Antiviral Library

HBV Subset

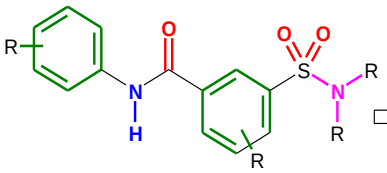
Focus on non-nucleoside compounds

YAI, Feb, 2015

ChemDiv
The chemistry of cures℠

Reference Compounds

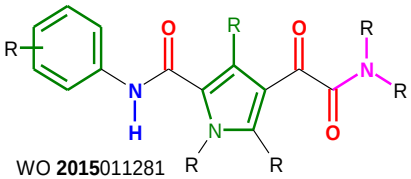
Isosteric transformations



WO **2014**106019

HBV replication inhibition in immortalized murine hepatocyte (AML12)-derived stable cell line (AML12HBV10) and liver Hep DES19 cells (EC_{50} < 1 μM) in MTT assays.

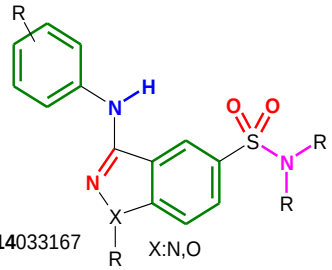
Baruch S Blumberg Institute



WO **2015**011281

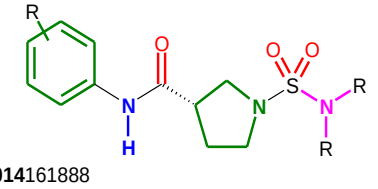
HBV replication inhibition in human hepatoma HepG2.2.15 (EC_{50} < 0.004 μM) and HepG2.117 (EC_{50} = 0.002 μM) cells in in vitro assays without cytotoxicity against HepG2 cells (CC_{50} > 100 μM) in resazurin assays

Janssen R&D Ireland



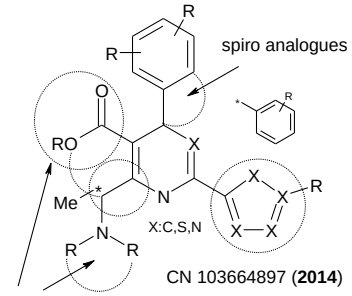
WO **2014**033167

HBV replication inhibition EC_{50} = 0.21 and 0.62 μM, in HepG2.2.15 and HepG2.117 cells, respectively



WO **2014**161888

activity against human hepatoma Hep G2.2.15 (stably transfected with HBV genome) and Hep G2.117 (stably inducible HBV producing cell line) cells (EC_{50} = 0.065 and 0.091 μM, respectively).

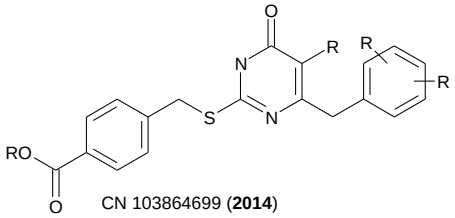


CN 103664897 (**2014**)

high diversity

HBV DNA replication inhibition (98% at 500 nM) in human hepatoma HepG2.2.15 cells in a qPCR-based assay.

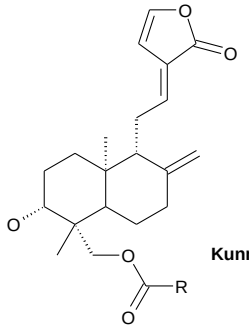
HEC Pharm



CN 103864699 (**2014**)

Reverse transcriptase inhibitors inhibit HIV-1 reverse transcriptase HBV with an IC_{50}=0.41 μM (in human liver HepG2 2.2.15 cancer cell)

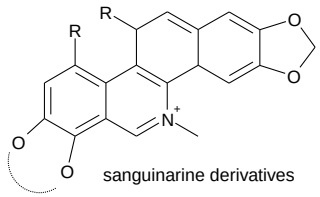
Peking University



CN 103739597 (**2014**)

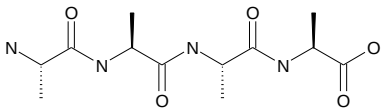
significant antiviral activity against HBsAg, HBeAg antigens and inhibited HBV DNA replication (IC_{50}=121.49, 19.73 and 23.51 mcM, respectively) in human hepatoma Hep G2.2.15 cells without showing any significant cytotoxicity (CC50 = 2466.06 mcM) in MTT assays.

Kunming Institute of Botany



sanguinarine derivatives

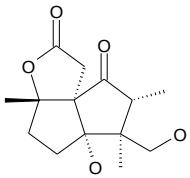
CN 103360402 (**2014**)



WO **2014**184350

HBV replication inhibition in human hepatoma HepG2.2.15 and HepG2.117 cells (EC_{50}<0.005 and 0.005 μM, respectively). It showed no cytotoxicity against HepG2 cells (CC_{50}>100 μM upon 4 days incubation), in resazurin assays.

Janssen R&D Ireland

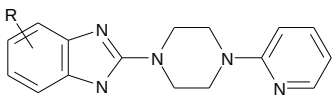


Zhengzhou University

CN 103304528 (**2013**)

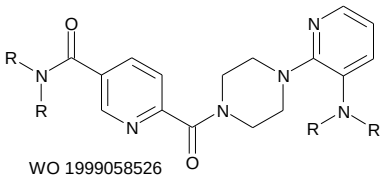
Compound extracted from *Lllicium henryi*

antiviral activity against HBsAg and HBeAg antigens (IC_{50}= 0.43 and 0.5 μM; in ELISA assays) and it also showed significant cytotoxicity (TC_{50}= 3.28 μM; using MTT method) in human hepatoma Hep G2 2.2.15 cells with therapeutic index values of 7.6 and 6.6, respectively.

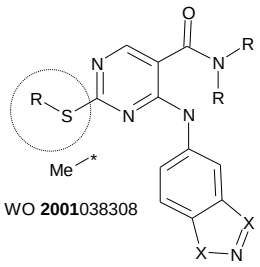


Antivir Res **2014**, 107: 6

BM601, a novel inhibitor of HBV

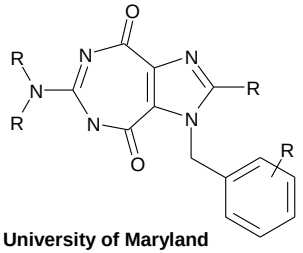


WO 1999058526



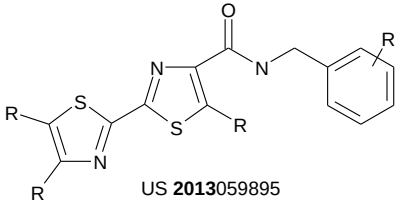
WO **2001**038308

examples



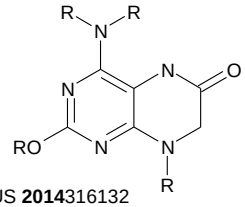
University of Maryland

Bioorg Med Chem Lett 2005, 15(24): 5397



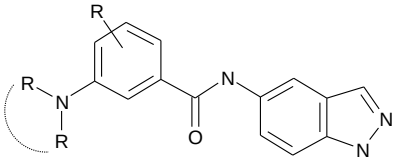
US **2013**059895

compound inhibited HBV-DNA (IC_{50}=5.4 μM and CC_{50}>100 μM)

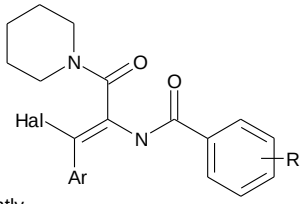


US **2014**316132

Toll-like receptor TLR7 ligand that stimulated IFN-alpha production in human peripheral blood mononuclear cells (MEC = 0.03 μM). Reported to be useful for the treatment of HBV



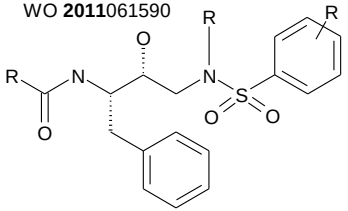
these compounds dose-dependently inhibit activity of HBV polymerase (by 42% at 1 mcg/ml) and also HCV RNA-dependent RNA-polymerase (NS5B, by 75% at 10 mcg/ml) *in vitro*



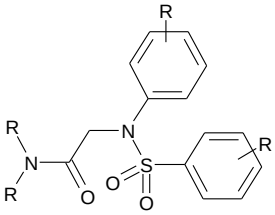
WO **1998**033501

Gilead Sciences

WO **2011**061590

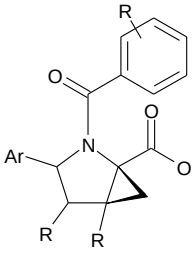


antiviral activity in lymphoid MT2 cells infected with 92HT599-MT2 HIV-1 strain with 104.5 and 80.45% inhibition at 1 and 0.1 μM, respectively, and IC_{50} values of 0.0117 and 0.0242 μM, in p24 estimation assays. It also showed cell viabilities of 99.97 and 89.93% at 1 and 0.1 mcM, respectively, against MT2 cells (CC_{50}>1 μM), in MTT cytotoxicity assays



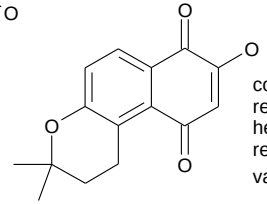
US **2015**038515

CCC-0975, dose-dependently reduced cccDNA (10, 20 and 70% reduction at 1, 3 and 10 mcM, respectively) and DP-rcDNA levels in HepDES19 cells.

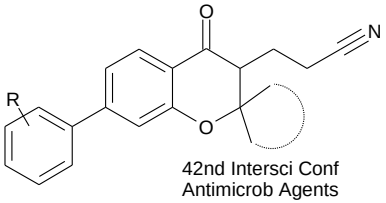


US **2009**324544

Enanta Pharmaceuticals, Inc.

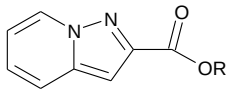


WO **2005**095376

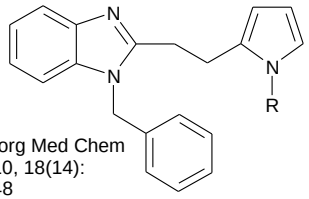


compound inhibited HBV replication in 2.2.15 human hepatoma cells with respective EC_{50} and EC_{90} values of 0.6 μM and 3.4 μM.

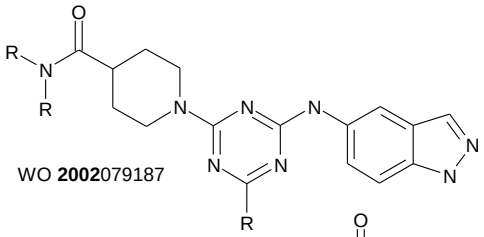
42nd Intersci Conf Antimicrob Agents Chemother (ICAAC) (September 27-30, San Diego) 2002, Abst F-1697



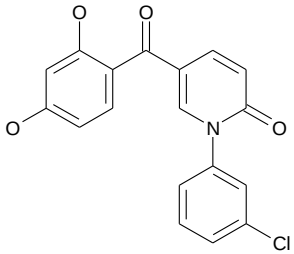
CN 102690262 (**2012**)



Bioorg Med Chem 2010, 18(14): 5048

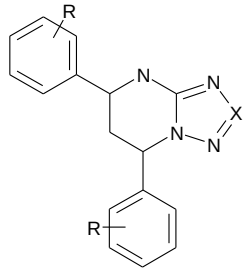


WO **2002**079187

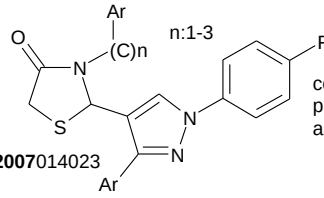


CH-04522, inhibited HBV DNA replication in HepG2 2.2.15 cells with IC_{50} and CC_{50} values of 1.46 and 221.11 μM (SI=151.06)

CN 102584690 (**2012**)

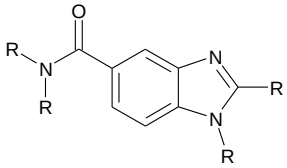


J Med Chem 2011, 54(16): 5660



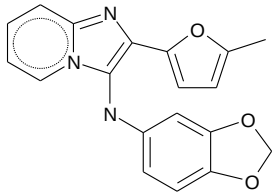
WO **2007**014023

compound inhibited HBV proliferation in HepG2 cellular assays (EC_{50}=0.01 μM).



IC_{50}<1.1 μM and SI>90.9

Arch Pharm 2011, 344(2): 78

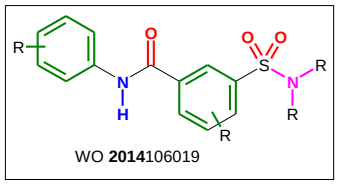


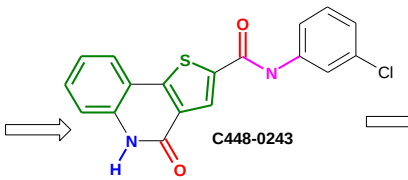
EC_{50}=4 μM,HBV-transfected human Hep G2 cells

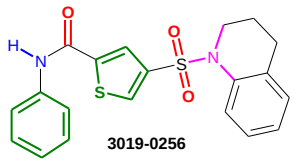
Topological analogues

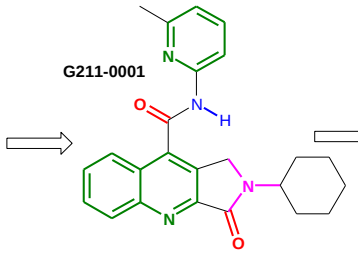
ChemDiv Compounds (examples)

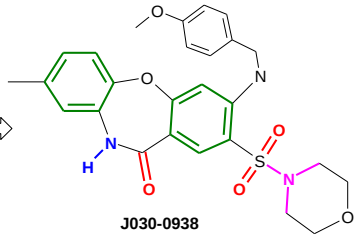
template

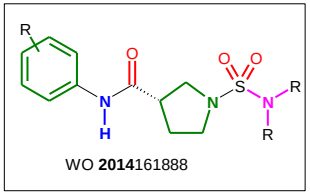


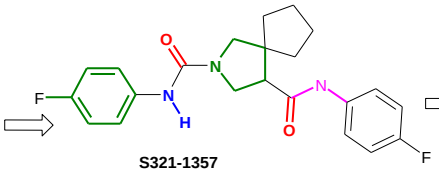


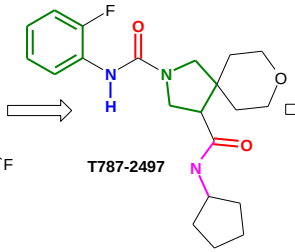


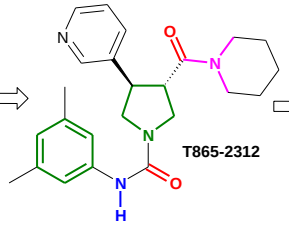


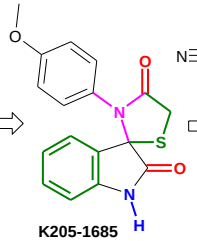


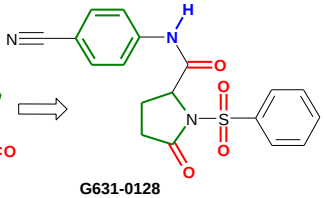


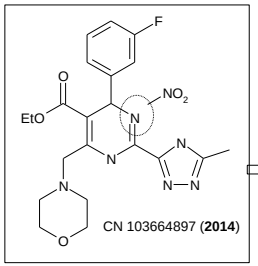


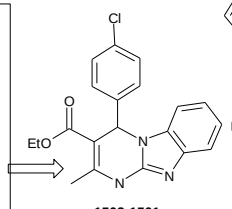


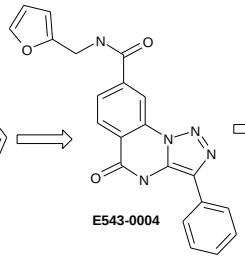


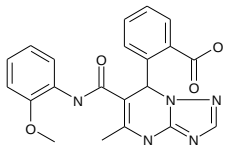


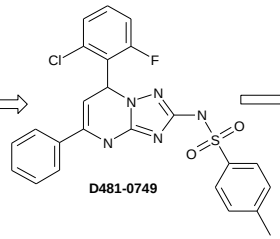


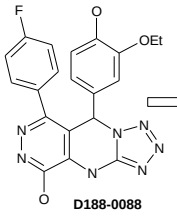


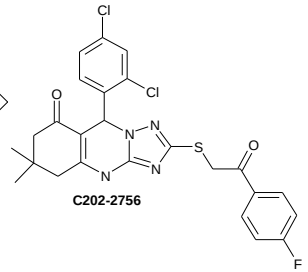


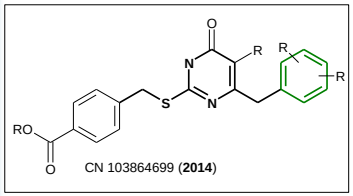


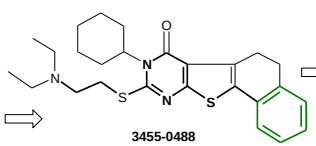


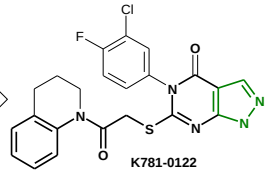


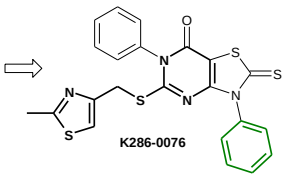


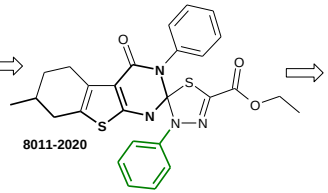


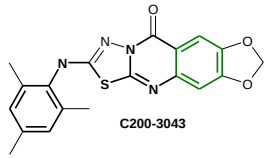












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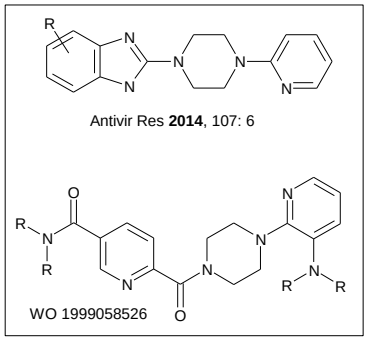

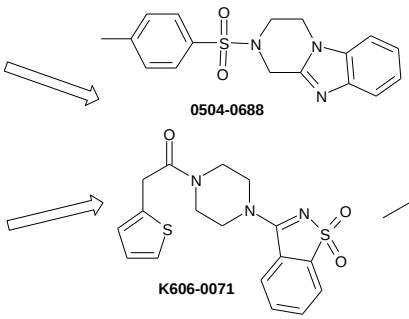

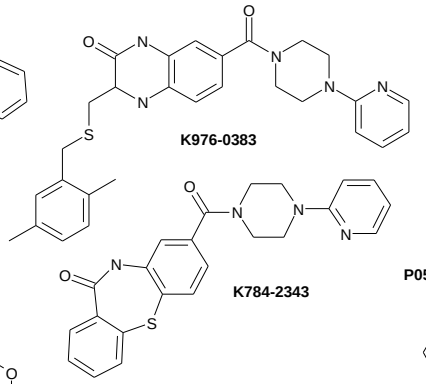

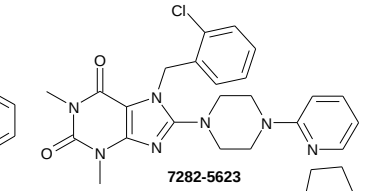

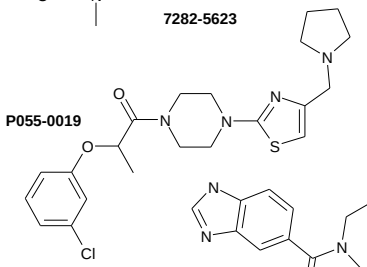

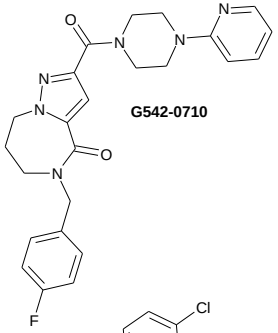

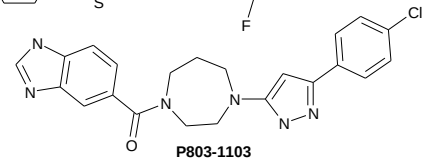

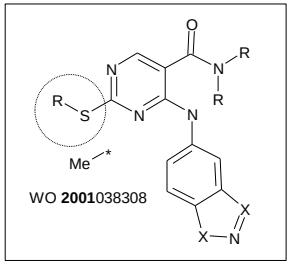

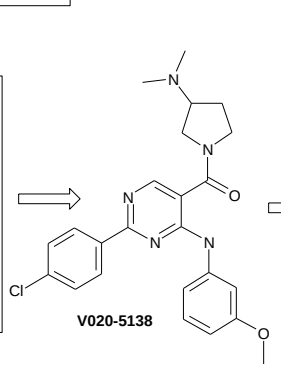

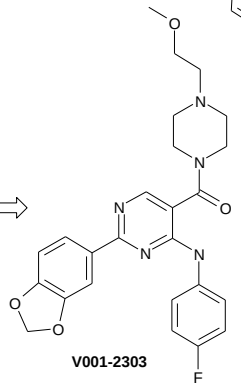

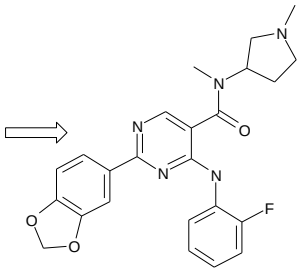

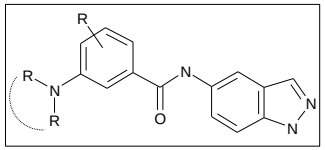

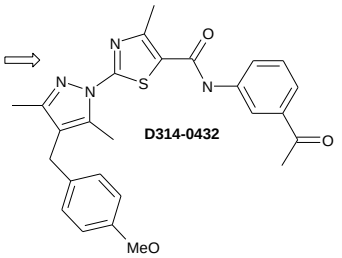

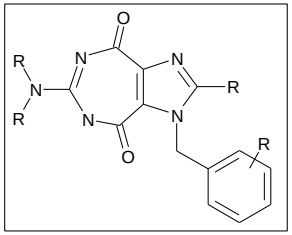

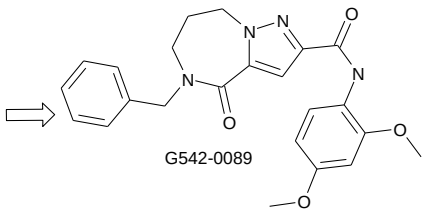

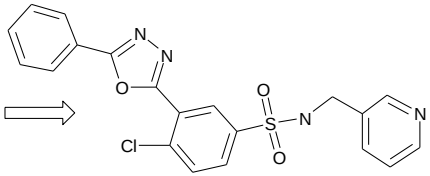

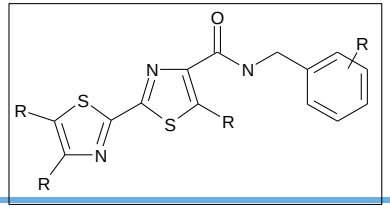

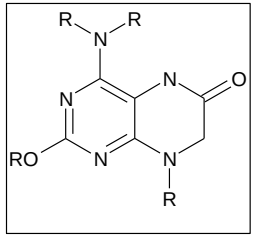

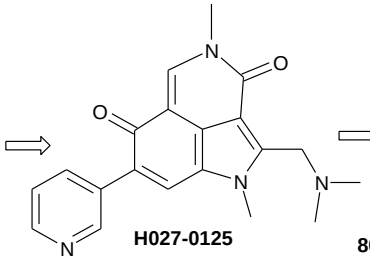

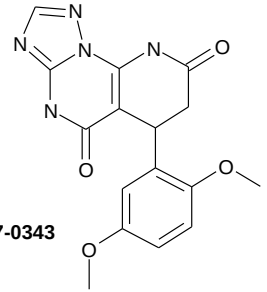

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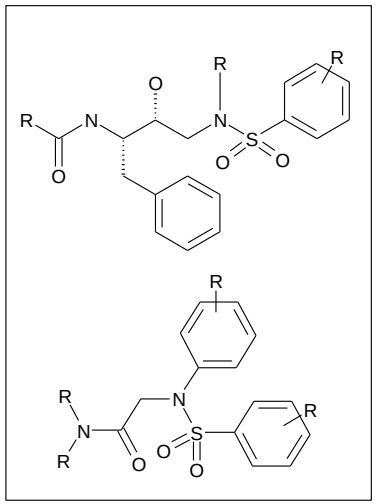

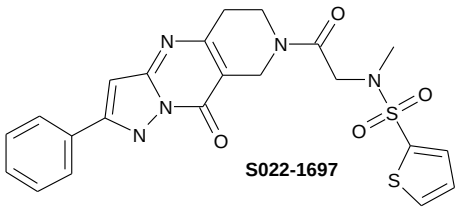

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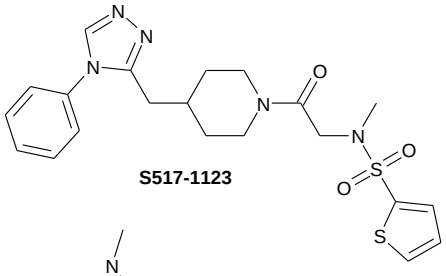

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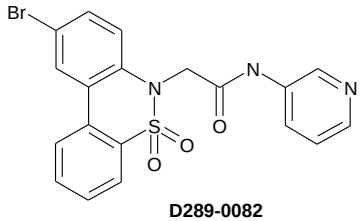

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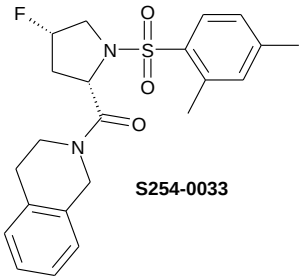

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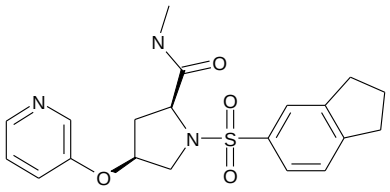

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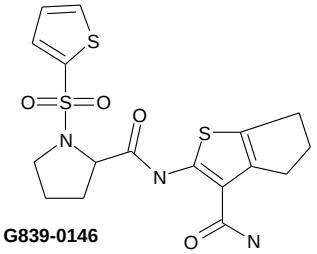

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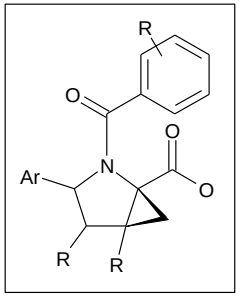

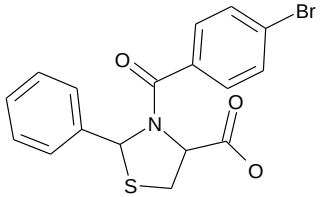

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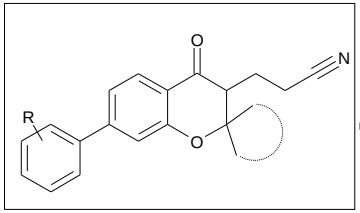

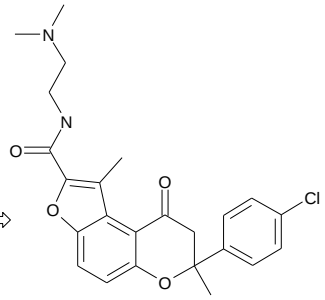

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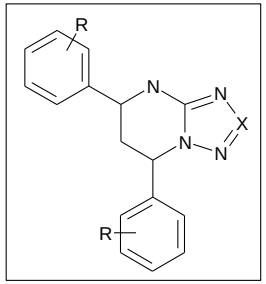

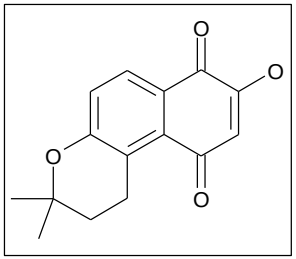

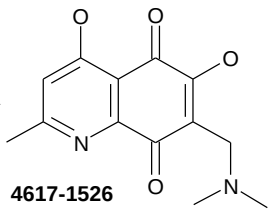

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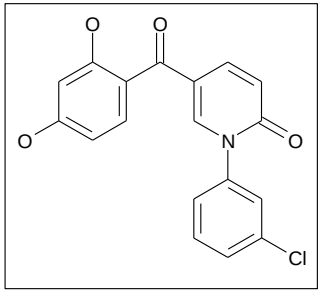

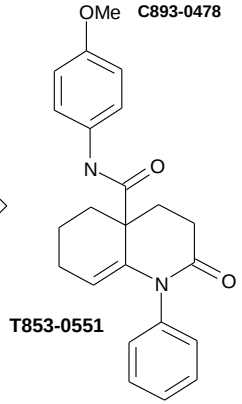

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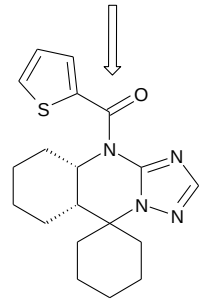

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