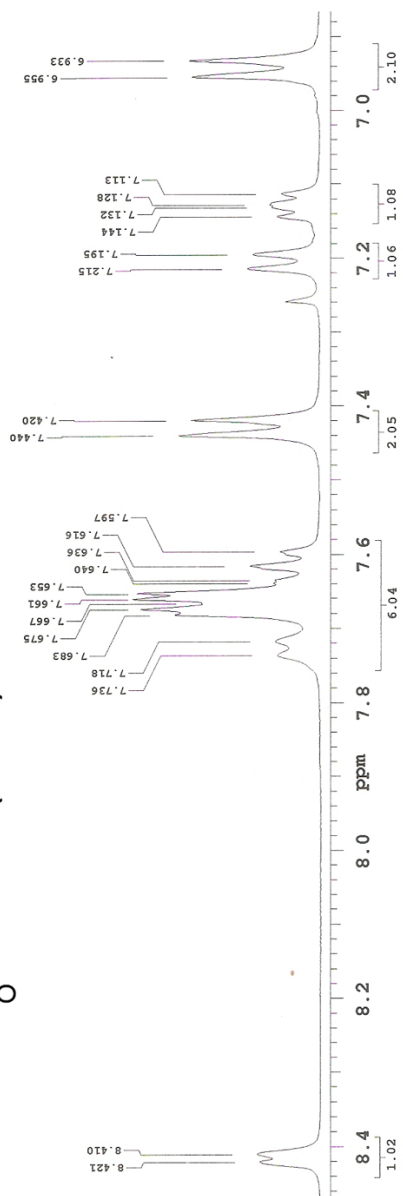
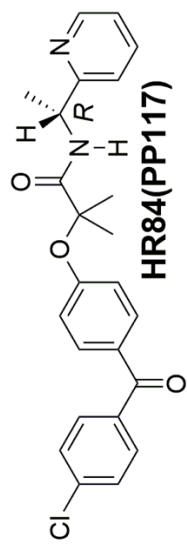
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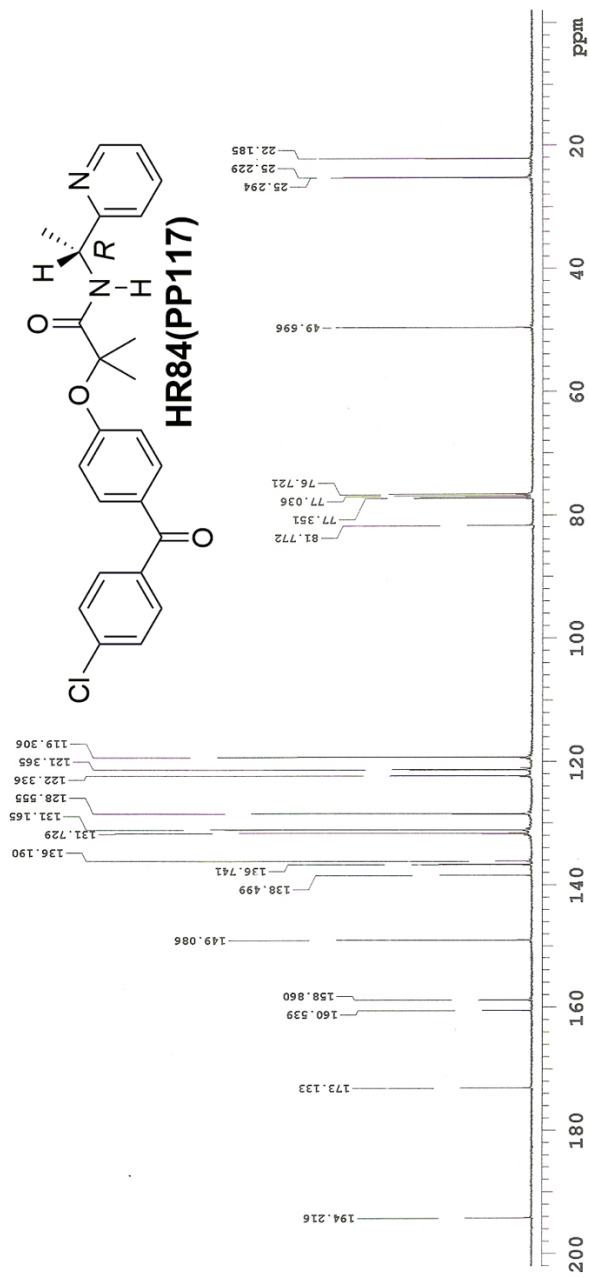
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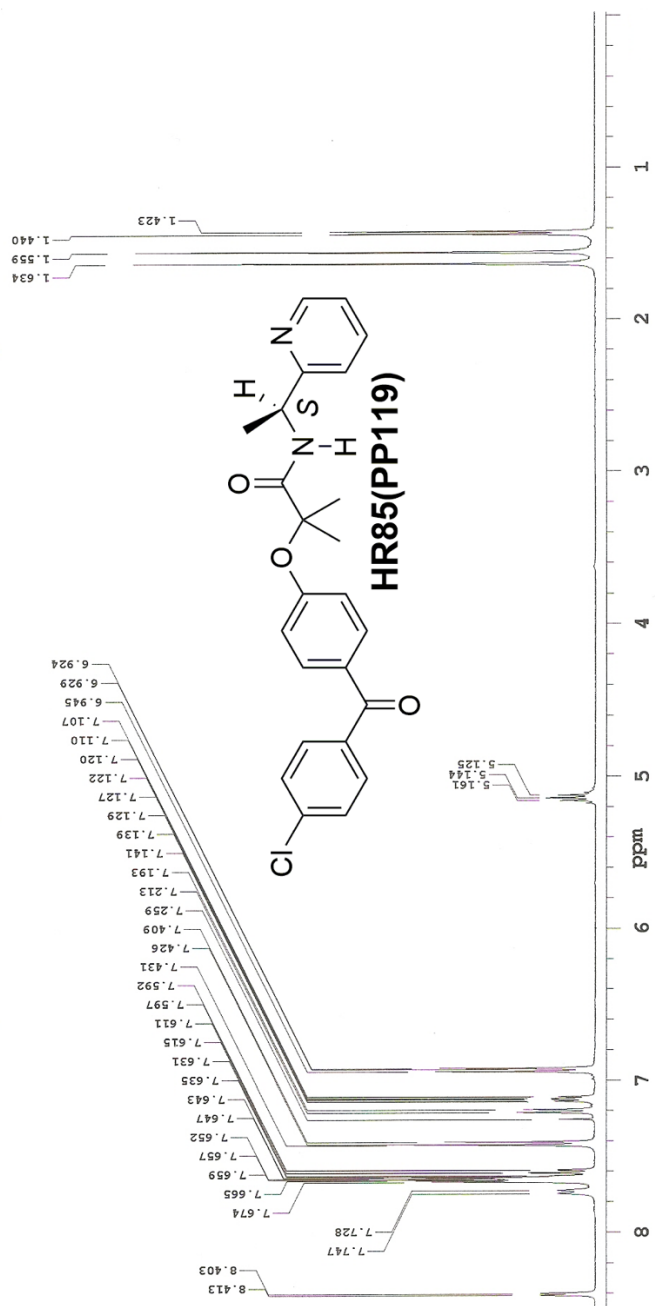
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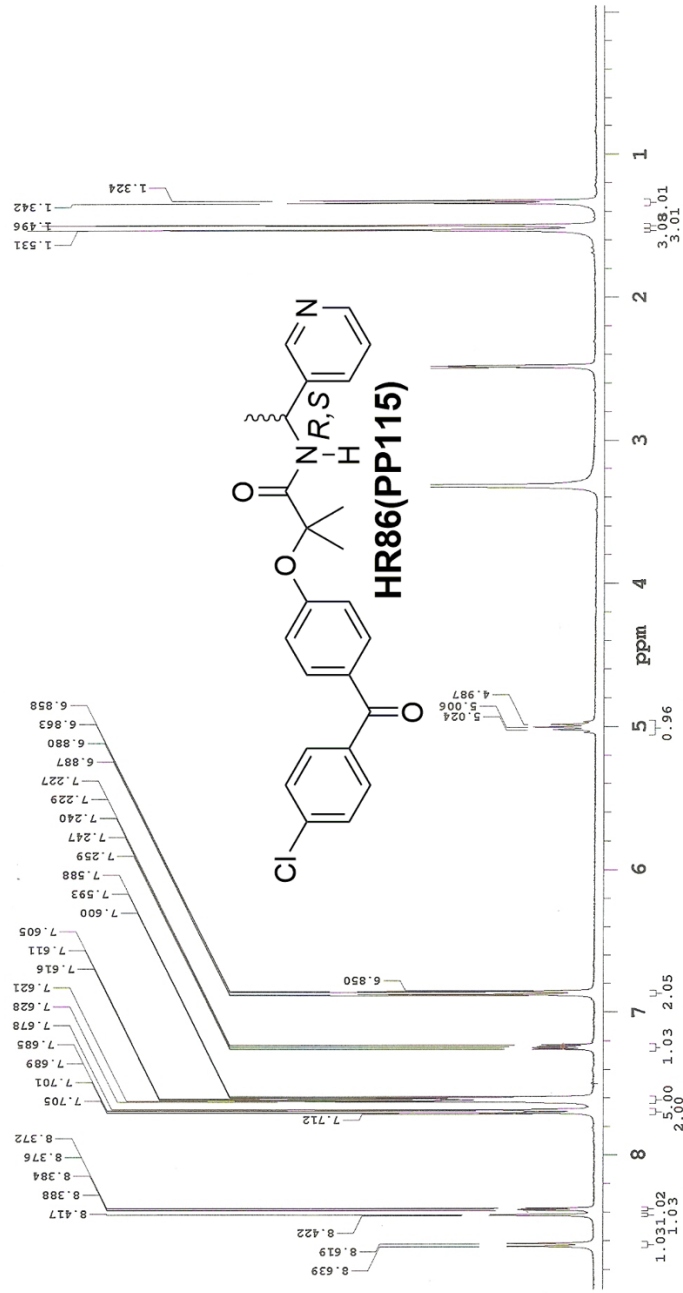
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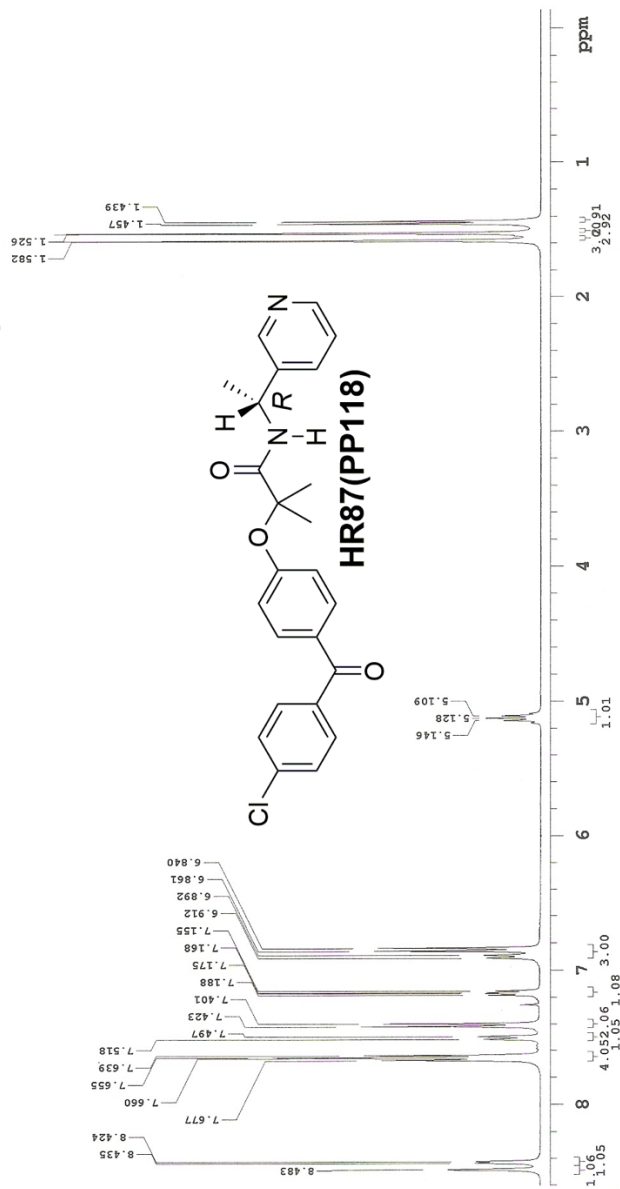
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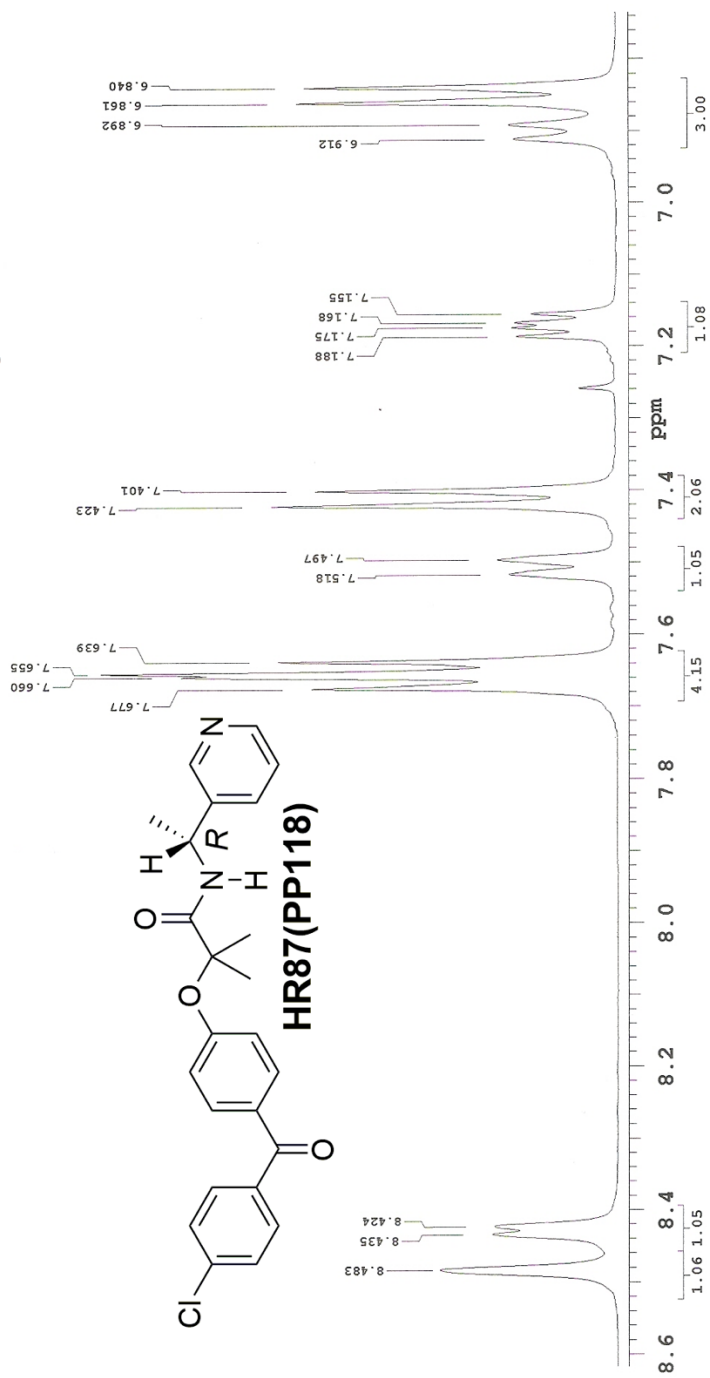
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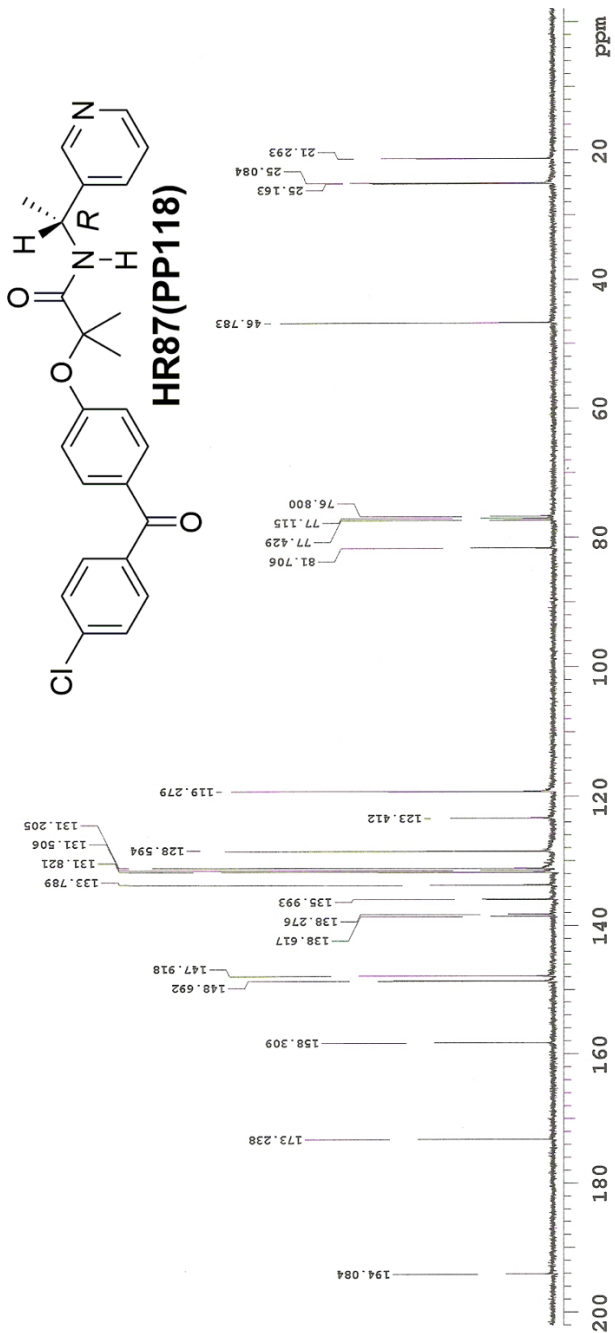
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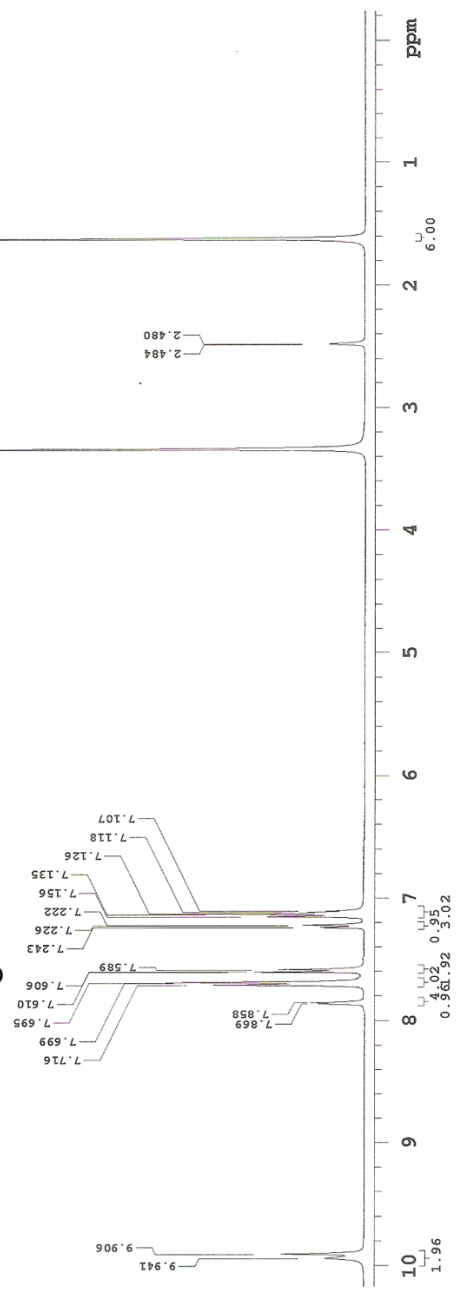
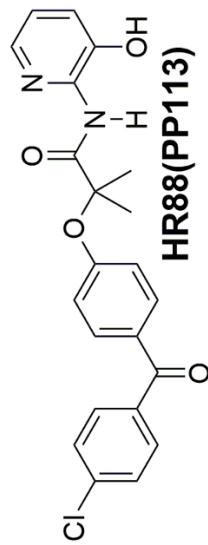
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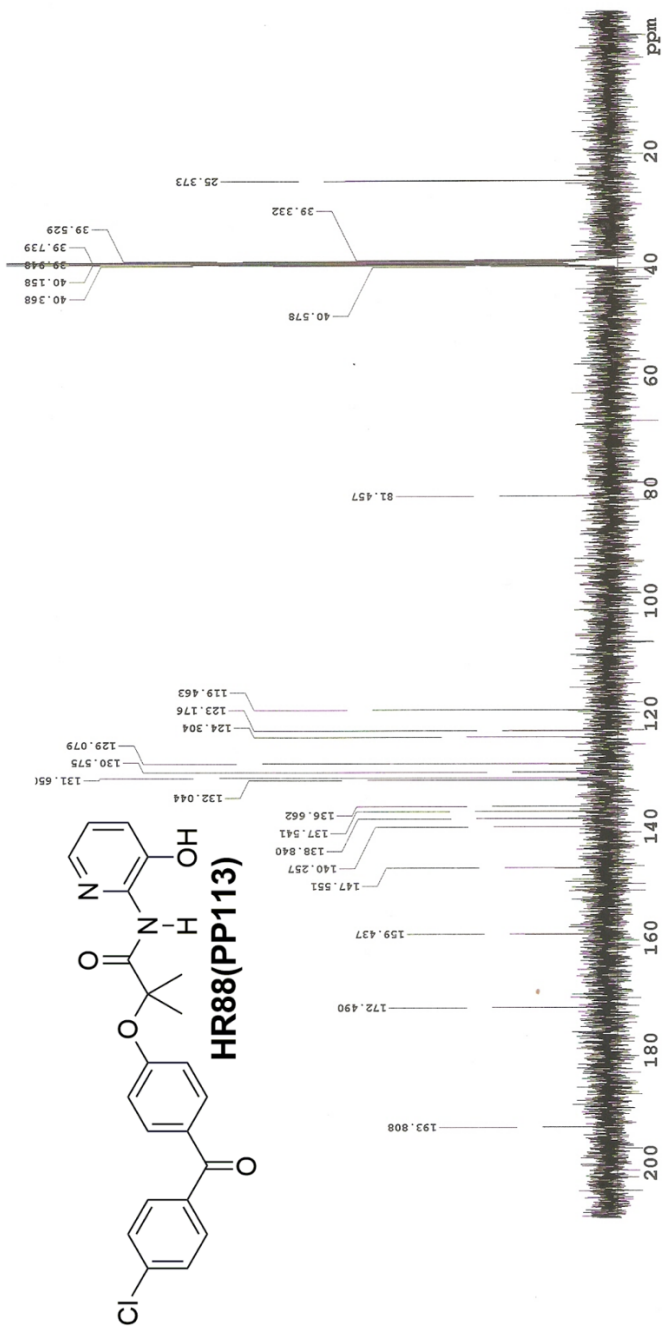
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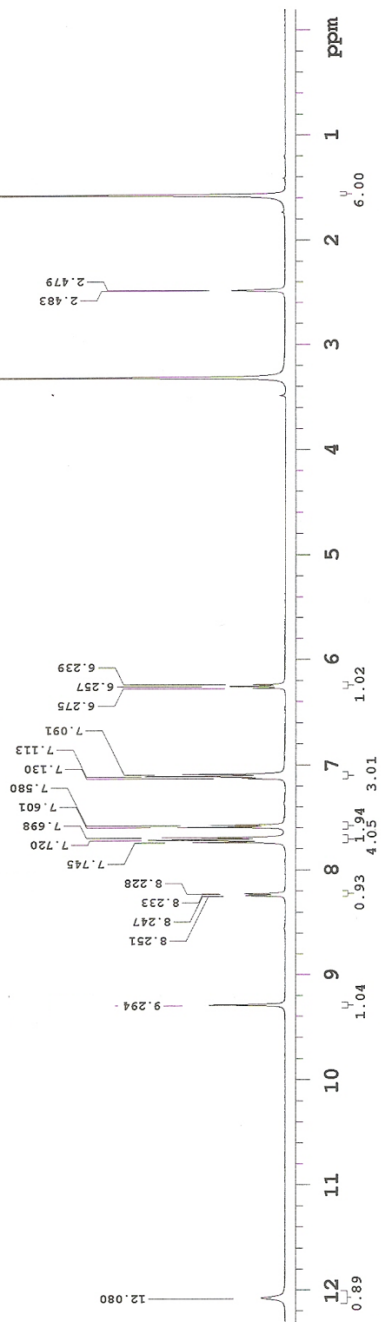
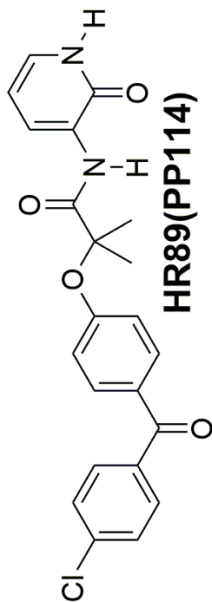
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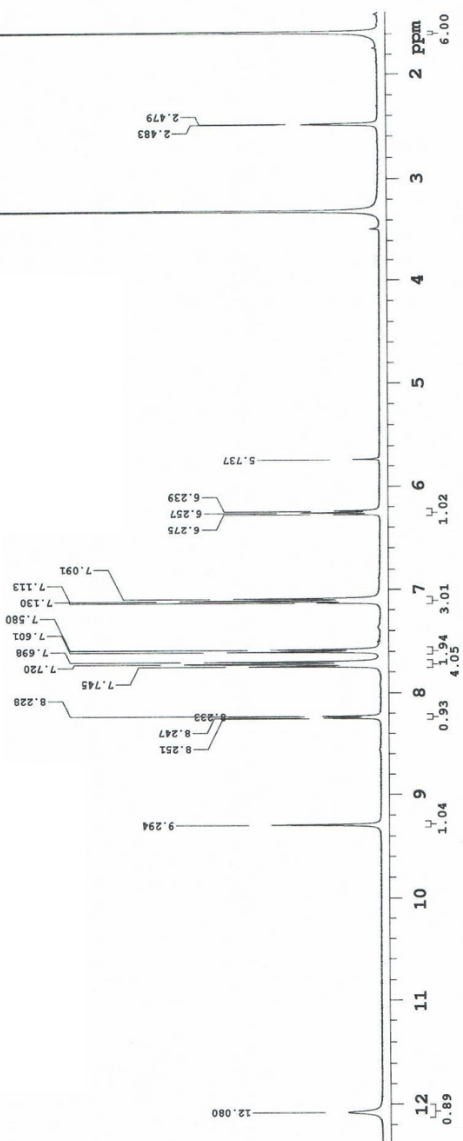
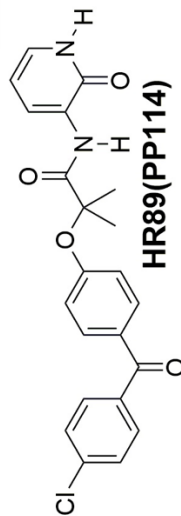
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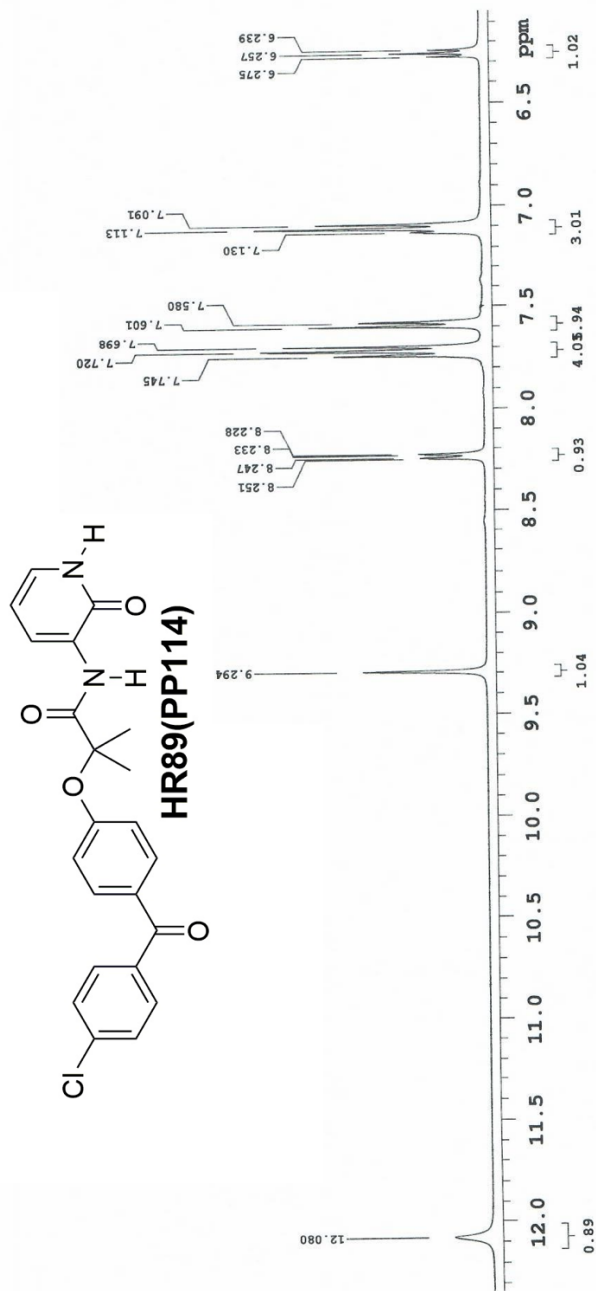
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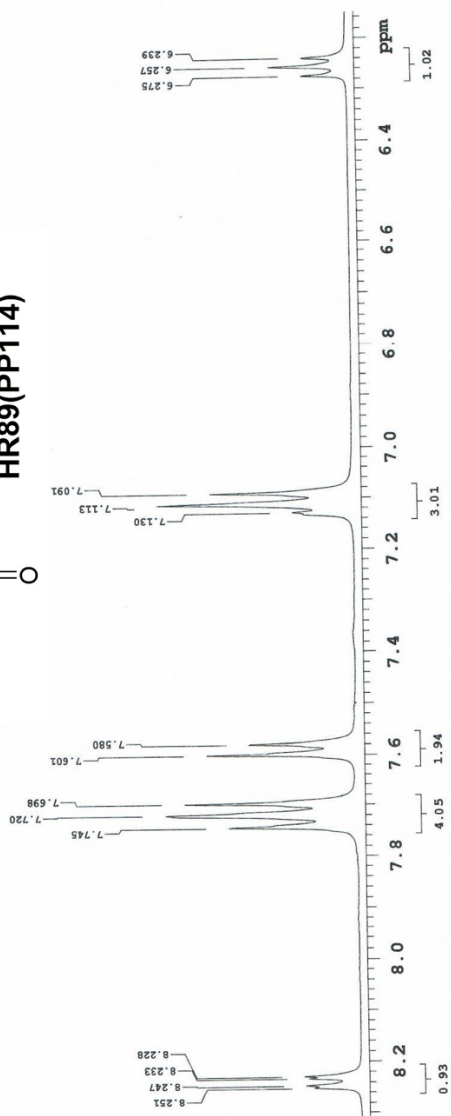
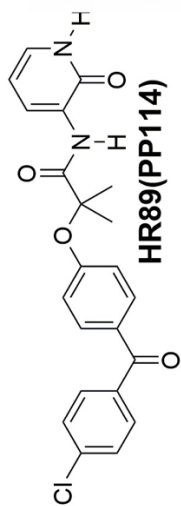
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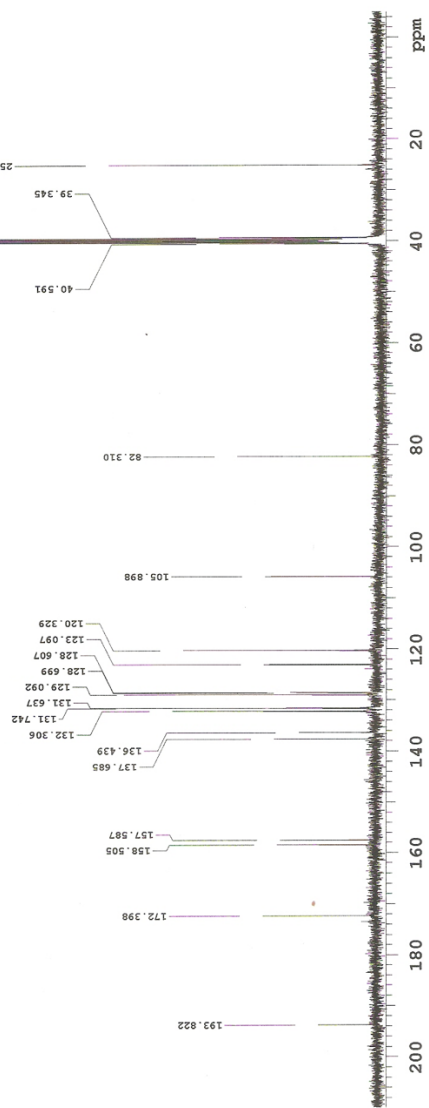
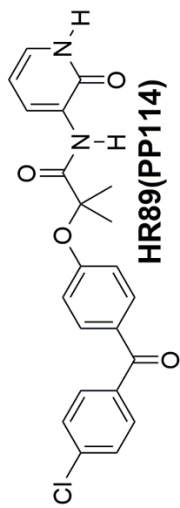
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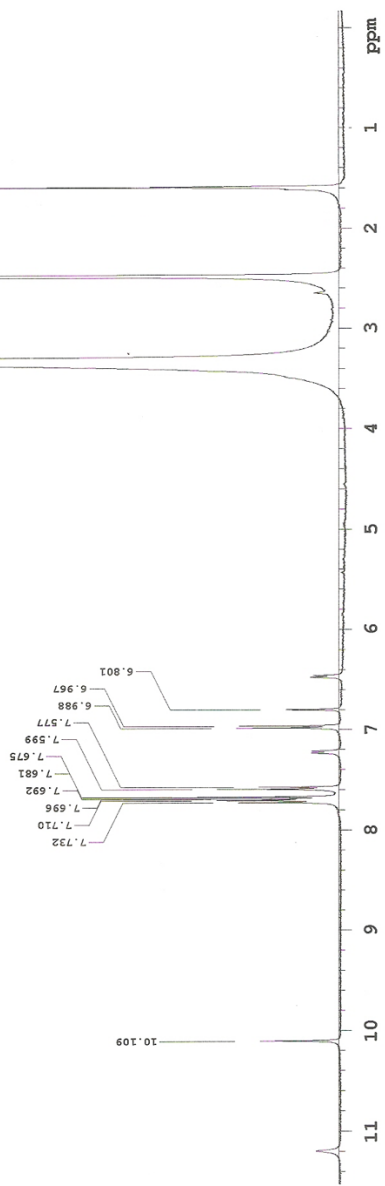
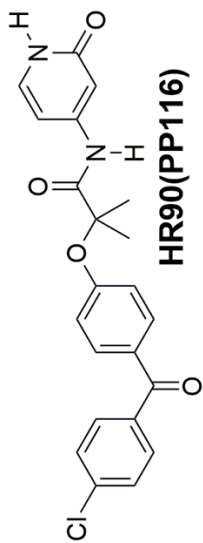
# <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) Varian Mercury 400 Plus



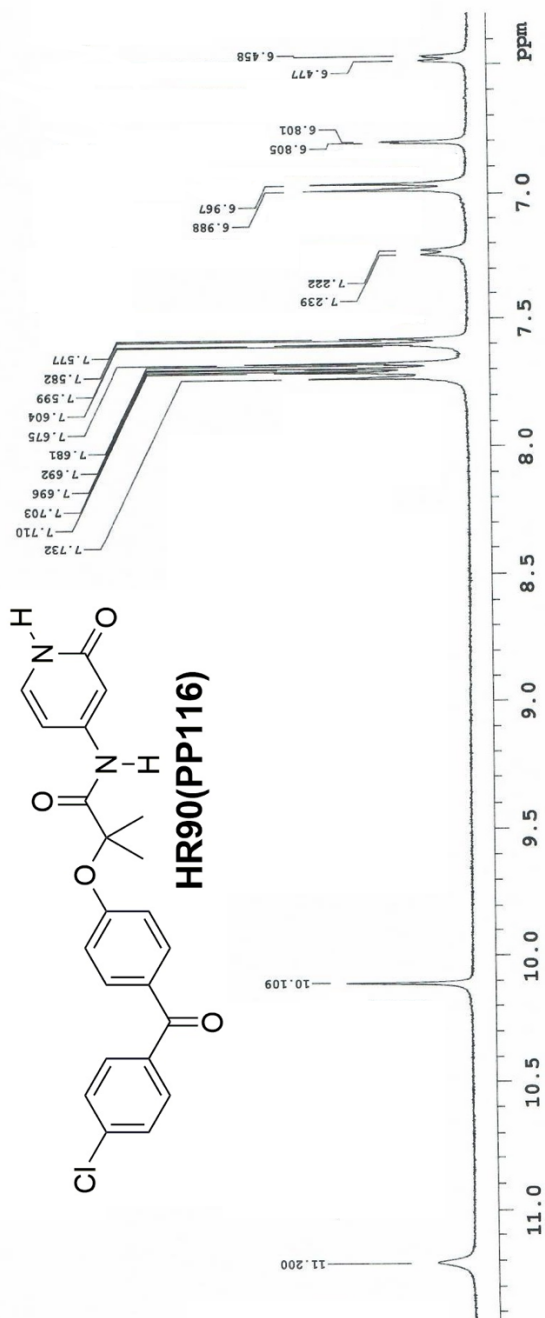
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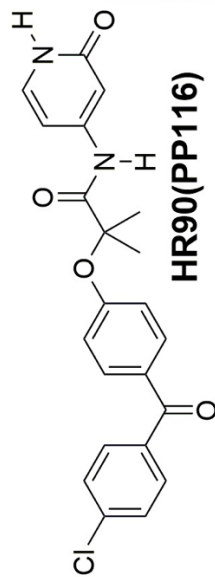
# <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) Varian Mercury 400 Plus



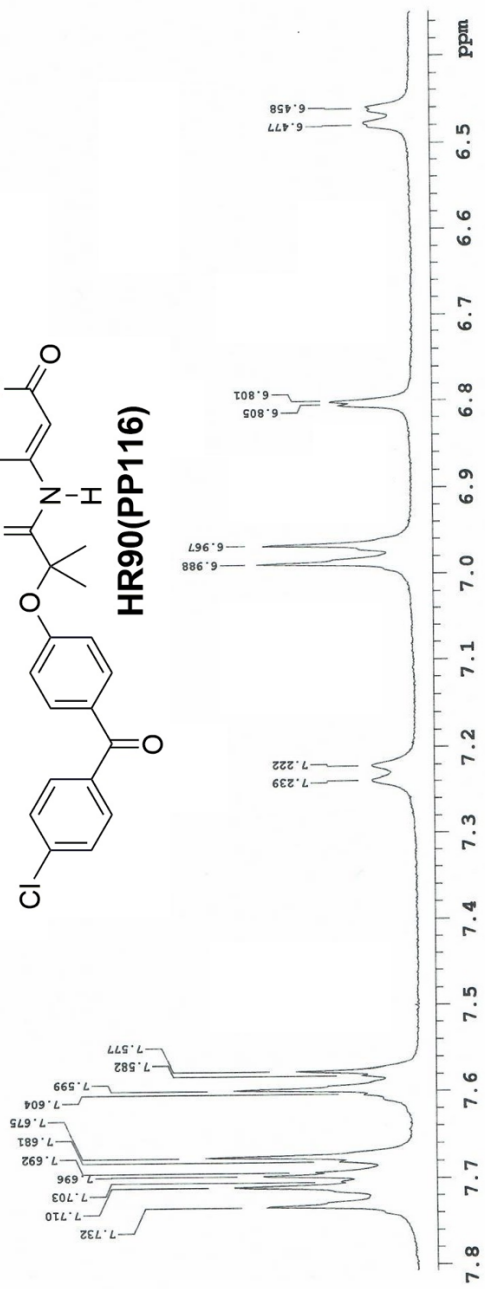
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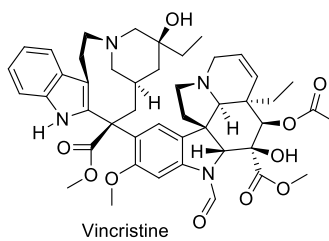
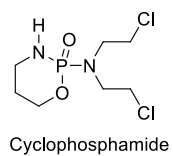
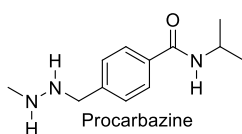
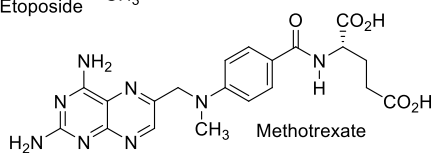
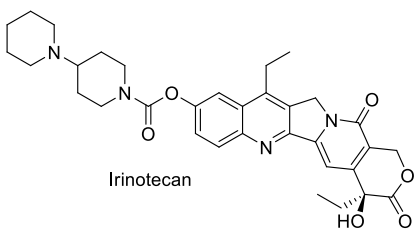
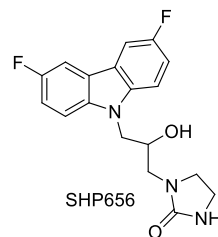
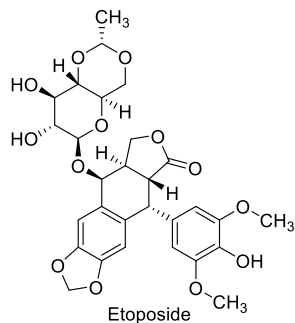
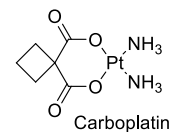
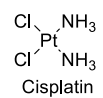
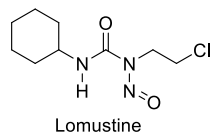
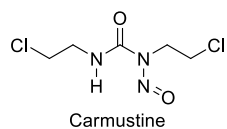
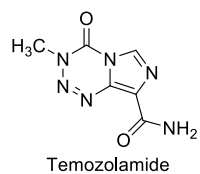


# $^1\text{H-NMR}$ (DMSO- $\text{d}_6$ ) Varian Mercury 400 Plus

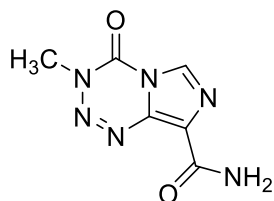


HR90(PP116)





The most common chemotherapy drug combination used to treat brain and spinal cord tumors is PCV (procarbazine, lomustine and vincristine)



Temozolamide

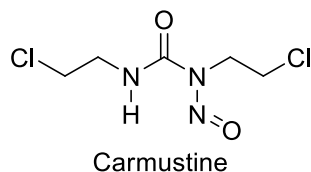
Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>	
		T <sub>0</sub>	NA	1	18.31	-0.90	16.08	26.31	232.02	7	47.86	3.67	safe
ClogP	-0.28	1.00											
ClogD	-0.28	1.00											
MW	194.15	1.00											
PSA	105.94	0.47											
HBD	2.00	0.50											
pKa	-0.96	1.00											
MPO	4.97												
BBB	3.44												
LogBB	-1.47												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area (Å<sup>2</sup>); HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138);

hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	2	1.00
HA_SCORE	14	0.89
MWHBN_SCORE	0.43	0.36
TPSA_SCORE	105.94	0.26
PKA_SCORE	8.81	1.00
BBB SCORE		3.44

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

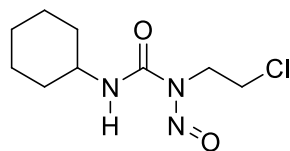


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
			NA	5	14.05	-2.38	17.32	29.69	61.77	4	46.98	3.49	safe
ClogP	1.02	1.00											
ClogD	1.02	1.00											
MW	214.05	1.00											
PSA	61.77	1.00											
HBD	1.00	0.75											
pKa	-5.34	1.00											
MPO	5.75												
BBB	4.26												
LogBB	-0.62												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	0	0.34
HA_SCORE	12	0.79
HWHBN_SCORE	0.21	1.00
TPSA_SCORE	61.77	0.57
PKA_SCORE	8.81	1.00
BBB_SCORE		4.26

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



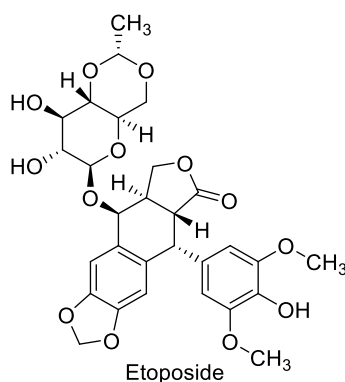
Lomustine

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	4	11.95	-3.28	21.92	33.97	351.15	4	58.65	3.70	safe
ClogP	2.16	1.00											
ClogD	2.16	0.92											
MW	233.70	1.00											
PSA	61.77	1.00											
HBD	1.00	0.75											
pKa	-5.35	1.00											
MPO	5.67												
BBB	4.40												
LogBB	-0.45												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	0	0.34
HA_SCORE	15	0.93
HWHBN_SCORE	0.20	1.00
TPSA_SCORE	61.77	0.57
PKA_SCORE	8.81	1.00
BBB_SCORE		4.40

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

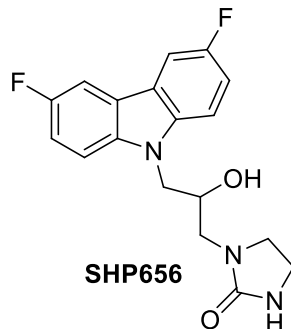


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	5	14.79	-3.40	55.93	73.05	781.41	24	139.02	4.94	safe
ClogP	1.16	1.00											
ClogD	1.16	1.00											
MW	588.56	0.00											
PSA	160.83	0.00											
HBD	3.00	0.25											
pKa	-3.69	1.00											
MPO	3.25												
BBB	1.74												
LogBB	-2.07												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	2	1.00
HA_SCORE	42	0.24
HWHBN_SCORE	0.62	0.00
TPSA_SCORE	160.83	0.00
PKA_SCORE	8.81	1.00
BBB_SCORE		1.74

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

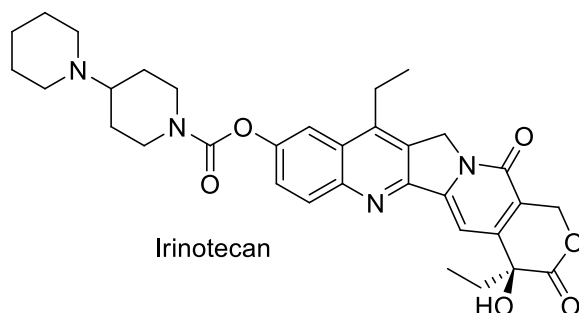


Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T <sub>0</sub>	5.95	4	12.29	-4.07	35.63	44.34	459.71	4	88.66	5.06	safe
ClogP	1.93	1.00										
ClogD	1.93	1.00										
MW	345.35	1.00										
PSA	57.50	1.00										
HBD	2.00	0.50										
pKa	-1.85	1.00										
MPO	5.50											
BBB	4.81											
LogBB	-0.42											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	25.00	0.52
HWHBN_SCORE	0.22	1.00
TPSA_SCORE	57.50	0.60
PKA_SCORE	8.81	1.00
BBB_SCORE		4.81

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

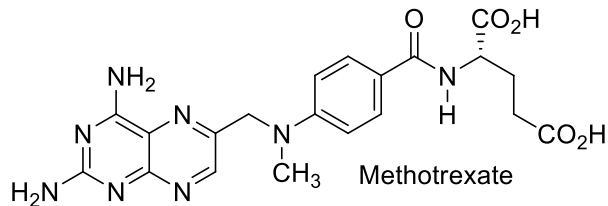


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	10.51	5	17.01	- 3.47	63.01	67.37	841.25	10	161.33	5.49	toxic
ClogP	2.78	1.00											
ClogD	1.00	1.00											
MW	586.69	0.00											
PSA	112.51	0.25											
HBD	1.00	0.75											
pKa	9.17	0.41											
MPO	3.41												
BBB	3.13												
LogBB	-1.10												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	43	0.21
HWHBN_SCORE	0.29	0.87
TPSA_SCORE	112.51	0.21
PKA_SCORE	9.17	0.99
BBB_SCORE		3.13

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

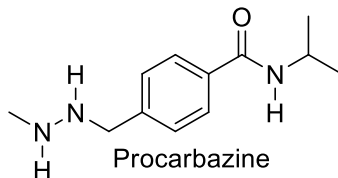


Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T <sub>0</sub>	3.16	9	15.30	0.00	43.52	55.08	601.64	17	119.21	4.71	safe
ClogP	-1.63	1.00										
ClogD	-5.70	1.00										
MW	454.45	0.33										
PSA	210.54	0.00										
HBD	7.00	0.00										
pKa	5.57	1.00										
MPO	3.33											
BBB	1.55											
LogBB	-3.04											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	33	0.61
HWHBN_SCORE	0.80	0.00
TPSA_SCORE	210.54	0.00
PKA_SCORE	5.57	0.48
BBB_SCORE		1.55

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

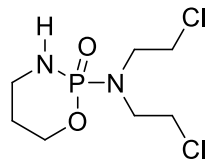


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	11.66	5	22.85	-1.02	25.22	38.17	376.41	4	86.98	4.84	Safe
ClogP	0.99	1.00											
ClogD	-0.01	1.00											
MW	221.30	1.00											
PSA	53.16	1.00											
HBD	3.00	0.25											
pKa	8.36	0.82											
MPO	5.07												
BBB	4.22												
LogBB	-0.49												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	1	0.82
HA_SCORE	16	0.95
HWHBN_SCORE	0.40	0.46
TPSA_SCORE	53.16	0.63
PKA_SCORE	8.36	0.99
BBB_SCORE		4.22

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



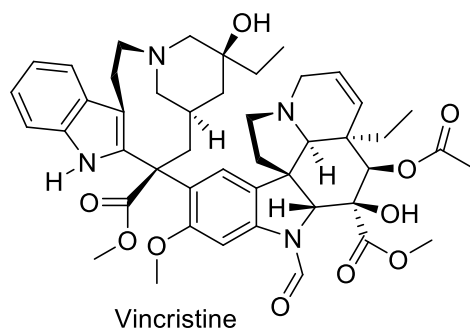
Cyclophosphamide

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	5	13.24	-1.27	23.02	44.34	355.40	2	58.48	3.32	safe
ClogP	0.10	1.00											
ClogD	0.10	1.00											
MW	261.08	1.00											
PSA	41.57	1.00											
HBD	1.00	0.75											
pKa	0.00	1.00											
MPO	5.75												
BBB	4.41												
LogBB	-0.46												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	0	0.34
HA_SCORE	14	0.89
HWHBN_SCORE	0.12	0.85
TPSA_SCORE	41.57	0.71
PKA_SCORE	8.81	1.00
BBB_SCORE		4.41

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

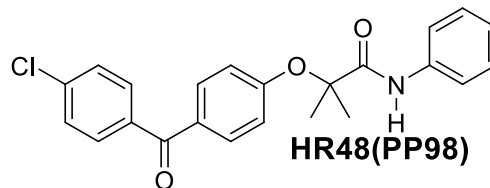


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	9.81	10	22.96	-2.04	87.84	99.55	NA	16	221.48	5.16	toxic
ClogP	3.13	0.94											
ClogD	1.54	1.00											
MW	824.97	0.00											
PSA	171.17	0.00											
HBD	3.00	0.25											
pKa	8.42	0.79											
MPO	2.97												
BBB	1.80												
LogBB	-1.92												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	60	0.00
HWHBN_SCORE	0.42	0.41
TPSA_SCORE	171.17	0.00
PKA_SCORE	8.42	0.99
BBB_SCORE		1.80

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

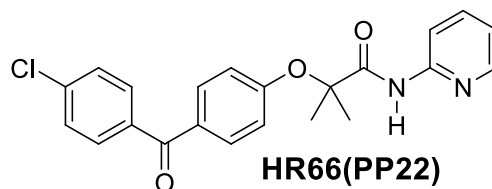


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	6	2.88	- 7.07	42.67	45.91	551.01	6	111.47	5.30	safe
ClogP	5.79	0.00											
ClogD	5.79	0.00											
MW	393.87	0.76											
PSA	55.40	1.00											
HBD	1.00	0.75											
pKa	-4.93	1.00											
MPO	3.51												
BBB	4.74												
LogBB	0.20												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	28	0.82
HWHBN_SCORE	0.20	1.00
TPSA_SCORE	55.40	0.61
PKA_SCORE	8.81	1.00
BBB_SCORE		4.74

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



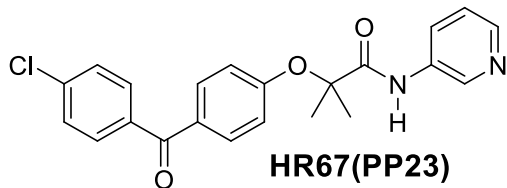
**HR66(PP22)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	7.57	6	3.99	- 6.45	41.78	49.64	543.63	7	109.63	5.19	safe
ClogP	5.17	0.00											
ClogD	5.17	0.00											
MW	394.86	0.75											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	3.99	1.00											
MPO	3.50												
BBB	4.50												
LogBB	-0.09												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	28	0.82
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.50

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



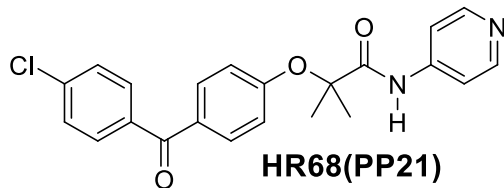
**HR67(PP23)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.39	6	4.54	-	41.78	41.15	543.37	7	109.31	5.28	safe
						5.8							
						9							
ClogP	4.58	0.21											
ClogD	4.57	0.00											
MW	394.86	0.75											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.37	1.00											
MPO	3.71												
BBB	4.50												
LogBB	-0.18												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	28	0.82
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.50

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



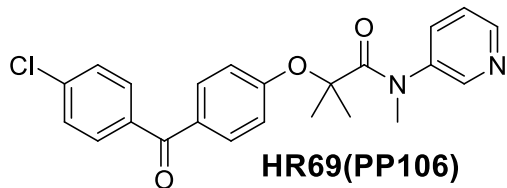
**HR68(PP21)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.96	6	4.54	- 5.89	41.78	44.70	453.10	7	109.31	5.28	Safe
ClogP	4.58	0.21											
ClogD	4.57	0.00											
MW	394.86	0.75											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.85	1.00											
MPO	3.71												
BBB	4.50												
LogBB	-0.18												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	28	0.82
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.50

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



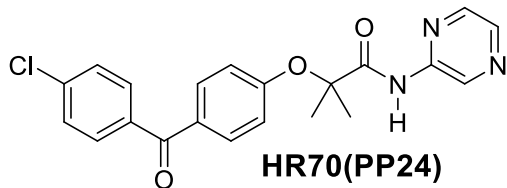
**HR69(PP106)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	6	4.69	-	43.62	50.87	575.89	7	112.43	5.44	safe
						5.9							
						7							
ClogP	4.44	0.28											
ClogD	4.44	0.00											
MW	408.88	0.65											
PSA	59.50	1.00											
HBD	0.00	1.00											
pKa	4.33	1.00											
MPO	3.93												
BBB	4.65												
LogBB	-0.07												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.20	1.00
TPSA_SCORE	59.50	0.58
PKA_SCORE	8.81	1.00
BBB_SCORE		4.65

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



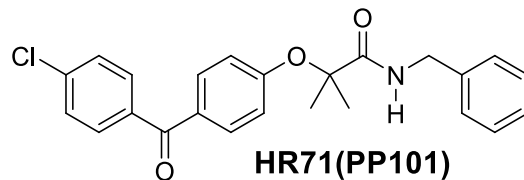
**HR70(PP24)**

Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	5.88	6	5.65	- 5.27	40.90	44.62	536.59	8	107.47	5.18	safe
ClogP	3.95	0.52										
ClogD	3.95	0.02										
MW	395.84	0.74										
PSA	81.18	1.00										
HBD	1.00	7.25										
pKa	0.07	1.00										
MPO	4.04											
BBB	4.14											
LogBB	-0.46											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	28.00	0.82
HWHBN_SCORE	0.30	0.84
TPSA_SCORE	81.18	0.43
PKA_SCORE	8.81	1.00
BBB_SCORE		4.14

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

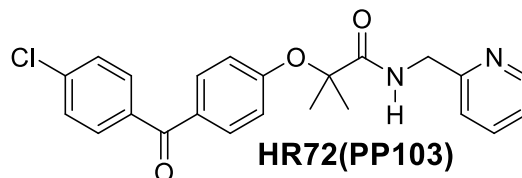


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	7	3.80	- 6.9 2	44.52	49.64	582.41	6	114.52	5.34	safe
ClogP	5.50	0.00											
ClogD	5.50	0.00											
MW	407.89	0.66											
PSA	55.40	1.00											
HBD	1.00	0.75											
pKa	2.70	1.00											
MPO	3.41												
BBB	4.70												
LogBB	0.15												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29.00	0.79
HWHBN_SCORE	0.20	1.00
TPSA_SCORE	55.40	0.61
PKA_SCORE	8.81	1.00
BBB_SCORE		4.70

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

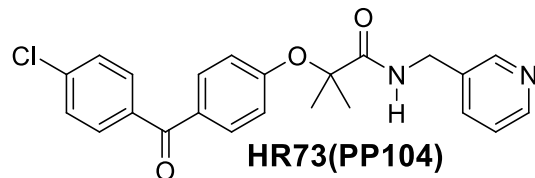


Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	8.23	7	5.41	- 5.97	43.63	53.16	575.97	4	111.85	5.28	safe
ClogP	4.36	0.32										
ClogD	4.36	0.00										
MW	408.88	0.65										
PSA	68.29	1.00										
HBD	1.00	0.75										
pKa	4.16	1.00										
MPO	3.72											
BBB	4.47											
LogBB	-0.21											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.47

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

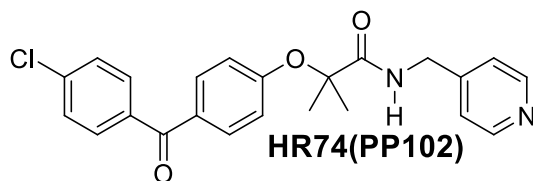


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.87	7	5.43	- 5.74	43.63	51.36	575.34	7	112.37	5.24	safe
ClogP	4.28	0.36											
ClogD	4.28	0.00											
MW	408.88	0.65											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.82	1.00											
MPO	3.76												
BBB	4.47												
LogBB	-0.22												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.47

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

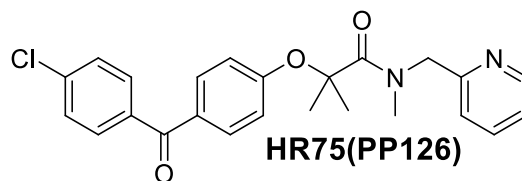


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.99	7	5.43	- 5.74	43.63	51.47	575.38	7	112.37	5.27	safe
ClogP	4.28	0.36											
ClogD	4.28	0.00											
MW	408.88	0.65											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	5.02	1.00											
MPO	3.76												
BBB	4.14												
LogBB	-0.22												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	5.02	0.34
BBB_SCORE		4.14

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



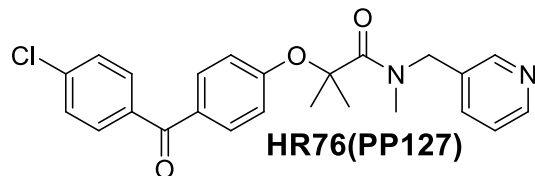
**HR75(PP126)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	7	5.56	- 5.91	45.47	57.15	608.71	7	116.74	5.35	safe
ClogP	4.59	0.21											
ClogD	4.59	0.00											
MW	422.91	0.55											
PSA	59.50	1.00											
HBD	0.00	1.00											
pKa	4.21	1.00											
MPO	3.76												
BBB	4.60												
LogBB	-0.04												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.19	1.00
TPSA_SCORE	59.50	0.58
PKA_SCORE	8.81	1.00
BBB_SCORE		4.60

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



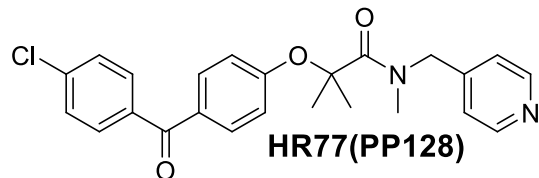
**HR76(PP127)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	7	5.58	- 5.77	45.47	57.81	608.06	7	117.26	5.41	safe
ClogP	4.51	0.25											
ClogD	4.50	0.00											
MW	422.91	0.55											
PSA	59.50	1.00											
HBD	0.00	1.00											
pKa	4.83	1.00											
MPO	3.80												
BBB	4.60												
LogBB	-0.06												

IP = Isoelectronic Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.19	1.00
TPSA_SCORE	59.50	0.58
PKA_SCORE	8.81	1.00
BBB_SCORE		4.60

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

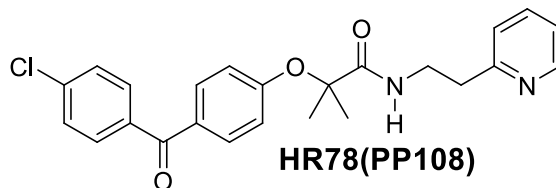


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	7	5.58	- 5.77	45.47	56.93	608.63	7	117.26	5.42	safe
ClogP	4.51	0.25											
ClogD	4.50	0.00											
MW	422.91	0.55											
PSA	59.50	1.00											
HBD	0.00	1.00											
pKa	5.03	1.00											
MPO	3.80												
BBB	4.27												
LogBB	-0.06												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.19	1.00
TPSA_SCORE	59.50	0.58
PKA_SCORE	5.03	0.34
BBB_SCORE		4.27

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



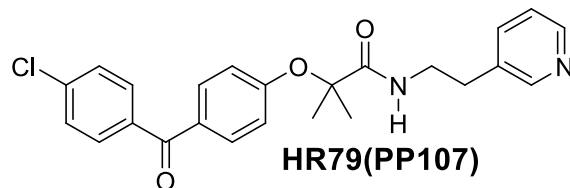
**HR78(PP108)**

Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	9.50	8	5.01	- 5.97	45.47	48.71	606.38	7	116.55	5.34	Safe
ClogP	4.60	0.20										
ClogD	4.60	0.00										
MW	422.91	0.55										
PSA	68.29	1.00										
HBD	1.00	0.75										
pKa	4.55	1.00										
MPO	3.50											
BBB	4.44											
LogBB	-0.17											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

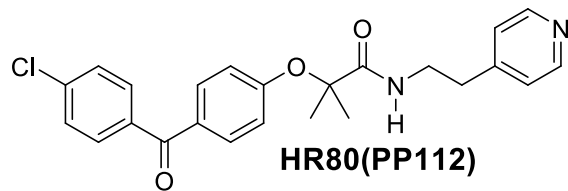


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	9.68	8	5.03	-5.74	45.47	46.89	605.78	7	117.12	5.39	safe
ClogP	4.57	0.21											
ClogD	4.57	0.00											
MW	422.91	0.55											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.93	1.00											
MPO	3.52												
BBB	4.44												
LogBB	-0.18												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

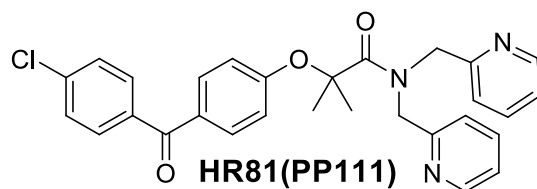


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	9.75	8	5.03	- 5.7 4	45.47	49.21	605.22	7	117.12	5.45	TOXIC
ClogP	4.57	0.21											
ClogD	4.57	0.00											
MW	422.91	0.55											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	5.05	1.00											
MPO	3.52												
BBB	4.11												
LogBB	-0.18												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	5.05	0.35
BBB_SCORE		4.11

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



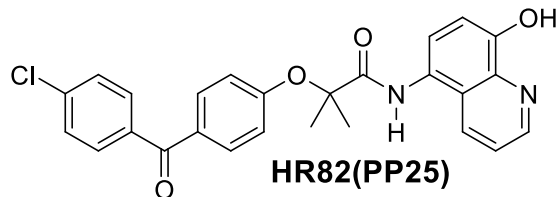
**HR81(PP111)**

Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	NA	9	4.76	- 6.41	54.16	77.69	707.76	8	138.68	5.24	safe
ClogP	5.18	0.00										
ClogD	5.17	0.00										
MW	500.00	0.00										
PSA	72.39	1.00										
HBD	0.00	1.00										
pKa	4.49	1.00										
MPO	3.00											
BBB	3.66											
LogBB	-0.15											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	4	0.20
HA_SCORE	36	0.48
HWHBN_SCORE	0.22	0.99
TPSA_SCORE	72.39	0.49
PKA_SCORE	8.81	1.00
BBB_SCORE		3.66

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

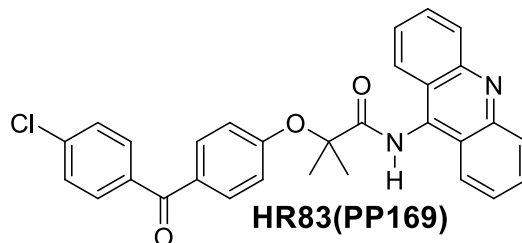


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	6.65	6	4.59	-7.05	49.90	50.89	615.89	9	127.37	5.27	safe
ClogP	5.65	0.00											
ClogD	5.65	0.00											
MW	460.91	0.28											
PSA	88.52	1.00											
HBD	2.00	0.50											
pKa	4.53	1.00											
MPO	2.78												
BBB	3.21												
LogBB	-0.31												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	4	0.20
HA_SCORE	33	0.61
HWHBN_SCORE	0.33	0.76
TPSA_SCORE	88.52	0.38
PKA_SCORE	8.81	1.00
BBB_SCORE		3.21

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

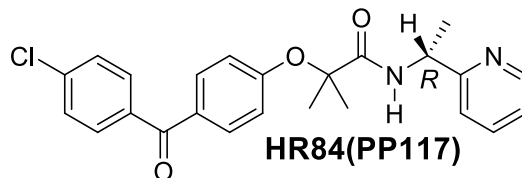


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	9.01	6	3.40	-9.08	56.85	56.88	666.84	7	141.47	5.62	Safe
ClogP	7.33	0.00											
ClogD	7.32	0.00											
MW	494.98	0.04											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	5.55	1.00											
MPO	2.79												
BBB	3.25												
LogBB	0.24												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	5	0.00
HA_SCORE	36	0.48
HWHBN_SCORE	0.22	0.99
TPSA_SCORE	68.29	0.52
PKA_SCORE	5.55	0.48
BBB_SCORE		3.25

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

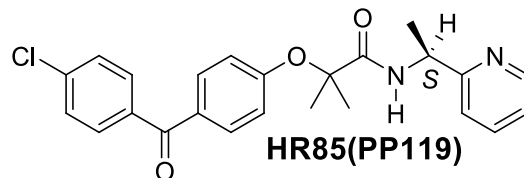


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.09	7	4.99	-6.28	45.47	56.50	603.44	7	116.34	5.24	Safe
ClogP	4.93	0.03											
ClogD	4.93	0.00											
MW	422.91	0.55											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.09	1.00											
MPO	3.33												
BBB	4.44												
LogBB	-0.12												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

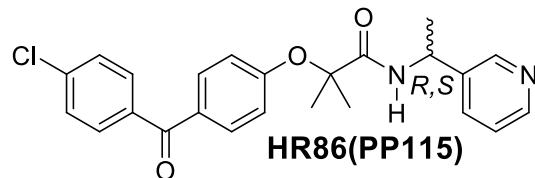


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.09	7	4.99	-6.28	45.47	56.50	603.44	7	116.34	5.26	safe
ClogP	4.93	0.03											
ClogD	4.93	0.00											
MW	422.91	0.55											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.09	1.00											
MPO	3.33												
BBB	4.44												
LogBB	-0.12												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

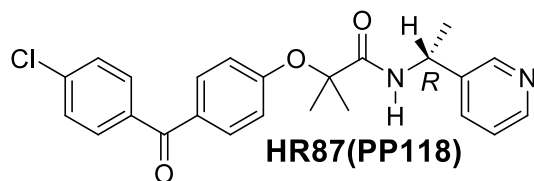


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.67	7	5.01	-6.05	45.67	57.16	604.58	7	116.79	5.39	safe
ClogP	4.70	0.15											
ClogD	4.70	0.00											
MW	422.91	0.55											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.80	1.00											
MPO	3.45												
BBB	4.44												
LogBB	-0.16												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

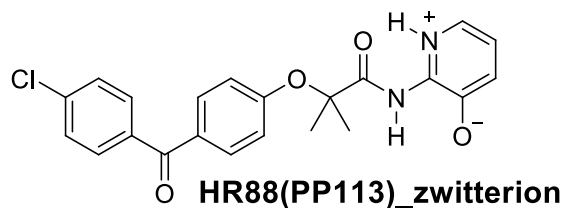


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.67	7	5.01	-6.05	45.67	57.16	604.58	7	116.79	5.36	safe
ClogP	4.70	0.15											
ClogD	4.70	0.00											
MW	422.91	0.55											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.79	1.00											
MPO	3.45												
BBB	3.40												
LogBB	-0.16												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

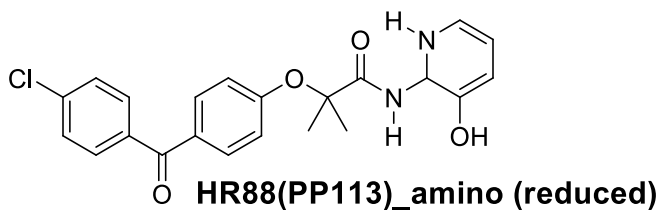


Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	NA	6	13.41	- 5.75	42.37	45.59	554.75	9	122.36	5.17	safe
ClogP	4.87	0.07										
ClogD	4.63	0.00										
MW	410.85	0.64										
PSA	92.60	0.91										
HBD	2.00	0.50										
pKa	3.92	1.00										
MPO	3.12											
BBB	3.92											
LogBB	-0.49											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	92.60	0.35
PKA_SCORE	7.52	0.90
BBB_SCORE		3.92

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

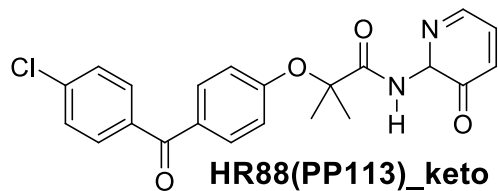


Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	9.52	6	12.54	- 5.97	42.86	47.06	540.14	9	112.46	5.52	toxic
ClogP	3.72	0.64										
ClogD	3.39	0.31										
MW	412.87	0.62										
PSA	87.66	1.00										
HBD	3.00	0.25										
pKa	4.84	1.00										
MPO	3.82											
BBB	3.75											
LogBB	-0.63											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	2	1.00
HA_SCORE	29	0.79
HWHBN_SCORE	0.39	0.50
TPSA_SCORE	87.66	0.39
PKA_SCORE	7.35	0.88
BBB_SCORE		3.75

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

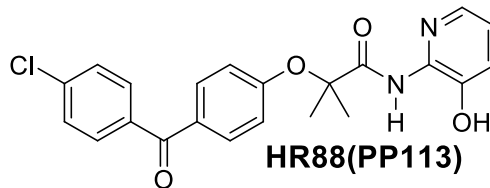


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	6.47	6	5.97	-7.20	42.15	54.68	535.28	9	110.48	5.33	safe
ClogP	4.07	0.46											
ClogD	4.07	0.00											
MW	410.85	0.64											
PSA	84.83	1.00											
HBD	1.00	0.75											
pKa	2.62	1.00											
MPO	3.85												
BBB	4.38												
LogBB	-0.50												

IP = Isoelectronic Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	2	1.00
HA_SCORE	29	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	84.83	0.41
PKA_SCORE	8.81	1.00
BBB_SCORE		3.75

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

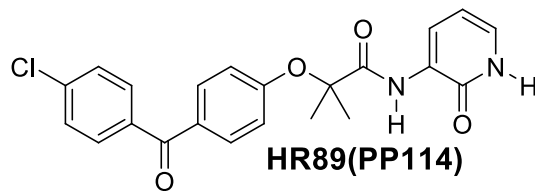


Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	6.16	6	5.62	- 5.90	42.40	45.14	553.00	9	111.61	5.22	safe
ClogP	4.87	0.07										
ClogD	4.63	0.00										
MW	410.85	0.64										
PSA	88.52	1.00										
HBD	2.00	0.50										
pKa	3.92	1.00										
MPO	3.20											
BBB	3.72											
LogBB	-0.43											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	84.52	0.38
PKA_SCORE	7.52	0.90
BBB_SCORE		3.72

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



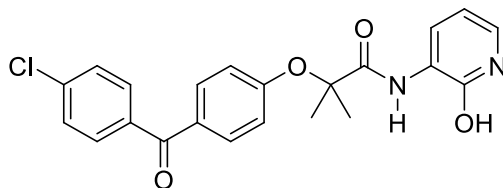
**HR89(PP114)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	6	7.23	- 6.49	42.32	43.44	529.29	8	111.66	5.13	safe
ClogP	3.53	0.73											
ClogD	3.53	0.24											
MW	410.85	0.64											
PSA	84.50	1.00											
HBD	2.00	0.50											
pKa	1.82	1.00											
MPO	4.11												
BBB	4.08												
LogBB	-0.57												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	84.50	0.41
PKA_SCORE	8.81	1.00
BBB_SCORE		4.08

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



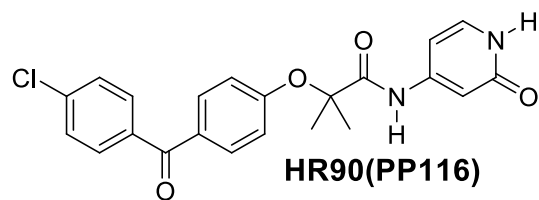
**HR89(PP114)\_aromatic**

Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	6.17	6	5.85	-6.00	42.40	43.69	552.22	9	111.61	5.21	Safe
ClogP	4.87	0.07										
ClogD	4.87	0.00										
MW	410.85	0.64										
PSA	88.52	1.00										
HBD	2.00	0.50										
pKa	1.82	1.00										
MPO	3.20											
BBB	3.77											
LogBB	-0.43											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	88.52	0.38
PKA_SCORE	8.81	1.00
BBB_SCORE		3.77

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



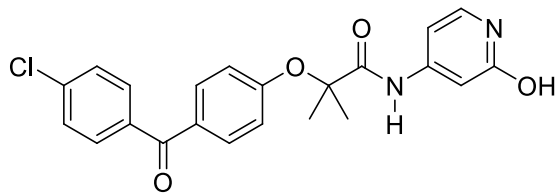
**HR90(PP116)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	6	7.23	- 6.49	42.32	42.75	530.46	8	111.59	5.16	safe
ClogP	3.38	0.81											
ClogD	3.38	0.31											
MW	410.85	0.64											
PSA	84.50	1.00											
HBD	2.00	0.50											
pKa	1.80	1.00											
MPO	4.26												
BBB	4.08												
LogBB	-0.60												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	84.50	0.41
PKA_SCORE	8.81	1.00
BBB_SCORE		4.08

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



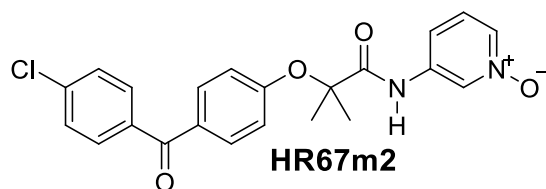
**HR90(PP116)\_aromatic**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	6.92	6	5.85	-6.00	42.40	44.16	554.21	9	111.61	5.21	safe
ClogP	4.87	0.07											
ClogD	4.87	0.00											
MW	410.85	0.64											
PSA	88.52	1.00											
HBD	2.00	0.5											
pKa	2.21	1.00											
MPO	3.20												
BBB	3.77												
LogBB	-0.43												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	88.52	0.38
PKA_SCORE	8.81	1.00
BBB_SCORE		3.77

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

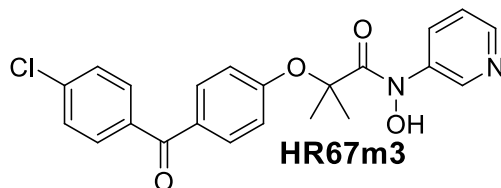


Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	6.13	6	11.51	-6.13	42.26	43.33	558.19	9	112.63	5.36	safe
ClogP	3.31	0.84										
ClogD	3.31	0.84										
MW	410.85	0.64										
PSA	82.34	1.00										
HBD	1.00	0.75										
pKa	0.81	1.00										
MPO	4.57											
BBB	4.28											
LogBB												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.25	0.97
TPSA_SCORE	82.34	0.43
PKA_SCORE	8.81	1.00
BBB_SCORE		4.28

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

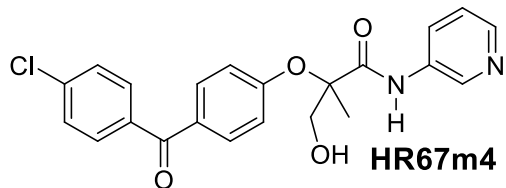


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	5.82	6	11.77	-5.06	42.41	51.70	556.21	9	109.30	5.63	safe
ClogP	4.21	0.39											
ClogD	4.06	0.00											
MW	410.85	0.64											
PSA	79.73	1.00											
HBD	1.00	0.75											
pKa	3.84	1.00											
MPO	3.78												
BBB	4.11												
LogBB													

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	29.00	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	79.73	0.44
PKA_SCORE	7.79	0.94
BBB_SCORE		4.11

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

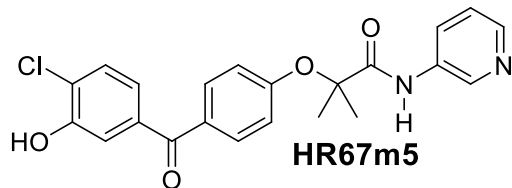


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.35	7	12.06	-5.44	42.41	40.63	553.24	9	110.86	5.40	safe
ClogP	3.53	0.74											
ClogD	3.53	0.24											
MW	410.85	0.64											
PSA	88.52	1.00											
HBD	2.00	0.50											
pKa	4.37	1.00											
MPO	4.11												
BBB	3.77												
LogBB													

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29.00	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	88.52	0.38
PKA_SCORE	8.81	1.00
BBB_SCORE		3.77

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

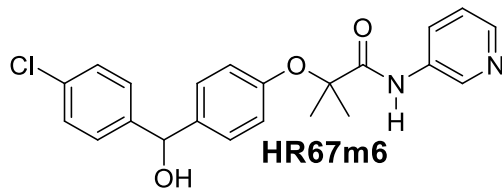


Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	6.10	6	12.02	-5.44	42.42	40.55	552.87	9	11.29	5.76	safe
ClogP	4.27	0.36											
ClogD	4.14	0.00											
MW	410.85	0.64											
PSA	88.52	1.00											
HBD	2.00	0.50											
pKa	4.37	1.00											
MPO	3.50												
BBB	3.75												
LogBB													

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	29.00	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	88.52	0.38
PKA_SCORE	7.85	0.95
BBB_SCORE		3.75

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.



Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	8.37	6	11.34	-4.95	42.17	53.36	554.15	7	109.84	5.49	safe
ClogP	4.13	0.43										
ClogD	4.13	0.00										
MW	396.87	0.74										
PSA	71.45	1.00										
HBD	2.00	0.50										
pKa	4.37	1.00										
MPO	3.67											
BBB	4.27											
LogBB												

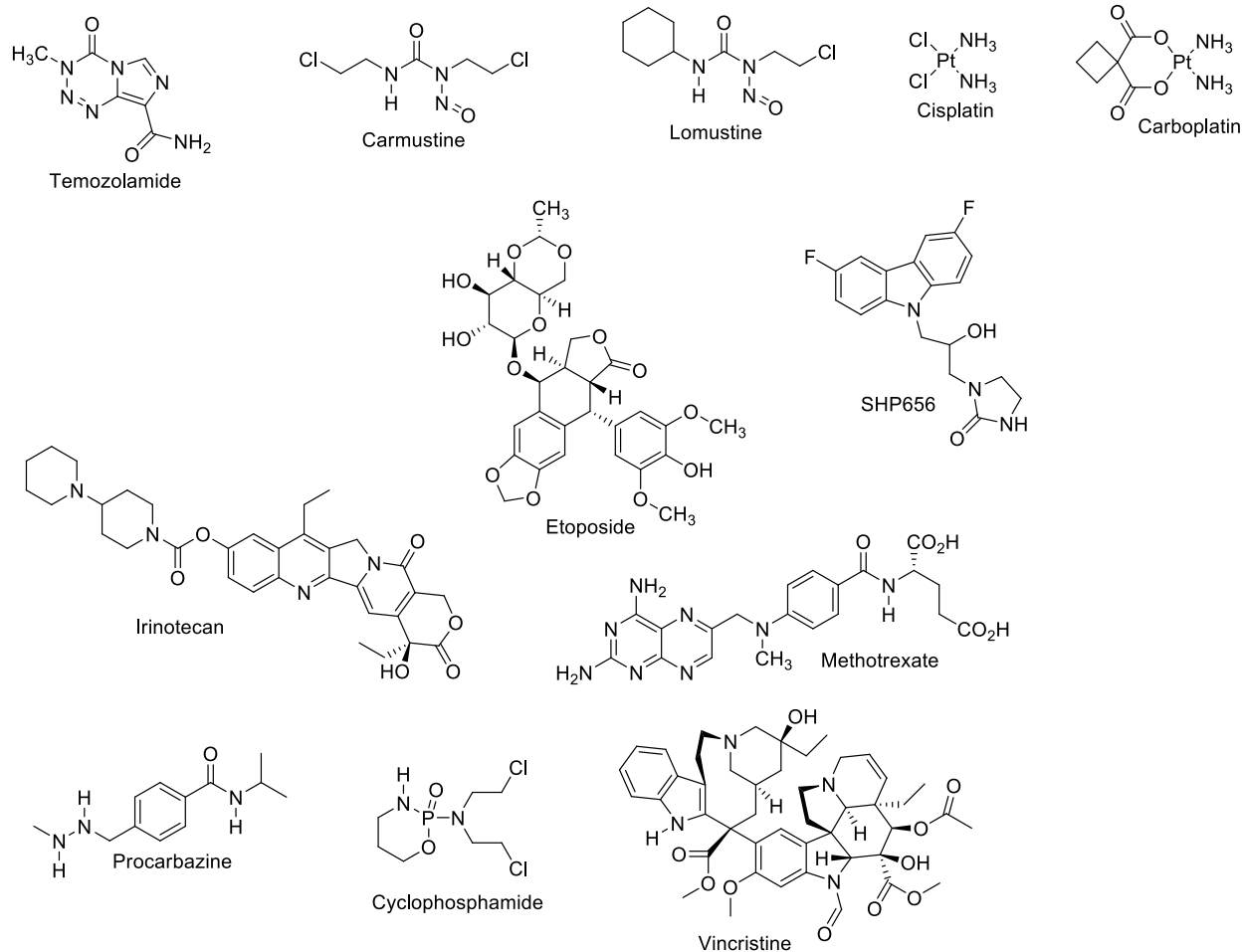
IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model.

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	28.00	0.82
HWHBN_SCORE	0.30	0.84
TPSA_SCORE	71.45	0.50
PKA_SCORE	8.81	1.00
BBB_SCORE		4.27

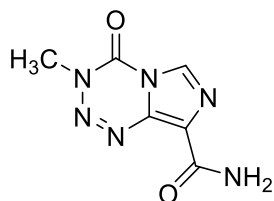
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.  
MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;  
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.; Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med. Chem. 2019, 62 (21), 9824-9836.

**2. MarvinSketch (Product version 22.21) Generated data including common chemotherapy drugs for CNS tumors compared to Pyridine-BPA variants:**

**(HR48-HR90)**



The most common chemotherapy drug combination used to treat brain and spinal cord tumours is PCV (procarbazine, lomustine and vincristine)



Temozolamide

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	1	18.31	-0.90	16.08	26.31	232.02	7	47.86	3.67	safe
ClogP	-0.28	1.00											
ClogD	-0.28	1.00											
MW	194.15	1.00											
PSA	105.94	0.47											
HBD	2.00	0.50											
pKa	-0.96	1.00											
MPO	4.97												
BBB	3.44												
LogBB	-1.47												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area ( $\text{\AA}^2$ ); HBD =

hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	2	1.00
HA_SCORE	14	0.89
MWHBN_SCORE	0.43	0.36
TPSA_SCORE	105.94	0.26
PKA_SCORE	8.81	1.00
BBB SCORE		3.44

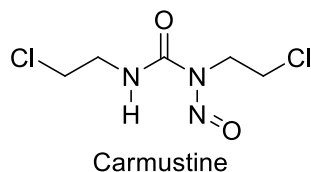
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
			NA	5	14.05	-2.38	17.32	29.69	61.77	4	46.98	3.49	safe
ClogP	1.02	1.00											
ClogD	1.02	1.00											
MW	214.05	1.00											
PSA	61.77	1.00											
HBD	1.00	0.75											
pKa	-5.34	1.00											
MPO	5.75												
BBB	4.26												
LogBB	-0.62												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	0	0.34
HA_SCORE	12	0.79
HWHBN_SCORE	0.21	1.00
TPSA_SCORE	61.77	0.57
PKA_SCORE	8.81	1.00
BBB_SCORE		4.26

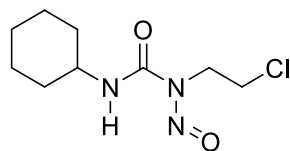
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



Lomustine

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	4	11.95	-3.28	21.92	33.97	351.15	4	58.65	3.70	safe
ClogP	2.16	1.00											
ClogD	2.16	0.92											
MW	233.70	1.00											
PSA	61.77	1.00											
HBD	1.00	0.75											
pKa	-5.35	1.00											
MPO	5.67												
BBB	4.40												
LogBB	-0.45												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	0	0.34
HA_SCORE	15	0.93
HWHBN_SCORE	0.20	1.00
TPSA_SCORE	61.77	0.57
PKA_SCORE	8.81	1.00
BBB_SCORE		4.40

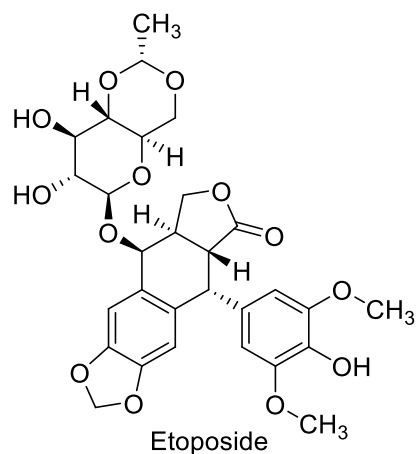
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	5	14.79	-3.40	55.93	73.05	781.41	24	139.02	4.94	safe
ClogP	1.16	1.00											
ClogD	1.16	1.00											
MW	588.56	0.00											
PSA	160.83	0.00											
HBD	3.00	0.25											
pKa	-3.69	1.00											
MPO	3.25												
BBB	1.74												
LogBB	-2.07												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>);

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	2	1.00
HA_SCORE	42	0.24
HWHBN_SCORE	0.62	0.00
TPSA_SCORE	160.83	0.00
PKA_SCORE	8.81	1.00
BBB_SCORE		1.74

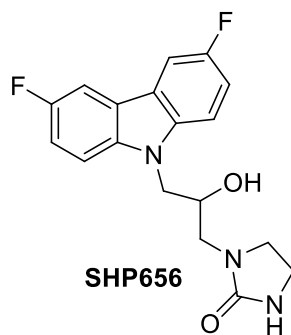
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	5.95	4	12.29	-4.07	35.63	44.34	459.71	4	88.66	5.06	safe
ClogP	1.93	1.00											
ClogD	1.93	1.00											
MW	345.35	1.00											
PSA	57.50	1.00											
HBD	2.00	0.50											
pKa	-1.85	1.00											
MPO	5.50												
BBB	4.81												
LogBB	-0.42												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>);

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	25.00	0.52
HWHBN_SCORE	0.22	1.00
TPSA_SCORE	57.50	0.60
PKA_SCORE	8.81	1.00
BBB_SCORE		4.81

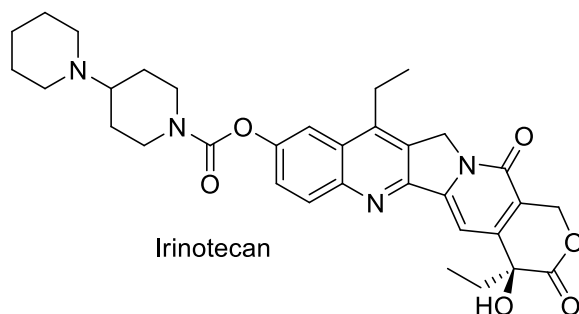
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	10.51	5	17.01	- 3.47	63.01	67.37	841.25	10	161.33	5.49	toxic
ClogP	2.78	1.00											
ClogD	1.00	1.00											
MW	586.69	0.00											
PSA	112.51	0.25											
HBD	1.00	0.75											
pKa	9.17	0.41											
MPO	3.41												
BBB	3.13												
LogBB	-1.10												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>);

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	43	0.21
HWHBN_SCORE	0.29	0.87
TPSA_SCORE	112.51	0.21
PKA_SCORE	9.17	0.99
BBB_SCORE		3.13

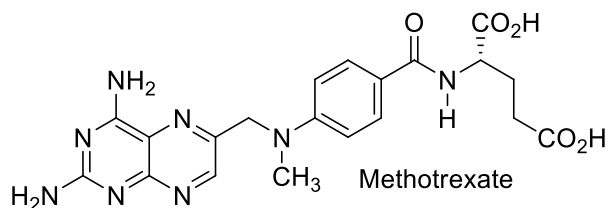
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T <sub>0</sub>	3.16	9	15.30	0.00	43.52	55.08	601.64	17	119.21	4.71	safe
ClogP	-1.63	1.00										
ClogD	-5.70	1.00										
MW	454.45	0.33										
PSA	210.54	0.00										
HBD	7.00	0.00										
pKa	5.57	1.00										
MPO	3.33											
BBB	1.55											
LogBB	-3.04											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	33	0.61
HWHBN_SCORE	0.80	0.00
TPSA_SCORE	210.54	0.00
PKA_SCORE	5.57	0.48
BBB_SCORE		1.55

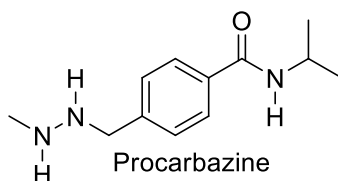
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	11.66	5	22.85	-1.02	25.22	38.17	376.41	4	86.98	4.84	Safe
ClogP	0.99	1.00											
ClogD	-0.01	1.00											
MW	221.30	1.00											
PSA	53.16	1.00											
HBD	3.00	0.25											
pKa	8.36	0.82											
MPO	5.07												
BBB	4.22												
LogBB	-0.49												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	1	0.82
HA_SCORE	16	0.95
HWHBN_SCORE	0.40	0.46
TPSA_SCORE	53.16	0.63
PKA_SCORE	8.36	0.99
BBB_SCORE		4.22

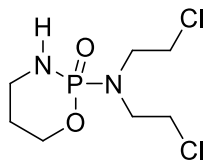
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



Cyclophosphamide

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	5	13.24	-1.27	23.02	44.34	355.40	2	58.48	3.32	safe
ClogP	0.10	1.00											
ClogD	0.10	1.00											
MW	261.08	1.00											
PSA	41.57	1.00											
HBD	1.00	0.75											
pKa	0.00	1.00											
MPO	5.75												
BBB	4.41												
LogBB	-0.46												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	0	0.34
HA_SCORE	14	0.89
HWHBN_SCORE	0.12	0.85
TPSA_SCORE	41.57	0.71
PKA_SCORE	8.81	1.00
BBB_SCORE		4.41

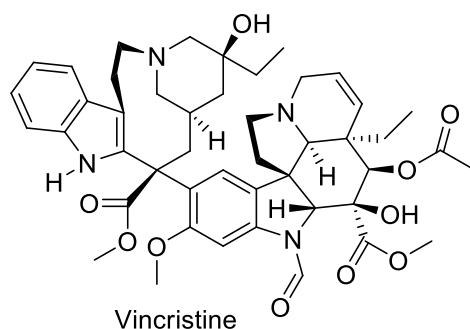
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T <sub>0</sub>	9.81	10	22.96	-2.04	87.84	99.55	NA	16	221.48	5.16	toxic
ClogP	3.13	0.94										
ClogD	1.54	1.00										
MW	824.97	0.00										
PSA	171.17	0.00										
HBD	3.00	0.25										
pKa	8.42	0.79										
MPO	2.97											
BBB	1.80											
LogBB	-1.92											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC<sub>50</sub>

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	60	0.00
HWHBN_SCORE	0.42	0.41
TPSA_SCORE	171.17	0.00
PKA_SCORE	8.42	0.99
BBB_SCORE		1.80

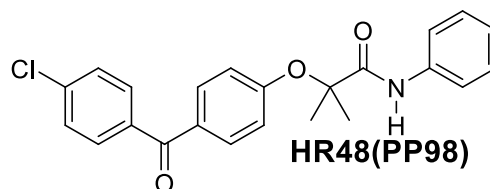
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T <sub>0</sub>	NA	6	2.88	- 7.07	42.67	45.91	551.01	6	111.47	5.30	safe
ClogP	5.79	0.00											
ClogD	5.79	0.00											
MW	393.87	0.76											
PSA	55.40	1.00											
HBD	1.00	0.75											
pKa	-4.93	1.00											
MPO	3.51												
BBB	4.74												
LogBB	0.20												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pH = 7.4; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	28	0.82
HWHBN_SCORE	0.20	1.00
TPSA_SCORE	55.40	0.61
PKA_SCORE	8.81	1.00
BBB_SCORE	4.74	

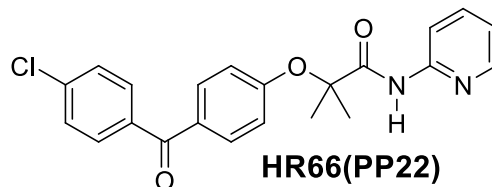
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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**HR66(PP22)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	7.57	6	3.99	- 6.45	41.78	49.64	543.63	7	109.63	5.19	safe
ClogP	5.17	0.00											
ClogD	5.17	0.00											
MW	394.86	0.75											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	3.99	1.00											
MPO	3.50												
BBB	4.50												
LogBB	-0.09												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	28	0.82
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.50

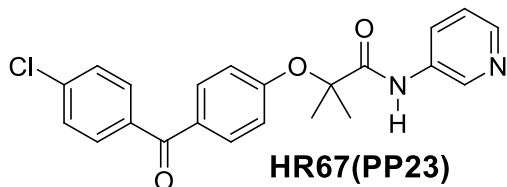
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



**HR67(PP23)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.39	6	4.54	-	41.78	41.15	543.37	7	109.31	5.28	safe
						5.8							
						9							
ClogP	4.58	0.21											
ClogD	4.57	0.00											
MW	394.86	0.75											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.37	1.00											
MPO	3.71												
BBB	4.50												
LogBB	-0.18												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	28	0.82
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.50

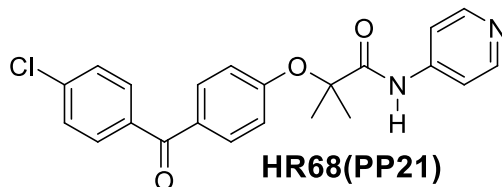
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



**HR68(PP21)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.96	6	4.54	- 5.89	41.78	44.70	453.10	7	109.31	5.28	Safe
ClogP	4.58	0.21											
ClogD	4.57	0.00											
MW	394.86	0.75											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.85	1.00											
MPO	3.71												
BBB	4.50												
LogBB	-0.18												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	28	0.82
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.50

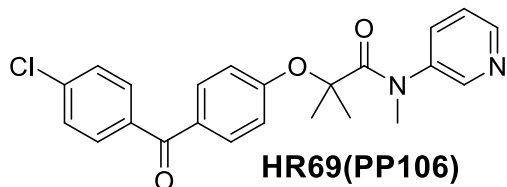
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



**HR69(PP106)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	6	4.69	-	43.62	50.87	575.89	7	112.43	5.44	safe
						5.9							
						7							
ClogP	4.44	0.28											
ClogD	4.44	0.00											
MW	408.88	0.65											
PSA	59.50	1.00											
HBD	0.00	1.00											
pKa	4.33	1.00											
MPO	3.93												
BBB	4.65												
LogBB	-0.07												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.20	1.00
TPSA_SCORE	59.50	0.58
PKA_SCORE	8.81	1.00
BBB_SCORE		4.65

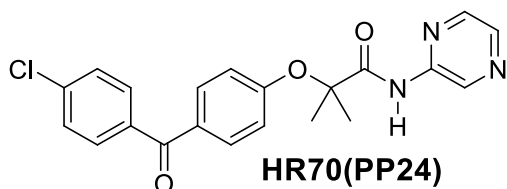
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



**HR70(PP24)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	5.88	6	5.65	- 5.27	40.90	44.62	536.59	8	107.47	5.18	safe
ClogP	3.95	0.52											
ClogD	3.95	0.02											
MW	395.84	0.74											
PSA	81.18	1.00											
HBD	1.00	7.25											
pKa	0.07	1.00											
MPO	4.04												
BBB	4.14												
LogBB	-0.46												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	28.00	0.82
HWHBN_SCORE	0.30	0.84
TPSA_SCORE	81.18	0.43
PKA_SCORE	8.81	1.00
BBB_SCORE		4.14

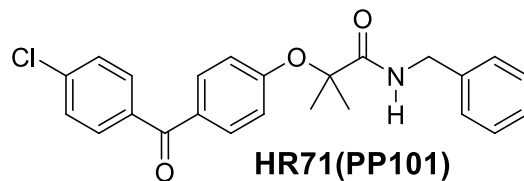
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	7	3.80	- 6.9 2	44.52	49.64	582.41	6	114.52	5.34	safe
ClogP	5.50	0.00											
ClogD	5.50	0.00											
MW	407.89	0.66											
PSA	55.40	1.00											
HBD	1.00	0.75											
pKa	2.70	1.00											
MPO	3.41												
BBB	4.70												
LogBB	0.15												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29.00	0.79
HWHBN_SCORE	0.20	1.00
TPSA_SCORE	55.40	0.61
PKA_SCORE	8.81	1.00
BBB_SCORE		4.70

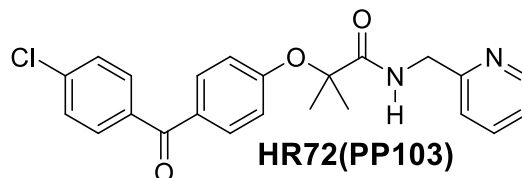
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



**HR72(PP103)**

Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.23	7	5.41	- 5.97	43.63	53.16	575.97	4	111.85	5.28	safe
ClogP	4.36	0.32											
ClogD	4.36	0.00											
MW	408.88	0.65											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.16	1.00											
MPO	3.72												
BBB	4.47												
LogBB	-0.21												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.47

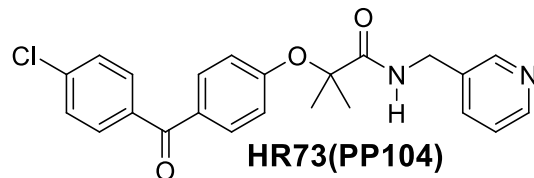
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.87	7	5.43	- 5.74	43.63	51.36	575.34	7	112.37	5.24	safe
ClogP	4.28	0.36											
ClogD	4.28	0.00											
MW	408.88	0.65											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.82	1.00											
MPO	3.76												
BBB	4.47												
LogBB	-0.22												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.47

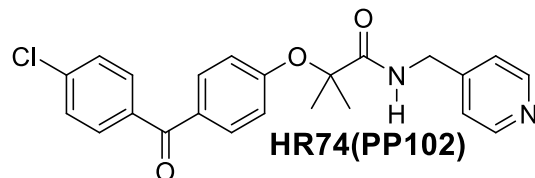
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	8.99	7	5.43	- 5.74	43.63	51.47	575.38	7	112.37	5.27	safe
ClogP	4.28	0.36										
ClogD	4.28	0.00										
MW	408.88	0.65										
PSA	68.29	1.00										
HBD	1.00	0.75										
pKa	5.02	1.00										
MPO	3.76											
BBB	4.14											
LogBB	-0.22											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.25	0.96
TPSA_SCORE	68.29	0.52
PKA_SCORE	5.02	0.34
BBB_SCORE		4.14

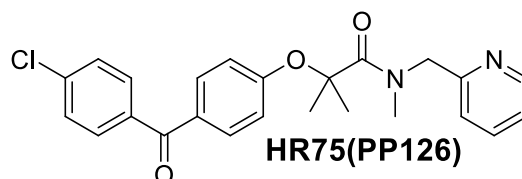
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	7	5.56	- 5.91	45.47	57.15	608.71	7	116.74	5.35	safe
ClogP	4.59	0.21											
ClogD	4.59	0.00											
MW	422.91	0.55											
PSA	59.50	1.00											
HBD	0.00	1.00											
pKa	4.21	1.00											
MPO	3.76												
BBB	4.60												
LogBB	-0.04												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ );

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.19	1.00
TPSA_SCORE	59.50	0.58
PKA_SCORE	8.81	1.00
BBB_SCORE		4.60

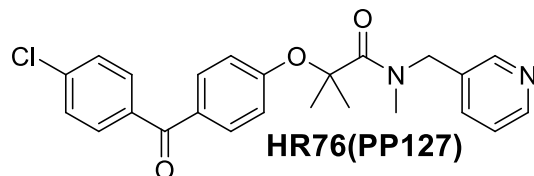
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>	
		T0	NA	7	5.58	-	45.47	57.81	608.06	7	117.26	5.41	safe
					5.77								
ClogP	4.51	0.25											
ClogD	4.50	0.00											
MW	422.91	0.55											
PSA	59.50	1.00											
HBD	0.00	1.00											
pKa	4.83	1.00											
MPO	3.80												
BBB	4.60												
LogBB	-0.06												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.19	1.00
TPSA_SCORE	59.50	0.58
PKA_SCORE	8.81	1.00
BBB_SCORE		4.60

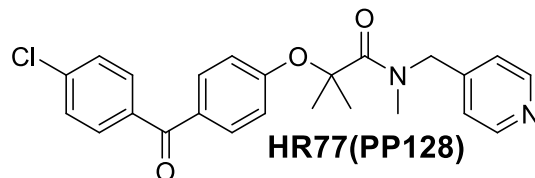
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	NA	7	5.58	- 5.77	45.47	56.93	608.63	7	117.26	5.42	safe
ClogP	4.51	0.25										
ClogD	4.50	0.00										
MW	422.91	0.55										
PSA	59.50	1.00										
HBD	0.00	1.00										
pKa	5.03	1.00										
MPO	3.80											
BBB	4.27											
LogBB	-0.06											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.19	1.00
TPSA_SCORE	59.50	0.58
PKA_SCORE	5.03	0.34
BBB_SCORE		4.27

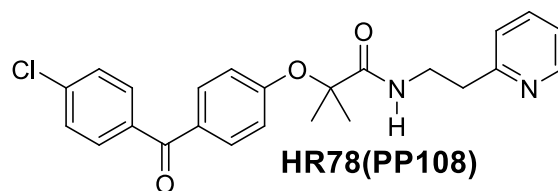
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	9.50	8	5.01	- 5.97	45.47	48.71	606.38	7	116.55	5.34	Safe
ClogP	4.60	0.20											
ClogD	4.60	0.00											
MW	422.91	0.55											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.55	1.00											
MPO	3.50												
BBB	4.44												
LogBB	-0.17												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE	4.44	

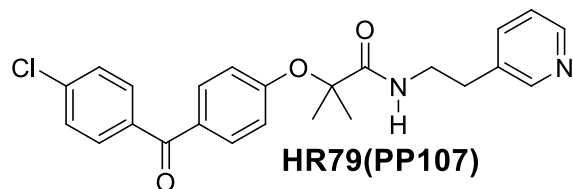
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	9.68	8	5.03	-5.74	45.47	46.89	605.78	7	117.12	5.39	safe
ClogP	4.57	0.21											
ClogD	4.57	0.00											
MW	422.91	0.55											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	4.93	1.00											
MPO	3.52												
BBB	4.44												
LogBB	-0.18												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

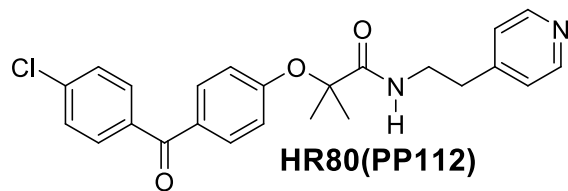
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	9.75	8	5.03	- 5.7 4	45.47	49.21	605.22	7	117.12	5.45	TOXIC
ClogP	4.57	0.21										
ClogD	4.57	0.00										
MW	422.91	0.55										
PSA	68.29	1.00										
HBD	1.00	0.75										
pKa	5.05	1.00										
MPO	3.52											
BBB	4.11											
LogBB	-0.18											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	5.05	0.35
BBB_SCORE		4.11

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

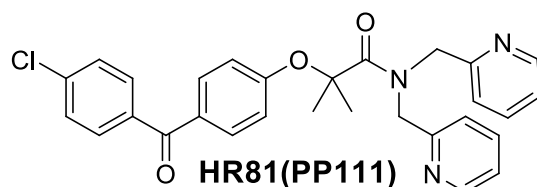
MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>	
		TO	NA	9	4.76	-	54.16	77.69	707.76	8	138.68	5.24	safe
					6.41								
ClogP	5.18	0.00											
ClogD	5.17	0.00											
MW	500.00	0.00											
PSA	72.39	1.00											
HBD	0.00	1.00											
pKa	4.49	1.00											
MPO	3.00												
BBB	3.66												
LogBB	-0.15												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	4	0.20
HA_SCORE	36	0.48
HWHBN_SCORE	0.22	0.99
TPSA_SCORE	72.39	0.49
PKA_SCORE	8.81	1.00
BBB_SCORE		3.66

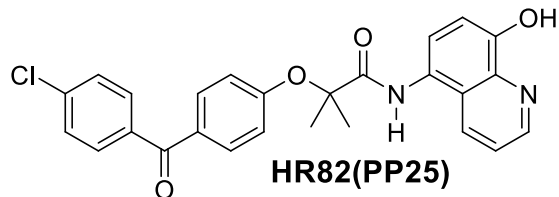
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	6.65	6	4.59	-7.05	49.90	50.89	615.89	9	127.37	5.27	safe
ClogP	5.65	0.00											
ClogD	5.65	0.00											
MW	460.91	0.28											
PSA	88.52	1.00											
HBD	2.00	0.50											
pKa	4.53	1.00											
MPO	2.78												
BBB	3.21												
LogBB	-0.31												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ );

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> =

hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	4	0.20
HA_SCORE	33	0.61
HWHBN_SCORE	0.33	0.76
TPSA_SCORE	88.52	0.38
PKA_SCORE	8.81	1.00
BBB_SCORE		3.21

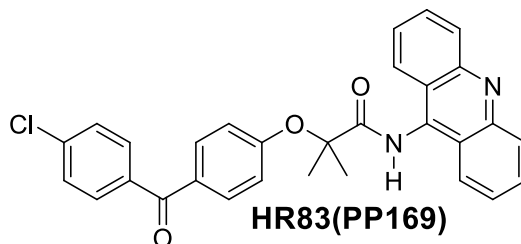
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>	
		T0	9.01	6	3.40	-9.08	56.85	56.88	666.84	7	141.47	5.62	Safe
ClogP	7.33	0.00											
ClogD	7.32	0.00											
MW	494.98	0.04											
PSA	68.29	1.00											
HBD	1.00	0.75											
pKa	5.55	1.00											
MPO	2.79												
BBB	3.25												
LogBB	0.24												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub> (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	5	0.00
HA_SCORE	36	0.48
HWHBN_SCORE	0.22	0.99
TPSA_SCORE	68.29	0.52
PKA_SCORE	5.55	0.48
BBB_SCORE		3.25

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	8.09	7	4.99	-6.28	45.47	56.50	603.44	7	116.34	5.24	Safe
ClogP	4.93	0.03										
ClogD	4.93	0.00										
MW	422.91	0.55										
PSA	68.29	1.00										
HBD	1.00	0.75										
pKa	4.09	1.00										
MPO	3.33											
BBB	4.44											
LogBB	-0.12											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ );

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub>

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> =

hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

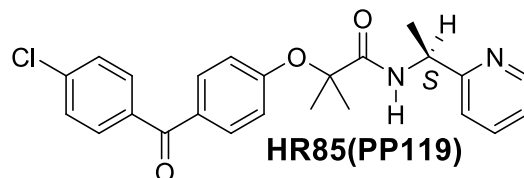
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	8.09	7	4.99	-6.28	45.47	56.50	603.44	7	116.34	5.26	safe
ClogP	4.93	0.03										
ClogD	4.93	0.00										
MW	422.91	0.55										
PSA	68.29	1.00										
HBD	1.00	0.75										
pKa	4.09	1.00										
MPO	3.33											
BBB	4.44											
LogBB	-0.12											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ );

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub>

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> =

hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

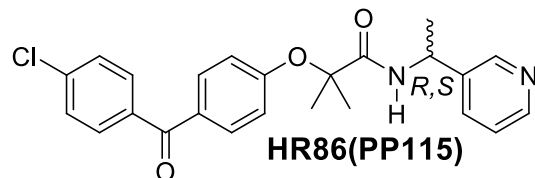
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	8.67	7	5.01	-6.05	45.67	57.16	604.58	7	116.79	5.39	safe
ClogP	4.70	0.15										
ClogD	4.70	0.00										
MW	422.91	0.55										
PSA	68.29	1.00										
HBD	1.00	0.75										
pKa	4.80	1.00										
MPO	3.45											
BBB	4.44											
LogBB	-0.16											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ );

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC<sub>50</sub>

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> =

hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

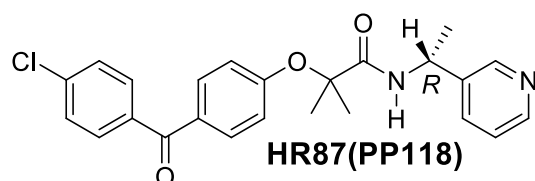
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	8.67	7	5.01	-6.05	45.67	57.16	604.58	7	116.79	5.36	safe
ClogP	4.70	0.15										
ClogD	4.70	0.00										
MW	422.91	0.55										
PSA	68.29	1.00										
HBD	1.00	0.75										
pKa	4.79	1.00										
MPO	3.45											
BBB	3.40											
LogBB	-0.16											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ );

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	30	0.75
HWHBN_SCORE	0.24	0.97
TPSA_SCORE	68.29	0.52
PKA_SCORE	8.81	1.00
BBB_SCORE		4.44

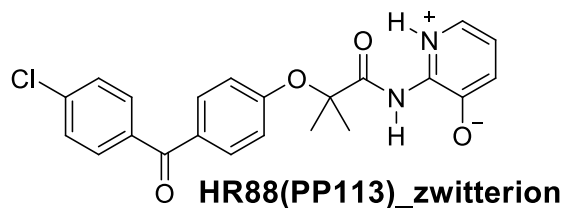
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	NA	6	13.41	- 5.75	42.37	45.59	554.75	9	122.36	5.17	safe
ClogP	4.87	0.07										
ClogD	4.63	0.00										
MW	410.85	0.64										
PSA	92.60	0.91										
HBD	2.00	0.50										
pKa	3.92	1.00										
MPO	3.12											
BBB	3.92											
LogBB	-0.49											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	92.60	0.35
PKA_SCORE	7.52	0.90
BBB_SCORE		3.92

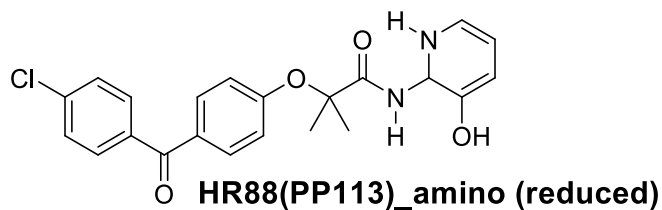
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	9.52	6	12.54	- 5.97	42.86	47.06	540.14	9	112.46	5.52	toxic
ClogP	3.72	0.64										
ClogD	3.39	0.31										
MW	412.87	0.62										
PSA	87.66	1.00										
HBD	3.00	0.25										
pKa	4.84	1.00										
MPO	3.82											
BBB	3.75											
LogBB	-0.63											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	2	1.00
HA_SCORE	29	0.79
HWHBN_SCORE	0.39	0.50
TPSA_SCORE	87.66	0.39
PKA_SCORE	7.35	0.88
BBB_SCORE		3.75

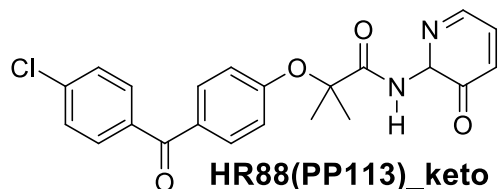
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	6.47	6	5.97	-7.20	42.15	54.68	535.28	9	110.48	5.33	safe
ClogP	4.07	0.46										
ClogD	4.07	0.00										
MW	410.85	0.64										
PSA	84.83	1.00										
HBD	1.00	0.75										
pKa	2.62	1.00										
MPO	3.85											
BBB	4.38											
LogBB	-0.50											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	2	1.00
HA_SCORE	29	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	84.83	0.41
PKA_SCORE	8.81	1.00
BBB_SCORE		3.75

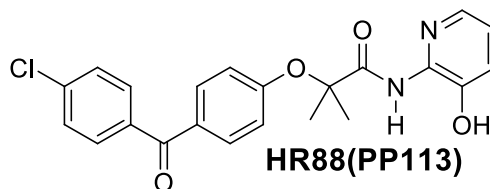
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	6.16	6	5.62	- 5.90	42.40	45.14	553.00	9	111.61	5.22	safe
ClogP	4.87	0.07											
ClogD	4.63	0.00											
MW	410.85	0.64											
PSA	88.52	1.00											
HBD	2.00	0.50											
pKa	3.92	1.00											
MPO	3.20												
BBB	3.72												
LogBB	-0.43												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	84.52	0.38
PKA_SCORE	7.52	0.90
BBB_SCORE		3.72

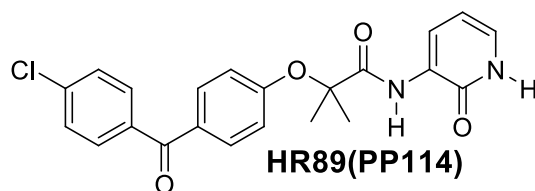
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	6	7.23	- 6.49	42.32	43.44	529.29	8	111.66	5.13	safe
ClogP	3.53	0.73											
ClogD	3.53	0.24											
MW	410.85	0.64											
PSA	84.50	1.00											
HBD	2.00	0.50											
pKa	1.82	1.00											
MPO	4.11												
BBB	4.08												
LogBB	-0.57												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	84.50	0.41
PKA_SCORE	8.81	1.00
BBB_SCORE	4.08	

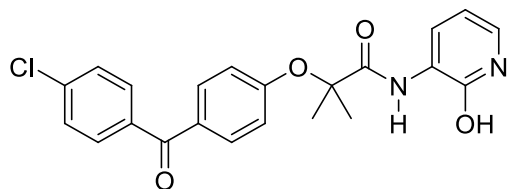
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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**HR89(PP114)\_aromatic**

Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	6.17	6	5.85	-6.00	42.40	43.69	552.22	9	111.61	5.21	Safe
ClogP	4.87	0.07										
ClogD	4.87	0.00										
MW	410.85	0.64										
PSA	88.52	1.00										
HBD	2.00	0.50										
pKa	1.82	1.00										
MPO	3.20											
BBB	3.77											
LogBB	-0.43											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	88.52	0.38
PKA_SCORE	8.81	1.00
BBB_SCORE		3.77

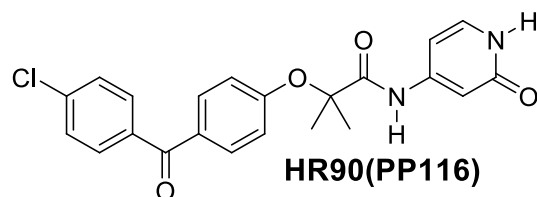
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	NA	6	7.23	- 6.49	42.32	42.75	530.46	8	111.59	5.16	safe
ClogP	3.38	0.81											
ClogD	3.38	0.31											
MW	410.85	0.64											
PSA	84.50	1.00											
HBD	2.00	0.50											
pKa	1.80	1.00											
MPO	4.26												
BBB	4.08												
LogBB	-0.60												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	84.50	0.41
PKA_SCORE	8.81	1.00
BBB_SCORE	4.08	

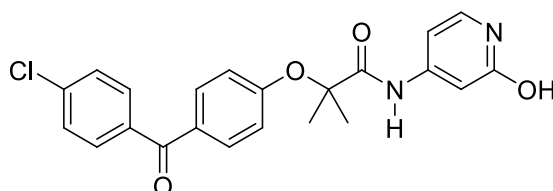
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

Chem. 2019, 62 (21), 9824-9836.



**HR90(PP116)\_aromatic**

Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	6.92	6	5.85	-6.00	42.40	44.16	554.21	9	111.61	5.21	safe
ClogP	4.87	0.07										
ClogD	4.87	0.00										
MW	410.85	0.64										
PSA	88.52	1.00										
HBD	2.00	0.5										
pKa	2.21	1.00										
MPO	3.20											
BBB	3.77											
LogBB	-0.43											

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	88.52	0.38
PKA_SCORE	8.81	1.00
BBB_SCORE	3.77	

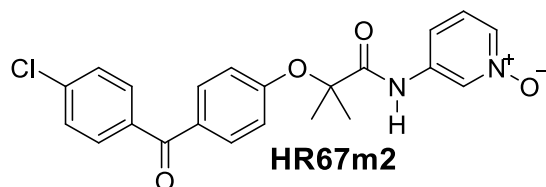
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5\text{MW}(\text{HBA}+\text{HBD})]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	6.13	6	11.51	-6.13	42.26	43.33	558.19	9	112.63	5.36	safe
ClogP	3.31	0.84											
ClogD	3.31	0.84											
MW	410.85	0.64											
PSA	82.34	1.00											
HBD	1.00	0.75											
pKa	0.81	1.00											
MPO	4.57												
BBB	4.28												
LogBB													

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ );

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29	0.79
HWHBN_SCORE	0.25	0.97
TPSA_SCORE	82.34	0.43
PKA_SCORE	8.81	1.00
BBB_SCORE		4.28

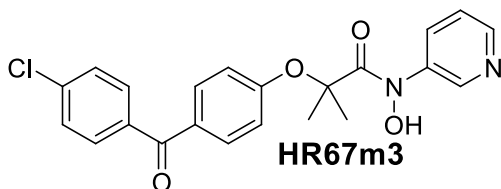
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	5.82	6	11.77	-5.06	42.41	51.70	556.21	9	109.30	5.63	safe
ClogP	4.21	0.39										
ClogD	4.06	0.00										
MW	410.85	0.64										
PSA	79.73	1.00										
HBD	1.00	0.75										
pKa	3.84	1.00										
MPO	3.78											
BBB	4.11											
LogBB												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	29.00	0.79
HWHBN_SCORE	0.30	0.85
TPSA_SCORE	79.73	0.44
PKA_SCORE	7.79	0.94
BBB_SCORE		4.11

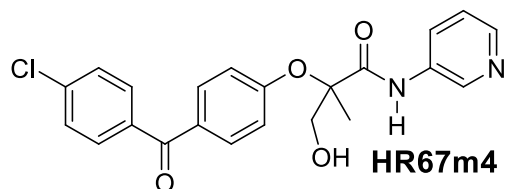
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	8.35	7	12.06	-5.44	42.41	40.63	553.24	9	110.86	5.40	safe
ClogP	3.53	0.74										
ClogD	3.53	0.24										
MW	410.85	0.64										
PSA	88.52	1.00										
HBD	2.00	0.50										
pKa	4.37	1.00										
MPO	4.11											
BBB	3.77											
LogBB												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic

balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ );

MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar

refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen

bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB

= blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3	0.69
HA_SCORE	29.00	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	88.52	0.38
PKA_SCORE	8.81	1.00
BBB_SCORE		3.77

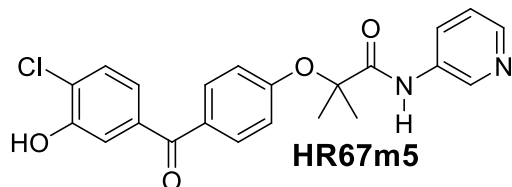
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch	IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
	T0	6.10	6	12.02	-5.44	42.42	40.55	552.87	9	11.29	5.76	safe
ClogP	4.27	0.36										
ClogD	4.14	0.00										
MW	410.85	0.64										
PSA	88.52	1.00										
HBD	2.00	0.50										
pKa	4.37	1.00										
MPO	3.50											
BBB	3.75											
LogBB												

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability( $\text{\AA}^3$ ); Minimal Projection Area ( $\text{\AA}^2$ ); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution ( $0.152\text{ClogP} - 0.0148\text{PSA} + 0.138$ ); hERG = estimated pIC50 (pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	29.00	0.79
HWHBN_SCORE	0.35	0.69
TPSA_SCORE	88.52	0.38
PKA_SCORE	7.85	0.95
BBB_SCORE		3.75

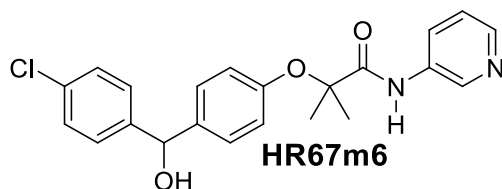
ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

Lee, H. J.; Barden, C. J.; Weaver, D. "The Blood-Brain Barrier (BBB) Score" J. Med.

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Calc.	MarvinSketch		IP	RB	HLB	logS	PL	MPA	MSA	HBA	MR	hERG <sub>AM</sub>	hERG <sub>CM</sub>
		T0	8.37	6	11.34	-4.95	42.17	53.36	554.15	7	109.84	5.49	safe
ClogP	4.13	0.43											
ClogD	4.13	0.00											
MW	396.87	0.74											
PSA	71.45	1.00											
HBD	2.00	0.50											
pKa	4.37	1.00											
MPO	3.67												
BBB	4.27												
LogBB													

IP = Isoelectric Point; RB = Number of rotatable bonds; HLB = hydrophilic-lipophilic balance; logS = water solubility; PL = polarizability(Å<sup>3</sup>); Minimal Projection Area (Å<sup>2</sup>); MSA = molecular surface area; HBA = hydrogen bond acceptors; MR = Molar refractivity; ClogD = distribution at pKa; PSA = polar surface area; HBD = hydrogen bond donors; pKa = estimated acid strength; MPO = score for CNS penetration; LogBB = blood-brain distribution (0.152ClogP – 0.0148PSA + 0.138); hERG = estimated pIC<sub>50</sub>

(pAct) value for hERG (the human ether-a-go-go (hERG) ion channel); hERG<sub>AM</sub> = hERG activity model; hERG<sub>CM</sub> = hERG classification model

BBB Score Calculator		
Property	Value	T <sub>0</sub>
ARO_R_SCORE	3.00	0.69
HA_SCORE	28.00	0.82
HWHBN_SCORE	0.30	0.84
TPSA_SCORE	71.45	0.50
PKA_SCORE	8.81	1.00
BBB_SCORE		4.27

ARO\_R\_SCORE = Number of aromatic rings; HA\_SCORE = Number of heavy atoms.

MWHNM\_SCORE =  $[-0.5MW(HBA+HBD)]$  where MW = molecular weight, HBA = number of hydrogen bond acceptor sites, and HBD = number of hydrogen bond donors;

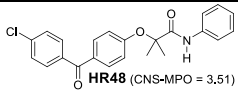
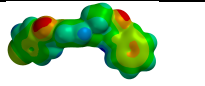
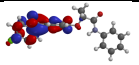
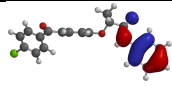
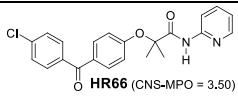
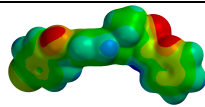
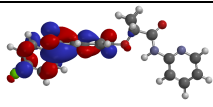
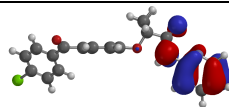
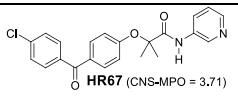
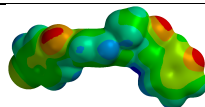
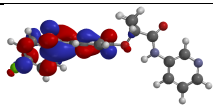
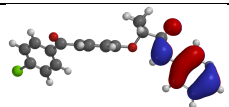
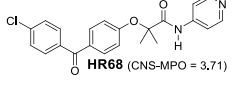
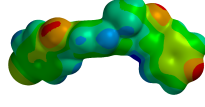
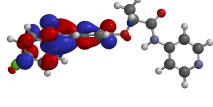
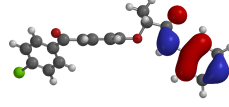
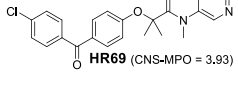
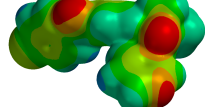
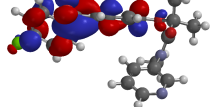
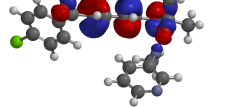
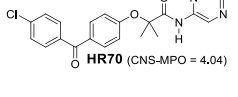
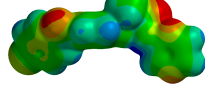
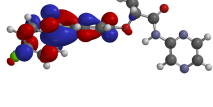
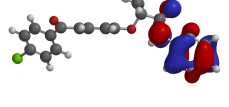
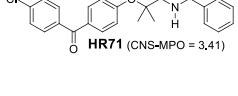
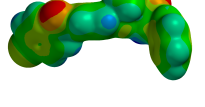
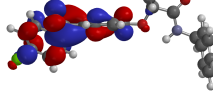
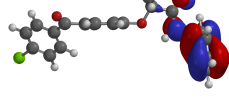
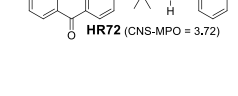
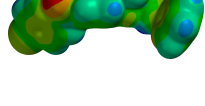
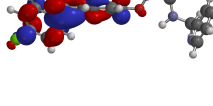
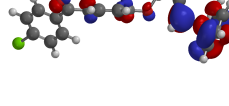
TPSA = topological polar surface area; PKA\_SCORE = Acidity strength. Gupta, M.;

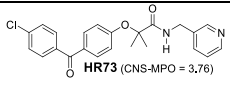
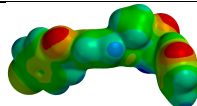
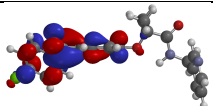
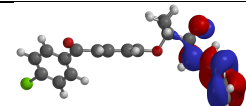
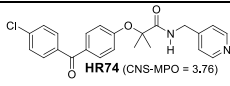
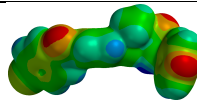
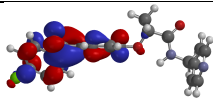
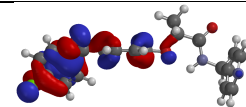
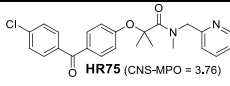
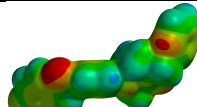
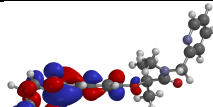
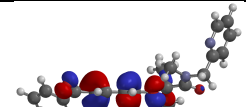
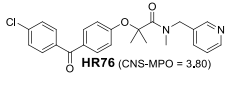
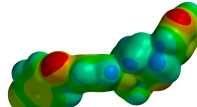
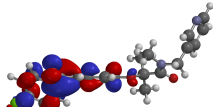
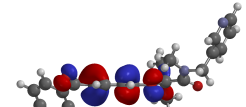
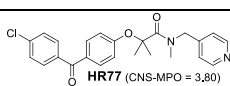
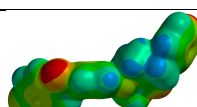
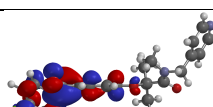
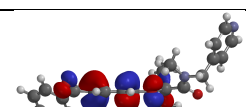
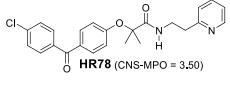
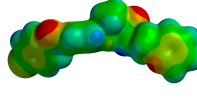
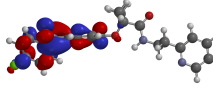
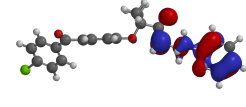
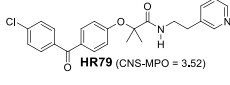
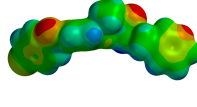
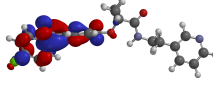
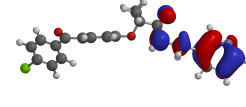
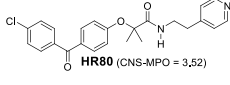
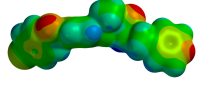

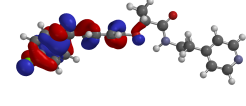
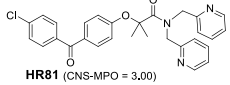
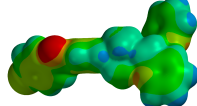
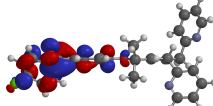
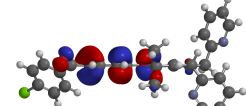
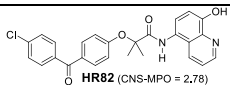
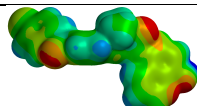
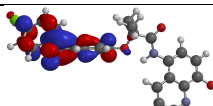
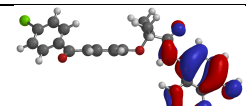
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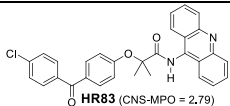
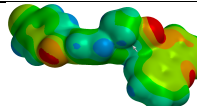
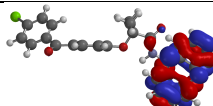
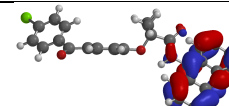
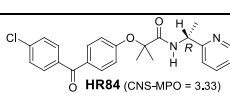
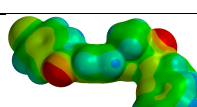
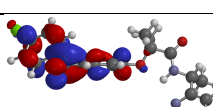
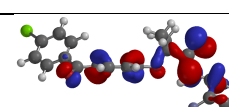
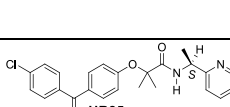
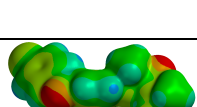
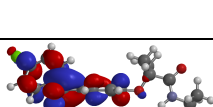
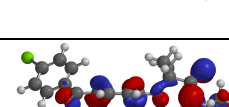
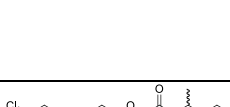
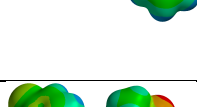
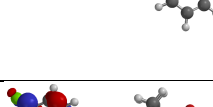
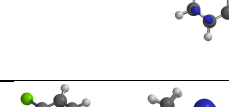
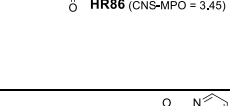
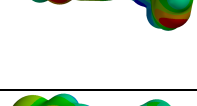


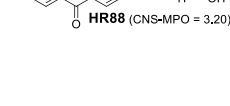
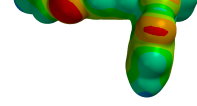
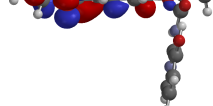
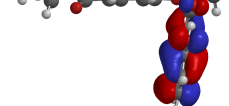
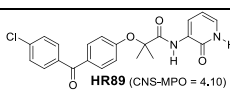
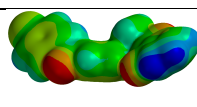
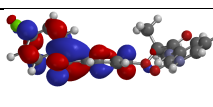
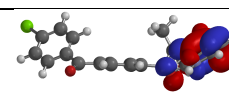
Chem. 2019, 62 (21), 9824-9836.

### 3. Density Functional Theory (DFT) with $\omega$ B97X-D/6-31G\* computed molecular properties.

DFT computed properties of aminopyridine derivatives **HR48**, **HR66**-**HR90**

Structure	EPM (solid)	LUMO	$E_{LUM}$ o	HOMO	$E_{LUM}$ o	$\Delta E_{FM}$ o	DM
 HR48 (CNS-MPO = 3,51)			-0.20		-7.98	7.68	1.8 1
 HR66 (CNS-MPO = 3,50)			-0.18		-8.37	8.19	3.4 9
 HR67 (CNS-MPO = 3,71)			-0.26		-8.33	8.07	3.5 9
 HR68 (CNS-MPO = 3,71)			-0.29		-8.73	8.44	2.8 9
 HR69 (CNS-MPO = 3,93)			-0.07		-8.44	8.37	4.1 4
 HR70 (CNS-MPO = 4,04)			-0.23		-8.66	8.43	1.2 7
 HR71 (CNS-MPO = 3,41)			-0.14		-8.60	8.46	2.2 3
 HR72 (CNS-MPO = 3,72)			-0.12		-8.86	8.74	1.6 1

 <b>HR73</b> (CNS-MPO = 3,76)			-0.17		-8.87	8.70	4.1 7
 <b>HR74</b> (CNS-MPO = 3,76)			-0.20		-8.96	8.76	3.4 0
 <b>HR75</b> (CNS-MPO = 3,76)			0.04		-8.37	8.41	3.5 7
 <b>HR76</b> (CNS-MPO = 3,80)			-0.02		-8.44	8.42	2.2 2
 <b>HR77</b> (CNS-MPO = 3,80)			-0.03		-8.45	8.42	0.3 9
 <b>HR78</b> (CNS-MPO = 3,50)			-0.13		-8.73	8.60	2.3 9
 <b>HR79</b> (CNS-MPO = 3,52)			-0.19		-8.79	8.60	3.7 8
 <b>HR80</b> (CNS-MPO = 3,52)			-0.21		-8.97	8.76	2.7 3
 <b>HR81</b> (CNS-MPO = 3,00)			0.25		-8.01	8.26	7.5 0
 <b>HR82</b> (CNS-MPO = 2,78)			-0.24		-7.35	7.11	2.1 4

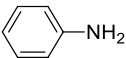
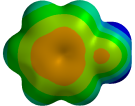
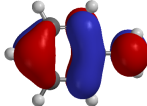
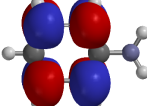
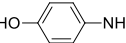
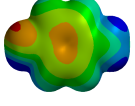
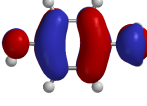
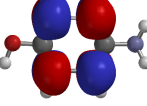
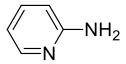
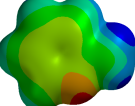
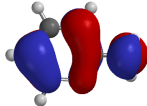
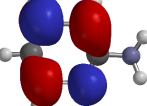
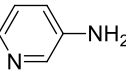
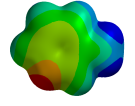
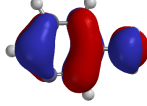
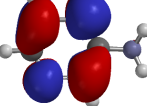
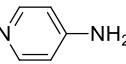
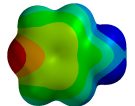
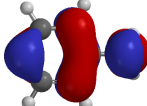
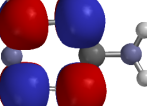
 HR83 (CNS-MPO = 2,79)			-0.39		-7.50	7.11	2.4 8
 HR84 (CNS-MPO = 3,33)			-0.05		-8.72	8.67	3.5 6
 HR85 (CNS-MPO = 3,33)			-0.04		-8.72	8.68	3.8 7
 HR86 (CNS-MPO = 3,45)			-0.18		-8.85	8.67	2.1 7
 HR88 (CNS-MPO = 3,20)			-0.04		-7.93	7.89	3.7 5
 HR89 (CNS-MPO = 4,10)			-0.01		-7.69	7.68	3.9 5
 HR90 (CNS-MPO = 4,26)			-0.11		-7.88	7.77	7.0 8

EPM = Electrostatic Potential Map; HOMO = Highest Occupied Molecular Orbital;

LUMO = Lowest Unoccupied Molecular Orbital;  $E_{\text{HOMO}}$  = Energy of HOMO in eV;  $E_{\text{LUMO}}$

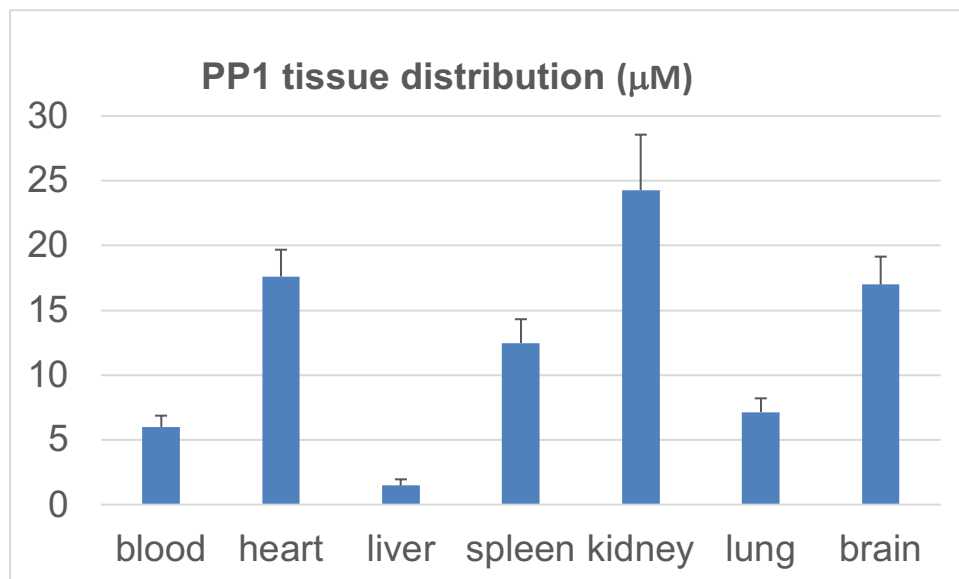
= Energy of LUMO in eV;  $\Delta E_{\text{FMO}} = E_{\text{LUMO}} - E_{\text{HOMO}}$  in eV; DP = dipole moment (Debye)

DFT ( $\omega$ B97X-D/6-31G\*) computed properties (nucleophilicity) of few selected anilines and aminopyridines.

Nucleophile	Structure	Electrostatic Potential	HOMO	LUMO	HOMO (eV)	LUMO (eV)	Dipole Moment (debye)
aniline					-7.12	2.29	1.89
4-aminophenol					-6.96	2.03	2.14
2-aminopyridine					-7.75	1.67	2.01
3-aminopyridine					-7.78	1.56	3.26
4-aminopyridine					-8.14	1.95	3.98

HOMO = Highest Occupied Molecular Orbital; LUMO = Lowest Unoccupied Molecular Orbital

**4. Detection of our prototype drug candidate, PP1, in mouse tissues following intraperitoneal drug delivery.**



*Tissue distribution of our BPA-based prototype glioblastoma drug candidate, PP1. Mice were treated intraperitoneally (ip) with PP1 dissolved in 20% cyclodextrin at 50 mg/kg and the levels of the compound in blood, heart, liver, kidney, spleen, lung and brain were evaluated by HPLC (see methods). Data represent average values with standard deviation (n=3).*