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(54) Title: CASEIN KINASE 1 δ (CK1 δ) INHIBITORS

(57) Abstract: The invention relates to pharmaceutical compositions comprising casein kinase 1 delta (CK1 δ) and to the use of said inhibitors in the treatment of neurodegenerative disorders such as Alzheimer's disease.



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CASEIN KINASE 1 δ (CK1 δ) INHIBITORS

The invention relates to pharmaceutical compositions comprising casein kinase 1 delta (CK1 δ) inhibitors and to the use of said inhibitors in the treatment of neurodegenerative disorders such as Alzheimer's disease.

Alzheimer's disease (AD; also known as senile dementia of the Alzheimer type (SDAT), primary degenerative dementia of the Alzheimer's type (PDDAT), or Alzheimer's) is the most common form of dementia. Most often, Alzheimer's disease is diagnosed in people over 65 years of age, although the less-prevalent early-onset Alzheimer's can occur much earlier. In 2006, there were 26.6 million sufferers worldwide. Alzheimer's is predicted to affect 1 in 85 people globally by 2050.

Alzheimer's disease is a neurodegenerative disease characterised by the presence of senile plaques and neurofibrillary tangles in the brain. The degree of dementia at death correlates better with neurofibrillary tangle numbers than with senile plaques counts. The presence of neurofibrillary tangles in neurons results in the death of those neurons, implying that prevention of tangle formation is an important therapeutic goal. The principal protein that forms the neurofibrillary tangle is the microtubule-associated protein, tau, which assembles into filaments that have the appearance of twisting about each other in pairs and are referred to as paired helical filaments (PHF). PHF are present in different locations in degenerating neurons in the Alzheimer brain and when many aggregate in the neuronal cell body, they produce the neurofibrillary tangle (Lee *et al*, 2001).

Intraneuronal deposits of tau in the form of typical neurofibrillary tangles of AD or other morphologically distinct tau aggregates in a number of other neurodegenerative diseases, is the basis for grouping these conditions as tauopathies. Thus, in addition to AD, the main examples of the tauopathies are frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), progressive supranuclear palsy (PSP), Pick's disease, corticobasal degeneration, and multisystem atrophy (MSA). The intracellular tau deposits (usually neuronal but can also be glial) are all filamentous and mostly in a hyperphosphorylated state compared to the level of phosphorylation of tau from control human brain. In the case of AD, this hyperphosphorylated tau is often referred to as PHF-tau because it is derived from the PHF.

Tau is a phosphoprotein, the function of phosphorylation remaining to be unequivocally

established. However, increased phosphorylation of tau on multiple serine and threonine residues reduces the ability of tau to promote microtubule assembly and to stabilise assembled microtubules, effects that have been demonstrated both *in vitro* and in cells. Many studies have shown that PHF-tau from AD brain is more heavily phosphorylated on serine and threonine than tau from control brain. This has been demonstrated partly by protein sequencing and partly by demonstrating that certain monoclonal antibodies only label either PHF-tau or non-phosphorylated tau and not PHF-tau; the epitopes for many of these antibodies have been mapped to particular phosphorylated residues present in PHF-tau and absent from control brain tau. The pathological tau from most other cases of other tauopathies seems to be similarly hyperphosphorylated to PHF-tau.

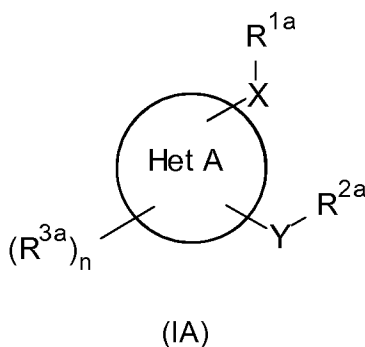
These findings strongly imply that similar abnormalities in regulating phosphorylation of tau are shared by all the tauopathies including AD.

A number of proline-directed and non-proline directed protein kinases have been suggested to have a role in the generation of PHF-tau in Alzheimer brain, including casein kinase 1. Mammalian casein kinase-1 exists as multiple isoforms CK1 α , CK1 β , CK1 γ 1, CK1 γ 2, CK1 γ 3, CK1 δ and CK1 ϵ . The role of CK1 δ as a potential tau kinase is of particular interest since it has been reported that CK1 δ protein is increased more than 30-fold in the hippocampus of Alzheimer brain compared to equivalent controls (Ghoshal, N. *et al* (1999) *Am. J. Pathol* 155, 1163-1172) while its mRNA content is increased 24-fold (Yasojima, K. *et al* (2000) *Brain Res* 865, 116-120) and CK1 has also been shown to be tightly associated with PHF (Kuret, J. *et al* (1997) *J. Neurochem* 69, 2506-2515). CK1 δ has also been reported to phosphorylate tau at two epitopes detecting using phospho-specific monoclonal antibodies to tau, and exogenous expression of CK1 δ in non-neuronal cells reduces binding of tau to microtubules (Li, G. *et al* (2004) *J. Biol. Chem.* 279, 15938-15945). Of note in the context of Alzheimer's disease is a report that CK1 activity is stimulated by amyloid beta-peptide (A β), a component of the senile neuritic plaques that, together with tangles, characterise Alzheimer brain (Chauhan, A. *et al* (1993) *Brain Res.* 629, 47-52). Additional evidence for possible involvement of CK1 in Alzheimer's disease comes from the reported influence of CK1 in the regulation of A β production in neurons (Flajolet, M. *et al* (2007) *PNAS USA* 104, 4159-4164). Further work has confirmed that at least 6 newly identified phosphorylation sites in PHF-tau (all on serine or threonine residues) can be generated by CK1 δ . The finding that a number of phosphorylation sites in PHF-tau for which CK1 is a strong candidate kinase, including three for which it is the only known kinase, implies that CK1 may make an important

contribution to the pathogenesis of Alzheimer's disease (Hanger *et al* (2007) J. Biol. Chem. 282, 23645-23654).

There is therefore a need for CK1δ inhibitors which may be of potential therapeutic benefit in the treatment of neurodegenerative diseases, such as tauopathies including Alzheimer's disease, frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), progressive supranuclear palsy (PSP), Pick's disease, corticobasal degeneration, and multisystem atrophy (MSA).

- 10 According to a first aspect of the invention there is provided a pharmaceutical composition comprising a compound of formula (IA) or a pharmaceutically acceptable salt or solvate thereof:



- 15 wherein

"Het A" represents a 4 or 5 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is optionally fused to one or more (e.g. 1-3) further rings to form a polycyclic ring system comprising up to 4 rings; X and Y independently represent a bond, $-C(R^{7a})(R^{8a})-$, $(CH_2)_2$, $-O-$, $-S-$, $-CH_2-O-$, $-(CH_2)_2-$, $O-$, NR^{6a} , $-N(R^{6a})-C(R^{7a})(R^{8a})-$, $-N(R^{6a})-(CH_2)_2-$, $-N(R^{6a})-(CH_2)_3-$, $-CH_2-N(R^{6a})-(CH_2)_2-$, $-N(R^{6a})-CO-$, $-CH_2-NH-CO-(CH_2)_2-$, $-N(R^{6a})-CO-CH_2-$, $-N(R^{6a})-CO-(CH_2)_2-$, $-CO-N(R^{6a})-CH_2-$, $=N-$, $-C(H)(CN)-$, $-C(=N-NH-COC_{1-6} \text{ alkyl})-$, $-CH=C(R^{6a})-CO-$, $=CH-$, $-CH=CH-$, $=CH-CO-$, $-N=CH-$, $-N=C(Me)-$, $-C(R^{6a})=CH-$, $-NH-N=C(H)-$, $-NH-CO-C(=CH-\text{heteroaryl})-$, $-C=C(Me)_2-$, $-CH=CH-CO-N(R^{6a})-$, $-CH=C(R^{6a})-NH-CO-$, $-CH=C(R^{6a})-CO-O-CH_2-$, $-CS-S-$, CH_2- , $-NH-CS-NH-$, $-NH-CS-NH-CH_2-$, $-NH-CS-NH-(CH_2)_2-$, $-CH_2-N(CSNH_2)-CH_2-$, $-S-$, CH_2- , $-S-(CH_2)_2-O-$, SO_2 , $-NH-SO_2-$, $-CH_2-N(R^{6a})-SO_2-$, CO , $-CH_2-CO-$, $-(CH_2)_2-CO-$, $-O-$, CH_2-CO- , $-(CH_2)_2-CO-$, COO , $-COO-C(R^{7a})CO-$, $-CH=C(R^{5a})-CONH-CH_2-$, $-CO-CH_2-$, $N(R^{6a})-CO-$, $-CO-CH_2-C(R^{6a})-CH_2-CO-$, $-CO-CH_2-N(R^{6a})-CH_2-$, $-CO-NH-N=C(R^{7a})-$, $-S-$, CH_2-CO- , $-S-CH_2-CO-N(R^{6a})-$, $-S-CH_2-CO-N(R^{6a})-CH_2-$, $-SO_2-N(R^{6a})-C(R^{7a})(R^{8a})-CONH-$, $-SO_2-N(R^{6a})-CH(-CH_2-\text{aryl})-CONH-CH_2-$, $-CH(-S-C_{1-6} \text{ alkyl})-C(Me)(OH)-$, $-CH_2-C(R^{6a})(OH)-$,

-C(OH)(CH(Me)(C₃₋₈ cycloalkyl))-CH₂-, -C(OH)(R^{6a})-CH₂-, -CH(Me)-NH-CO-CH₂-, -CO-N(R^{6a})-CH₂-, -CO-N(R^{6a})-CH₂-CH₂-, -CO-N(R^{6a})-CH₂-CH₂-CO-NH-CH₂-, -CO-NH-C(-CONH₂)=CH-, -CO-NH-CH(-CONH₂)-CH₂-, -CH₂-C(H)(Me)-CH₂-S-, -O-CH₂-CO-NH-, -CH₂-N(R^{6a})-CO-CH₂-O-, -N(R^{6a})-CO-CH₂-O-, -C(H)(-CH₂-aryl)-, -C(H)(-CH₂-heteroaryl)-, -C(NH-aryl)=N-N=CH-, -C(NH-aryl)=N-N=CH-, -NH-N=C(-aryl)-, -NH-N=C(-aryl)-CO-, -NH-C(=N-CO-C₁₋₆ alkyl)-NH-(CH₂)₂-, -C(-NH-aryl)=N-N=CH-, -NH-C(-NH-aryl)=N-CONH-, -C(=CH-aryl)-CONH-CH₂-, -CH=C(R^{6a})-CONH-, -CH(-CH₂-aryl)-NH-CO- or -CH(OH)-, wherein said aryl or heteroaryl groups of X and Y may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, NO₂ or hydroxyl groups;

10 R^{5a} represents hydrogen, C₁₋₆ alkyl or cyano;

R^{6a} represents hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, cyano, C₃₋₈ cycloalkyl, -CH₂-C₃₋₈ cycloalkyl, aryl, heteroaryl, -C₁₋₆ alkylene-aryl, -CO-aryl, -CO-heteroaryl or -C(R^{7a})(R^{8a})-heteroaryl, wherein said aryl groups of R^{6a} may be optionally substituted by one or more halogen or C₁₋₆ alkoxy groups;

15 R^{7a} and R^{8a} independently represent hydrogen or C₁₋₆ alkyl;

R^{1a} and R^{2a} independently represent aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1a} and R^{2a} may be substituted by one or more (e.g. 1, 2 or 3) R^{4a} groups;

R^{4a} represents halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-aryl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, -NH-aryl, -NH-SO₂-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{4a} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{4a} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;

n represents an integer from 0 to 3;

R^{3a} represents halogen, haloC₁₋₆ alkyl, C₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -S-C₁₋₆ alkyl, -CH₂-S-C₁₋₆ alkyl, -S-C₂₋₆ alkynyl, amino, cyano, NO₂, =O, =S, -SO₂-C₁₋₆ alkyl, -CONH₂, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -NH-C₁₋₆ alkyl, -NH-CO-C₁₋₆ alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH,

-NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein said aryl, heterocyclyl or heteroaryl groups of R^{3a} may be optionally substituted by one or more (e.g. 1, 2 or 3) R^{4a} groups and wherein said C₁₋₆ alkyl groups of R^{3a} may be optionally substituted by one or more hydroxyl groups;

with the proviso that the compound is other than compound number 38, 138, 212, 243, 378, 415, 441, 480, 577, 579, 580, 587-589, 593, 598, 600, 629, 636, 678, 684, 747, 760, 802, 861, 871, 873, 879, 883, 897-899, 904-905, 907, 909, 915, 917-919, 922-923, 925, 929-930, 938-939, 961.

In one embodiment, the compound of formula (IA) is selected from any of compounds:

1, 4-17, 19-25, 36-37, 39-40, 42, 44-45, 52, 61, 71-76, 80-83, 86-91, 93-97, 102-107, 110-112, 114, 117-122, 139-143, 149-151, 153, 158-160, 163-170, 174-177, 185-197, 200, 202-203, 208-209, 211, 213-221, 223-224, 226, 228-229, 232, 234, 237-240, 256, 261-264, 267-268, 270, 272, 275-283, 296, 304, 313, 319, 321-323, 326-328, 332, 334-335, 342-345, 350, 356, 361-365, 367-369, 372, 377, 379, 383, 393, 398, 403, 406, 412-413, 416-423, 431-432, 434, 436, 438-440, 442-447, 460, 463, 465-466, 468-476, 478, 481, 487-488, 492-494, 499, 501, 506, 508-510, 512-515, 517-518, 521-522, 525, 527-529, 531-532, 534, 551-552, 554-555, 558, 562-563, 569, 573, 576, 578, 581-582, 584, 586, 599, 604-605, 610-614, 617, 619, 623-625, 628, 630, 633-635, 639, 643-644, 650-652, 654, 656, 664-667, 670, 672, 676-677, 679, 683, 695, 697-698, 704, 707-708, 710, 714, 717, 733, 736, 741-743, 750, 761-766, 768, 773, 782, 787, 791, 794, 807, 809-812, 815-816, 820, 841-843, 846, 849-856, 859-860, 862-864, 931, 947-948, 967, 970, 982, 984, 989, 991-992, 1000 and 1002 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a further embodiment, the compound of formula (IA) is selected from any of compounds:

5-6, 9-11, 16-17, 19-20, 23-25, 37, 39-40, 42, 44-45, 52, 71, 73, 76, 80-83, 86-87, 89, 91, 93-94, 96-97, 102, 104-106, 111-112, 114, 117-122, 139-143, 149-151, 153, 159, 164, 166, 168, 174-177, 185-187, 190, 192, 195-197, 202-203, 208-209, 211, 214-221, 223-224, 226, 228-229, 232, 234, 237-238, 240, 261-264, 267, 270, 275-283, 313, 319, 321-322, 327-328, 332, 334-335, 342-345, 350, 361-365, 367, 369, 372, 377, 379, 383, 393, 398, 403, 406, 412-413, 416-419, 421, 423, 431-432, 440, 442-445, 447, 463, 465-466, 469-472, 474-476, 478, 481, 488, 494, 499, 501, 506, 508-510, 512-513, 515, 518, 521-

522, 525, 528, 532, 552, 554-555, 558, 562, 569, 576, 578, 582, 584 and 586 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a yet further embodiment, the compound of formula (IA) is selected from any of compounds:

10, 25, 45, 223, 240, 281-282, 321, 465, 506, 512, 611-614, 623-624, 633, 654, 656, 670, 676-677, 697, 717, 736, 766, 851 and 856 as described herein or a pharmaceutically acceptable salt or solvate thereof.

10 In a still yet further embodiment, the compound of formula (IA) is selected from any of compounds:

10, 45, 240, 654, 656, 766 and 856 as described herein or a pharmaceutically acceptable salt or solvate thereof, such as compounds 10, 654 and 856.

15 In one embodiment, the compound of formula (IA) is selected from any of compounds:

10, 25, 42, 45, 223, 240, 281-282, 321, 439, 465, 506, 512, 611-614, 619, 623-624, 633, 639, 654, 656, 670, 672, 676-677, 683, 697, 717, 736, 761, 765-766, 768, 809-810, 820, 842, 851, 856, 859-860, 863, 931, 947-948, 967, 970, 982, 984, 989, 991-992, 1000 and 1002 as described herein or a pharmaceutically acceptable salt or solvate thereof. The

20 compounds of this embodiment were tested in the CK1 δ inhibition assay as described herein and exhibited inhibition of greater than 5%.

In one embodiment, the compound of formula (IA) is selected from any of compounds:

10, 42, 45, 240, 654, 656, 766, 856, 859, 863, 931, 947-948 and 967 as described herein

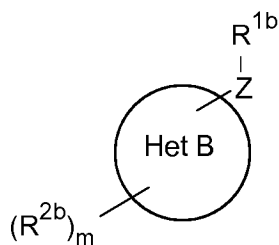
25 or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1 δ inhibition assay as described herein and exhibited inhibition of greater than 50%.

In one embodiment, the compound of formula (IA) is selected from any of compounds:

30 10, 654, 856, 859, 931 and 947 as described herein or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1 δ inhibition assay as described herein and exhibited inhibition of greater than 90%.

According to a second aspect of the invention there is provided a pharmaceutical

35 composition comprising a compound of formula (IB) or a pharmaceutically acceptable salt or solvate thereof:



(IB)

wherein

“Het B” represents a 5 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is fused to one or more (e.g. 1-3) further rings to form a polycyclic ring system comprising up to 4 rings;

Z represents a bond, $-\text{C}(\text{R}^{7b})(\text{R}^{8b})-$, $(\text{CH}_2)_2$, $-\text{O}-$, $-\text{S}-$, $-\text{CH}_2-\text{O}-$, $-(\text{CH}_2)_2-\text{O}-$, NR^{6b} , $-\text{N}(\text{R}^{6b})-\text{C}(\text{R}^{7b})(\text{R}^{8b})-$, $-\text{N}(\text{R}^{6b})-(\text{CH}_2)_2-$, $-\text{N}(\text{R}^{6b})-(\text{CH}_2)_3-$, $-\text{CH}_2-\text{N}(\text{R}^{6b})-(\text{CH}_2)_2-$, $-\text{N}(\text{R}^{6b})-\text{CO}-$, $-\text{CH}_2-\text{NH}-\text{CO}-(\text{CH}_2)_2-$, $-\text{N}(\text{R}^{6b})-\text{CO}-\text{CH}_2-$, $=\text{N}-$, $-\text{C}(\text{H})(\text{CN})-$, $-\text{C}(=\text{N}-\text{NH}-\text{COC}_{1-6} \text{ alkyl})-$, $-\text{CH}=\text{C}(\text{R}^{6b})-\text{CO}-$, $=\text{CH}-$, $-\text{N}=\text{CH}-$, $-\text{N}=\text{C}(\text{Me})-$, $-\text{C}(\text{R}^{6b})=\text{CH}-$, $-\text{NH}-\text{CO}-\text{C}(=\text{CH}-\text{heteroaryl})-$, $-\text{C}=\text{C}(\text{Me})_2-$, $-\text{CH}=\text{CH}-\text{CO}-\text{N}(\text{R}^{6b})-$, $-\text{CH}=\text{C}(\text{R}^{6b})-\text{CO}-\text{NH}-\text{CH}_2-$, $-\text{CH}=\text{C}(\text{R}^{6b})-\text{NH}-\text{CO}-$, $-\text{CH}=\text{C}(\text{R}^{6b})-\text{CO}-\text{O}-\text{CH}_2-$, $-\text{CS}-\text{S}-\text{CH}_2-$, $-\text{NH}-\text{CS}-\text{NH}-$, $-\text{NH}-\text{CS}-\text{NH}-\text{CH}_2-$, $-\text{NH}-\text{CS}-\text{NH}-(\text{CH}_2)_2-$, $-\text{CH}_2-\text{N}(\text{CSNH}_2)-\text{CH}_2-$, $-\text{S}-\text{C}(\text{R}^{5b})(\text{R}^{6b})-$, $-\text{S}-(\text{CH}_2)_2-\text{O}-$, SO_2 , $-\text{NH}-\text{SO}_2-$, $-\text{CH}_2-\text{NH}-\text{SO}_2-$, CO , $-\text{CH}_2-\text{CO}-$, $-(\text{CH}_2)_2-\text{CO}-$, $-\text{O}-\text{CH}_2-\text{CO}-$, $-(\text{CH}_2)_2-\text{CO}-$, COO , $-\text{COO}-\text{C}(\text{R}^{7b})\text{CO}-$, $-\text{CH}=\text{C}(\text{R}^{5b})-\text{CONH}-\text{CH}_2-$, $-\text{CO}-\text{CH}_2-\text{N}(\text{R}^{6b})-\text{CO}-$, $-\text{CO}-\text{CH}_2-\text{C}(\text{R}^{6b})-\text{CH}_2-\text{CO}-$, $-\text{CO}-\text{CH}_2-\text{N}(\text{R}^{6b})-\text{CH}_2-$, $-\text{CO}-\text{NH}-\text{N}=\text{C}(\text{R}^{7b})-$, $-\text{S}-\text{CH}_2-\text{CO}-$, $-\text{S}-\text{CH}_2-\text{CO}-\text{N}(\text{R}^{6b})-$, $-\text{S}-\text{CH}_2-\text{CO}-\text{N}(\text{R}^{6b})-\text{CH}_2-$, $-\text{SO}_2-\text{N}(\text{R}^{6b})-\text{C}(\text{R}^{7b})(\text{R}^{8b})-\text{CONH}-$, $-\text{SO}_2-\text{N}(\text{R}^{6b})-\text{CH}(-\text{CH}_2-\text{aryl})-\text{CONH}-\text{CH}_2-$, $-\text{CH}(-\text{S}-\text{C}_{1-6} \text{ alkyl})-\text{C}(\text{Me})(\text{OH})-$, $-\text{CH}_2-\text{C}(\text{R}^{6b})(\text{OH})-$, $-\text{C}(\text{OH})(\text{CH}(\text{Me})(\text{C}_{3-8} \text{ cycloalkyl}))-\text{CH}_2-$, $-\text{C}(\text{OH})(\text{R}^{6b})-\text{CH}_2-$, $-\text{CH}(\text{Me})-\text{NH}-\text{CO}-\text{CH}_2-$, $-\text{CO}-\text{N}(\text{R}^{6b})-\text{CH}_2-$, $-\text{C}(\text{H})(\text{R}^{6b})-\text{CO}-\text{N}(\text{R}^{5b})-\text{CH}_2-$, $-\text{CO}-\text{N}(\text{R}^{6b})-\text{CH}_2-\text{CH}_2-$, $-\text{CO}-\text{N}(\text{R}^{6b})-\text{CH}_2-\text{CH}_2-\text{CO}-\text{NH}-\text{CH}_2-$, $-\text{CO}-\text{NH}-\text{C}(-\text{CONH}_2)=\text{CH}-$, $-\text{CO}-\text{NH}-\text{CH}(-\text{CONH}_2)-\text{CH}_2-$, $-\text{CH}_2-\text{C}(\text{H})(\text{Me})-\text{CH}_2-\text{S}-$, $-\text{O}-\text{CH}_2-\text{CO}-\text{NH}-$, $-\text{CH}_2-\text{N}(\text{R}^{6b})-\text{CO}-\text{CH}_2-\text{O}-$, $-\text{N}(\text{R}^{6b})-\text{CO}-\text{CH}_2-\text{O}-$, $-\text{C}(\text{H})(-\text{CH}_2-\text{aryl})-$, $-\text{C}(\text{H})(-\text{CH}_2-\text{heteroaryl})-$, $-\text{C}(\text{NH}-\text{aryl})=\text{N}-\text{N}=\text{CH}-$, $-\text{C}(\text{NH}-\text{aryl})=\text{N}-\text{N}=\text{CH}-$, $-\text{NH}-\text{CO}-\text{CH}_2-\text{N}(\text{R}^{6b})-$, $-\text{NH}-\text{N}=\text{C}(-\text{aryl})-$, $-\text{NH}-\text{N}=\text{C}(-\text{aryl})-\text{CO}-$, $-\text{NH}-\text{C}(=\text{N}-\text{CO}-\text{C}_{1-6} \text{ alkyl})-\text{NH}-(\text{CH}_2)_2-$, $-\text{C}(-\text{NH}-\text{aryl})=\text{N}-\text{N}=\text{CH}-$, $-\text{NH}-\text{C}(-\text{NH}-\text{aryl})=\text{N}-\text{CONH}-$, $-\text{C}(=\text{CH}-\text{aryl})-\text{CONH}-\text{CH}_2-$, $-\text{CH}=\text{C}(\text{R}^{6b})-\text{CONH}-$, $-\text{CH}(-\text{CH}_2-\text{aryl})-\text{NH}-\text{CO}-$ or $-\text{CH}(\text{OH})-$,

wherein said aryl or heteroaryl groups of Z may be optionally substituted by one or more halogen, C_{1-6} alkyl, C_{1-6} alkoxy, NO_2 or hydroxyl groups;

R^{5b} represents hydrogen, C_{1-6} alkyl or cyano;

R^{6b} represents hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, cyano, COOH , $-\text{COOC}_{1-6} \text{ alkyl}$, C_{3-8}

cycloalkyl, $-\text{CH}_2-\text{C}_{3-8} \text{ cycloalkyl}$, aryl, heteroaryl, $-\text{C}_{1-6} \text{ alkylene-aryl}$, $-\text{CO-aryl}$, $-\text{O-CO-}$

heteroaryl, -CO-heteroaryl or $-C(R^{7b})(R^{8b})$ -heteroaryl, wherein said aryl groups of R^{6b} may be optionally substituted by one or more halogen or C_{1-6} alkoxy groups;

R^{7b} and R^{8b} independently represent hydrogen or C_{1-6} alkyl;

R^{1b} represents aryl, C_{3-8} cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1b} may be substituted by one or more (e.g. 1, 2 or 3) R^{4b} groups;

R^{4b} represents halogen, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, C_{3-8} cycloalkyl, halo C_{1-6} alkyl, hydroxyl, C_{1-6} alkoxy, -O- C_{1-6} alkenyl, halo C_{1-6} alkoxy, -COOH, -CO- C_{1-6} alkyl, -COO- C_{1-6} alkyl, -CONH₂, -CH₂-CONH₂, -NH- C_{1-6} alkyl, -NH- C_{2-6} alkenyl, -NH-CO- C_{1-6} alkyl, -CO-NH- C_{1-6} alkyl, -O-CH₂-CO-NH- C_{1-6} alkyl, -CH₂-CH₂-CO-NH- C_{1-6} alkyl, -S- C_{1-6} alkyl, -SO- C_{1-6} alkyl, -SO₂- C_{1-6} alkyl, -SO₂-NH- C_{1-6} alkyl, -S-CH₂-CO- C_{2-6} alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH- C_{3-8} cycloalkyl, -CH₂-CO-NH- C_{3-8} cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, -NH-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{4b} may be optionally substituted by one or more halogen, C_{1-6} alkyl, C_{1-6} alkoxy, =S or hydroxyl groups and wherein said C_{1-6} alkyl or C_{2-6} alkenyl groups of R^{4b} may be optionally substituted by one or more hydroxyl, amino, cyano, C_{1-6} alkoxy, CONH₂ or -COO- C_{1-6} alkyl groups;

m represents an integer from 0 to 3;

R^{2b} represents halogen, halo C_{1-6} alkyl, C_{1-6} alkyl, hydroxyl, C_{1-6} alkoxy, -S- C_{1-6} alkyl, -CH₂-S- C_{1-6} alkyl, -S- C_{2-6} alkynyl, amino, cyano, NO₂, =O, =S, -SO₂- C_{1-6} alkyl, -CONH₂, -CO- C_{1-6} alkyl, -COO- C_{1-6} alkyl, -NH- C_{1-6} alkyl, -NH-CO- C_{1-6} alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C_{1-6} alkyl, -CO-NH- C_{1-6} alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH, -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH- C_{1-6} alkyl, wherein said C_{1-6} alkyl groups of R^{2b} may be optionally substituted by one or more hydroxyl groups;

with the proviso that the compound is other than compound number 54, 373, 458, 496, 585, 590, 594, 596-597, 601-602, 649, 703, 778, 877, 891, 910, 912, 926 and 962-963.

In one embodiment, the compound of formula (IB) is selected from any of compounds 2-3, 26-28, 30-33, 35, 47-48, 51, 57-60, 63-64, 78, 84, 113, 123, 127-129, 145, 155-157, 171-173, 204, 206-207, 210, 225, 227, 233, 235-236, 241-242, 244, 249, 269, 285, 288, 303, 307-312, 314-316, 320, 324-325, 333, 336, 351, 357-360, 374-375, 384-391, 396, 399-402, 404-405, 407-411, 414, 424-425, 427-428, 437, 448, 456-457, 482, 484-485, 489-491, 495, 497-498, 505, 507, 516, 519, 524, 526, 553, 559-560, 568, 570, 575, 609, 615-

616, 618, 626-627, 638, 653, 669, 692-694, 705, 709, 712, 716, 719, 725, 734, 738, 740, 746, 749, 753-754, 756, 758-759, 767, 770, 777, 784-785, 790, 792, 796, 800-801, 804-805, 808, 819, 821, 827-828, 831, 833, 838, 844, 847, 857-858, 869, 872, 875, 933, 952, 955, 969, 987, 990 and 999 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a further embodiment, the compound of formula (IB) is selected from any of compounds:

2-3, 26-28, 30, 32-33, 47-48, 51, 59-60, 84, 113, 123, 127, 129, 145, 155, 157, 172-173, 204, 206-207, 210, 225, 233, 235-236, 241, 244, 269, 285, 288, 307-311, 315-316, 320, 324-325, 333, 336, 351, 357-360, 374-375, 385-386, 388-391, 396, 399-402, 404-405, 407-410, 414, 424, 427-428, 437, 457, 482, 490, 495, 497-498, 505, 516, 519, 553, 559-560 and 568 as described herein or a pharmaceutically acceptable salt or solvate thereof.

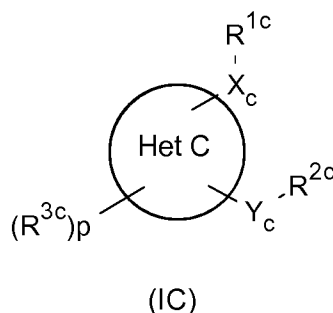
In a yet further embodiment, the compound of formula (IB) is selected from any of compounds:

30, 314, 324-325, 391, 405, 626, 705, 753-754, 759, 770, 784, 808, 833 and 847 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a still yet further embodiment, the compound of formula (IB) is selected from any of compounds:

324-325, 405, 754 and 847 as described herein or a pharmaceutically acceptable salt or solvate thereof, such as compound 324.

According to a third aspect of the invention there is provided a pharmaceutical composition comprising a compound of formula (IC) or a pharmaceutically acceptable salt or solvate thereof:



wherein

"Het C" represents a 6 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is optionally fused to one or more (e.g. 1-3) further rings to form a polycyclic ring system comprising up to 4 rings;

X_c and Y_c independently represent a bond, -C(R^{7c})(R^{8c})-, (CH₂)₂-, -O-, -S-, -CH₂-O-, -

- 5 (CH₂)₂-O-, NR^{6c}-, -N(R^{6c})-C(R^{7c})(R^{8c})-, -N(R^{6c})-(CH₂)₂-, -N(R^{6c})-(CH₂)₃-, -CH₂-N(R^{6c})-(CH₂)₂-, -N(R^{6c})-CO-, -CH₂-NH-CO-(CH₂)₂-, -N(R^{6c})-CO-CH₂-, -CO-N(R^{6c})-CH₂-, =N-, -C(H)(CN)-, -C(=N-NH-COC₁₋₆ alkyl)-, -CH=C(R^{6c})-CO-, =CH-, -N=CH-, -N=C(Me)-, -C(R^{6c})=CH-, -NH-CO-C(=CH-heteroaryl)-, -C=C(Me)₂-, -CH=CH-CO-N(R^{6c})-, -CH=C(R^{6c})-NH-CO-, -CH=C(R^{6c})-CO-O-CH₂-, -CS-S-CH₂-, -NH-CS-NH-, -NH-CS-NH-CH₂-, -NH-CS-NH-(CH₂)₂-, -CH₂-N(CSNH₂)-CH₂-, -S-CH₂-, -S-(CH₂)₂-O-, SO₂-, -NH-SO₂-, -CH₂-NH-SO₂-, CO-, -CH₂-CO-, -(CH₂)₂-CO-, -O-CH₂-CO-, -(CH₂)₂-CO-, COO-, -COO-C(R^{6c})(R^{7c})CO-, -CH=C(R^{5c})-CONH-CH₂-, -CO-CH₂-N(R^{6c})-CO-, -CO-CH₂-C(R^{6c})-CH₂-CO-, -CO-CH₂-N(R^{6c})-CH₂-, -CO-NH-N=C(R^{7c})-, -S-CH₂-CO-, -S-CH₂-CO-N(R^{6c})-, -S-CH₂-CO-N(R^{6c})-CH₂-, -SO₂-N(R^{6c})-C(R^{7c})(R^{8c})-CONH-, -SO₂-N(R^{6c})-CH(-CH₂-aryl)-CONH-CH₂-, -CH(-S-C₁₋₆ alkyl)-C(Me)(OH)-, -CH₂-C(R^{6c})(OH)-, -C(OH)(CH(Me)(C₃₋₈ cycloalkyl))-CH₂-, -C(OH)(R^{6c})-CH₂-, -CH(Me)-NH-CO-CH₂-, -CO-N(R^{6c})-CH₂-, -CO-N(R^{6c})-CH₂-CH₂-, -CO-N(R^{6c})-CH₂-CH₂-CO-NH-CH₂-, -CO-NH-C(-CONH₂)=CH-, -CO-NH-CH(-CONH₂)-CH₂-, -CH₂-C(H)(Me)-CH₂-S-, -O-CH₂-CO-NH-, -CH₂-N(R^{6c})-CO-CH₂-O-, -N(R^{6c})-CO-CH₂-O-, -C(H)(-CH₂-aryl)-, -C(H)(-CH₂-heteroaryl)-, -C(NH-aryl)=N-N=CH-, -C(NH-aryl)=N-N=CH-, -NH-N=C(-aryl)-, -NH-N=C(-aryl)-CO-, -NH-C(=N-CO-C₁₋₆ alkyl)-NH-(CH₂)₂-, -C(-NH-aryl)=N-N=CH-, -NH-C(-NH-aryl)=N-CONH-, -C(=CH-aryl)-CONH-CH₂-, -CH=C(R^{6c})-CONH-, -CH(-CH₂-aryl)-NH-CO- or -CH(OH)-, wherein said aryl or heteroaryl groups of X_c and Y_c may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, NO₂ or hydroxyl groups;

- 25 R^{5c} represents hydrogen, C₁₋₆ alkyl or cyano;

R^{6c} represents hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, cyano, C₃₋₈ cycloalkyl, -CH₂-C₃₋₈ cycloalkyl, aryl, heteroaryl, -C₁₋₆ alkylene-aryl, -CO-aryl, -CO-heteroaryl or -C(R^{7c})(R^{8c})-heteroaryl, wherein said aryl groups of R^{6c} may be optionally substituted by one or more halogen or C₁₋₆ alkoxy groups;

- 30 R^{7c} and R^{8c} independently represent hydrogen or C₁₋₆ alkyl;

R^{1c} and R^{2c} independently represent aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1c} and R^{2c} may be substituted by one or more (e.g. 1, 2 or 3) R^{4c} groups;

- R^{4c} represents halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-

- NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{4c} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{4c} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;
- 5 p represents an integer from 0 to 3;
- R^{3c} represents halogen, haloC₁₋₆ alkyl, C₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -S-C₁₋₆ alkyl, -CH₂-S-C₁₋₆ alkyl, -S-C₂₋₆ alkynyl, amino, cyano, NO₂, =O, =S, -SO₂-C₁₋₆ alkyl, -CONH₂, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -NH-C₁₋₆ alkyl, -NH-CO-C₁₋₆ alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH,
- 15 -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein said aryl, heterocyclyl or heteroaryl groups of R^{3c} may be optionally substituted by one or more (e.g. 1, 2 or 3) R^{4c} groups and wherein said C₁₋₆ alkyl groups of R^{3c} may be optionally substituted by one or more
- 20 hydroxyl groups;
- with the proviso that the compound is other than compound number 161, 648, 658, 680, 726, 824, 867, 880, 892, 896, 901, 903, 906, 928 and 944.

- In one embodiment, Het C represents a 6 membered heterocyclic ring system containing
- 25 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is optionally fused to one further ring to form a bicyclic ring system. In a further embodiment, Het C represents a 6 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is optionally fused to a phenyl ring to form a bicyclic ring system. In a yet further embodiment, Het C represents a 6 membered
- 30 heterocyclic ring system containing 1 or 2 nitrogen atoms, wherein said ring system is optionally fused to a phenyl ring to form a bicyclic ring system. In a yet further embodiment, Het C represents pyridinyl, pyrimidinyl or quinazolinyl. In a yet further embodiment, Het C represents quinazolinyl.
- 35 In one embodiment, X_c and Y_c independently represent a bond or NR^{6c}. In a further embodiment, X_c and Y_c independently represent a bond or NH. In a yet further

embodiment, one of X_c and Y_c represents a bond and the other represents a bond or NH. In a yet further embodiment, one of X_c and Y_c represents a bond and the other represents NH.

- 5 In one embodiment, R^{1c} and R^{2c} independently represent aryl, bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1c} and R^{2c} may be substituted by one or more (e.g. 1, 2 or 3) R^{4c} groups. In a further embodiment, R^{1c} and R^{2c} independently represent aryl (e.g. phenyl), bicyclic heterocyclyl (e.g. benzodioxinyl), monocyclic heteroaryl (e.g. pyridinyl, pyrazolyl or thiophenyl) or bicyclic heteroaryl ring
10 system (e.g. benzoxazolyl), wherein R^{1c} and R^{2c} may be substituted by one or more (e.g. 1, 2 or 3) R^{4c} groups. In a yet further embodiment, R^{1c} and R^{2c} independently represent aryl (e.g. phenyl), bicyclic heterocyclyl (e.g. benzodioxinyl), monocyclic heteroaryl (e.g. pyridinyl, pyrazolyl or thiophenyl) or bicyclic heteroaryl ring system (e.g. benzoxazolyl), wherein R^{1c} and R^{2c} may be substituted by one or more (e.g. 1) R^{4c} groups selected from
15 hydroxyl, C_{1-6} alkoxy (e.g. methoxy) or $-CONH_2$.

- In a yet further embodiment, R^{1c} and R^{2c} independently represent aryl (e.g. phenyl) or monocyclic heteroaryl (e.g. pyridinyl, pyrazolyl or thiophenyl) wherein R^{1c} and R^{2c} may be substituted by one or more (e.g. 1) R^{4c} groups selected from hydroxyl, C_{1-6} alkoxy (e.g.
20 methoxy) or $-CONH_2$.

In a yet further embodiment, R^{1c} and R^{2c} independently represent unsubstituted aryl (e.g. phenyl) or unsubstituted monocyclic heteroaryl (e.g. pyridinyl or pyrazolyl).

- 25 In a yet further embodiment, one of R^{1c} and R^{2c} represents unsubstituted aryl (e.g. phenyl) and the other represents unsubstituted monocyclic heteroaryl (e.g. pyridinyl or pyrazolyl).

- In one embodiment, p represents an integer from 0 to 2. In one embodiment, p represents 0. In an alternative embodiment, p represents 1. In an alternative embodiment, p
30 represents 2.

In one embodiment, R^{3c} represents $=O$, cyano or a monocyclic heteroaryl ring system (e.g. pyridinyl).

- 35 In one embodiment, when p represents 1, R^{3c} represents a monocyclic heteroaryl ring system (e.g. pyridinyl).

In one embodiment, when p represents 2, R^{3c} represents =O and cyano.

In one embodiment, the compound of formula (IC) is selected from any of compounds:

5 43, 46, 49, 147, 152, 154, 178-181, 183-184, 294-295, 305, 329, 339-341, 366, 370-371, 376, 435, 455, 459, 462, 486, 520, 539-543, 546-549, 556-557, 567, 631-632, 640-642, 645, 657, 661, 668, 671, 674, 681, 700-702, 727, 735, 755, 817-818, 823, 826, 845 or 865-866, 868, 870, 888-890, 894, 946, 949-951, 953, 957, 973, 977, 981, 983, 985-986, 993 and 995 as described herein or a pharmaceutically acceptable salt or solvate thereof.

10

In a further embodiment, the compound of formula (IC) is selected from any of compounds:

46, 147, 294-295, 329, 341, 435, 486, 520, 539, 542-543, 547-549, 556 and 567 as described herein or a pharmaceutically acceptable salt or solvate thereof.

15

In a yet further embodiment, the compound of formula (IC) is selected from any of compounds:

567, 631, 640, 661 and 700 as described herein or a pharmaceutically acceptable salt or solvate thereof, such as compound 700.

20

In one embodiment, the compound of formula (IC) is selected from any of compounds:

567, 631, 640, 661, 668, 700, 727, 823, 868, 870, 888-890, 894, 946, 949-951, 953, 957, 973, 977, 981, 983, 985-986, 993 and 995 as described herein or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the
25 CK1δ inhibition assay as described herein and exhibited inhibition of greater than 5%.

In one embodiment, the compound of formula (IC) is selected from any of compounds:

2-Phenyl-N-(pyridin-4-yl)quinazolin-4-amine (Compound 700);

N-(2,3-Dihydro-1,4-benzodioxin-6-yl)-2-phenylquinazolin-4-amine (Compound 868);

30 4-[[2-(Thiophen-3-yl)quinazolin-4-yl]amino]benzamide (Compound 870);

2-Phenyl-N-(1H-pyrazol-4-yl)quinazolin-4-amine (Compound 894);

2-[2-Methyl-4-(pyridin-4-yl)pyrimidin-5-yl]-1,3-benzoxazole (Compound 949);

2-[2-(Pyridin-2-yl)-4-(pyridin-4-yl)pyrimidin-5-yl]-1,3-benzoxazole (Compound 950);

5-(1,3-Benzoxazol-2-yl)-2-oxo-6-(pyridin-4-yl)-1,2-dihydropyridine-3-carbonitrile

35 (Compound 951);

4-[(2-Phenylquinazolin-4-yl)amino]phenol (Compound 957);

N-(4-Methoxyphenyl)-2-(thiophen-2-yl)quinazolin-4-amine (Compound 973);
 N-(4-Methoxyphenyl)-2-(pyridin-2-yl)quinazolin-4-amine (Compound 977);
 6-Phenyl-2-(pyridin-2-yl)-N-(pyridin-4-yl)pyrimidin-4-amine (Compound 986); and
 4-[(2-Phenylquinazolin-4-yl)amino]benzamide (Compound 993);

- 5 or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1δ inhibition assay as described herein and exhibited inhibition of greater than 25%.

10 In a further embodiment, the compound of formula (IC) is selected from any of compounds:

2-Phenyl-N-(pyridin-4-yl)quinazolin-4-amine (Compound 700);
 2-Phenyl-N-(1H-pyrazol-4-yl)quinazolin-4-amine (Compound 894);
 2-[2-Methyl-4-(pyridin-4-yl)pyrimidin-5-yl]-1,3-benzoxazole (Compound 949); and
 6-Phenyl-2-(pyridin-2-yl)-N-(pyridin-4-yl)pyrimidin-4-amine (Compound 986);

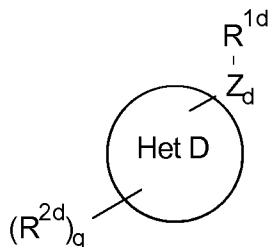
- 15 or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1δ inhibition assay as described herein and exhibited inhibition of greater than 50%.

20 In a yet further embodiment, the compound of formula (IC) is selected from any of compounds:

2-Phenyl-N-(pyridin-4-yl)quinazolin-4-amine (Compound 700); and
 2-Phenyl-N-(1H-pyrazol-4-yl)quinazolin-4-amine (Compound 894);

- or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1δ inhibition assay as described herein and exhibited
 25 inhibition of greater than 80%.

According to a fourth aspect of the invention there is provided a pharmaceutical composition comprising a compound of formula (ID) or a pharmaceutically acceptable salt or solvate thereof:



(ID)

wherein

"Het D" represents a 6 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is fused to one or more (e.g. 1-3) further rings to form a polycyclic ring system comprising up to 4 rings;

- 5 Z_d represents a bond, $-C(R^{7d})(R^{8d})-$, $-(CH_2)-C(R^{7d})(R^{8d})-$, $-O-$, $-S-$, $-CH_2-O-$, $-(CH_2)_2-O-$, NR^{6d} , $-N(R^{6d})-C(R^{7d})(R^{8d})-$, $-N(R^{6d})-(CH_2)_2-$, $-N(R^{6d})-(CH_2)_3-$, $-CH_2-N(R^{6d})-(CH_2)_2-$, $-N(R^{6d})-CO-$, $-CH_2-NH-CO-(CH_2)_2-$, $-N(R^{6d})-CO-CH_2-$, $-CO-N(R^{6d})-CH_2-$, $=N-$, $-C(H)(CN)-$, $-C(=N-NH-COC_{1-6} \text{ alkyl})-$, $-CH=C(R^{6d})-CO-$, $=CH-$, $-N=CH-$, $-N=C(Me)-$, $-C(R^{6d})=CH-$, $-NH-CO-C(=CH\text{-heteroaryl})-$, $-C=C(Me)_2-$, $-CH=CH-CO-N(R^{6d})-$, $-CH=C(R^{6d})-NH-CO-$, $-CO-O-CH_2-$,
 10 $-CH=C(R^{6d})-CO-O-CH_2-$, $-CS-S-CH_2-$, $-NH-CO-NH-$, $-NH-CS-NH-$, $-NH-CS-NH-CH_2-$, $-NH-CS-NH-(CH_2)_2-$, $-CH_2-N(CSNH_2)-CH_2-$, $-S-CH_2-$, $-S-(CH_2)_2-O-$, SO_2 , $-NH-SO_2-$, $-CH_2-NH-SO_2-$, CO , $-CH_2-CO-$, $-(CH_2)_2-CO-$, $-O-CH_2-CO-$, $-(CH_2)_2-CO-$, COO , $-COO-C(R^{7d})CO-$, $-CH=C(R^{5d})-CONH-CH_2-$, $-CO-CH_2-N(R^{6d})-CO-$, $-CO-CH_2-C(R^{6d})-CH_2-CO-$, $-CO-CH_2-N(R^{6d})-CH_2-$, $-CO-NH-N=C(R^{7d})-$, $-S-CH_2-CO-$, $-S-CH_2-CO-N(R^{6d})-$, $-S-CH_2-CO-N(R^{6d})-CH_2-$, $-SO_2-N(R^{6d})-C(R^{7d})(R^{8d})-CONH-$, $-SO_2-N(R^{6d})-CH(-CH_2\text{-aryl})-CONH-CH_2-$, $-CH(-S-C_{1-6} \text{ alkyl})-C(Me)(OH)-$, $-CH_2-C(R^{6d})(OH)-$, $-C(OH)(CH(Me)(C_{3-8} \text{ cycloalkyl})) -CH_2-$, $-C(OH)(R^{6d})-CH_2-$, $-CH(Me)-NH-CO-CH_2-$, $-CO-N(R^{6d})-CH_2-$, $-CO-N(R^{6d})-CH_2-CH_2-$, $-CO-N(R^{6d})-CH_2-CH_2-CO-NH-CH_2-$, $-CO-NH-C(-CONH_2)=CH-$, $-CO-NH-CH(-CONH_2)-CH_2-$, $-CH_2-C(H)(Me)-CH_2-S-$, $-O-CH_2-CO-NH-$, $-CH_2-N(R^{6d})-CO-CH_2-O-$, $-N(R^{6d})-CO-CH_2-O-$,
 20 $-C(H)(-CH_2\text{-aryl})-$, $-C(H)(-CH_2\text{-heteroaryl})-$, $-C(NH\text{-aryl})=N-N=CH-$, $-C(NH\text{-aryl})=N-N=CH-$, $-NH-N=C(-aryl)-$, $-NH-N=C(-aryl)-CO-$, $-NH-C(=N-CO-C_{1-6} \text{ alkyl})-NH-(CH_2)_2-$, $-C(-NH\text{-aryl})=N-N=CH-$, $-NH-C(-NH\text{-aryl})=N-CONH-$, $-C(=CH\text{-aryl})-CONH-CH_2-$, $-CH=C(R^{6d})-CONH-$, $-CH(-CH_2\text{-aryl})-NH-CO-$ or $-CH(OH)-$, wherein said aryl or heteroaryl groups of Z_d may be optionally substituted by one or more halogen, C_{1-6} alkyl, C_{1-6} alkoxy, NO_2 or
 25 hydroxyl groups;

R^{5d} represents hydrogen, C_{1-6} alkyl or cyano;

R^{6d} represents hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, cyano, C_{3-8} cycloalkyl, $-CH_2-C_{3-8}$ cycloalkyl, aryl, heteroaryl, $-C_{1-6}$ alkylene-aryl, $-CO\text{-aryl}$, $-CO\text{-heteroaryl}$ or $-C(R^{7d})(R^{8d})\text{-heteroaryl}$, wherein said aryl groups of R^{6d} may be optionally substituted by one or more

- 30 halogen or C_{1-6} alkoxy groups;

R^{7d} and R^{8d} independently represent hydrogen or C_{1-6} alkyl;

R^{1d} represents aryl, C_{3-8} cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1d} may be substituted by one or more (e.g. 1, 2 or 3) R^{4d} groups;

- 35 R^{4d} represents halogen, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, C_{3-8} cycloalkyl, halo C_{1-6} alkyl, hydroxyl, C_{1-6} alkoxy, $-O-C_{1-6}$ alkenyl, halo C_{1-6} alkoxy, $-COOH$, $-CO-C_{1-6}$ alkyl, $-COO-C_{1-6}$

alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{4d} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{4d} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;

q represents an integer from 0 to 3;

R^{2d} represents halogen, haloC₁₋₆ alkyl, C₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -S-C₁₋₆ alkyl, -CH₂-S-C₁₋₆ alkyl, -S-C₂₋₆ alkynyl, amino, cyano, NO₂, =O, =S, =NH, -SO₂-C₁₋₆ alkyl, -CONH₂, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -NH-C₁₋₆ alkyl, -NH-CO-C₁₋₆ alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH, -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, wherein said C₁₋₆ alkyl groups of R^{2d} may be optionally substituted by one or more hydroxyl groups;

with the proviso that the compound is other than compound number 273, 286, 467, 533, 544, 571, 591, 662, 783, 795, 806, 884, 887, 895, 902, 908, 921, 932, 934, 942, 959-960 and 1001.

In one embodiment, the compound of formula (ID) is selected from any of compounds: 29, 34, 41, 65-70, 92, 109, 116, 126, 130-137, 162, 182, 231, 246, 252-255, 258, 274, 290-293, 297-298, 317-318, 330-331, 347-349, 352, 450-454, 483, 536-538, 545, 550, 564-565, 572, 620, 637, 655, 663, 675, 682, 686, 691, 696, 706, 711, 724, 728-729, 737, 744-745, 748, 752, 774-776, 781, 797-799, 832, 834, 954, 958, 964-965, 971, 974-976, 978-980, 994 and 997-998 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a further embodiment, the compound of formula (ID) is selected from any of compounds:

34, 41, 65-66, 68-69, 109, 126, 130, 132-137, 162, 182, 231, 246, 252-255, 258, 274, 290, 293, 297-298, 317-318, 348-349, 352, 450-453, 536, 545, 550, 564-565 and 572 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a yet further embodiment, the compound of formula (ID) is selected from any of compounds:

663, 682, 696, 737, 748, 832 and 834 as described herein or a pharmaceutically acceptable salt or solvate thereof, such as compound 682.

5

In one embodiment, the compound of formula (ID) is selected from any of compounds:

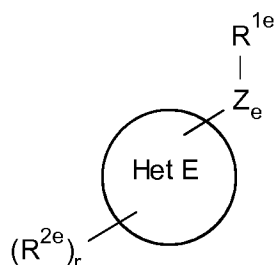
663, 675, 682, 696, 706, 737, 748, 797, 832, 834, 954, 958, 964-965, 971, 974-976, 978-980, 994 and 997-998 as described herein or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1 δ inhibition assay as described herein and exhibited inhibition of greater than 5%.

10

In one embodiment, the compound of formula (ID) is selected from any of compounds: 682, 954, 964, 978-979 and 997 as described herein or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1 δ inhibition assay as described herein and exhibited inhibition of greater than 50%.

15

According to a fifth aspect of the invention there is provided a pharmaceutical composition comprising a compound of formula (IE) or a pharmaceutically acceptable salt or solvate thereof:



20

(IE)

wherein

"Het E" represents a 6 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S;

25 Z_e represents a bond, $-C(R^{7e})(R^{8e})-$, $(CH_2)_2$, $-O-$, $-S-$, $-CH_2-O-$, $-(CH_2)_2-O-$, NR^{6e} , $-N(R^{6e})-C(R^{7e})(R^{8e})-$, $-N(R^{6e})-(CH_2)_2-$, $-N(R^{6e})-(CH_2)_3-$, $-CH_2-N(R^{6e})-(CH_2)_2-$, $-N(R^{6e})-CO-$, $-CH_2-NH-CO-(CH_2)_2-$, $-N(R^{6e})-CO-CH_2-$, $-CO-N(R^{6e})-CH_2-$, $=N-$, $-C(H)(CN)-$, $-C(=N-NH-COC_{1-6}alkyl)-$, $-C(R^{6e})=N-NH-CO-$, $-CH=C(R^{6e})-CO-$, $=CH-$, $-N=CH-$, $-N=C(Me)-$, $-C(R^{6e})=CH-$, $-NH-CO-C(=CH-heteroaryl)-$, $-C=C(Me)_2-$, $-CH=CH-CO-N(R^{6e})-$, $-CH=C(R^{6e})-NH-CO-$, $-CH=C(R^{6e})-CO-O-CH_2-$, $-CS-S-CH_2-$, $-NH-CS-NH-$, $-N(R^{6e})-CO-N(R^{7e})-$, $-NH-CS-N(R^{6e})-$

30

$\text{CH(R}^{7e}\text{)-}$, $-\text{CO-NH-CS-N(R}^{6e}\text{)-}$, $-\text{NH-CS-NH-(CH}_2\text{)}_2\text{-}$, $-\text{CH}_2\text{-N(CSNH}_2\text{)-CH}_2\text{-}$, $-\text{S-CH}_2\text{-}$, $-\text{S-}$
 $(\text{CH}_2)_2\text{-O-}$, $\text{SO}_2\text{-}$, $-\text{NH-SO}_2\text{-}$, $-\text{CH}_2\text{-N(R}^{6e}\text{)-SO}_2\text{-}$, CO- , $-\text{CH}_2\text{-CO-}$, $-(\text{CH}_2)_2\text{-CO-}$, $-\text{O-CH}_2\text{-CO-}$, $-\text{}$
 $(\text{CH}_2)_2\text{-CO-}$, COO- , $-\text{COO-C(R}^{7e}\text{)CO-}$, $-\text{CH=C(R}^{5e}\text{)-CONH-CH}_2\text{-}$, $-\text{CO-CH}_2\text{-N(R}^{6e}\text{)-CO-}$, $-\text{}$
 $\text{CO-CH}_2\text{-C(R}^{6e}\text{)-CH}_2\text{-CO-}$, $-\text{C(R}^{6e}\text{)-CO-CH}_2\text{-}$, $-\text{CO-CH}_2\text{-N(R}^{6e}\text{)-CH}_2\text{-}$, $-\text{CO-NH-N=C(R}^{7e}\text{)-}$, $-\text{}$
 $\text{S-CH}_2\text{-CO-}$, $-\text{S-CH}_2\text{-CO-N(R}^{6e}\text{)-}$, $-\text{S-CH}_2\text{-CO-N(R}^{6e}\text{)-CH}_2\text{-}$, $-\text{SO}_2\text{-N(R}^{6e}\text{)-C(R}^{7e}\text{)(R}^{8e}\text{)-CONH-}$
 $-\text{SO}_2\text{-N(R}^{6e}\text{)-CH(-CH}_2\text{-aryl)-CONH-CH}_2\text{-}$, $-\text{CH(-S-C}_{1-6}\text{ alkyl)-C(Me)(OH)-}$, $-\text{CH}_2\text{-}$
 $\text{C(R}^{6e}\text{)(OH)-}$, $-\text{C(OH)(CH(Me)(C}_{3-8}\text{ cycloalkyl))-CH}_2\text{-}$, $-\text{C(OH)(R}^{6e}\text{)-CH}_2\text{-}$, $-\text{CH(Me)-NH-CO-}$
 $\text{CH}_2\text{-}$, $-\text{CO-N(R}^{6e}\text{)-CH}_2\text{-}$, $-\text{CO-N(R}^{6e}\text{)-CH}_2\text{-CH}_2\text{-}$, $-\text{CO-N(R}^{6e}\text{)-CH}_2\text{-CH}_2\text{-O-CO-}$, $-\text{CO-N(R}^{6e}\text{)-}$
 $\text{CH}_2\text{-CH}_2\text{-CO-NH-CH}_2\text{-}$, $-\text{CO-NH-C(-CONH}_2\text{)=CH-}$, $-\text{CO-NH-CH(-CONH}_2\text{)-CH}_2\text{-}$, $-\text{CH}_2\text{-}$
 $\text{C(H)(Me)-CH}_2\text{-S-}$, $-\text{O-CH}_2\text{-CO-NH-}$, $-\text{CH}_2\text{-N(R}^{6e}\text{)-CO-CH}_2\text{-O-}$, $-\text{N(R}^{6e}\text{)-CO-CH}_2\text{-O-}$, $-\text{C(H)-}$
 $\text{CH}_2\text{-aryl)-}$, $-\text{C(H)-CH}_2\text{-heteroaryl)-}$, $-\text{C(NH-aryl)=N-N=CH-}$, $-\text{C(NH-aryl)=N-N=CH-}$, $-\text{NH-}$
 N=C(-aryl)- , $-\text{NH-C(R}^{6e}\text{)=N-SO}_2\text{-}$, $-\text{NH-N=C(-aryl)-CO-}$, $-\text{NH-C(=N-CO)(R}^{6e}\text{)-}$, $-\text{NH-C(=N-}$
 $\text{CO-C}_{1-6}\text{ alkyl)-NH-(CH}_2\text{)}_2\text{-}$, $-\text{C(-NH-aryl)=N-N=CH-}$, $-\text{NH-C(-NH-aryl)=N-CONH-}$, $-\text{C(=CH-}$
 $\text{aryl)-CONH-CH}_2\text{-}$, $-\text{CH=C(R}^{6e}\text{)-CONH-}$, $-\text{CH(-CH}_2\text{-aryl)-NH-CO-}$ or $-\text{CH(OH)-}$, wherein
said aryl or heteroaryl groups of Z_e may be optionally substituted by one or more halogen,
 C_{1-6} alkyl, C_{1-6} alkoxy, NO_2 or hydroxyl groups;
 R^{5e} represents hydrogen, C_{1-6} alkyl or cyano;
 R^{6e} represents hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, cyano, C_{3-8} cycloalkyl, $-\text{}$
 $\text{CH}_2\text{-C}_{3-8}\text{ cycloalkyl}$, aryl, heteroaryl, $-\text{C}_{1-6}\text{ alkylene-aryl}$, $-\text{C}_{1-6}\text{ alkylene-heteroaryl}$, $-\text{NH-CO-}$
 aryl , $-\text{CO-aryl}$, $-\text{CO-heteroaryl}$ or $-\text{C(R}^{7e}\text{)(R}^{8e}\text{)-heteroaryl}$, wherein said aryl groups of R^{6e}
may be optionally substituted by one or more halogen or C_{1-6} alkoxy groups;
 R^{7e} and R^{8e} independently represent hydrogen or C_{1-6} alkyl;
 R^{1e} represents aryl, C_{3-8} cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or
bicyclic heteroaryl ring system, wherein R^{1d} may be substituted by one or more (e.g. 1, 2
or 3) R^{4e} groups;
 R^{4e} represents halogen, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, C_{3-8} cycloalkyl, halo C_{1-6} alkyl,
hydroxyl, C_{1-6} alkoxy, $-\text{O-C}_{1-6}\text{ alkenyl}$, halo C_{1-6} alkoxy, $-\text{COOH}$, $-\text{CO-C}_{1-6}\text{ alkyl}$, $-\text{COO-C}_{1-6}$
 alkyl , $-\text{CONH}_2$, $-\text{SO}_2\text{NH}_2$, $-\text{CH}_2\text{-CONH}_2$, $-\text{NH-C}_{1-6}\text{ alkyl}$, $-\text{NH-C}_{2-6}\text{ alkenyl}$, $-\text{NH-CO-C}_{1-6}$
 alkyl , $-\text{CO-NH-C}_{1-6}\text{ alkyl}$, $-\text{NH-NH}_2$, $-\text{O-CH}_2\text{-CO-NH-C}_{1-6}\text{ alkyl}$, $-\text{CH}_2\text{-CH}_2\text{-CO-NH-C}_{1-6}\text{ alkyl}$,
 $-\text{S-C}_{1-6}\text{ alkyl}$, $-\text{SO-C}_{1-6}\text{ alkyl}$, $-\text{SO}_2\text{-C}_{1-6}\text{ alkyl}$, $-\text{SO}_2\text{-NH-C}_{1-6}\text{ alkyl}$, $-\text{S-CH}_2\text{-CO-C}_{2-6}\text{ alkenyl}$, $-\text{}$
 $\text{SO}_2\text{-OH}$, amino, cyano, NO_2 , $=\text{O}$, $-\text{CO-NH-(CH}_2\text{)}_2\text{-OMe}$, $-\text{NH-C}_{3-8}\text{ cycloalkyl}$, $-\text{CO-}$
 heterocyclyl , $-\text{CO-heteroaryl}$, $-\text{COO-(CH}_2\text{)}_2\text{-heterocyclyl}$, $-\text{OCH}_2\text{-aryl}$, $-\text{OCH}_2\text{-heteroaryl}$, $-\text{}$
 $\text{CH}_2\text{-O-CO-aryl}$, $-\text{O-aryl}$, $-\text{CO-NH-aryl}$, $-\text{NH-SO}_2\text{-aryl}$, $-\text{NH-CO-heteroaryl}$, $-\text{NH-C}_{1-4}$
 $\text{alkylene-heteroaryl}$, $-\text{NH-CO-CH}_2\text{-aryl}$, aryl or heteroaryl groups, wherein said C_{1-6} alkynyl,
aryl, heterocyclyl or heteroaryl groups of R^{4e} may be optionally substituted by one or more
halogen, C_{1-6} alkyl, C_{1-6} alkoxy, $=\text{S}$ or hydroxyl groups and wherein said C_{1-6} alkyl or C_{2-6}

alkenyl groups of R^{4e} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;

r represents an integer from 0 to 3;

R^{2e} represents halogen, haloC₁₋₆ alkyl, C₁₋₆ alkyl, C₁₋₆ alkynyl, hydroxyl, C₁₋₆ alkoxy, -S-C₁₋₆

- 5 alkyl, -CH₂-S-C₁₋₆ alkyl, -S-C₂₋₆ alkynyl, amino, cyano, NO₂, =O, =S, -SO₂-C₁₋₆ alkyl, -CONH₂, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -NH-C₁₋₆ alkyl, -NH-CO-C₁₋₆ alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH, -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, wherein said C₁₋₆ alkyl or C₁₋₆ alkynyl,
- 10 groups of R^{2e} may be optionally substituted by one or more hydroxyl or alkylamino groups; with the proviso that the compound is other than compound number 250, 647, 685, 751, 769, 803, 874, 876, 893, 900, 911, 913-914, 916, 920, 927, 936-937, 940, 943 and 945.

In one embodiment, the compound of formula (IE) is selected from any of compounds:

- 15 18, 50, 55-56, 62, 77, 85, 108, 115, 144, 146, 148, 198-199, 201, 222, 230, 245, 247, 251, 265, 284, 287, 300, 306, 337-338, 346, 381-382, 392, 426, 429-430, 479, 561, 566, 583, 603, 606-608, 621-622, 646, 659-660, 687-688, 690, 699, 715, 718, 720-723, 730-732, 739, 771-772, 780, 793, 813-814, 822, 829-830, 835-837, 840, 848, 885-886, 941, 966 and 988 as described herein or a pharmaceutically acceptable salt or solvate thereof.

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In a further embodiment, the compound of formula (IE) is selected from any of compounds:

18, 62, 115, 146, 148, 222, 230, 251, 265, 300, 306, 338, 346, 381, 392, 426, 561 and 583 as described herein or a pharmaceutically acceptable salt or solvate thereof.

25

In a yet further embodiment, the compound of formula (IE) is selected from any of compounds:

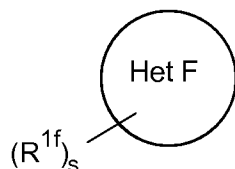
583, 660, 822 and 830 as described herein or a pharmaceutically acceptable salt or solvate thereof.

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In one embodiment, the compound of formula (IE) is selected from any of compounds: 583, 646, 660, 723, 730, 780, 822, 830, 885-886, 941, 966 and 988 as described herein or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1δ inhibition assay as described herein and exhibited

35 inhibition of greater than 5%.

According to a sixth aspect of the invention there is provided a pharmaceutical composition comprising a compound of formula (IF) or a pharmaceutically acceptable salt or solvate thereof:



(IF)

wherein

"Het F" represents a heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is fused to one or more (e.g. 1-3) further rings to form a polycyclic ring system comprising up to 4 rings;

R^{1f} represents halogen, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, C_{3-8} cycloalkyl, halo C_{1-6} alkyl, hydroxyl, C_{1-6} alkoxy, -O- C_{1-6} alkenyl, halo C_{1-6} alkoxy, -COOH, -CO- C_{1-6} alkyl, -COO- C_{1-6} alkyl, -CONH₂, -CH₂-CONH₂, -NH- C_{1-6} alkyl, -NH- C_{2-6} alkenyl, -NH-CO- C_{1-6} alkyl, -CO-NH- C_{1-6} alkyl, -O-CH₂-CO-NH- C_{1-6} alkyl, -CH₂-CH₂-CO-NH- C_{1-6} alkyl, -S- C_{1-6} alkyl, -SO- C_{1-6} alkyl, -SO₂- C_{1-6} alkyl, -SO₂-NH- C_{1-6} alkyl, -S-CH₂-CO- C_{2-6} alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH- C_{3-8} cycloalkyl, wherein said C_{1-6} alkyl or C_{2-6} alkenyl groups of R^{1f} may be optionally substituted by one or more hydroxyl, amino, cyano, C_{1-6} alkoxy, CONH₂ or -COO- C_{1-6} alkyl groups;

s represents an integer from 1 to 3;

with the proviso that the compound is other than compound number 592 and 595.

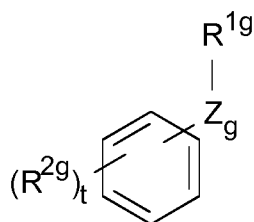
In one embodiment, the compound of formula (IF) is selected from any of compounds: 53, 79, 124-125, 205, 289, 299, 301-302, 353-355, 397, 500 and 511 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a further embodiment, the compound of formula (IF) is selected from any of compounds:

79, 125, 205, 289, 299, 301-302, 353-355, 397, 500 and 511 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In one embodiment, the compound of formula (IF) is Compound 205 as described herein or a pharmaceutically acceptable salt or solvate thereof. The compound of this embodiment was tested in the CK1δ inhibition assay as described herein and exhibited inhibition of greater than 50%.

According to a sixth aspect of the invention there is provided a pharmaceutical composition comprising a compound of formula (IG) or a pharmaceutically acceptable salt or solvate thereof:



wherein

- Z_g represents a bond, $-C(R^{7g})(R^{8g})-$, $(CH_2)_2$, $-O-$, $-S-$, $-CH_2-O-$, $-(CH_2)_2-O-$, NR^{6g} , $-N(R^{6g})-$, $C(R^{7g})(R^{8g})-$, $-N(R^{6g})-(CH_2)_2-$, $-N(R^{6g})-(CH_2)_3-$, $-CH_2-N(R^{6g})-(CH_2)_2-$, $-N(R^{6g})-CO-$, $-CH_2-NH-$, $CO-(CH_2)_2-$, $-N(R^{6g})-CO-CH_2-$, $=N-$, $-C(H)(CN)-$, $-C(=N-NH-COC_{1-6} \text{ alkyl})-$, $-CH=C(R^{6g})-$, $CO-$, $=CH-$, $-N=CH-$, $-N=C(Me)-$, $-C(R^{6g})=CH-$, $-NH-CO-C(=CH-\text{heteroaryl})-$, $-C=C(Me)_2-$, $-CH=CH-CO-N(R^{6g})-$, $-CH=C(R^{6g})-NH-CO-$, $-CH=C(R^{6g})-CO-O-CH_2-$, $-CS-S-CH_2-$, $-NH-CS-NH-$, $-NH-CS-NH-CH_2-$, $-NH-CS-NH-(CH_2)_2-$, $-CH_2-N(CSNH_2)-CH_2-$, $-S-CH_2-$, $-S-(CH_2)_2-O-$, SO_2 , $-NH-SO_2-$, $-CH_2-NH-SO_2-$, CO , $-CH_2-CO-$, $-(CH_2)_2-CO-$, $-O-CH_2-CO-$, $-(CH_2)_2-CO-$, $COO-$, $-COO-C(R^{7g})CO-$, $-CH=C(R^{5g})-CONH-CH_2-$, $-CO-CH_2-N(R^{6g})-CO-$, $-CO-CH_2-C(R^{6g})-CH_2-CO-$, $-CO-CH_2-N(R^{6g})-CH_2-$, $-CO-NH-N=C(R^{7g})-$, $-S-C(R^{6g})(R^{7g})-CO-$, $-S-CH_2-CO-N(R^{6g})-$, $-S-CH_2-CO-N(R^{6g})-CH_2-$, $-SO_2-N(R^{6g})-C(R^{7g})(R^{8g})-CONH-$, $-SO_2-N(R^{6g})-CH(-CH_2-\text{aryl})-CONH-CH_2-$, $-CH(-S-C_{1-6} \text{ alkyl})-C(Me)(OH)-$, $-CH_2-C(R^{6g})(OH)-$, $-C(OH)(CH(Me)(C_{3-8} \text{ cycloalkyl}))$, $-CH_2-$, $-C(OH)(R^{6g})-CH_2-$, $-CH(Me)-NH-CO-CH_2-$, $-CO-N(R^{6g})-CH_2-$, $-CO-N(R^{6g})-CH_2-CH_2-$, $-CO-N(R^{6g})-CH_2-CH_2-CO-NH-CH_2-$, $-CO-NH-C(-CONH_2)=CH-$, $-CO-NH-CH(-CONH_2)-CH_2-$, $-CH_2-C(H)(Me)-CH_2-S-$, $-O-CH_2-CO-NH-$, $-CH_2-N(R^{6g})-CO-CH_2-O-$, $-N(R^{6g})-CO-CH_2-O-$, $-C(H)(-CH_2-\text{aryl})-$, $-C(H)(-CH_2-\text{heteroaryl})-$, $-C(NH-\text{aryl})=N-N=CH-$, $-C(NH-\text{aryl})=N-N=CH-$, $-NH-N=C(-\text{aryl})-$, $-NH-N=C(-\text{aryl})-CO-$, $-NH-C(=N-CO-C_{1-6} \text{ alkyl})-$, $NH-(CH_2)_2-$, $-C(-NH-\text{aryl})=N-N=CH-$, $-NH-C(-NH-\text{aryl})=N-CONH-$, $-C(=CH-\text{aryl})-CONH-CH_2-$, $-CH=C(R^{6g})-CONH-$, $-CH(-CH_2-\text{aryl})-NH-CO-$ or $-CH(OH)-$, wherein said aryl or heteroaryl groups of Z_g may be optionally substituted by one or more halogen, C_{1-6} alkyl, C_{1-6} alkoxy, NO_2 or hydroxyl groups;
- R^{5g} represents hydrogen, C_{1-6} alkyl or cyano;
- R^{6g} represents hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, cyano, C_{3-8} cycloalkyl, $-CH_2-C_{3-8}$ cycloalkyl, aryl, heteroaryl, $-C_{1-6}$ alkylene-aryl, $-CO-\text{aryl}$, $-CO-\text{heteroaryl}$ or $-C(R^{7g})(R^{8g})-$

heteroaryl, wherein said aryl groups of R^{6g} may be optionally substituted by one or more halogen or C₁₋₆ alkoxy groups;

R^{7g} and R^{8g} independently represent hydrogen or C₁₋₆ alkyl;

R^{1g} represents aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1g} may be substituted by one or more (e.g. 1, 2 or 3) R^{4g} groups;

R^{4g} represents halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{4g} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{4g} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;

t represents an integer from 0 to 3;

R^{2g} represents halogen, haloC₁₋₆ alkyl, C₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -S-C₁₋₆ alkyl, -CH₂-S-C₁₋₆ alkyl, -S-C₂₋₆ alkynyl, amino, cyano, NO₂, =O, =S, -SO₂-C₁₋₆ alkyl, -CONH₂, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -NH-C₁₋₆ alkyl, -NH-CO-C₁₋₆ alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH, -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, wherein said C₁₋₆ alkyl groups of R^{2g} may be optionally substituted by one or more hydroxyl groups;

with the proviso that the compound is other than compound number 789, 839 and 924.

In one embodiment, the compound of formula (IG) is selected from any of compounds:

98-101, 248, 257, 259-260, 266, 271, 380, 394, 449, 461, 464, 477, 502-504, 523, 530, 535, 574, 673, 713, 779, 788, 825, 881-882, 935, 956, 968, 972 and 996 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a further embodiment, the compound of formula (IG) is selected from any of

compounds:

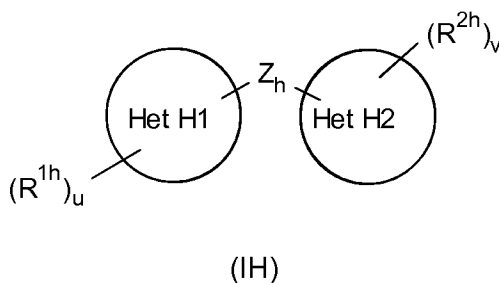
98, 101, 248, 257, 259-260, 266, 271, 380, 394 and 530 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In a yet further embodiment, the compound of formula (IG) is compound 825 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In one embodiment, the compound of formula (IG) is selected from any of compounds: 825, 881-882, 935, 956, 968, 972 and 996 as described herein or a pharmaceutically acceptable salt or solvate thereof. The compounds of this embodiment were tested in the CK1δ inhibition assay as described herein and exhibited inhibition of greater than 5%.

In one embodiment, the compound of formula (IG) is Compound 972 as described herein or a pharmaceutically acceptable salt or solvate thereof. The compound of this embodiment was tested in the CK1δ inhibition assay as described herein and exhibited inhibition of greater than 50%.

According to a seventh aspect of the invention there is provided a pharmaceutical composition comprising a compound of formula (IH) or a pharmaceutically acceptable salt or solvate thereof:



wherein

“Het H1” and “Het H2” independently represent a 5 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S;

Z_h represents a bond, $-C(R^{7h})(R^{8h})-$, $(CH_2)_2$, $-O-$, $-S-$, $-CH_2-O-$, $-(CH_2)_2-O-$, NR^{6h} , $-N(R^{6h})-C(R^{6h})(R^{7h})-$, $-N(R^{6h})-(CH_2)_2-$, $-N(R^{6h})-(CH_2)_3-$, $-CH_2-N(R^{6h})-(CH_2)_2-$, $-N(R^{6h})-CO-$, $-CH_2-NH-CO-(CH_2)_2-$, $-N(R^{6h})-CO-CH_2-$, $=N-$, $-C(H)(CN)-$, $-C(=N-NH-COC_{1-6} \text{ alkyl})-$, $-CH=C(R^{6h})-CO-$, $=CH-$, $-N=CH-$, $-N=C(Me)-$, $-C(R^{6h})=CH-$, $-NH-CO-C(=CH-\text{heteroaryl})-$, $-C=C(Me)_2-$, $-CH=CH-CO-N(R^{6h})-$, $-CH=C(R^{6h})-NH-CO-$, $-CH=C(R^{6h})-CO-O-CH_2-$, $-CS-S-CH_2-$, $-NH-CS-NH-$, $-NH-CS-NH-CH_2-$, $-NH-CS-NH-(CH_2)_2-$, $-CH_2-N(CSNH_2)-CH_2-$, $-S-CH_2-$, $-S-(CH_2)_2-O-$, SO_2 , $-NH-SO_2-$, $-CH_2-NH-SO_2-$, CO , $-CH_2-CO-$, $-(CH_2)_2-CO-$, $-O-CH_2-CO-$, $-(CH_2)_2-CO-$, $COO-$, $-COO-C(R^{7h})CO-$, $-CH=C(R^{5h})-CONH-CH_2-$, $-CO-CH_2-N(R^{6h})-CO-$, $-CO-CH_2-C(R^{6h})-$

- CH₂-CO-, -CO-CH₂-N(R^{6h})-CH₂-, -CO-NH-N=C(R^{7h})-, -S-CH₂-CO-, -S-CH₂-CO-N(R^{6h})-, -S-CH₂-CO-N(R^{6h})-CH₂-, -SO₂-N(R^{6h})-C(R^{7h})(R^{8h})-CONH-, -SO₂-N(R^{6h})-CH(-CH₂-aryl)-CONH-CH₂-, -CH(-S-C₁₋₆ alkyl)-C(Me)(OH)-, -CH₂-C(R^{6h})(OH)-, -C(OH)(CH(Me)(C₃₋₈ cycloalkyl))-CH₂-, -C(OH)(R^{6h})-CH₂-, -CH(Me)-NH-CO-CH₂-, -CO-N(R^{6h})-CH₂-, -CO-N(R^{6h})-CH₂-CH₂-, -CO-N(R^{6h})-CH₂-CH₂-CO-NH-CH₂-, -CO-NH-C(-CONH₂)=CH-, -CO-NH-CH(-CONH₂)-CH₂-, -CH₂-C(H)(Me)-CH₂-S-, -O-CH₂-CO-NH-, -CH₂-N(R^{6h})-CO-CH₂-O-, -N(R^{6h})-CO-CH₂-O-, -C(H)(-CH₂-aryl)-, -C(H)(-CH₂-heteroaryl)-, -C(NH-aryl)=N-N=CH-, -C(NH-aryl)=N-N=CH-, -NH-N=C(-aryl)-, -NH-N=C(-aryl)-CO-, -NH-C(=N-CO-C₁₋₆ alkyl)-NH-(CH₂)₂-, -C(-NH-aryl)=N-N=CH-, -NH-C(-NH-aryl)=N-CONH-, -C(=CH-aryl)-CONH-CH₂-, -CH=C(R^{6h})-CONH-, -CH(-CH₂-aryl)-NH-CO- or -CH(OH)-, wherein said aryl or heteroaryl groups of Z_h may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, NO₂ or hydroxyl groups;
- R^{5h} represents hydrogen, C₁₋₆ alkyl or cyano;
- R^{6h} represents hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, cyano, C₃₋₈ cycloalkyl, -CH₂-C₃₋₈ cycloalkyl, aryl, heteroaryl, -C₁₋₆ alkylene-aryl, -CO-aryl, -CO-heteroaryl or -C(R^{7h})(R^{8h})-heteroaryl, wherein said aryl groups of R^{6h} may be optionally substituted by one or more halogen or C₁₋₆ alkoxy groups;
- R^{7h} and R^{8h} independently represent hydrogen or C₁₋₆ alkyl;
- R^{1h} and R^{2h} independently represent halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{1h} and R^{2h} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{1h} and R^{2h} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;
- u and v independently represent an integer from 0 to 3;
- with the proviso that the compound is other than compound number 757 and 878.

- In one embodiment, the compound of formula (IH) is selected from any of compounds:

395, 433, 689 and 786 as described herein or a pharmaceutically acceptable salt or solvate thereof.

In the present context, the term "pharmaceutically acceptable salt" is intended to indicate salts which are not harmful to the patient. Such salts include pharmaceutically acceptable acid addition salts, pharmaceutically acceptable metal salts and pharmaceutically acceptable alkaline addition salts. Acid addition salts include salts of inorganic acids as well as organic acids.

Representative examples of suitable inorganic acids include hydrochloric, hydrobromic, hydroiodic, phosphoric, sulfuric, nitric acids and the like. Representative examples of suitable organic acids include formic, acetic, trichloroacetic, trifluoroacetic, propionic, benzoic, cinnamic, citric, fumaric, glycolic, lactic, maleic, malic, malonic, mandelic, oxalic, picric, pyruvic, salicylic, succinic, methanesulfonic, ethanesulfonic, tartaric, ascorbic, pantoic, bismethylene salicylic, ethanedisulfonic, gluconic, citraconic, aspartic, stearic, palmitic, EDTA, glycolic, p-aminobenzoic, glutamic, benzenesulfonic, p-toluenesulfonic acids and the like. Further examples of pharmaceutically acceptable inorganic or organic acid addition salts include the pharmaceutically acceptable salts listed in J. Pharm. Sci. 1977, **66**, 2, which is incorporated herein by reference. Examples of metal salts include lithium, sodium, potassium, magnesium salts and the like. Examples of ammonium and alkylated ammonium salts include ammonium, methylammonium, dimethylammonium, trimethylammonium, ethylammonium, hydroxyethylammonium, diethylammonium, butylammonium, tetramethylammonium salts and the like.

Representative examples of alkaline salts include, for example, sodium, potassium, lithium, calcium, magnesium or ammonium or organic bases such as, for example, methylamine, ethylamine, propylamine, trimethylamine, diethylamine, triethylamine, N,N-dimethylethanolamine, tris(hydroxymethyl)aminomethane, ethanolamine, pyridine, piperidine, piperazine, picoline, dicyclohexylamine, morpholine, benzylamine, procaine, lysine, arginine, histidine, N-methylglucamine.

According to the invention, the compounds of formulae (IA)-(IH) can be in racemic forms, as well as in the form of pure enantiomers or non racemic (scalemic) mixture of enantiomers, including when the compounds of formulae (IA)-(IH) have more than one stereogenic centre. In case the compounds of formulae (IA)-(IH) have unsaturated carbon

carbon double bonds, both the cis (Z) and trans (E) isomers and their mixtures belong to the invention.

References herein to "halogen" means a fluorine, chlorine, bromine or iodine atom.

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References herein to "C₁₋₆ alkyl" means any linear, branched hydrocarbon groups having 1 to 6 carbon atoms, or cyclic hydrocarbon groups having 3 to 6 carbon atoms. Representative examples of such alkyl groups include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and t-butyl, n-pentyl, isopentyl, neopentyl, cyclopropyl, cyclobutyl, 10 cyclopentyl and cyclohexyl. References to "haloC₁₋₆alkyl" mean a C₁₋₆ alkyl group substituted by one or more halogen atoms as herein defined.

References herein to "C₁₋₆ alkylene" means a saturated divalent hydrocarbon chain having the specified number of member atoms. For example, C₁₋₆ alkylene refers to a bond or an 15 alkylene group having from 1 to 6 member atoms. Alkylene groups may be straight or branched. Representative branched alkylene groups have one or two branches. Alkylene includes methylene, ethylene, propylene (n-propylene and isopropylene) and butylene (n-butylene, isobutylene, and t-butylene).

20 References herein to "C₂₋₆ alkenyl" means any linear, branched hydrocarbon groups of 2 to 6 carbon atoms, or cyclic hydrocarbon group having 3 to 6 carbon atoms having at least one double bond. Representative examples of such alkenyl groups include ethenyl, propenyl, butenyl and cyclohexenyl.

25 References herein to "C₂₋₆ alkynyl" means any linear, or branched hydrocarbon groups of 2 to 6 carbon atoms, having at least one triple bond. Representative examples of such alkynyl groups include ethynyl, propargyl and butynyl.

References herein to 'C₁₋₆ alkoxy' means an -O-C₁₋₆ alkyl group wherein C₁₋₆ alkyl is as 30 defined herein. Examples of such groups include methoxy, ethoxy, propoxy, butoxy, pentoxy or hexoxy and the like.

References herein to 'C₃₋₈ cycloalkyl' means a saturated monocyclic hydrocarbon ring of 3 to 8 carbon atoms. Examples of such groups include cyclopropyl, cyclobutyl, cyclopentyl, 35 cyclohexyl, cycloheptyl or cyclooctyl and the like.

References herein to 'aryl' means a C₆₋₁₂ monocyclic or bicyclic hydrocarbon ring wherein at least one ring is aromatic. Examples of such groups include phenyl, indyl or naphthyl and the like.

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References herein to "heteroatom" means a nitrogen, sulphur, or oxygen atom.

References herein to "heterocyclyl" means a saturated or unsaturated non-aromatic ring containing from 1 to 4 heteroatoms as member atoms in the ring. Heterocyclyl groups containing more than one heteroatom may contain different heteroatoms. Heterocyclyl groups may be optionally substituted with one or more substituents as defined herein. Heterocyclyl groups are monocyclic ring systems or fused bicyclic or polycyclic ring systems or bicyclic structures known as heterocyclic "spiro" ring systems. In certain embodiments, heterocyclyl is saturated. In other embodiments, heterocyclyl is unsaturated and non-aromatic. Non-limiting examples of monocyclic heterocyclyl ring systems include pyrrolidinyl, tetrahydrofuranyl, dihydrofuranyl, pyranyl, tetrahydropyranyl, dihydropyranyl, tetrahydrothienyl, pyrazolidinyl, oxazolidinyl, thiazolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 1,3-dioxolanyl, 1,3-dioxanyl, 1,4-dioxanyl, 1,3-oxathiolanyl, 1,3-oxathianyl, 1,3-dithianyl, and azetidiny.

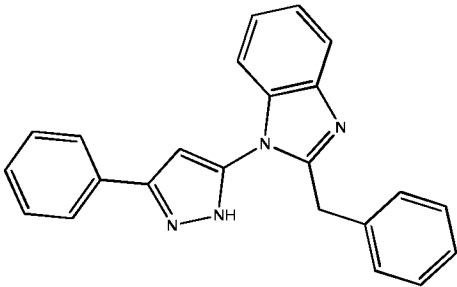
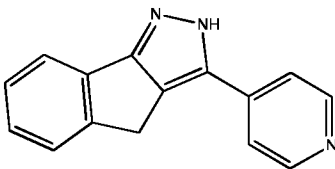
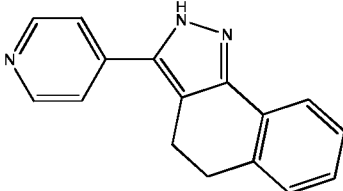
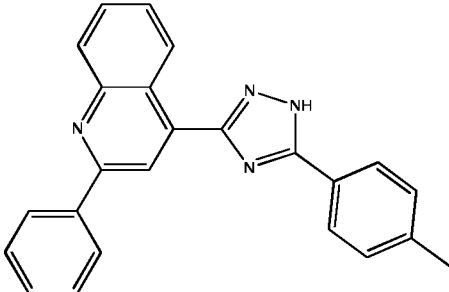
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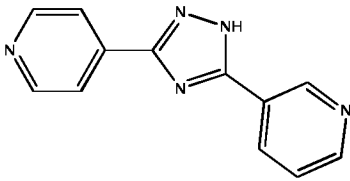
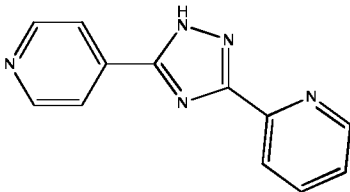
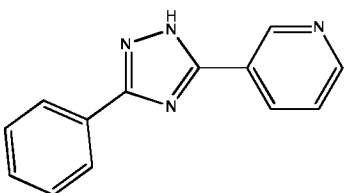
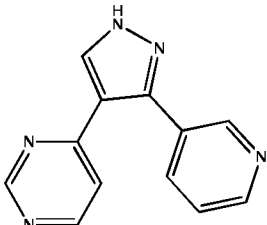
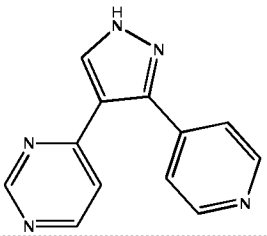
References herein to "heteroaryl" means an aromatic ring containing from 1 to 4 heteroatoms as member atoms in the ring. Heteroaryl groups containing more than one heteroatom may contain different heteroatoms. Heteroaryl groups may be optionally substituted with one or more substituents as defined herein. Heteroaryl groups are monocyclic ring systems or are fused bicyclic or polycyclic ring systems. Monocyclic heteroaryl rings have 5 or 6 member atoms. Bicyclic heteroaryl rings have from 7 to 11 member atoms. Bicyclic heteroaryl rings include those rings wherein phenyl and a monocyclic heterocyclyl ring are attached forming a fused bicyclic ring system, and those rings wherein a monocyclic heteroaryl ring and a monocyclic cycloalkyl, cycloalkenyl, heterocyclyl, or heteroaryl ring are attached forming a fused bicyclic ring system. Non-limiting examples of heteroaryl includes pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, furanyl, furazanyl, thienyl, triazolyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, indolyl, isoindolyl, indoliziny, indazolyl, purinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, pteridinyl, cinnolinyl, benzimidazolyl, benopyranly, benzoxazolyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzothienyl, furopyridinyl, and naphthyridinyl.

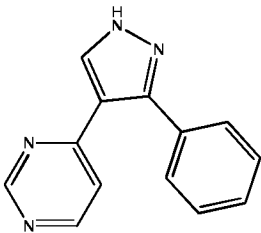
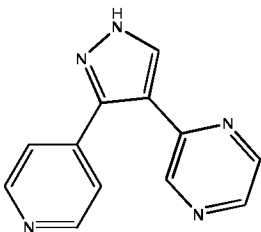
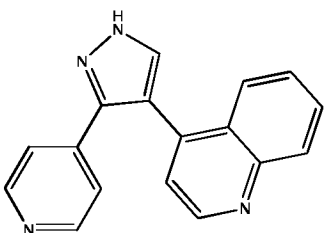
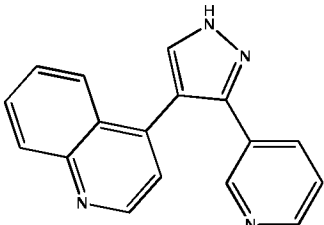
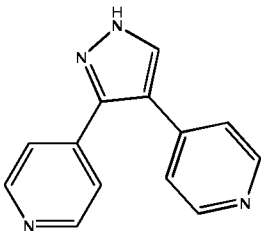
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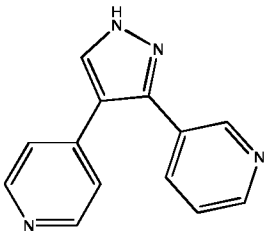
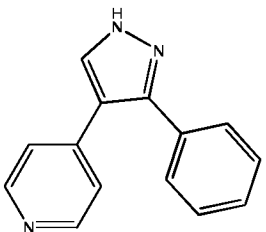
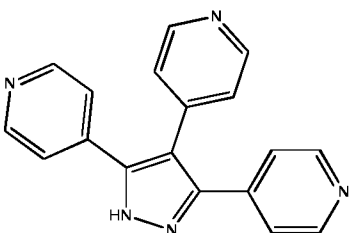
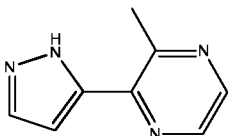
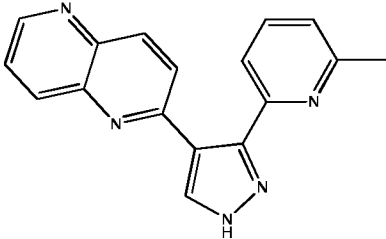
References herein to "heterocyclic ring system" mean either a heterocyclcyl ring system or a heteroaryl ring system as hereinbefore defined.

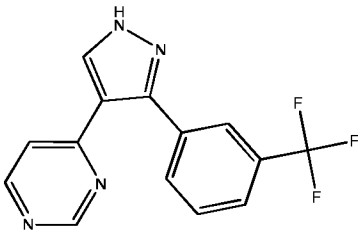
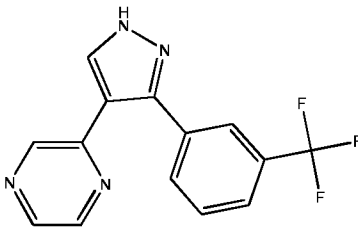
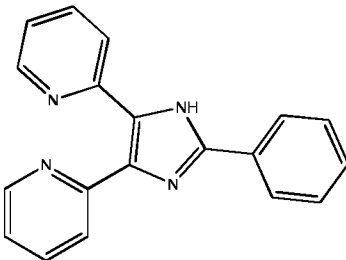
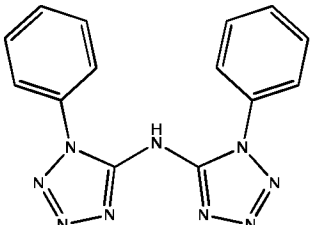
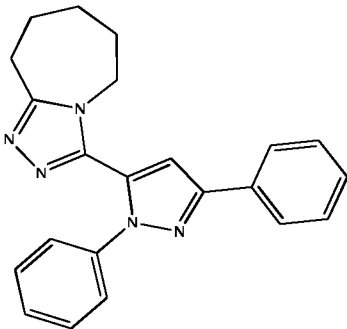
- 5 Representative compounds of the invention include compounds 1-1002 as set forth below:

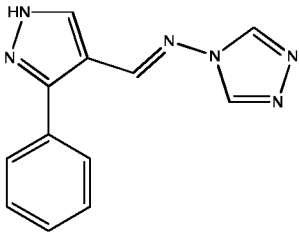
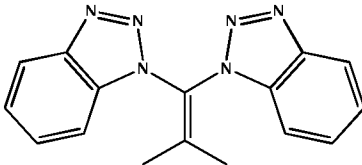
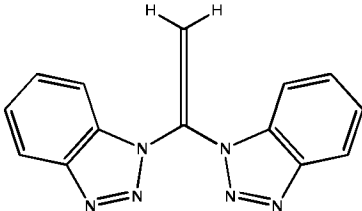
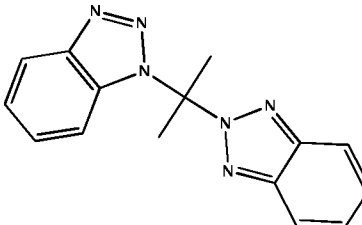
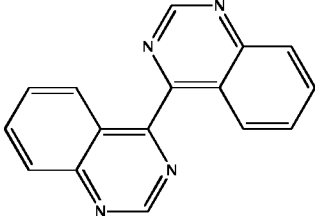
Compound Number	Structure
1	
2	
3	
4	

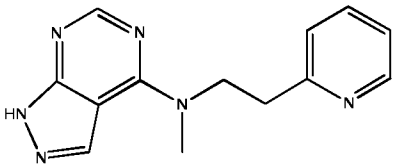
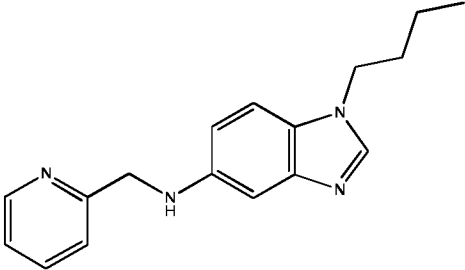
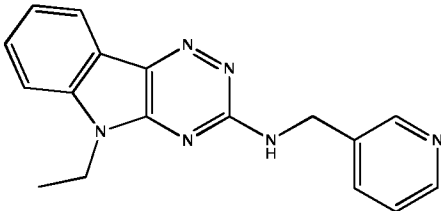
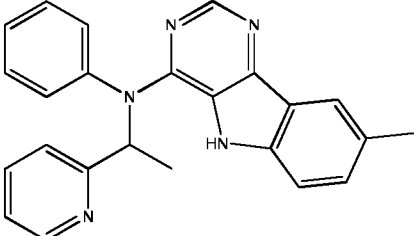
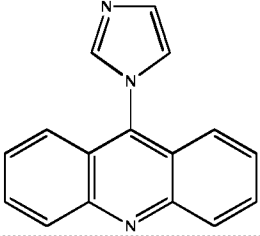
5	 <chem>c1ccncc1-c1nn[nH]c1-c1ccccn1</chem>
6	 <chem>c1ccncc1-c1nn[nH]c1-c1cccnc1</chem>
7	 <chem>c1ccccc1-c1nn[nH]c1-c1ccccn1</chem>
8	 <chem>c1ccncc1-c1nn[nH]c1-c1ccccn1</chem>
9	 <chem>c1ccncc1-c1nn[nH]c1-c1cccnc1</chem>

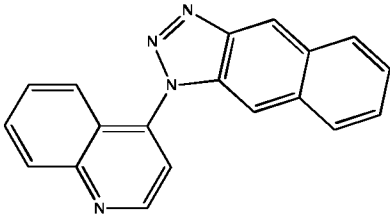
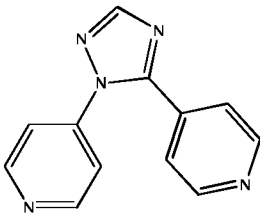
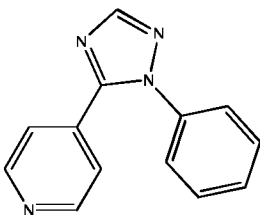
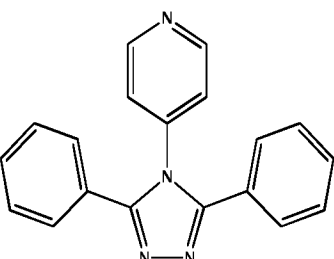
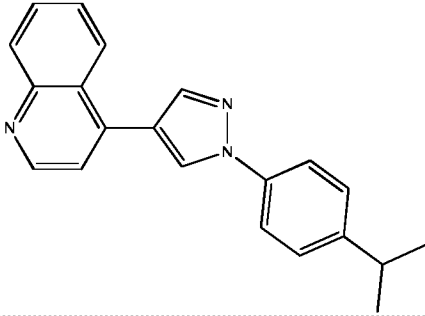
10	 <chem>c1ccccc1C2=CN=C(C=C2)c3ccncc3</chem>
11	 <chem>c1ccncc1C2=CN=C(C=C2)c3ccncc3</chem>
12	 <chem>c1ccc2c(c1)c(c[nH]2)C3=CN=C(C=C3)c4ccncc4</chem>
13	 <chem>c1ccc2c(c1)c(c[nH]2)C3=CN=C(C=C3)c4ccncc4</chem>
14	 <chem>c1ccncc1C2=CN=C(C=C2)c3ccncc3</chem>

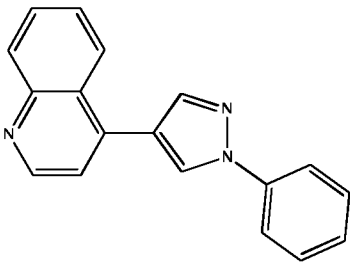
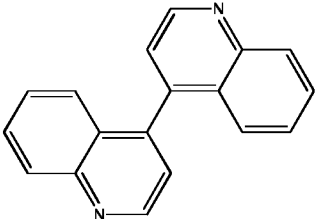
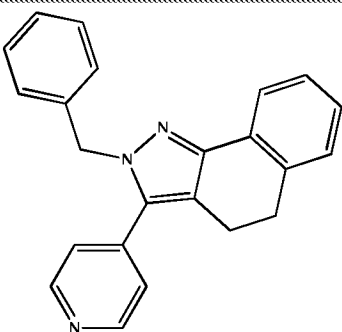
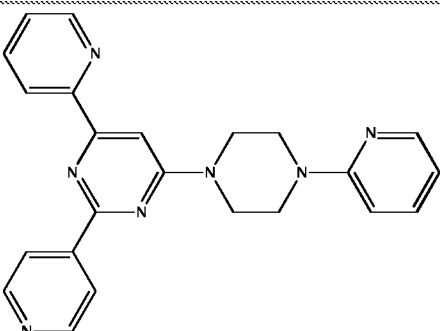
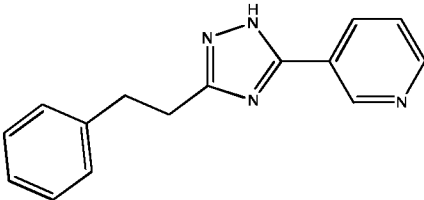
15	 <chem>c1ccncc1C2=CN=C(C=C2)c3ccncc3</chem>
16	 <chem>c1ccncc1C2=CN=C(C=C2)c3ccccc3</chem>
17	 <chem>c1ccncc1C2=NC(=C(N2)c3ccncc3)c4ccncc4</chem>
18	 <chem>Cc1ccncc1C2=CN=C(C=C2)c3ccncc3</chem>
19	 <chem>Cc1ccncc1C2=CN=C(C=C2)c3cc4c(cnc34)c5ccncc5</chem>

20	 <chem>c1cc(C2=CN=CN2C3=CC=CC=C3C(F)(F)F)ccn1</chem>
21	 <chem>c1cc(C2=CN=CN2C3=CC=CC=C3C(F)(F)F)ccn1</chem>
22	 <chem>c1cc(C2=NC(C3=CC=CC=C3)N=C2C4=CC=CC=N4)ccn1</chem>
23	 <chem>c1ccccc1N2C3=CC=CC=C3N=N2C4=CC=CC=C4N5C6=CC=CC=C6N=N5</chem>
24	 <chem>c1ccccc1N2C3=CC=CC=C3N=N2C4=CC=CC=C4N5C6=CC=CC=C6N=N5C7=CC=CC=C7</chem>

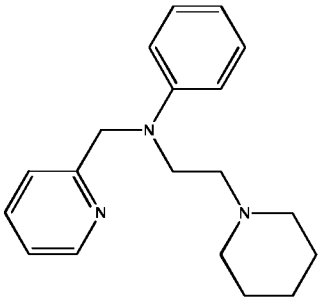
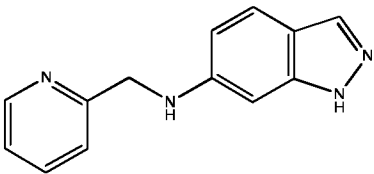
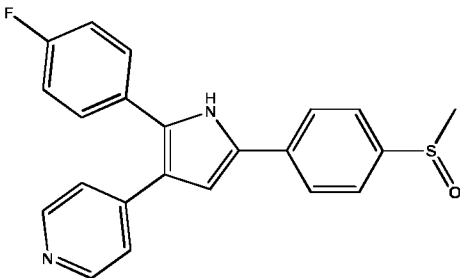
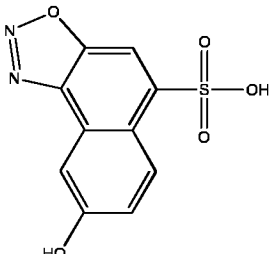
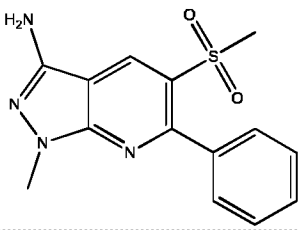
25	 <chem>c1ccc(cc1)-c2nc3cc[nH]3c2C=Nc4cc[nH]4</chem>
26	 <chem>C=C(C)c1nc2ccccc2n1-c3cc4c(cc3)ncn4</chem>
27	 <chem>C=Cc1nc2ccccc2n1-c3cc4c(cc3)ncn4</chem>
28	 <chem>C(C)(C)c1nc2ccccc2n1-c3cc4c(cc3)ncn4</chem>
29	 <chem>C=Cc1nc2ccccc2n1-c3cc4c(cc3)ncn4</chem>

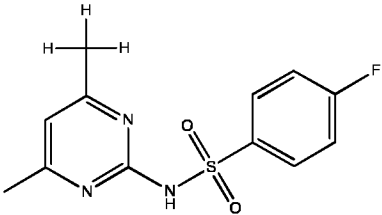
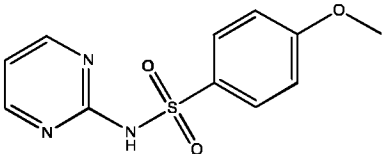
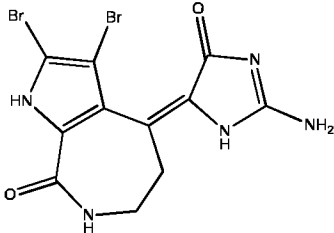
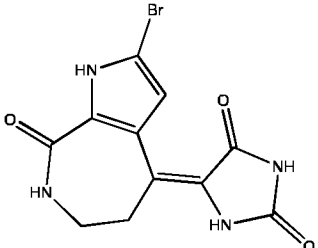
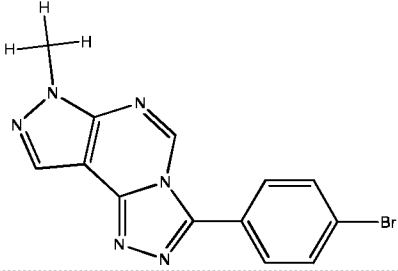
30	 <chem>CN1C=CN2C(=N1)C=CC2N(CCC3=CC=CC=N3)</chem>
31	 <chem>CCCCN1C=CN2C=C(C=C1)C=C(C2)NC3=CC=CC=N3</chem>
32	 <chem>CCN1C=NC2=C(N1)C=CC=C2C3=NC=NC3NC4=CC=CC=N4</chem>
33	 <chem>CC1=CC=C(C=C1)N(C2=CC=CC=C2)C3=NC=NC4=CC=C(C=C3)C=C4C5=CC=CC=N5</chem>
34	 <chem>c1ccc2c(c1)c3ccccc3c2n1c2ccccc21</chem>

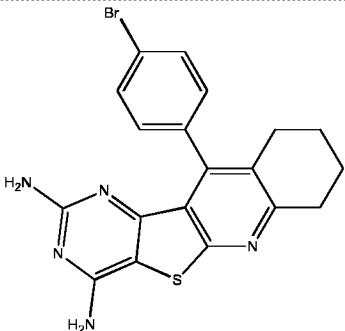
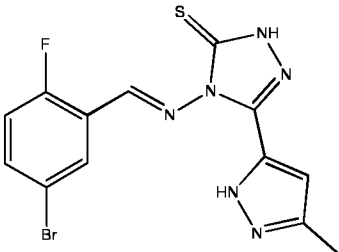
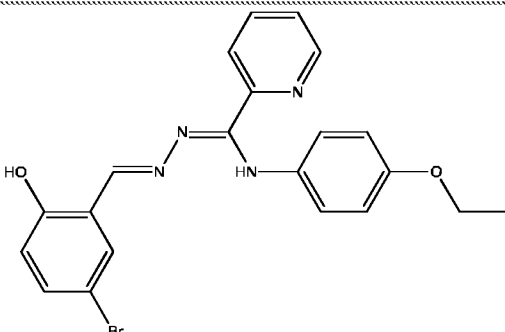
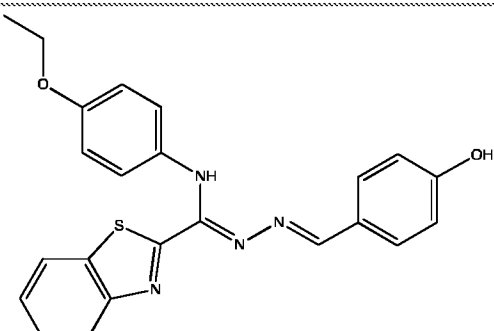
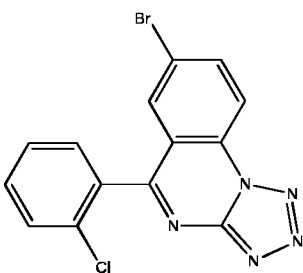
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36	 <chem>c1ccncc1n2c3ccncc3n2</chem>
37	 <chem>c1ccccc1n2c3ccncc3n2</chem>
38	 <chem>c1ccccc1n2c3ccncc3n2c4ccccc4</chem>
39	 <chem>CC(C)c1ccc(cc1)n2c3ccncc3n2c4cc5ccccc5cc4n</chem>

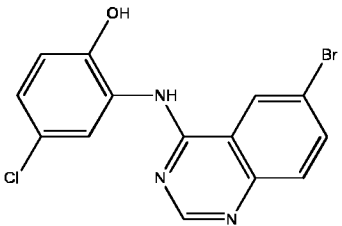
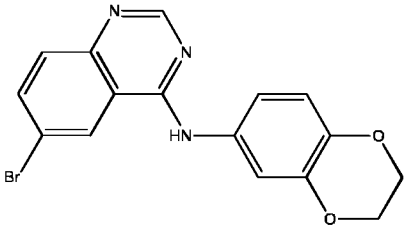
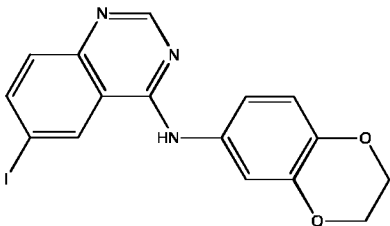
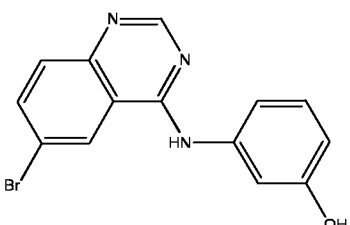
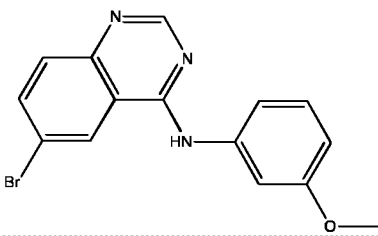
40	 <chem>c1ccc(cc1)n2cc3ccccc3cc2c2ccncc21</chem>
41	 <chem>c1ccc2c(c1)cnc3ccccc3c2c2ccncc21</chem>
42	 <chem>c1ccc(cc1)CN2C(=N3C(=CC4C(C3)CCCC4)N2)c5ccncc5</chem>
43	 <chem>c1ccc(cc1)c2nc3ccncc3nc2N4CCN(CC4)c5ccncc5</chem>
44	 <chem>c1ccc(cc1)CCc2nc3ccncc3n2c4ccncc4</chem>

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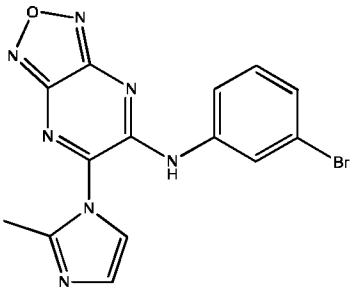
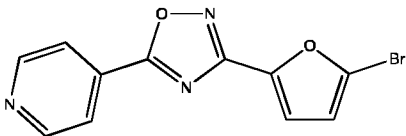
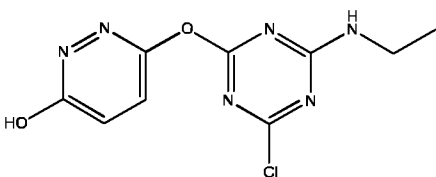
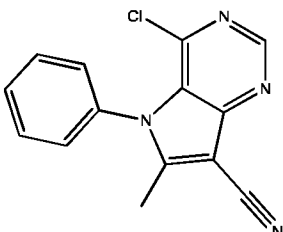
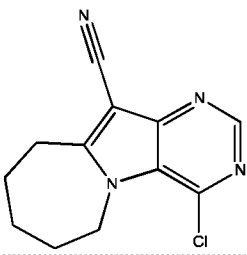
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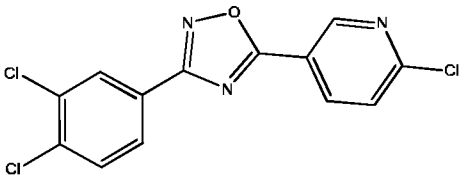
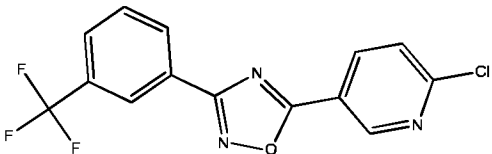
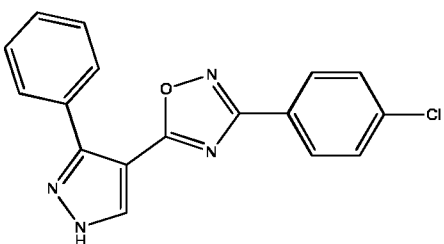
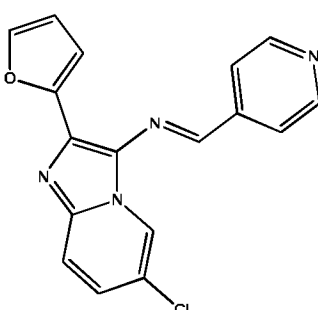
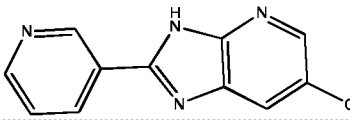
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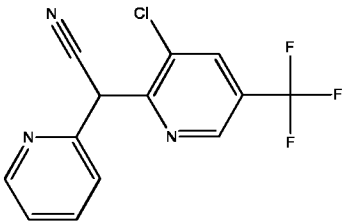
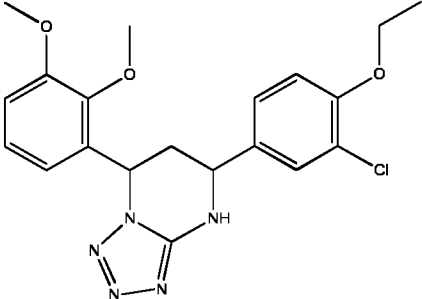
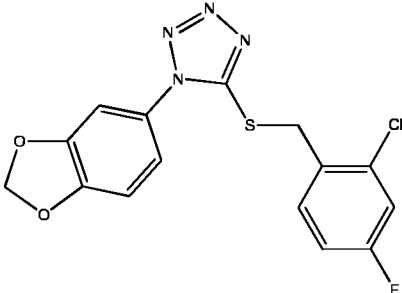
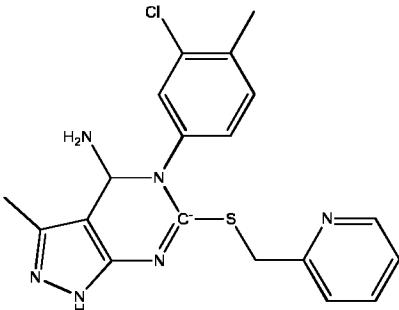
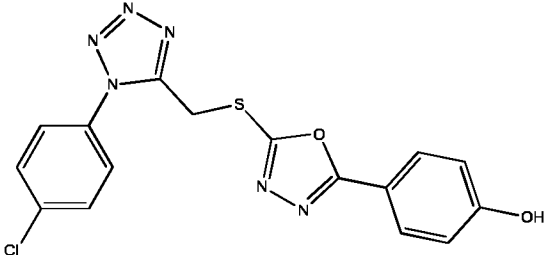
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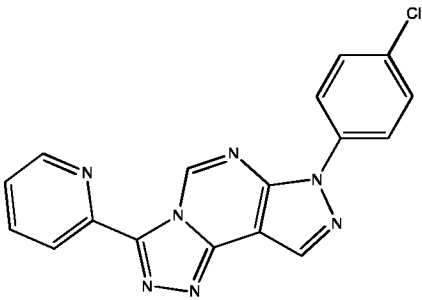
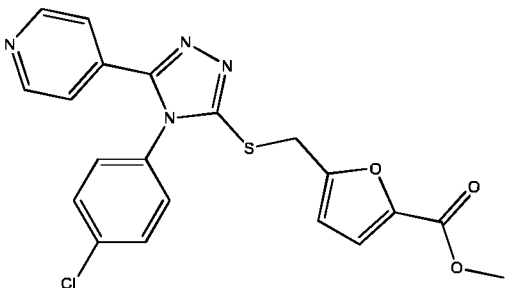
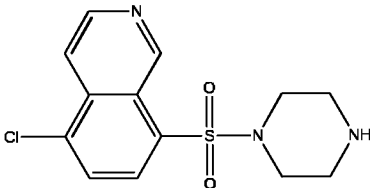
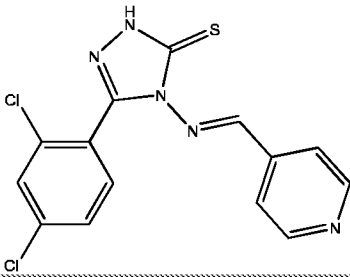
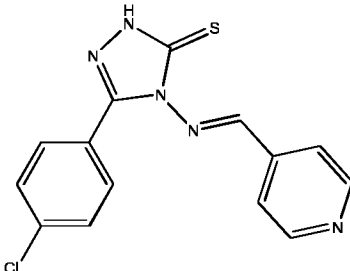
65	 <chem>Oc1ccc(Nc2nc3ccc(Br)cc3n2)cc1Cl</chem>
66	 <chem>Brc1ccc2nc3cc(Nc4ccc5c(c4)OCCO5)ccc3n2</chem>
67	 <chem>Ic1ccc2nc3cc(Nc4ccc5c(c4)OCCO5)ccc3n2</chem>
68	 <chem>Oc1ccc(Nc2nc3ccc(Br)cc3n2)cc1</chem>
69	 <chem>COc1ccc(Nc2nc3ccc(Br)cc3n2)cc1</chem>

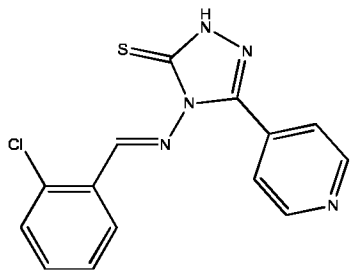
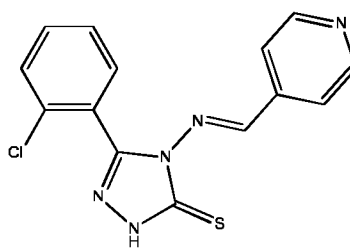
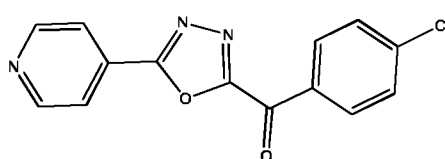
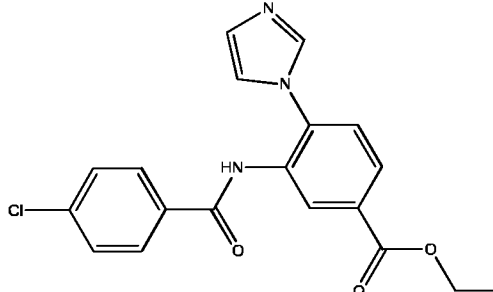
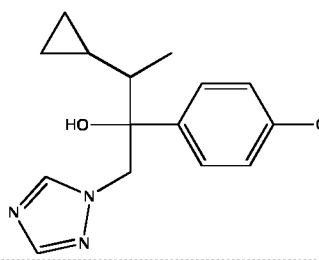
70	Chemical structure 70: A quinazoline ring system with an iodine atom at the 4-position and a 4-hydroxyphenyl group at the 2-position. <chem>Oc1ccc(Nc2nc3cc(I)ccc3nc2)cc1</chem>
71	Chemical structure 71: A 1,3,4-thiadiazine ring system with a pyridin-2-yl group at the 4-position and a 3-bromophenyl group at the 2-position. <chem>Brc1ccc(cc1)C2=NC3=NC(=N2)SC3c4ccncc4</chem>
72	Chemical structure 72: A 1,3,4-thiadiazine-5-carboxamide ring system with a 4-bromophenyl group at the 2-position and a 1H-indol-3-yl group at the 4-position. <chem>O=C1NC(=S1)C(=N2C(=NC(=N2)SC2=CC=C(C=C2)N3C=CC=CC=C3)C4=CC=C(C=C4)Br)N5C=CC=C(C=C5)Br</chem>
73	Chemical structure 73: A 1,3,4-thiadiazine-5-carboxamide ring system with a 4-chlorophenyl group at the 2-position and a pyridin-2-yl group at the 4-position. <chem>O=C1NC(=S1)C(=N2C(=NC(=N2)SC2=CC=C(C=C2)N3C=CC=CC=C3)C4=CC=C(C=C4)Cl)N5C=CC=C(C=C5)Br</chem>
74	Chemical structure 74: A 1,3,4-thiadiazine-5-carboxamide ring system with a 4-fluorophenyl group at the 2-position and a 3-methoxy-4-hydroxyphenyl group at the 4-position. <chem>COc1cc(O)ccc1C=C2C(=O)NC(=N2)N3C=CC=C(C=C3)F</chem>

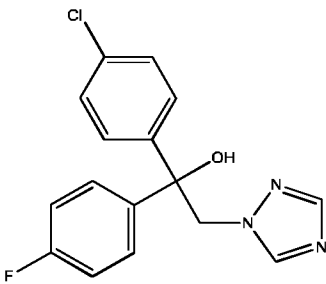
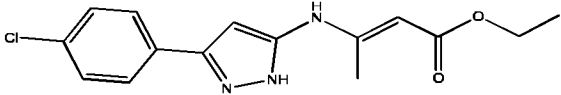
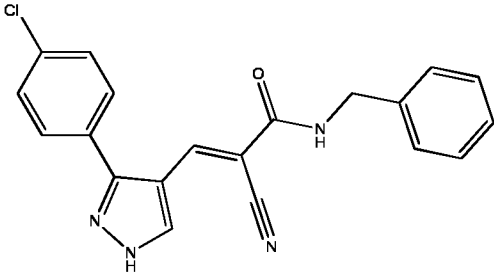
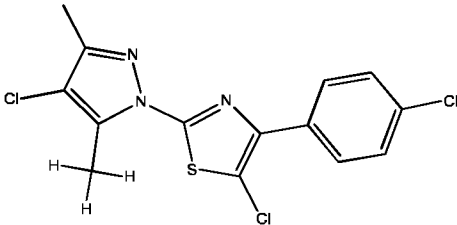
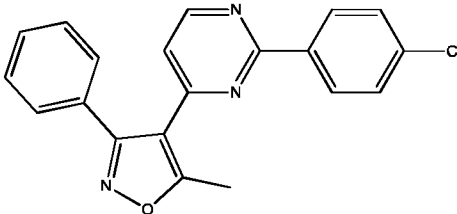
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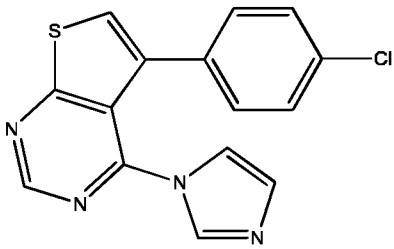
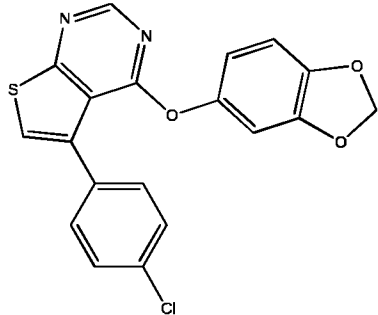
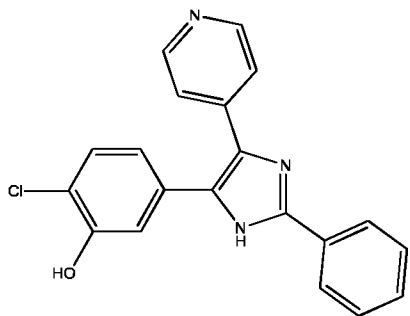
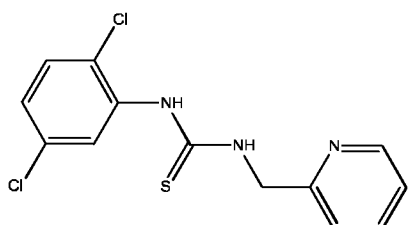
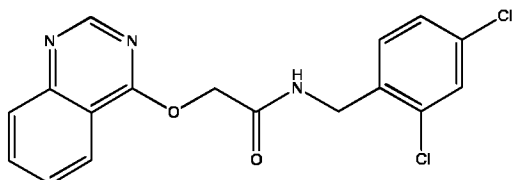
80	 <chem>Clc1ccc(Cl)cc1-c1nc2cc(Cl)ccn2n1</chem>
81	 <chem>Fc1cc(F)cc-c1-c1nc2cc(Cl)ccn2n1</chem>
82	 <chem>c1ccccc1-c1nc2cc(Cl)ccn2n1</chem>
83	 <chem>c1cc(Cl)ccn1-c1nc2cc(Cl)ccn2n1</chem>
84	 <chem>c1cc(Cl)ccn1-c1nc2cc(Cl)ccn2n1</chem>

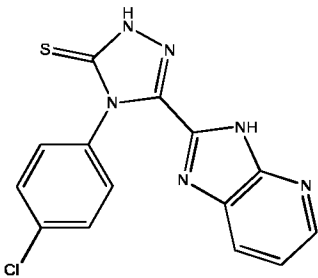
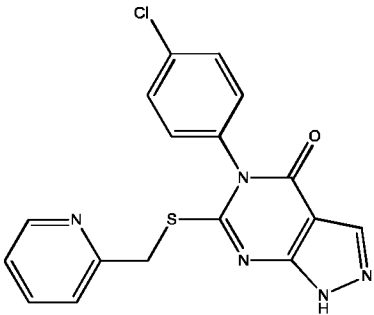
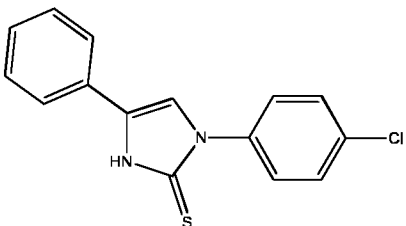
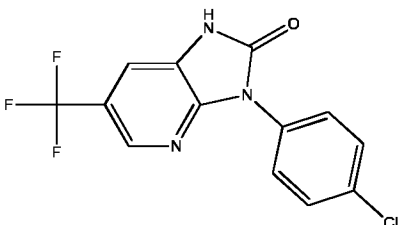
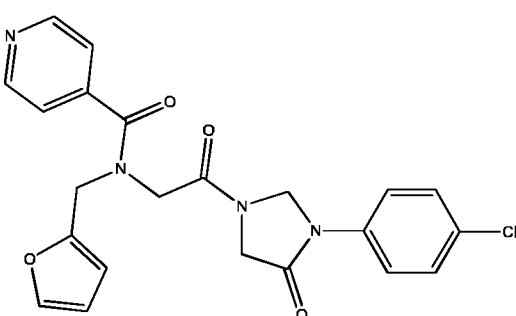
85	 <chem>N#CC(C1=CC=CC=N1)c2cc(Cl)cc(CF(F)F)c2</chem>
86	 <chem>COc1cc(OC)ccc1C2=NN=C(N2)C3=CC=C(OC)C(Cl)=C3</chem>
87	 <chem>Fc1ccc(Cl)cc1SC2=CN=CN=C2N3C=CC4=CC=CC3O4</chem>
88	 <chem>Cc1nc2c(nc[nH]2)C(N)C3=NN=C(N3)C4=CC=C(Cl)C=C4SC5=CC=CC=N5</chem>
89	 <chem>Oc1ccc(cc1)-c2nn[nH]2SC3=CC=CC=C3N4=CC=CC=C4Cl</chem>

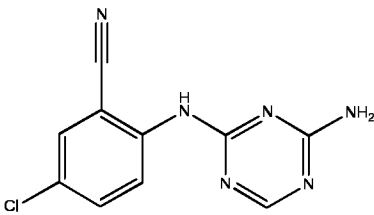
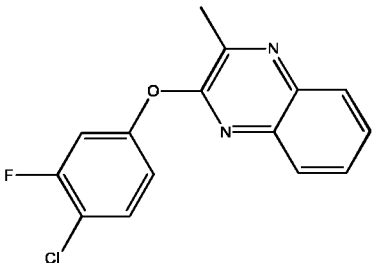
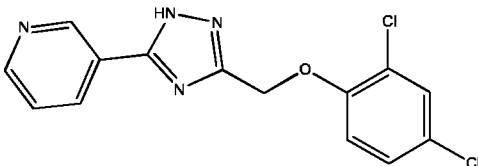
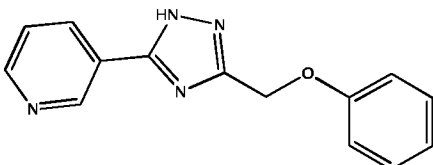
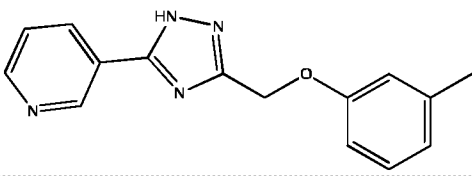
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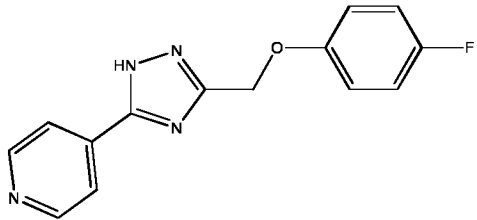
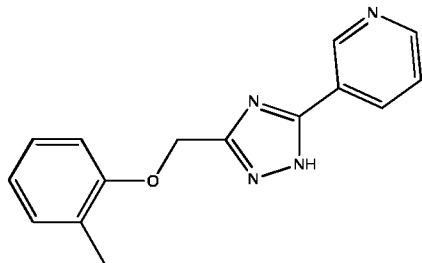
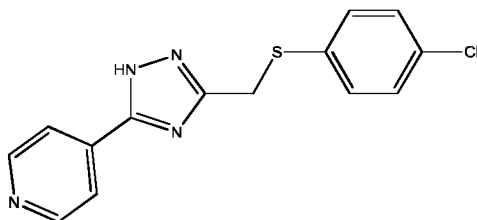
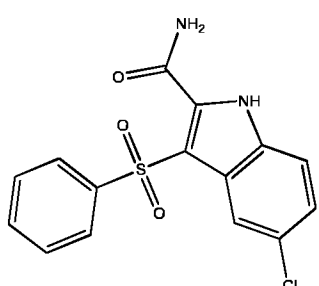
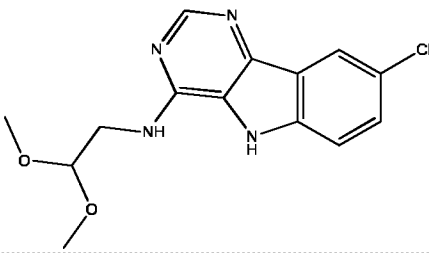
95	 <chem>Clc1ccccc1/C=N/N2C(=S)N=C(N2)c3ccccn3</chem>
96	 <chem>c1ccc(cc1)/N2C(=S)N=C(N2)/N=C/c3ccccn3</chem>
97	 <chem>Clc1ccc(cc1)C(=O)c2nc3ccccc3o2</chem>
98	 <chem>CCOC(=O)c1ccc(NC(=O)c2ccc(Cl)cc2)c(N3C=CN=C3)c1</chem>
99	 <chem>CC1CC1C(O)(Cc2nn[nH]2)c3ccc(Cl)cc3</chem>

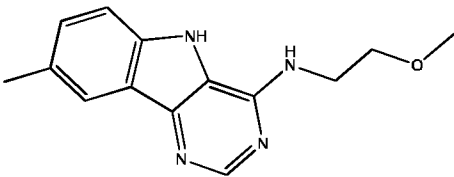
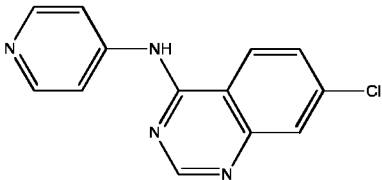
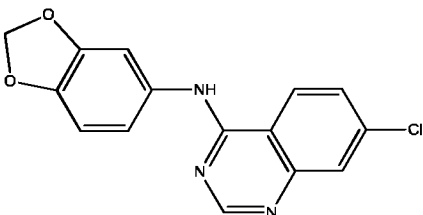
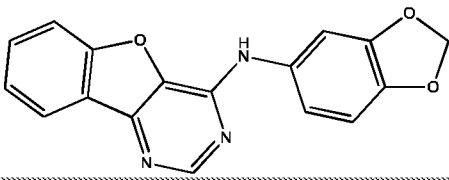
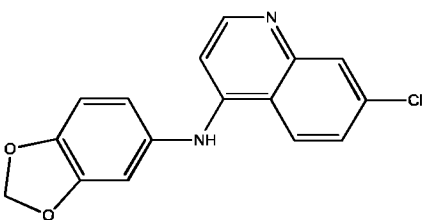
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101	 <chem>Clc1ccc(cc1)-c2nc[nH]2N/C=C/C(=O)OCC</chem>
102	 <chem>Clc1ccc(cc1)-c2nc[nH]2/C=C/C(=O)NCCc3ccccc3</chem>
103	 <chem>Clc1ccc(cc1)-c2nc3sc(N4C=CC(Cl)=C4C)c3n2</chem>
104	 <chem>Clc1ccc(cc1)-c2nc3ccn(c3n2)-c4c5ccccc5on4C</chem>

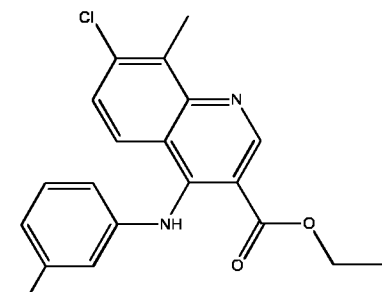
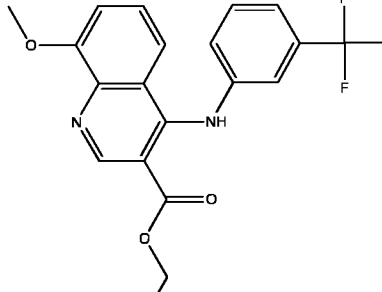
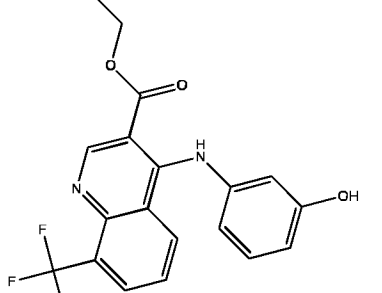
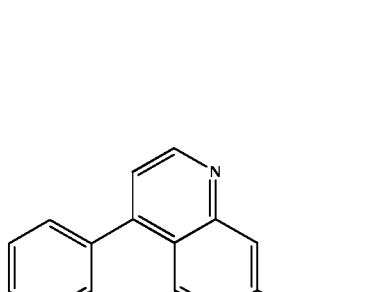
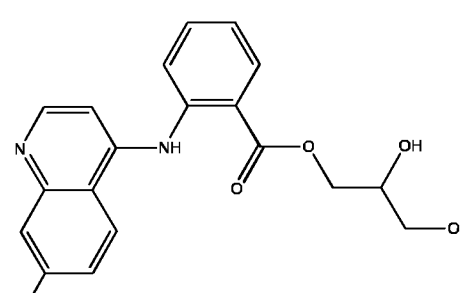
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106	 <chem>Clc1ccc(cc1)-c2sc3nc4c(n3)Oc5ccc6c(c5)OCO6</chem>
107	 <chem>Oc1cc(Cl)ccc1-c2c(c3ccccc3n2)c4ccncc4</chem>
108	 <chem>Clc1cc(Cl)ccc1NC(=S)NCc2ccncc2</chem>
109	 <chem>Clc1ccc(Cl)cc1NC(=O)CCOc2c3ccccc3nc2</chem>

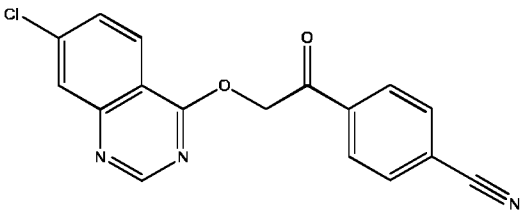
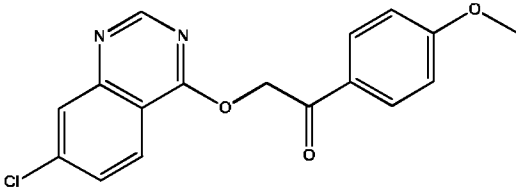
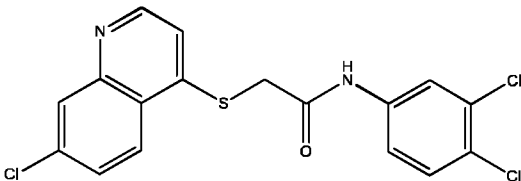
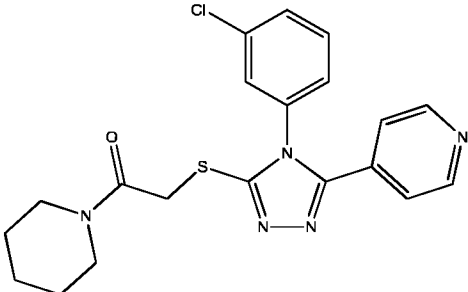
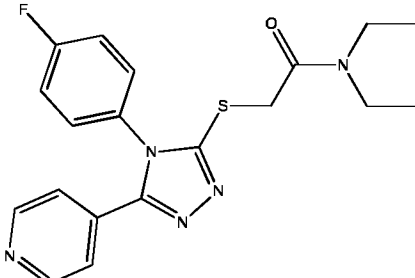
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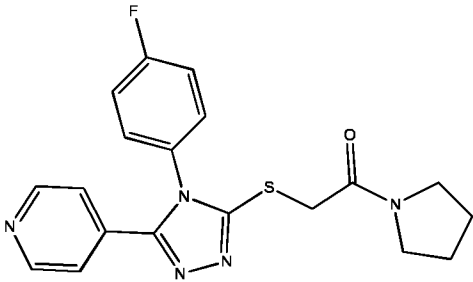
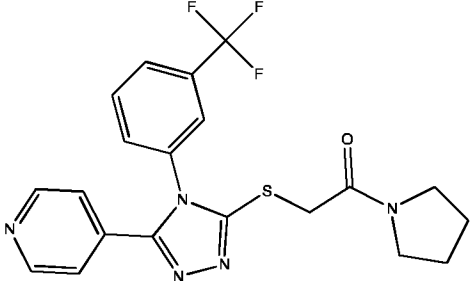
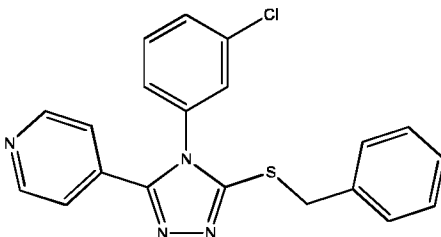
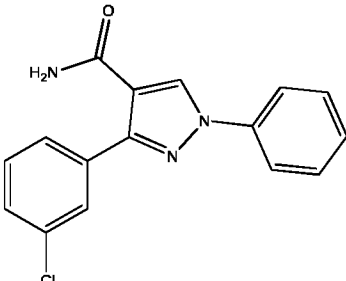
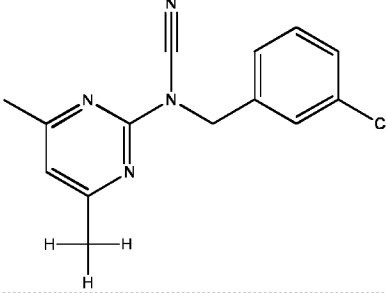
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116	 <chem>Cc1nc2ccccc2n1Oc3cc(Cl)cc(F)c3</chem>
117	 <chem>Clc1cc(Cl)cc(OCc2nn[nH]c2c3ccncc3)n1</chem>
118	 <chem>c1ccccc1OCc2nn[nH]c2c3ccncc3</chem>
119	 <chem>Cc1ccc(OCc2nn[nH]c2c3ccncc3)cc1</chem>

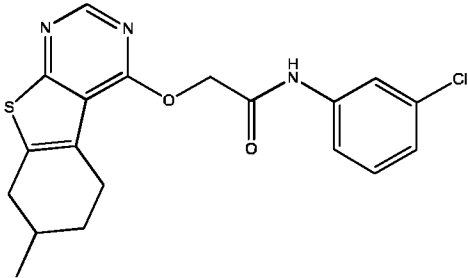
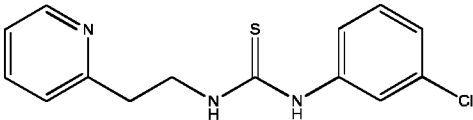
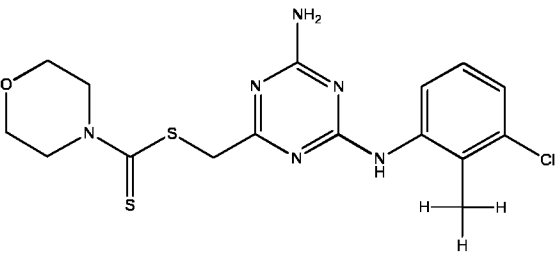
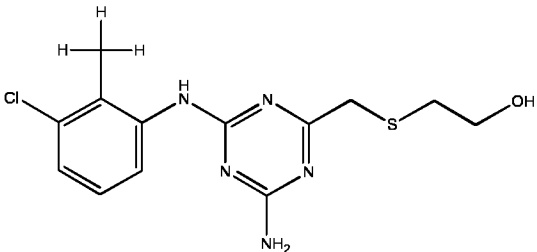
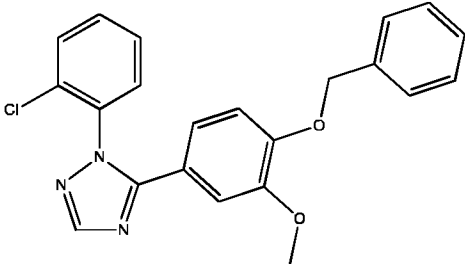
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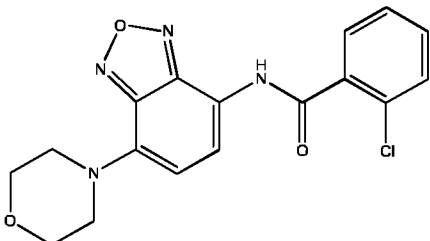
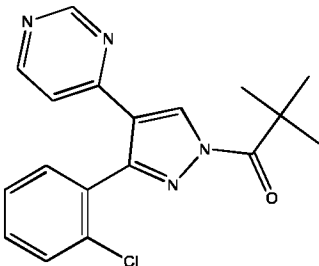
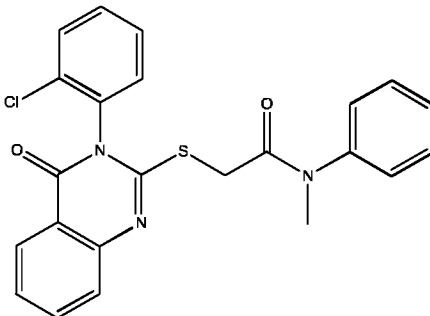
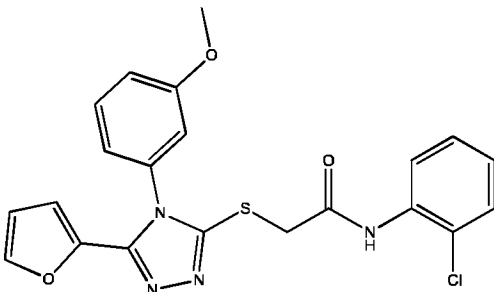
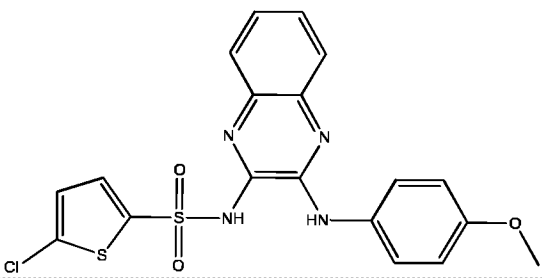
125	 <chem>COCCCNc1nc2ccccc2n1C</chem>
126	 <chem>Clc1ccc2nc3ccccc3n2Nc4ccncc4</chem>
127	 <chem>Clc1ccc2nc3cc4c(c3n2)Nc5ccc6c(c5)OCO6</chem>
128	 <chem>c1ccc2c(c1)oc3ccccc3n2Nc4ccc5c(c4)OCO5</chem>
129	 <chem>Clc1ccc2nc3cc4c(c3n2)Nc5ccc6c(c5)OCO6</chem>

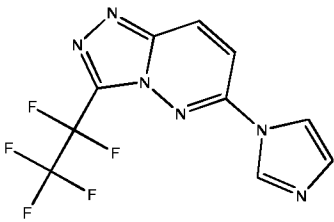
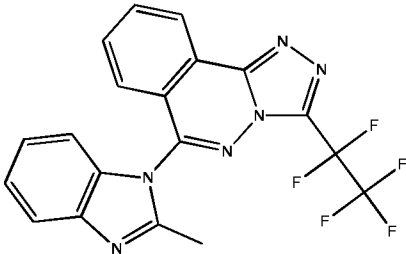
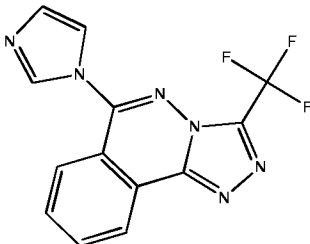
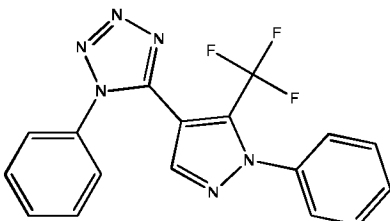
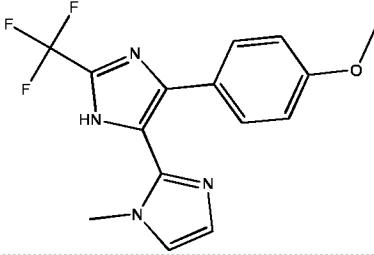
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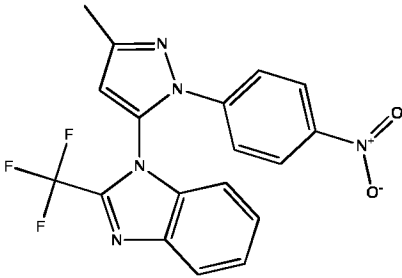
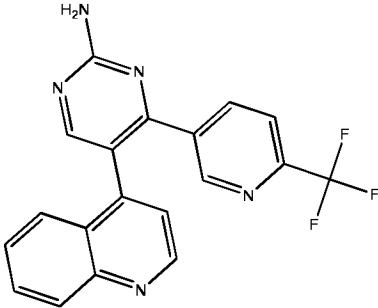
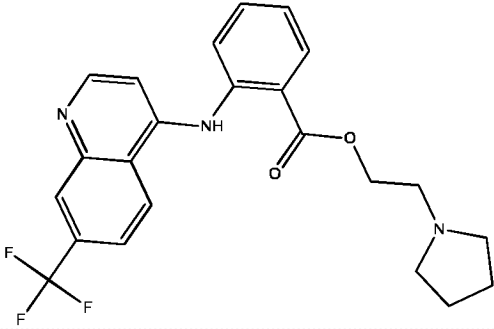
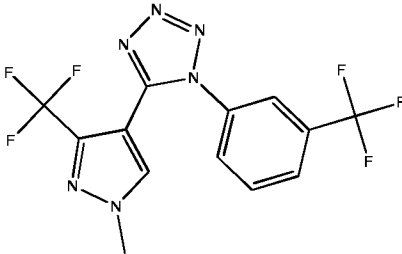
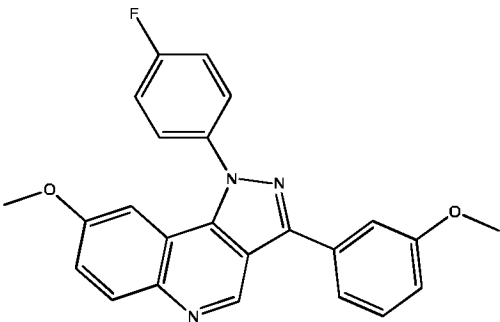
135	 <chem>N#Cc1ccc(cc1)C(=O)COc2nc3ccc(Cl)cc3n2</chem>
136	 <chem>COc1ccc(cc1)C(=O)COc2nc3ccc(Cl)cc3n2</chem>
137	 <chem>Clc1cc(Cl)ccc1NC(=O)CSc2nc3ccc(Cl)cc3n2</chem>
138	 <chem>Clc1ccc(cc1)n2nc3ccncc3n2SCC(=O)N4CCCCC4</chem>
139	 <chem>CCN(CC)C(=O)SCc1nn2c(c1n2)c3ccncc3c4ccc(F)cc4</chem>

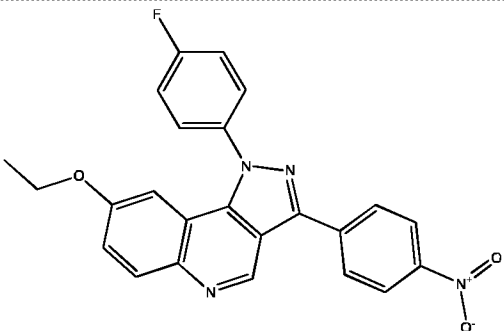
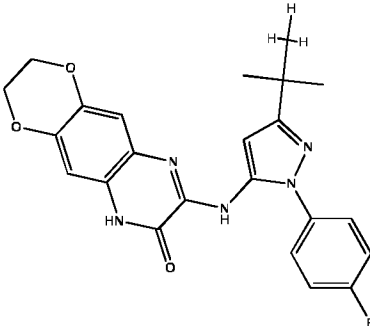
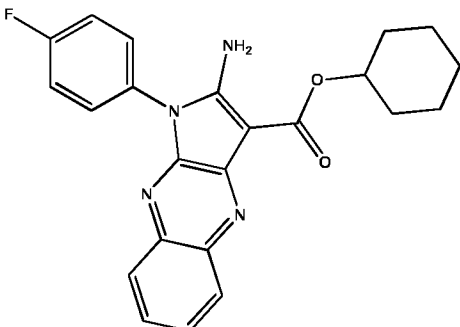
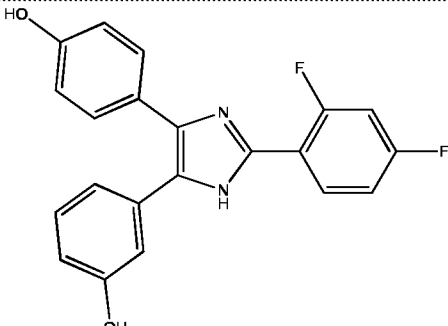
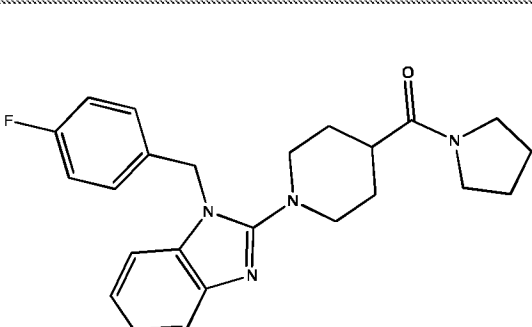
140	 <chem>Fc1ccc(cc1)n2nc(cc2c3ccncc3)SCCC(=O)N4CCCC4</chem>
141	 <chem>FC(F)(F)c1ccc(cc1)n2nc(cc2c3ccncc3)SCCC(=O)N4CCCC4</chem>
142	 <chem>Clc1cccc(c1)n2nc(cc2c3ccncc3)SCCc4ccccc4</chem>
143	 <chem>Nc1cc(C(=O)N)nn(c1c2ccccc2)c3cc(Cl)ccc3</chem>
144	 <chem>Cc1nc(NC#NCCc2ccc(Cl)cc2)nn1N</chem>

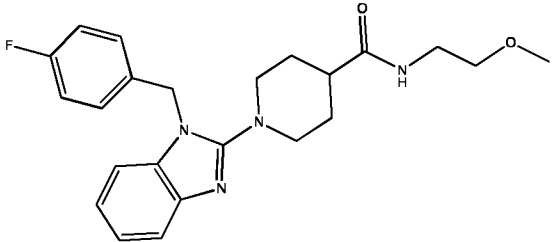
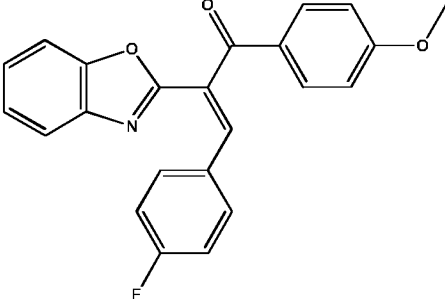
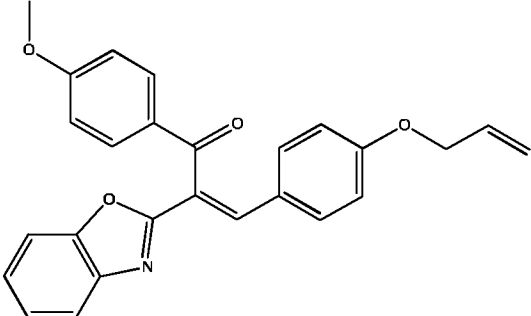
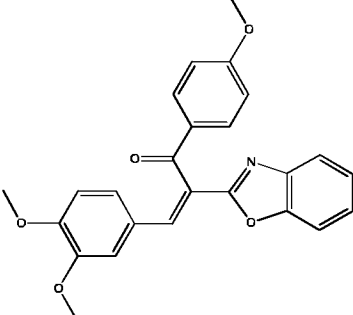
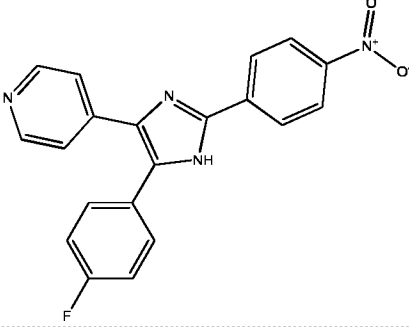
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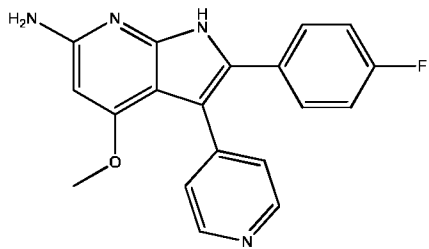
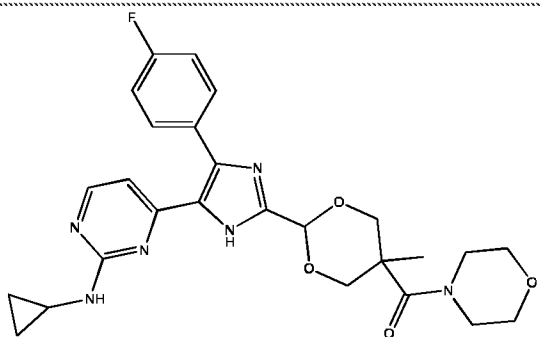
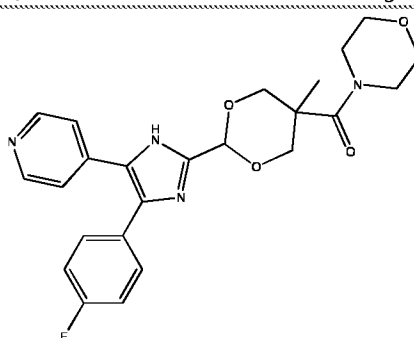
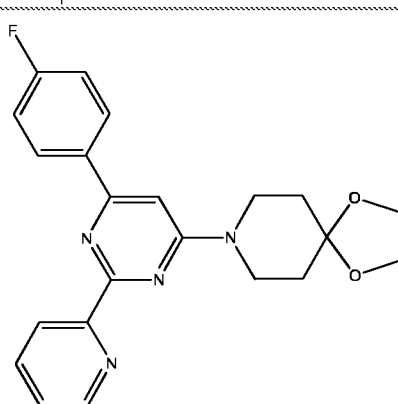
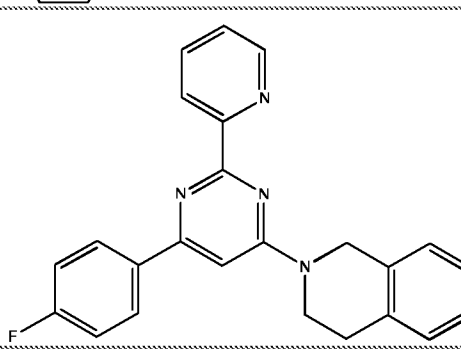
150	 <chem>Clc1ccccc1C(=O)Nc2cc3nc4ccccc4n3cc2N5CCOCC5</chem>
151	 <chem>CC(C)(C)C(=O)N1C=NC(C2=CC=CC=C2Cl)=C1C3=CC=NC=N3</chem>
152	 <chem>Clc1ccccc1C(=O)NCCSc2nc3ccccc3c(=O)n2C4=CC=CC=C4Cl</chem>
153	 <chem>COc1ccc(cc1)n2nc3ccccc3n2C(=O)NCCSc4cc(Cl)ccccc4</chem>
154	 <chem>COc1ccc(cc1)NC(=O)Nc2nc3ccccc3n2NS(=O)(=O)c4cc(Cl)ccs4</chem>

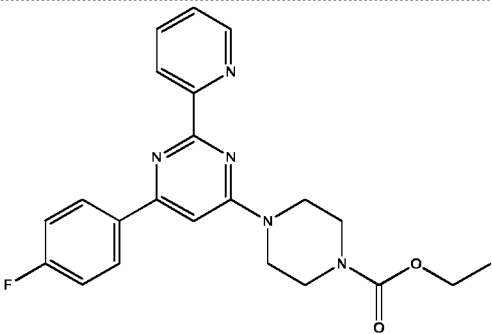
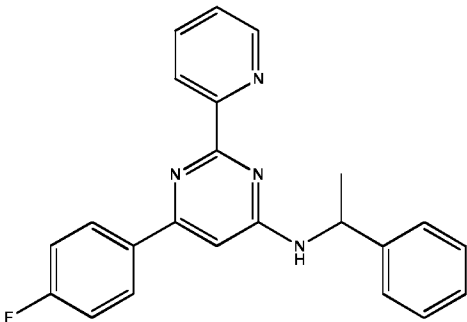
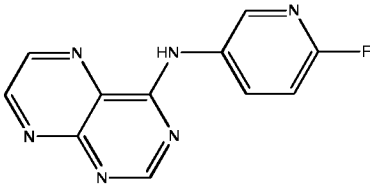
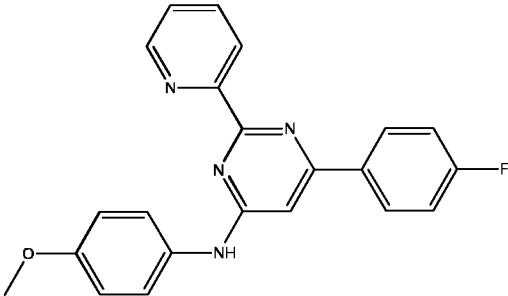
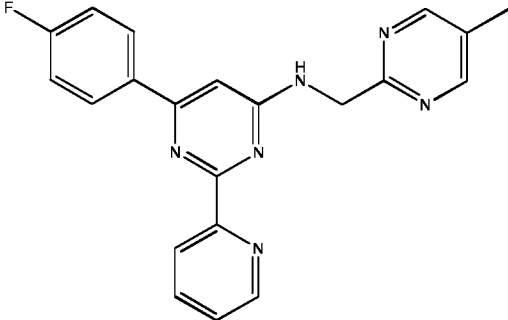
155	 <chem>Fc1c(C(F)(F)F)n2cnc3ccn(c3n2)c4ccn4</chem>
156	 <chem>Cc1nc2ccccc2n1-c1cnc2c3ccccc3n12C(F)(F)F</chem>
157	 <chem>Fc1c(C(F)(F)F)n2cnc3ccn(c3n2)c4ccn4</chem>
158	 <chem>Fc1c(C(F)(F)F)n2cnc3ccn(c3n2)c4ccccc4</chem>
159	 <chem>COc1ccc(cc1)-c2c(C(F)(F)F)n3cnc4ccn(c4n3)c5ccn5</chem>

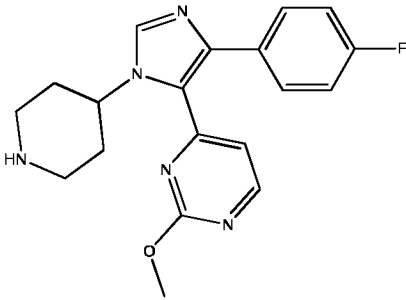
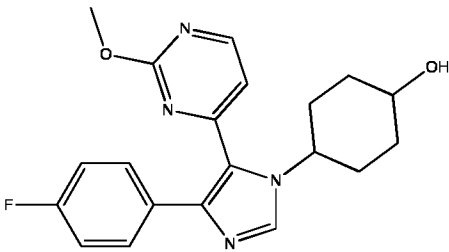
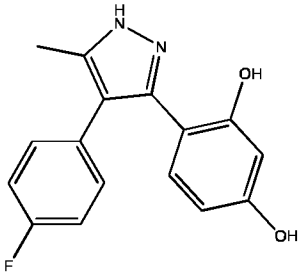
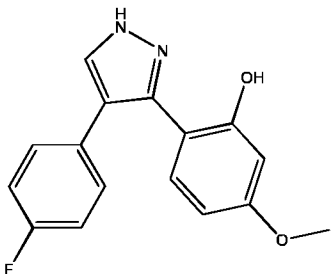
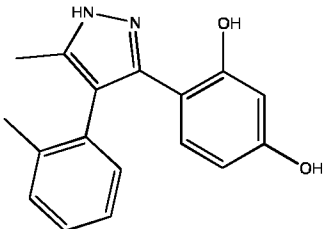
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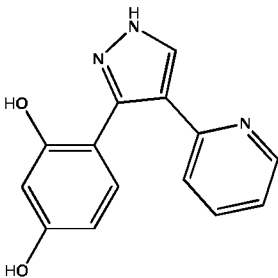
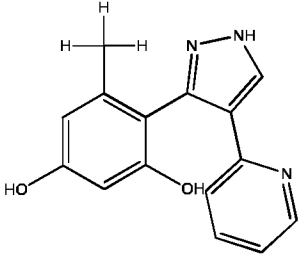
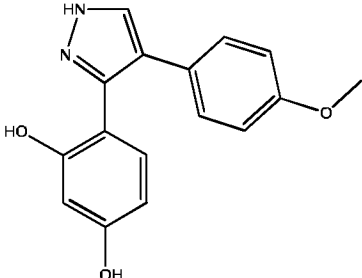
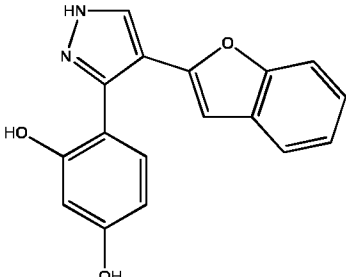
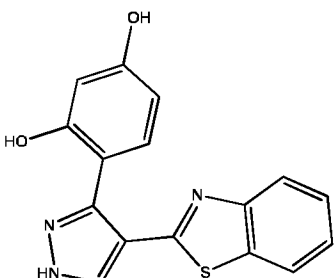
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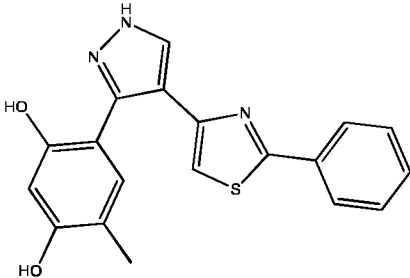
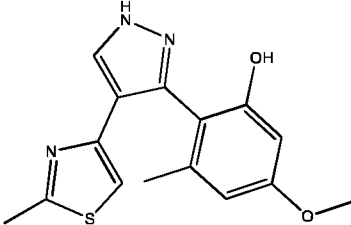
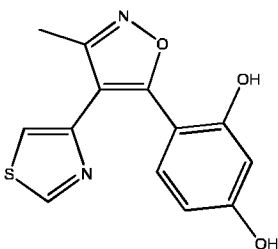
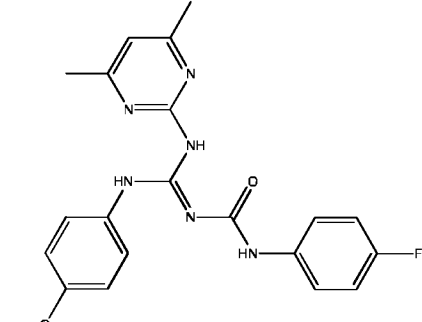
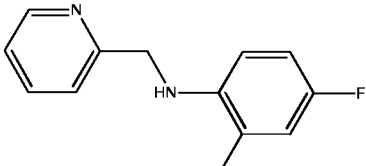
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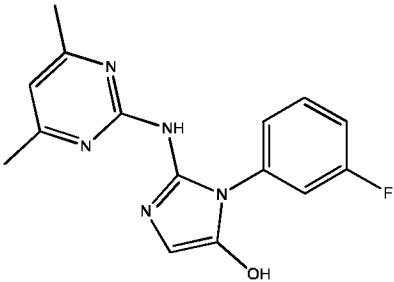
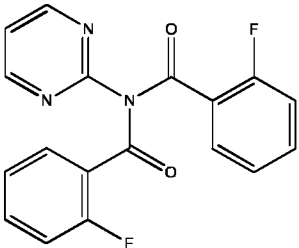
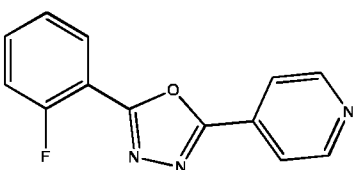
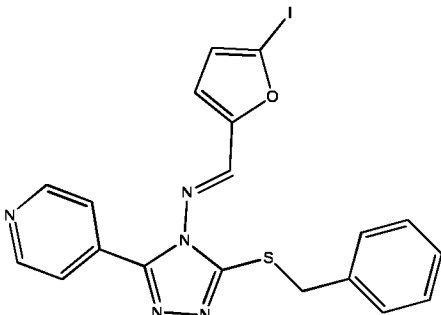
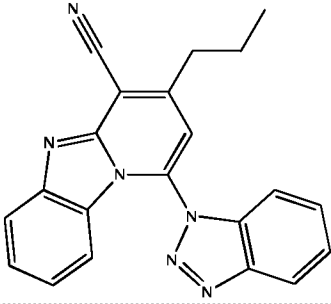
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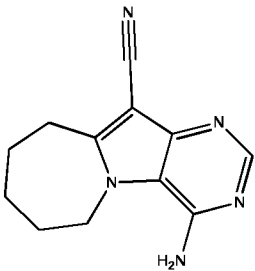
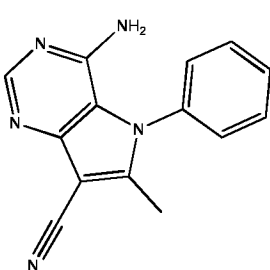
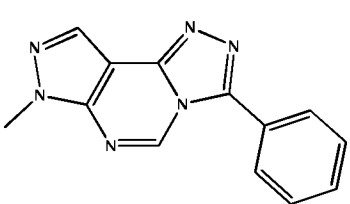
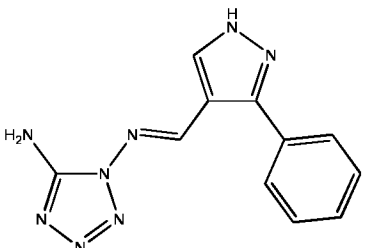
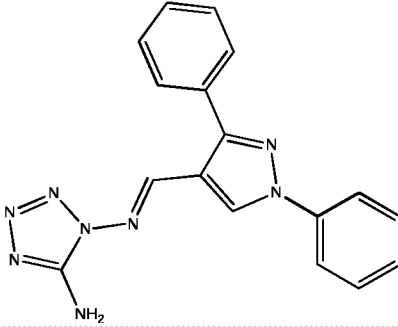
180	 <chem>CCOC(=O)N1CCN(CC1)c2nc(C3=CC=C(F)C=C3)c4nc(C5=CC=CC=N5)n4</chem>
181	 <chem>CC(C)Nc1nc(C2=CC=C(F)C=C2)c3nc(C4=CC=CC=N4)n3</chem>
182	 <chem>Fc1ccc(Nc2nc3ncnc3n2)cc1</chem>
183	 <chem>COc1ccc(Nc2nc(C3=CC=C(F)C=C3)c4nc(C5=CC=CC=N5)n4)cc1</chem>
184	 <chem>CC1=CN=CN=C1Nc2nc(C3=CC=C(F)C=C3)c4nc(C5=CC=CC=N5)n4</chem>

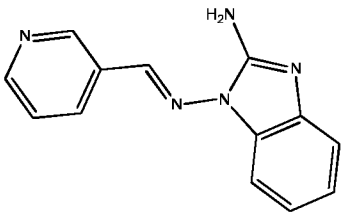
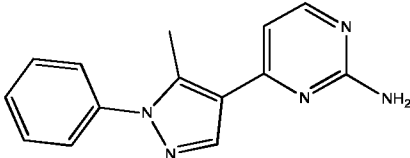
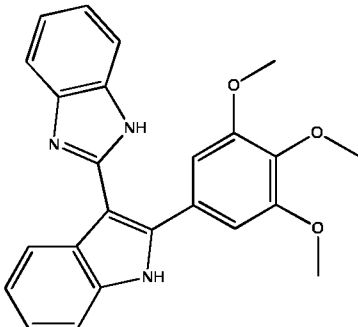
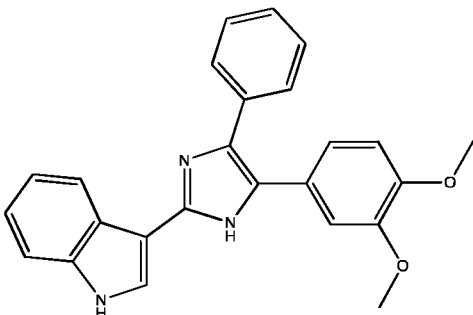
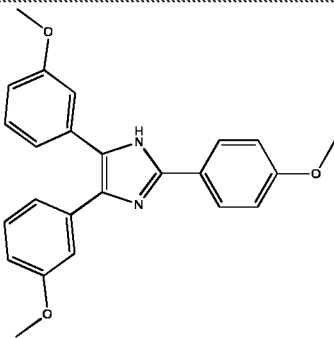
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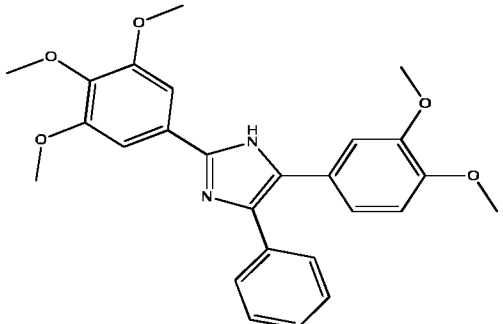
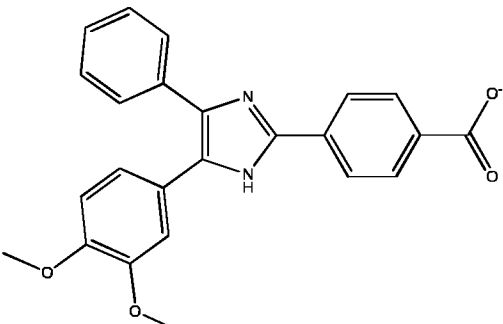
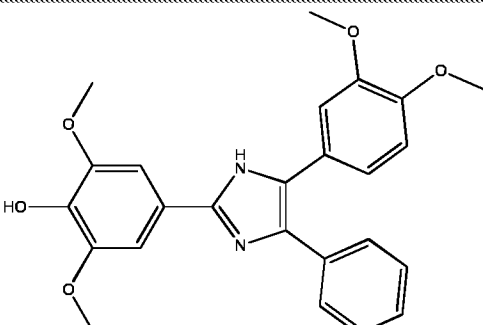
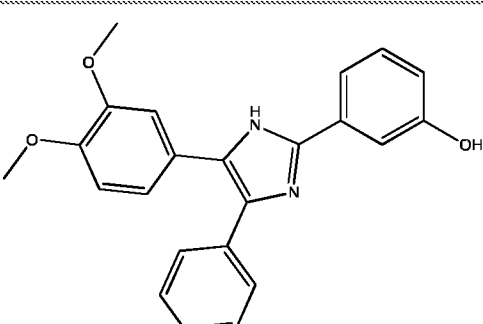
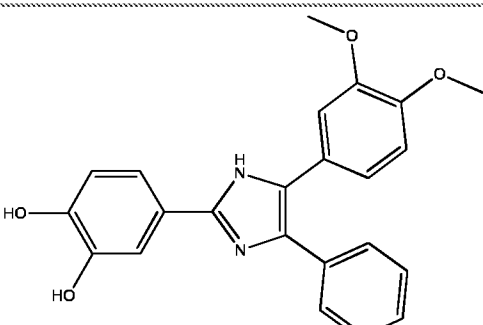
190	 <chem>Oc1cc(O)cc(cc1)-c2nc3ccncc3n2-c4ccccn4</chem>
191	 <chem>Oc1ccc2c(c1)cc(O)c3ccncc32</chem>
192	 <chem>COc1ccc(cc1)-c2nc3ccncc3n2-c4cc(O)cc(O)cc4</chem>
193	 <chem>Oc1cc(O)cc(cc1)-c2nc3ccncc3n2-c4cc5ccccc5o4</chem>
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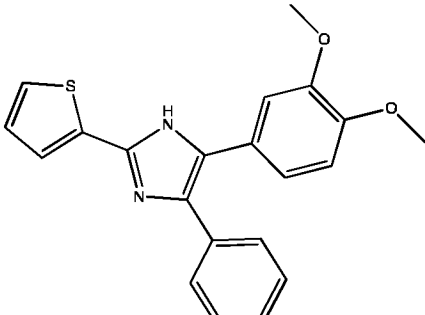
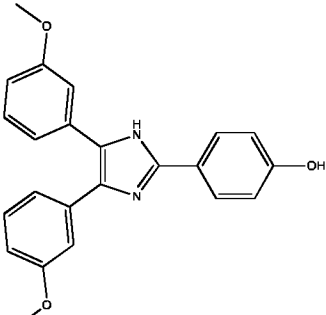
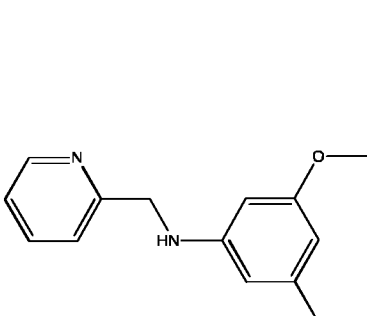
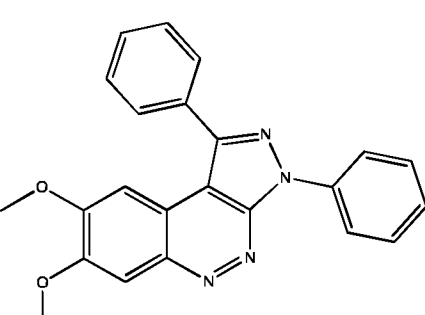
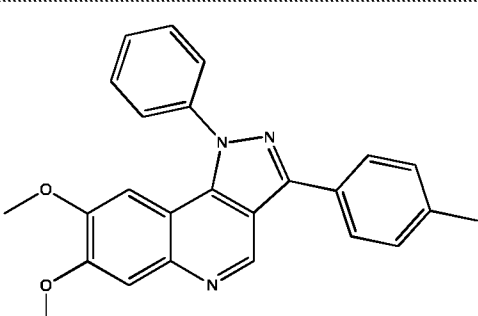
195	 <chem>Oc1cc(O)c(C2=CN=C(C2c3ccccc3S4=NC=CC4)c5ccc(O)c5)c1</chem>
196	 <chem>COc1cc(O)c(C2=CN=C(C2c3ccccc3S4=NC=CC4)c5ccc(O)c5)c1</chem>
197	 <chem>COc1cc(O)c(C2=NO=C(C2c3ccccc3S4=NC=CC4)c5ccc(O)c5)c1</chem>
198	 <chem>COc1cc(O)c(C2=NO=C(C2c3ccccc3S4=NC=CC4)c5ccc(O)c5)c1</chem>
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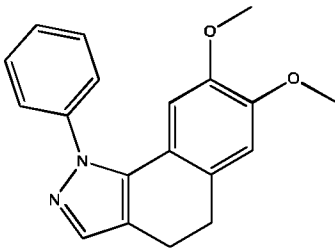
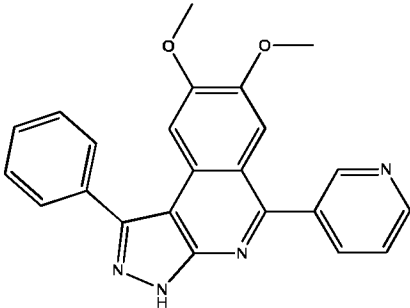
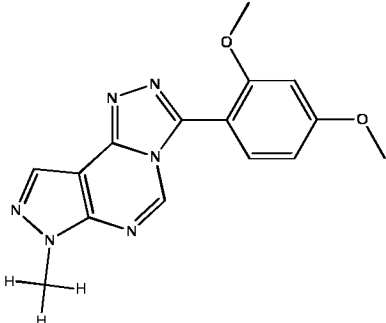
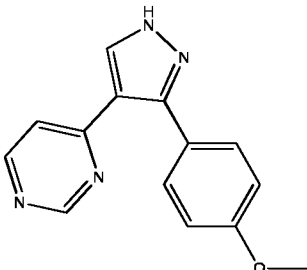
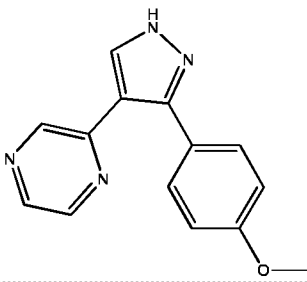
200	 <chem>Cc1cc(C)nc(Nc2nc(CO)c(Nc3ccc(F)cc3)c2)n1</chem>
201	 <chem>Fc1ccccc1C(=O)N(c2ccncn2)C(=O)c3ccccc3F</chem>
202	 <chem>Fc1cccc(c1)c2nc3ccncc3o2</chem>
203	 <chem>COc1cc(I)cc1C=N2C(c3ccncc3)N(CS4Cc5ccccc54)N2</chem>
204	 <chem>CCCN1C(=CN2C(=C1N3C4=CC=CC=C4N=C3N5C6=CC=CC=C6N=N5)C7=CC=CC=C7C2=C1C#N)C8=CC=CC=C8</chem>

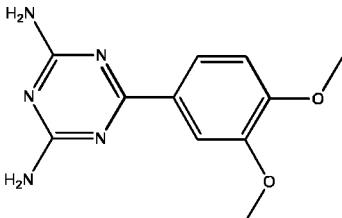
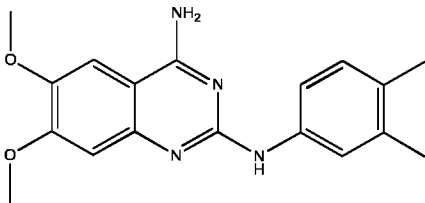
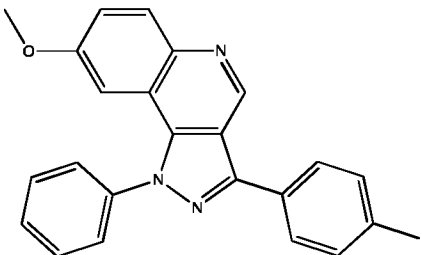
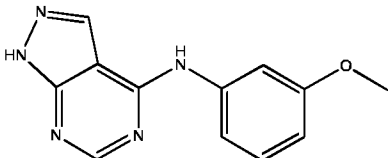
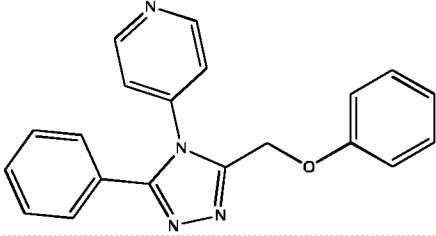
205	 <chem>N#CC1=C2C(=N1)N=CN=C2N3CCCCC13</chem>
206	 <chem>CN1=C(C#N)C2=C(N1)N=CN=C2N3C=CC=CC=C3</chem>
207	 <chem>CN1C=NC2=C1N=CN=C2N3C=CC=CC=C3</chem>
208	 <chem>N#CC1=NC=NC=N1N=CN2C=CC=CC=C2</chem>
209	 <chem>N#CC1=NC=NC=N1N=CN2C=CC=CC=C2</chem>

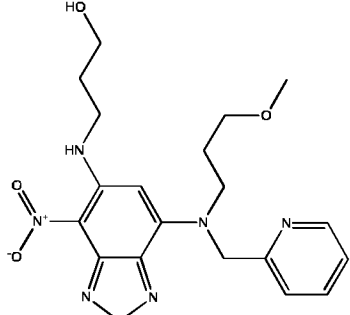
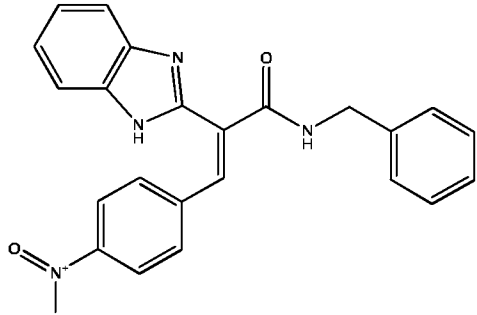
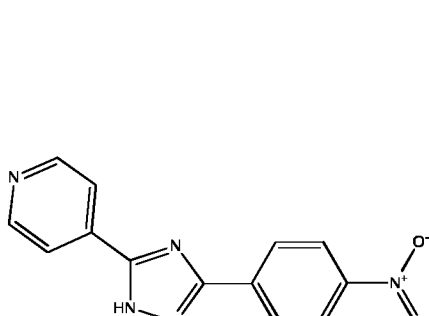
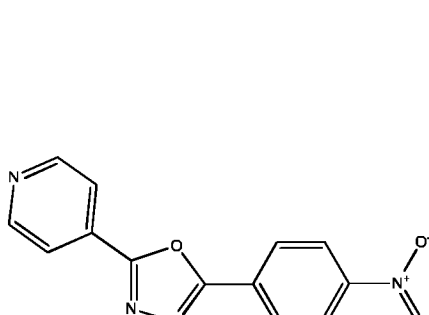
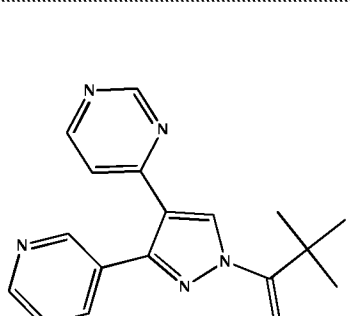
210	 <chem>Nc1nc2ccccc2n1N=Cc3ccncc3</chem>
211	 <chem>Cc1nc2ccccc2n1-c3ccnc(N)c3</chem>
212	 <chem>COc1cc(OC)c(OC)cc1-c2c3ccccc3[nH]2-c4c5ccccc5[nH]4</chem>
213	 <chem>COc1cc(OC)ccc1-c2c3ccccc3[nH]2-c4c5ccccc5[nH]4</chem>
214	 <chem>COc1ccc(cc1)-c2c3ccccc3[nH]2-c4ccc(OC)cc4</chem>

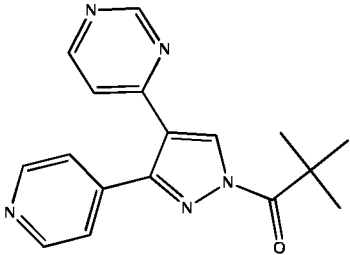
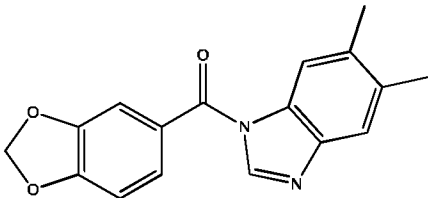
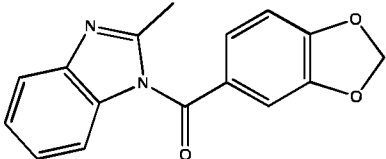
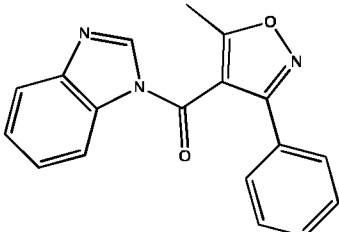
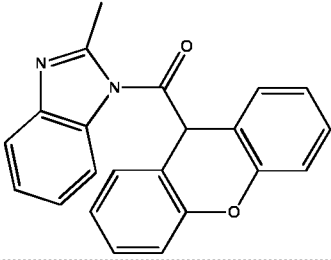
215	 <chem>COc1cc(OC)c(OC)cc1-c1c[nH]c2c1ccccc2-c3cc(OC)cc(OC)cc3</chem>
216	 <chem>COc1cc(OC)ccc1-c1c[nH]c2c1ccccc2-c3ccc(cc3)C(=O)OC</chem>
217	 <chem>COc1cc(OC)ccc1-c1c[nH]c2c1ccccc2-c3cc(OC)c(O)cc3OC</chem>
218	 <chem>COc1cc(OC)ccc1-c1c[nH]c2c1ccccc2-c3ccc(O)cc3</chem>
219	 <chem>COc1cc(OC)ccc1-c1c[nH]c2c1ccccc2-c3cc(O)c(O)cc3</chem>

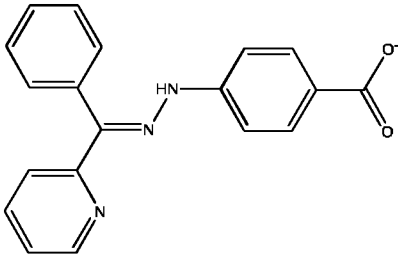
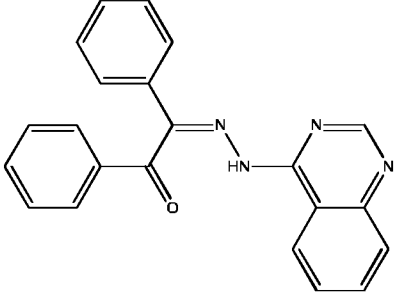
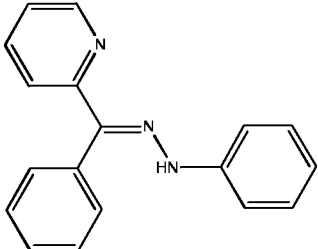
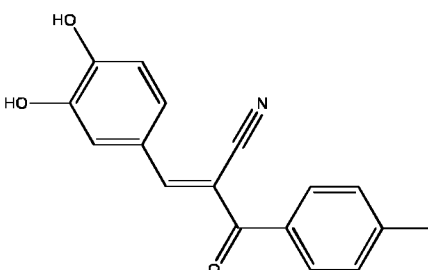
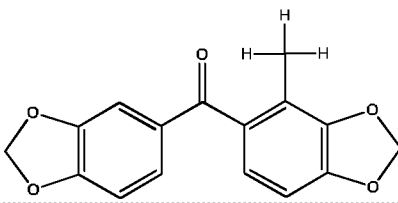
220	 <chem>COc1cc(OC)ccc1c2nc(c3ccccc3n2)c4ccsc4</chem>
221	 <chem>COc1ccc(cc1)c2nc(c3ccc(O)cc3n2)c4ccc(OC)cc4</chem>
222	 <chem>COc1cc(OC)ccc1NCc2ccccn2</chem>
223	 <chem>COc1cc2nc3ccccc3n2cc1OC</chem>
224	 <chem>COc1cc2nc3ccccc3n2cc1OC</chem>

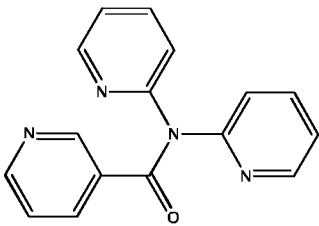
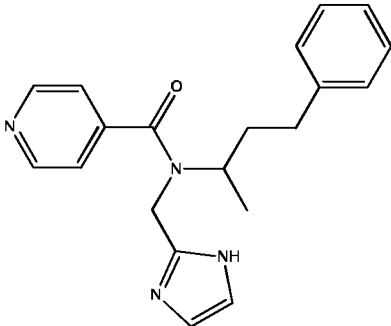
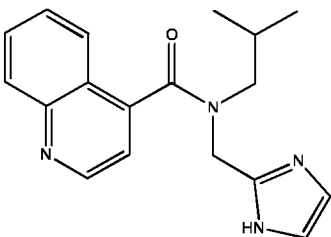
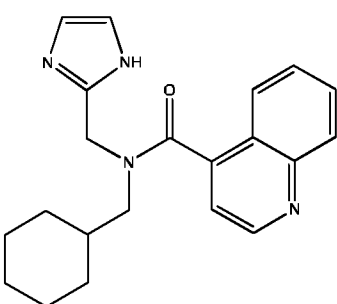
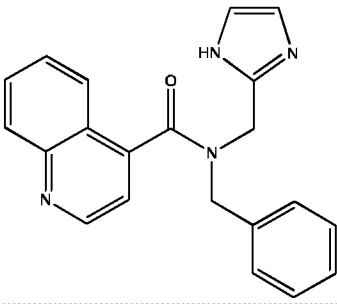
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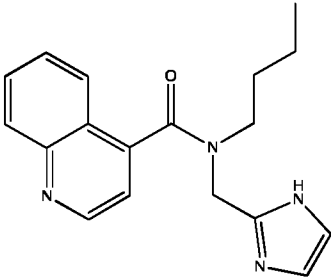
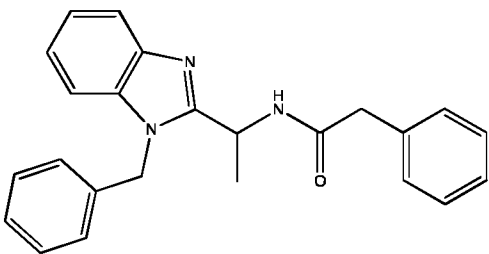
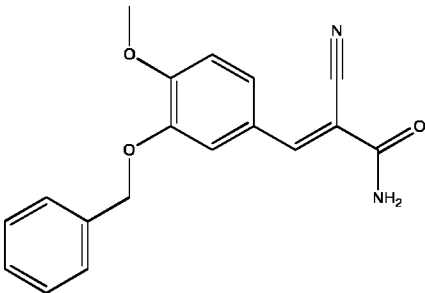
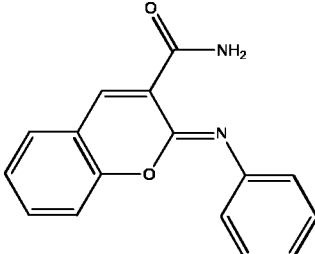
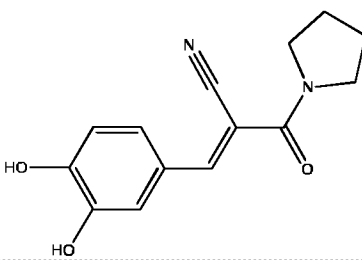
230	 <chem>Nc1nc(N)cnc1-c1ccc(OC)c(OC)c1</chem>
231	 <chem>COc1cc2nc(N)c(Nc3cc(C)c(C)cc3)cnc2cc(OC)c1</chem>
232	 <chem>COc1ccc2c(c1)c3cc4c(c2)n(c3)c5ccc(C)cc5</chem>
233	 <chem>COC1=CC=C(C=C1)Nc2nc3c(ncn3)c2</chem>
234	 <chem>c1ccncc1N1C(C2=CC=CC=C2)N1CCOC3=CC=CC=C3</chem>

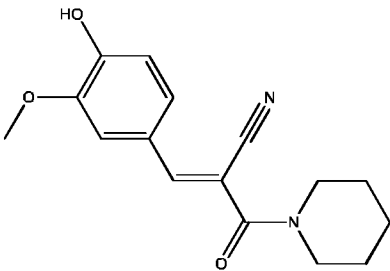
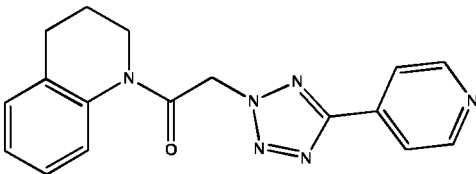
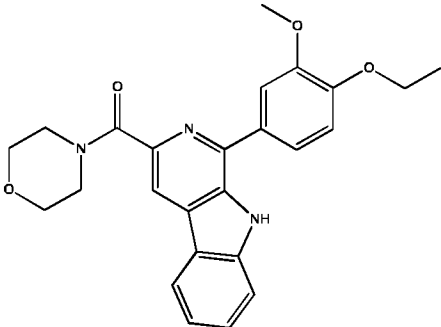
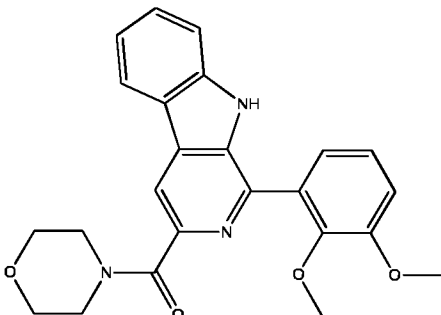
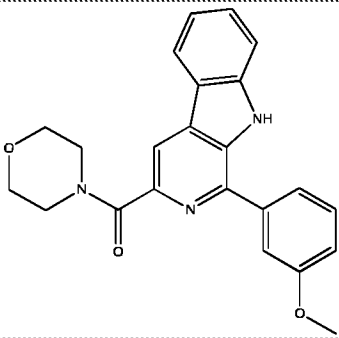
235	 <chem>COCCN(CCN)C1=CC=C2C(=C1)O=C2N3C(=CC=C3[N+](=O)[O-])NCCO</chem>
236	 <chem>O=C(NCc1ccccc1)C2=C(C=Cc3ccc([N+](=O)[O-])cc3)N3C(=NC4=CC=CC=C4N3)c5ccccc5</chem>
237	 <chem>[O-][N+](=O)c1ccc(cc1)-c2nc3ccn(c3n2)c4cccnc4</chem>
238	 <chem>[O-][N+](=O)c1ccc(cc1)-c2nc3ccn(c3o2)c4cccnc4</chem>
239	 <chem>CC(C)(C)C(=O)N1C(=CN2C(=CC=C2N)C3=CC=CC=N3)C4=CC=CC=N4</chem>

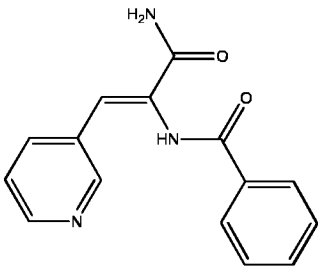
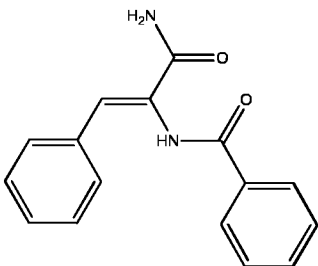
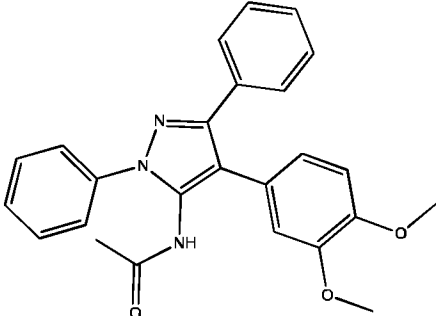
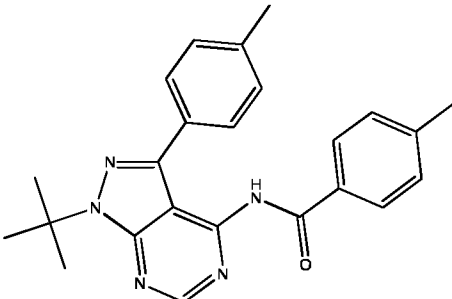
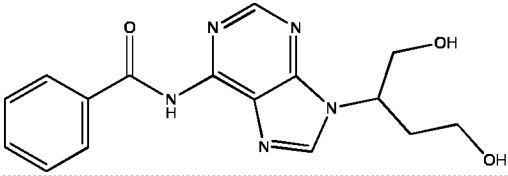
240	 <chem>CC(C)(C)C(=O)N1C=NC(C2=CC=CC=N2)=C1C3=CC=NC=N3</chem>
241	 <chem>CC1=C(C)C2=CC=C(C=C2N1)N(C(=O)C3=CC=C4C(=C3)OC5=CC=CC=C4O5)C6=CC=CC=C6</chem>
242	 <chem>CC1=C2C(=N1)C3=CC=CC=C3N2C(=O)C4=CC=C5C(=C4)OC6=CC=CC=C5O6</chem>
243	 <chem>CC1=C(C2=CC=CC=C2)N3C=CC(=N3)C(=O)N1C2=CC=CC=C2</chem>
244	 <chem>CC1=C2C(=N1)C3=CC=CC=C3N2C(=O)C4=CC=C5C(=C4)OC6=CC=CC=C5O6</chem>

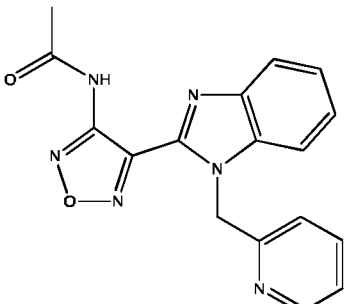
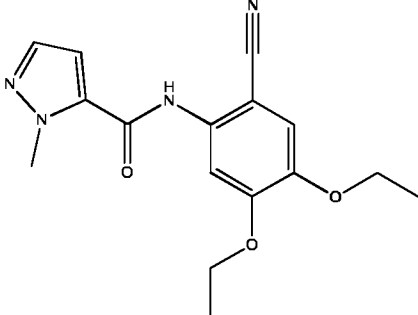
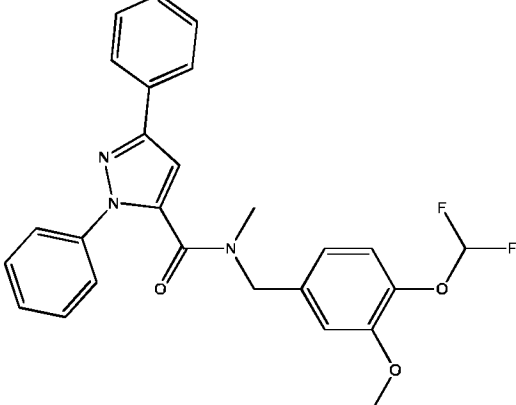
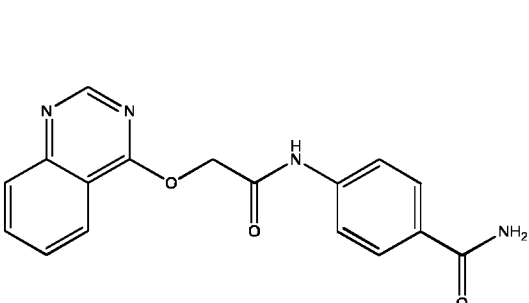
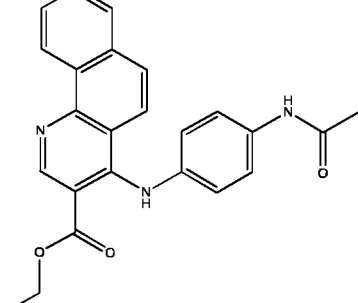
245	 <chem>O=C([O-])c1ccc(NC(=N)C2=CC=CC=C2C3=CC=CC=N3)cc1</chem>
246	 <chem>O=C(c1ccccc1)C(=NNC2=CC3=CC=CC=C3N=C2)c4ccccc4</chem>
247	 <chem>C1=CC=CC=C1C(=NNC2=CC=CC=C2C3=CC=CC=N3)C4=CC=CC=C4</chem>
248	 <chem>CC1=CC=C(C=C1)C(=O)C(=C(C#N)C=Cc2cc(O)c(O)cc2)C(=O)O</chem>
249	 <chem>O=C1C2=CC3=C(C=C2OC3)C(=O)C4=CC5=C(C=C4)OC6=CC=CC=C56</chem>

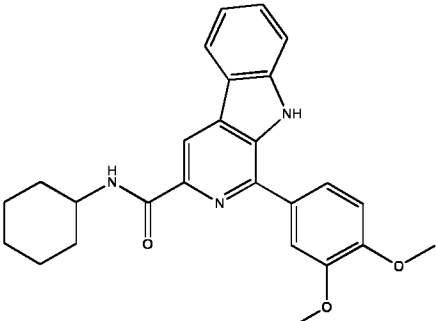
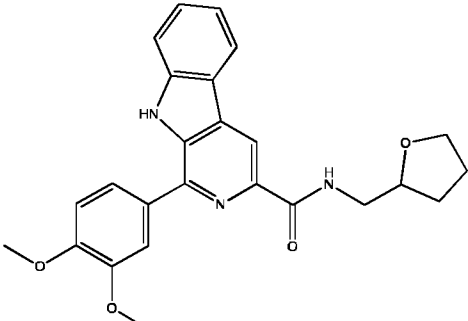
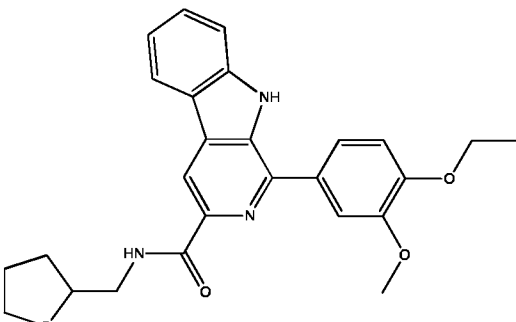
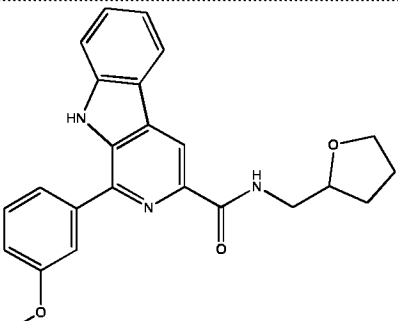
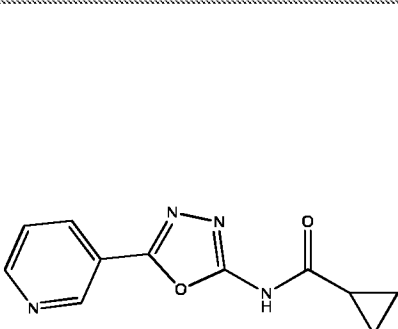
250	 <chem>O=C1C(=CN2C=CC=CC2)N(C3=CC=CC=N3)C4=CC=CC=N41</chem>
251	 <chem>O=C1C(=CN2C=CC=CC2)N(C3=CC=CC=N3)C4=CC=CC=N41CC5=CN=CNC5CCC6=CC=CC=C6</chem>
252	 <chem>O=C1C(=CN2C=CC=CC2)N(C3=CC=CC=N3)C4=CC=CC=N41CC5=CN=CNC5CC(C)C</chem>
253	 <chem>O=C1C(=CN2C=CC=CC2)N(C3=CC=CC=N3)C4=CC=CC=N41CC5=CN=CNC5CC6CCCCC6</chem>
254	 <chem>O=C1C(=CN2C=CC=CC2)N(C3=CC=CC=N3)C4=CC=CC=N41CC5=CN=CNC5CC6=CC=CC=C6</chem>

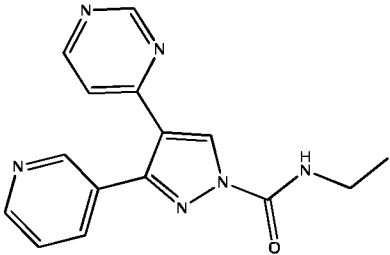
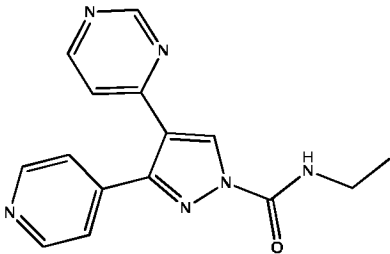
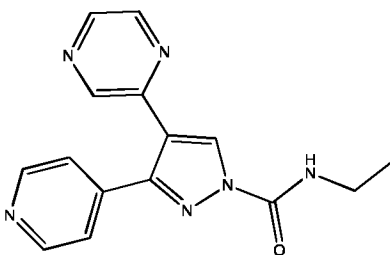
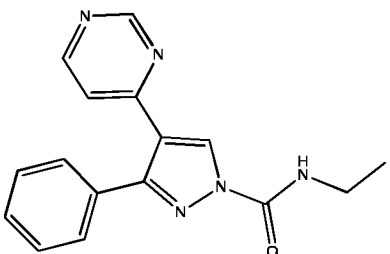
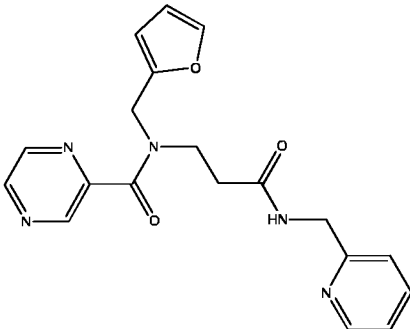
255	 <chem>CCCC(=O)c1ccc2ncncc2c1CN1C=CN=C1</chem>
256	 <chem>CC(NC(=O)Cc1ccccc1)c2nc3ccccc3n2Cc4ccccc4</chem>
257	 <chem>COc1cc(OCc2ccccc2)ccc1/C=C/C(=O)N#N</chem>
258	 <chem>NC(=O)c1cc2ccccc2oc1=Cc3ccccc3</chem>
259	 <chem>Oc1cc(O)ccc1/C=C/C(=O)N1CCCC1#N</chem>

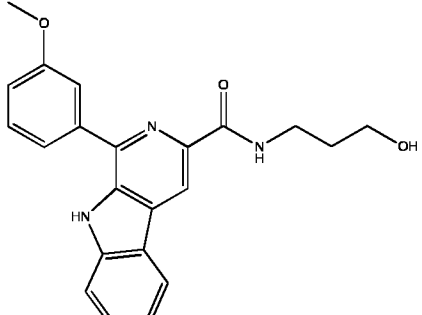
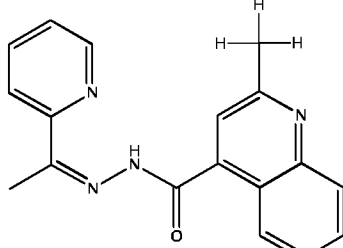
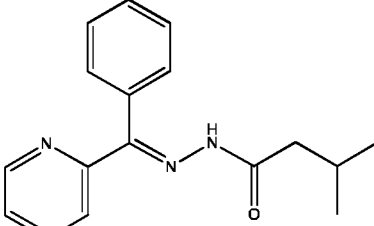
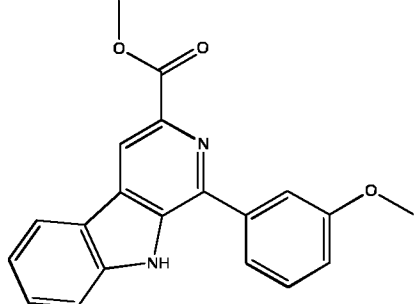
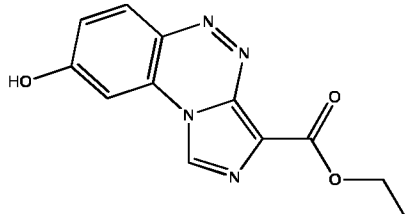
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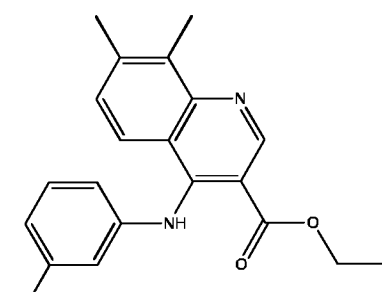
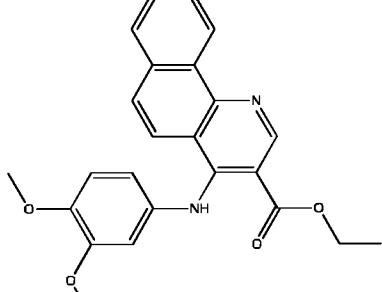
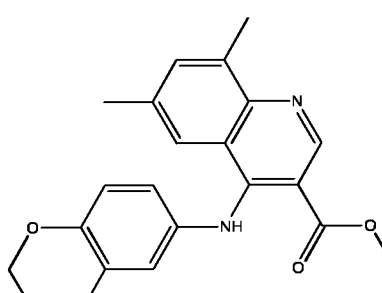
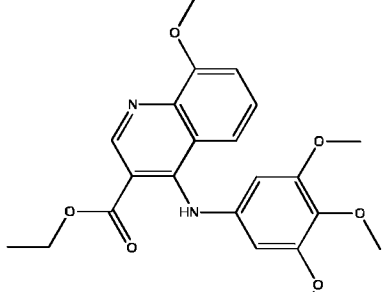
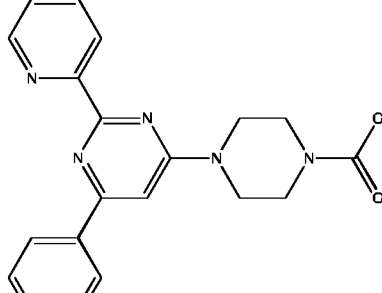
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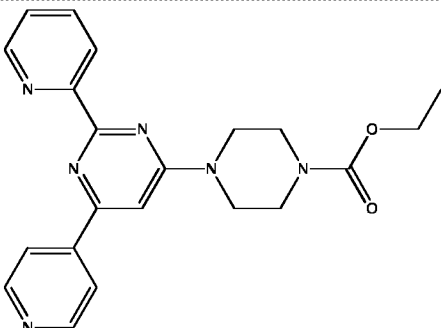
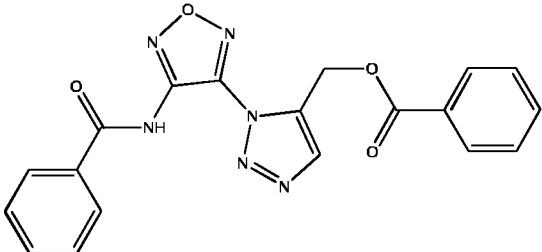
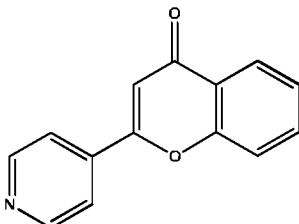
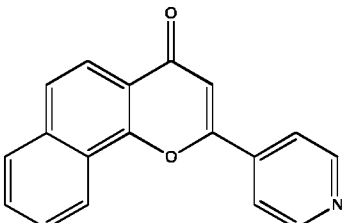
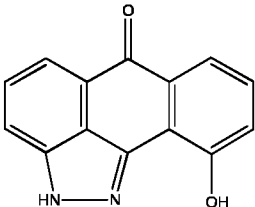
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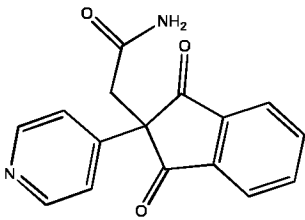
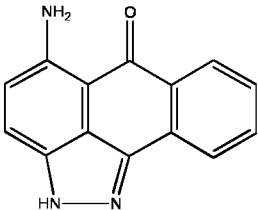
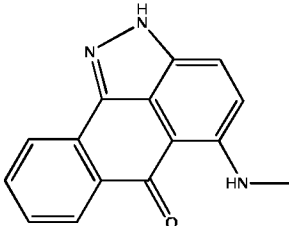
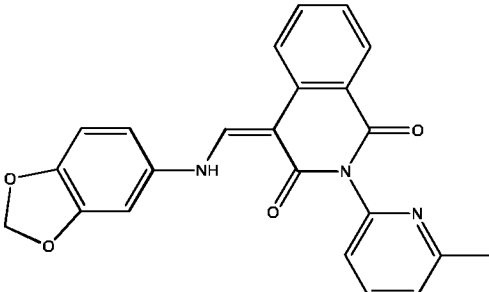
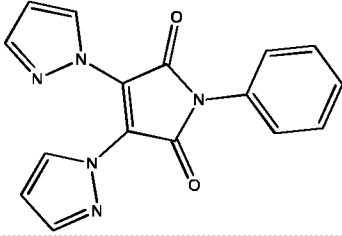
275	 <chem>COc1cc(OC)c(OC)cc1-c2nc3c(c2)c4ccccc4[nH]3C(=O)NCC5CCCCC5</chem>
276	 <chem>COc1cc(OC)ccc1-c2nc3c(c2)c4ccccc4[nH]3C(=O)NCC5COC5</chem>
277	 <chem>CCOc1ccc(OC)cc1-c2nc3c(c2)c4ccccc4[nH]3C(=O)NCC5COC5</chem>
278	 <chem>COc1ccc(cc1)-c2nc3c(c2)c4ccccc4[nH]3C(=O)NCC5COC5</chem>
279	 <chem>O=C1CC1NC2=NC=CC=C2O3=NN=C3c4ccncc4</chem>

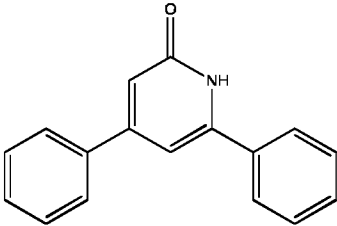
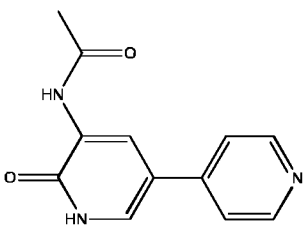
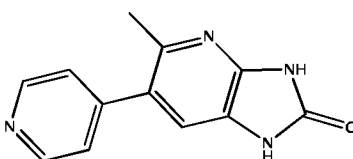
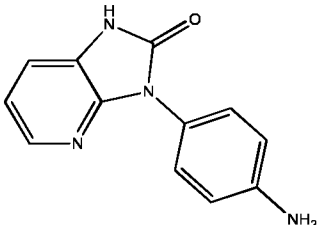
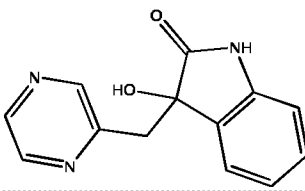
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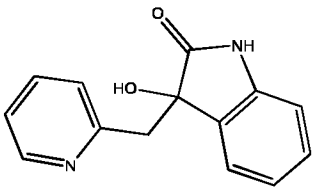
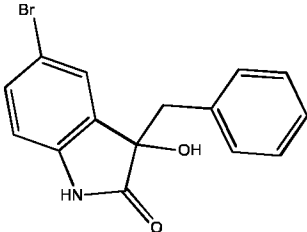
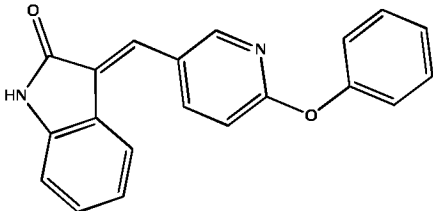
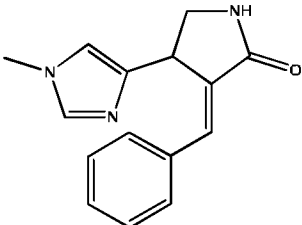
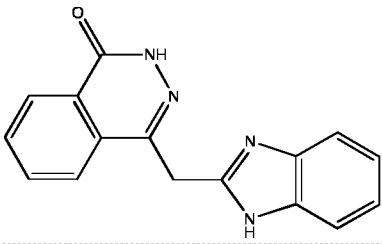
285	 <chem>COc1ccc(cc1)c2nc3ccccc3[nH]2C(=O)NCCCO</chem>
286	 <chem>CC1=CC=CC=C1N=C(NC(=O)c2cnc3ccccc23)C4=CC=CC=C4N4</chem>
287	 <chem>CC(C)CC(=O)NNC(=C1C=CC=CC=C1)c2ccncc2</chem>
288	 <chem>COc1ccc(cc1)c2nc3ccccc3[nH]2C(=O)OC</chem>
289	 <chem>CCOC(=O)c1nc2nc3cc(O)ccc3n2n1</chem>

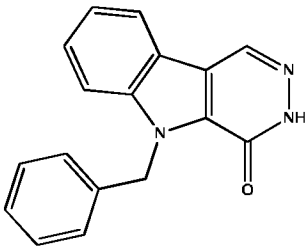
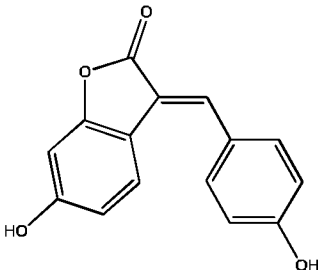
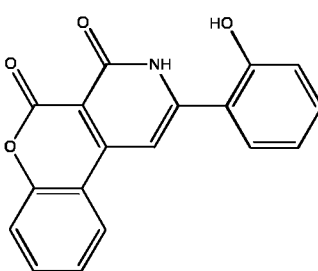
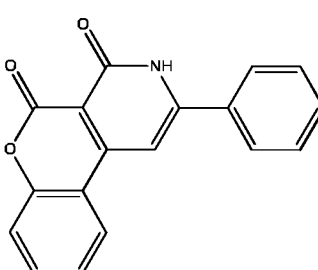
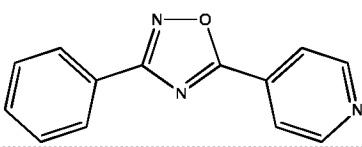
290	 <chem>CCOC(=O)C1=C(C2=CC(=C(C)C)N2)C(=NC3=CC=CC=C3N1Cc4ccc(O)cc4)</chem>
291	 <chem>CCOC(=O)C1=C(C2=CC=CC=C2N1)C(=NC3=CC=CC=C3N1Cc4cc(OC)cc(OC)c4)</chem>
292	 <chem>CCOC(=O)C1=C(C2=CC(=C(C)C)N2)C(=NC3=CC=CC=C3N1Cc4ccc(OCCOCCO4)cc4)</chem>
293	 <chem>CCOC(=O)C1=C(C2=CC(=CC=C2)N1)C(=NC3=CC(=CC=C3)N3Cc4ccc(OC)cc4C(=O)OCC</chem>
294	 <chem>CCOC(=O)N1CCN(CC1)C2=CN(C(=N2)C3=CC=CC=C3N3)C4=CC=CC=C4N4</chem>

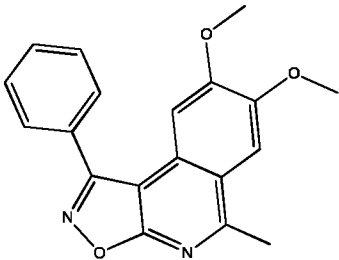
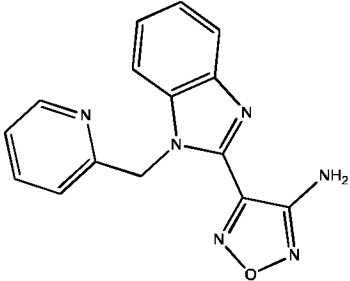
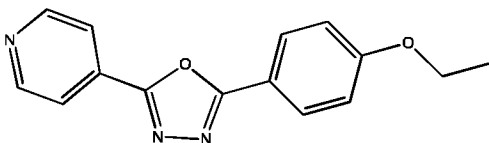
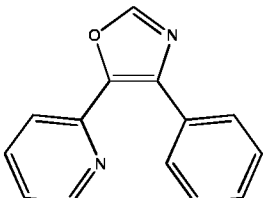
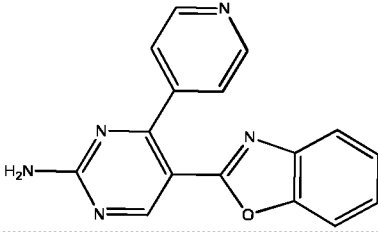
295	 <chem>CCOC(=O)N1CCN(CC1)c2cc(C3=CC=CC=N3)c4c(n2)C5=CC=CC=N5</chem>
296	 <chem>O=C(Nc1nnoc1-c2c[nH]cn2)C(=O)c3ccccc3COCC(=O)c4ccccc4</chem>
297	 <chem>O=C1C(=Cc2ccccc2O1)c3ccncc3</chem>
298	 <chem>O=C1C(=Cc2ccccc2O1)c3ccncc3</chem>
299	 <chem>O=C1C(=O)c2cc3c(c1)c[nH]n3c4cc(O)ccc42</chem>

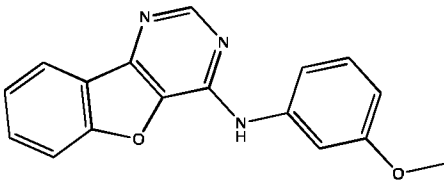
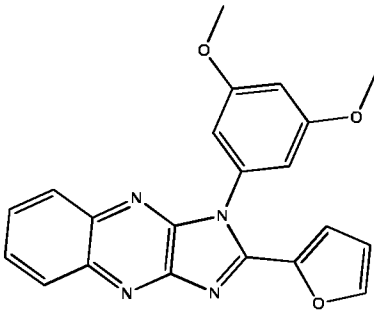
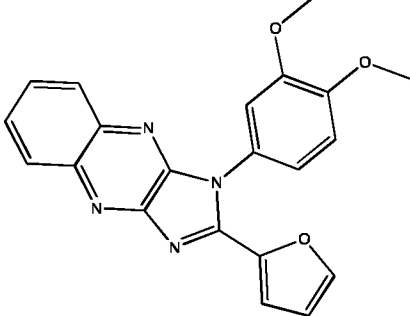
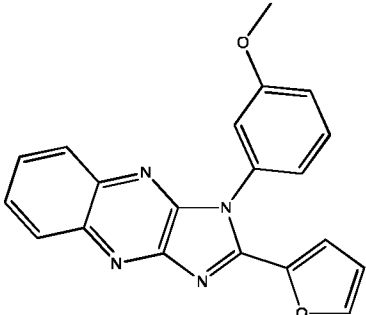
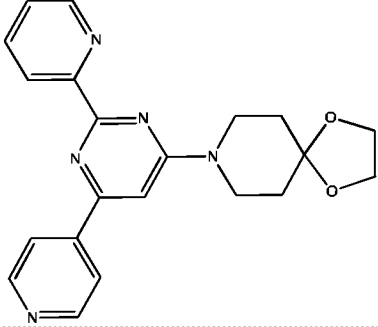
300	 <chem>NC(=O)CC1(=O)c2ccccc2C(=O)C1c3ccncc3</chem>
301	 <chem>Nc1ccc2c(c1)c3ccccc3n[nH]2</chem>
302	 <chem>CN1C=CC2=C1C(=O)c3ccccc3N2</chem>
303	 <chem>Cc1ccc2nc(C(=O)N=Cc3ccc4c(c3)OCO4)c(C(=O)c5ccccc5)n2</chem>
304	 <chem>c1ccncc1N2C(=O)C(c3ccccc3)C(=O)N2c4ccncc4</chem>

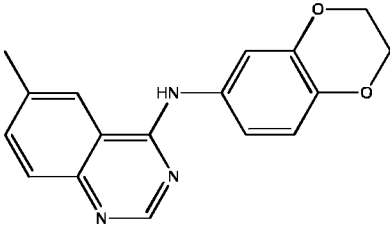
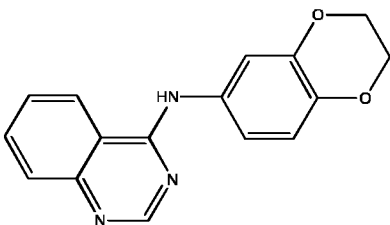
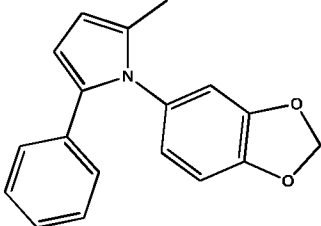
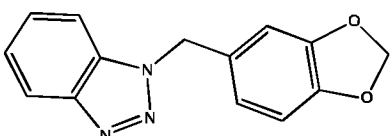
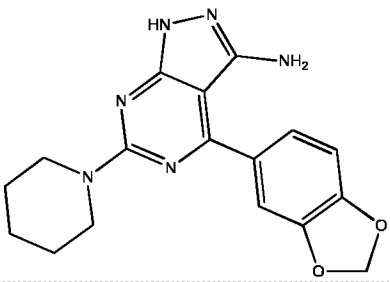
305	 <chem>O=C1NC(=C(C2=CC=CC=C2)C(=C(C3=CC=CC=C3)C1)C4=CC=CC=C4</chem>
306	 <chem>CC(=O)Nc1cc(C2=CC=CC=C2)c(=O)[nH]1C3=CC=CC=N3</chem>
307	 <chem>Cc1nc2cc(C3=CC=CC=N3)cc2[nH]1C4=CC=CC=C4</chem>
308	 <chem>Nc1ccc(NC2=CC=CC=C2C3=CC=CC=N3C4=CC=CC=C4)cc1</chem>
309	 <chem>O=C1NC(=C(C2=CC=CC=C2)C(=C(C3=CC=CC=C3)C1)C4=CC=CC=C4</chem>

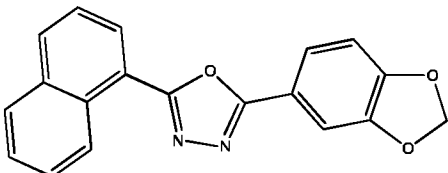
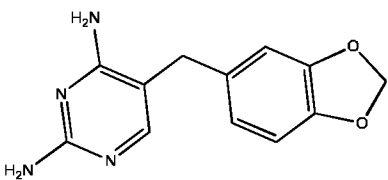
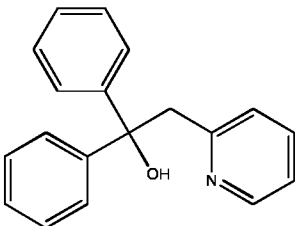
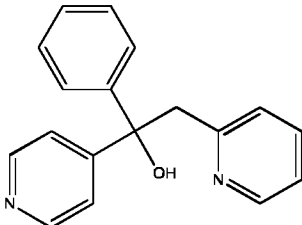
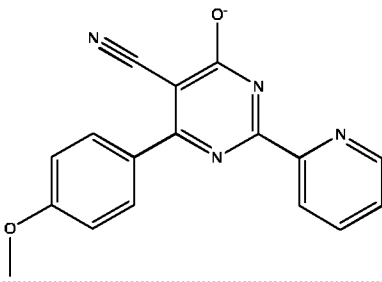
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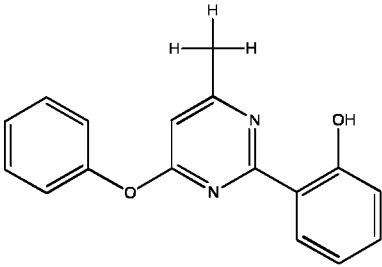
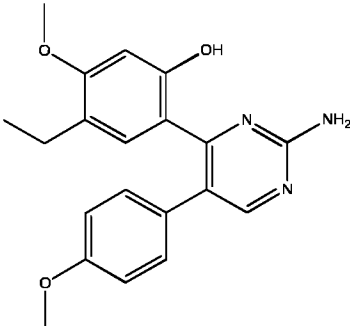
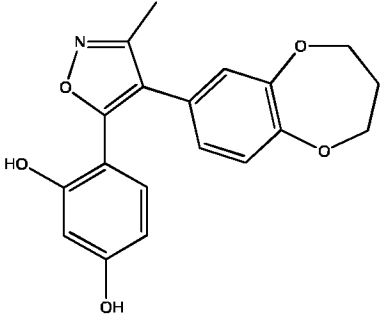
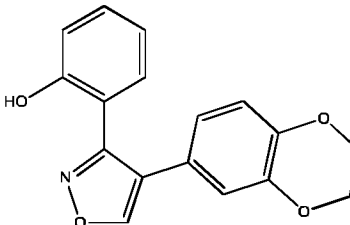
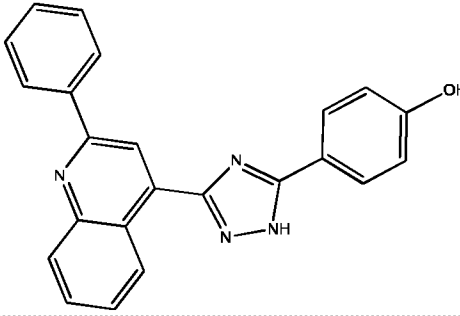
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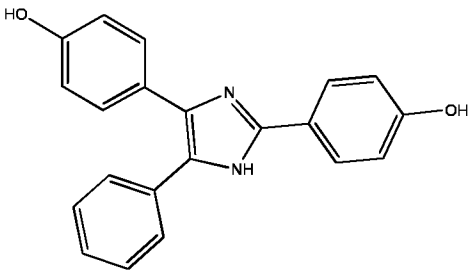
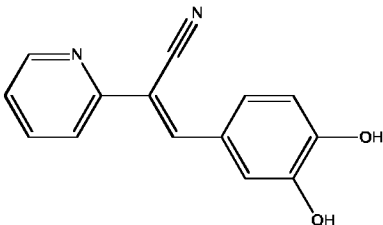
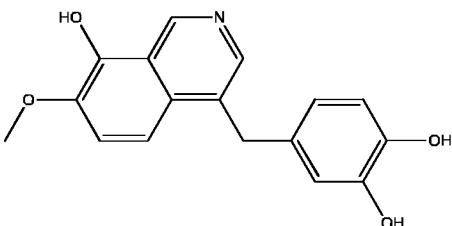
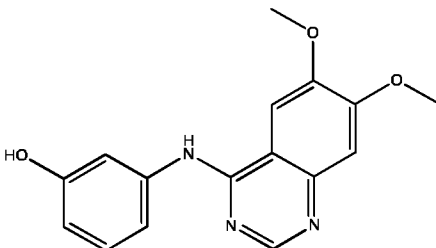
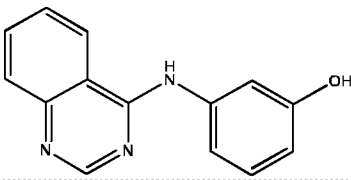
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321	 <chem>Nc1ncnc2c1n(c2c3ccccc3)CC4=CC=CC=N4</chem>
322	 <chem>CCOC1=CC=C(C=C1)c2nn(c2)c3ccncc3</chem>
323	 <chem>c1ccccc1C2=CC=C(C=C2)c3oc4ccncc4O3</chem>
324	 <chem>Nc1nc2c(ncn2C3=CC=C(C=C3)c4oc5ccccc5n4)cc(C6=CC=CC=N6)n1</chem>

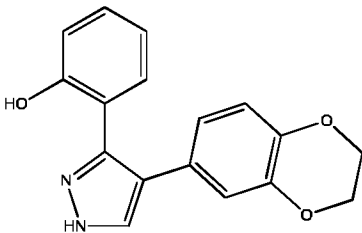
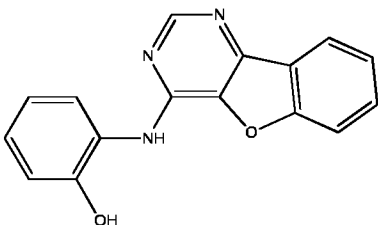
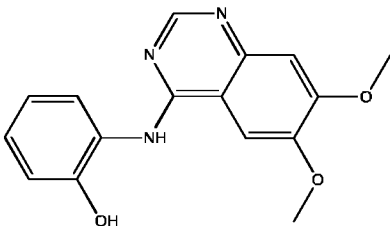
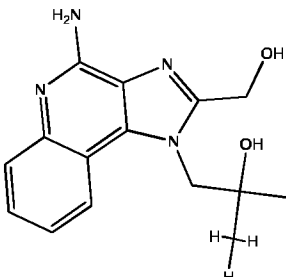
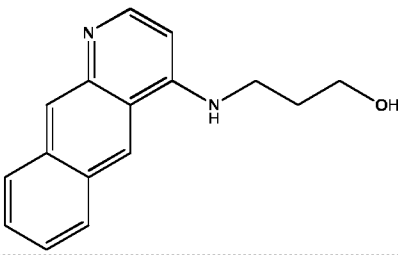
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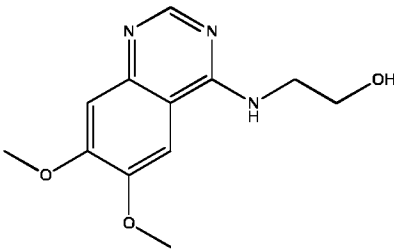
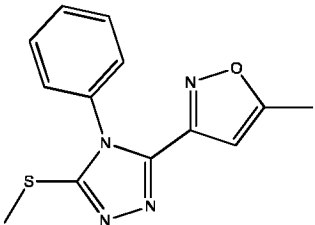
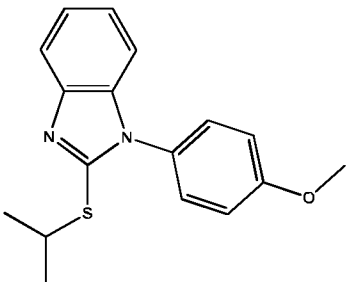
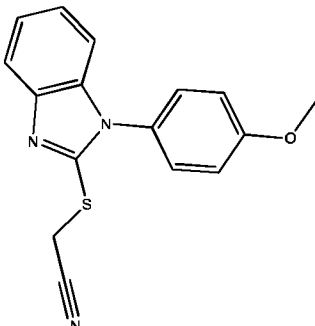
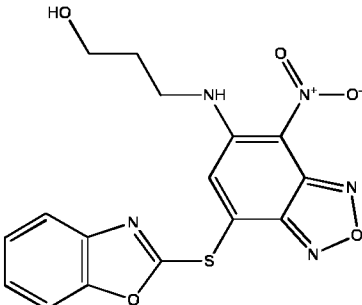
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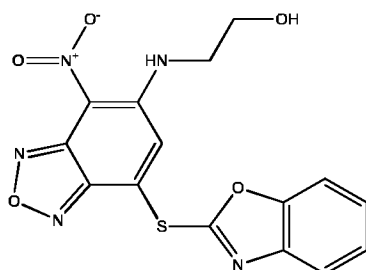
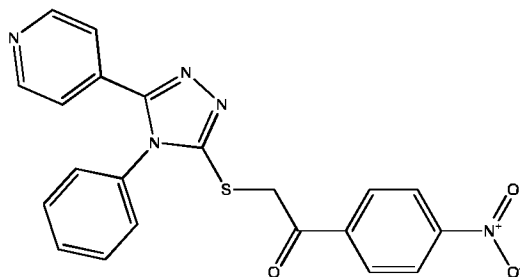
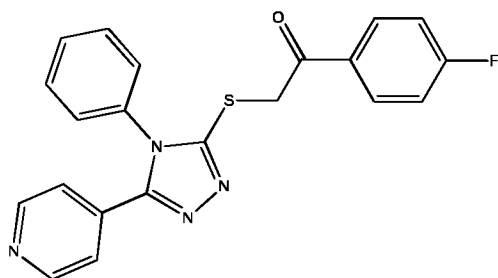
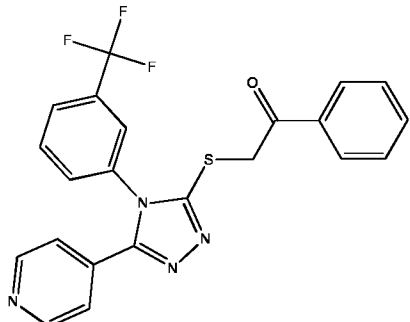
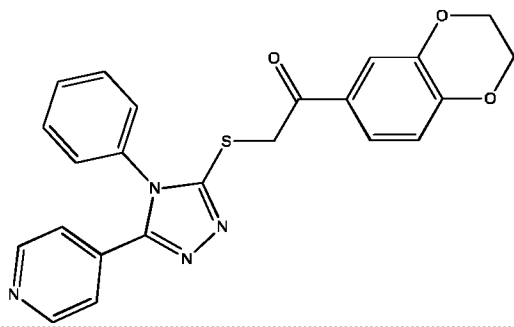
335	 <chem>c1ccc2c(c1)ccc3c2c(c4ccccc4)cc5ccccc53-c6nnoc6-c7ccc8c(c7)OCO8</chem>
336	 <chem>Nc1nc(N)nc(Cc2ccc3c(c2)OCO3)c1</chem>
337	 <chem>c1ccccc1C(O)(Cc2ccccc2-c3ccccn3)c4ccccc4</chem>
338	 <chem>c1ccccc1C(O)(Cc2ccncc2-c3ccccn3)c4ccncc4</chem>
339	 <chem>[O-]c1nc(C#N)c(Cc2ccc(OC)cc2)n1-c3ccccn3</chem>

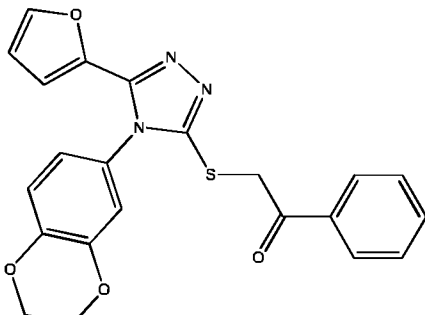
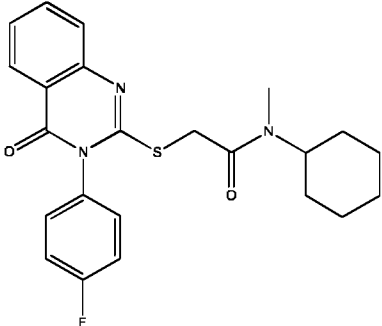
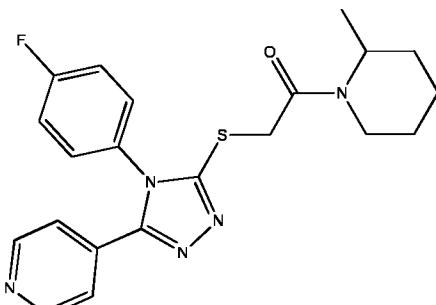
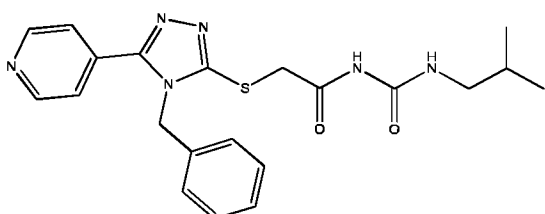
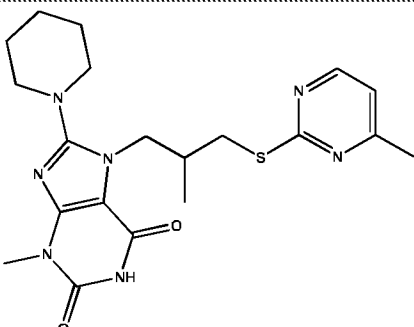
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341	 <chem>CCOc1cc(O)ccc1C2=CN=C(N)N=C2c3ccc(OC)cc3</chem>
342	 <chem>COc1nc(C)c(Oc2cc(O)cc(O)c2)c1-c3cc4ccccc3O4</chem>
343	 <chem>Oc1ccccc1C2=CN(C)C=C2-c3cc4ccccc3O4</chem>
344	 <chem>Oc1ccc(cc1)C2=NN=C2c3cc4ccccc4n3</chem>

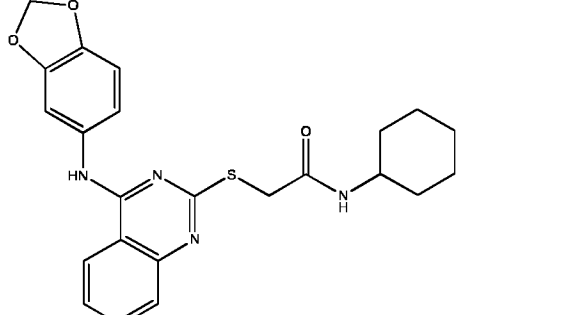
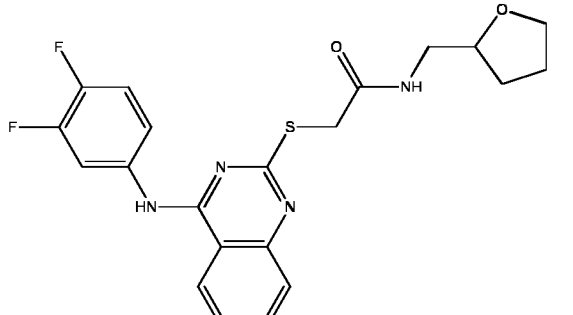
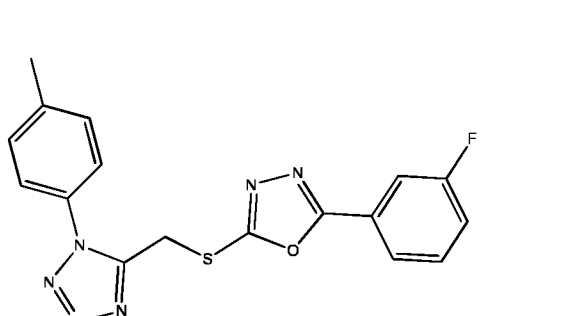
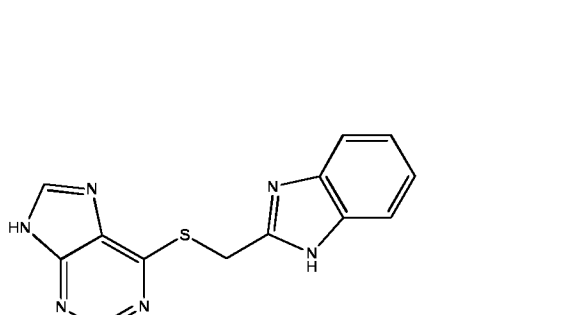
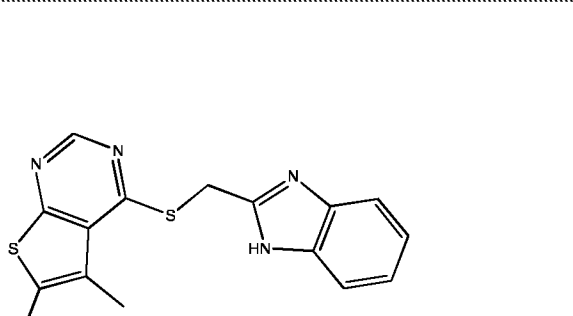
345	 <chem>Oc1ccc(cc1)-c2nc(c3ccccc23)-c4ccc(O)cc4</chem>
346	 <chem>N#CC(=Cc1cc(O)c(O)cc1)c2ccncc2</chem>
347	 <chem>COc1cc2c(cc1O)ncnc2Cc3cc(O)c(O)cc3</chem>
348	 <chem>COc1cc(OC)cc2nc3cc(O)ccc3n2c1</chem>
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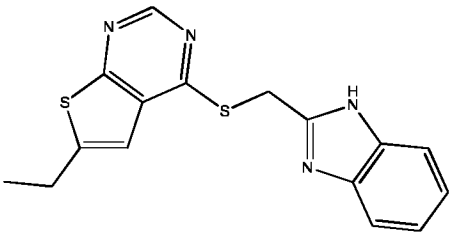
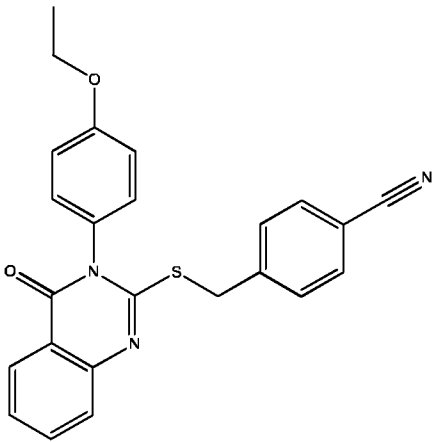
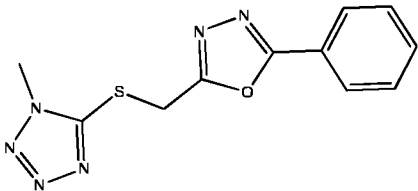
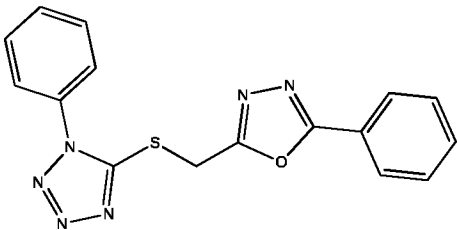
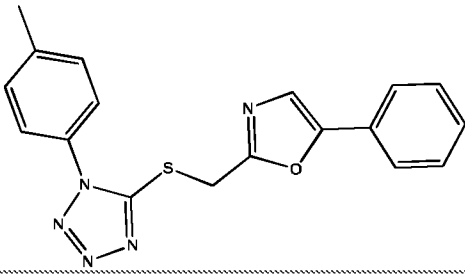
350	 <chem>Oc1ccccc1-c2nc3ccccc3[nH]2-c4ccc5c(c4)OCCO5</chem>
351	 <chem>Oc1ccccc1-Nc2nc3ccccc3o2-c4nc5ccccc5n4</chem>
352	 <chem>COc1cc2nc3ccccc3[nH]2c(c1)C4=CC(OC)=CC=C4</chem>
353	 <chem>CC(C)(O)CN1C2=CC=CC=C2N3C(=N1)C(=NC=C3N)N</chem>
354	 <chem>OCCCCNc1nc2ccccc2c3ccccc13</chem>

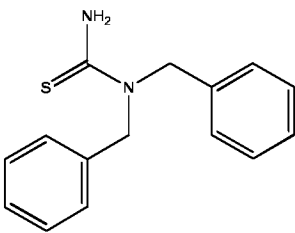
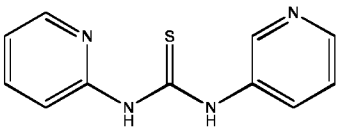
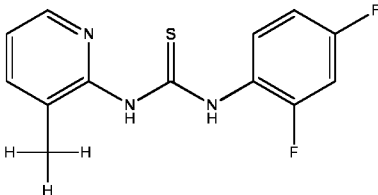
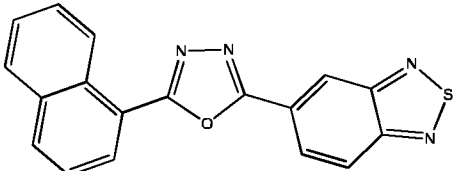
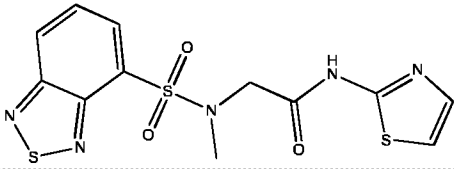
355	 <chem>COc1cc2ncnc2c(c1)NCCO</chem>
356	 <chem>COc1nn[nH]1C2=CN(C)CS2c3ccccc3</chem>
357	 <chem>CC(C)S1=C2C(=N1)C3=CC=CC=C3N2c4ccc(OC)cc4</chem>
358	 <chem>CC#CCS1=C2C(=N1)C3=CC=CC=C3N2c4ccc(OC)cc4</chem>
359	 <chem>CC#CCS1=C2C(=N1)C3=CC(=C(C=C3)N(C2)CCO)C(=C4C(=C(C=C5C(=O)N(C5)C4)C6=CC=CC=C6[N+](=O)[O-])</chem>

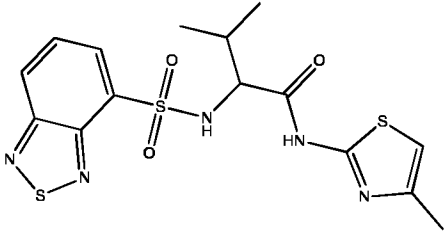
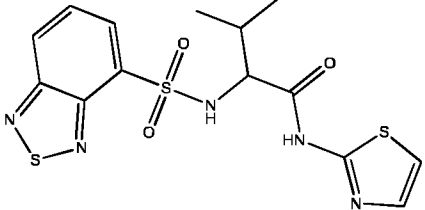
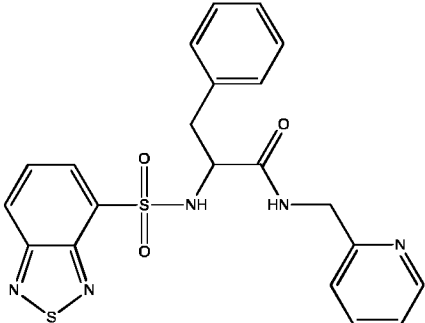
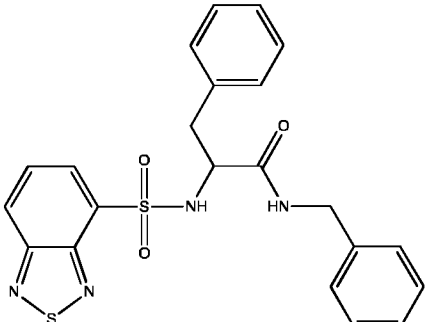
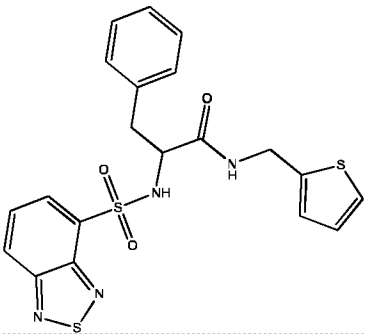
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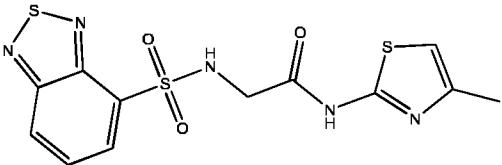
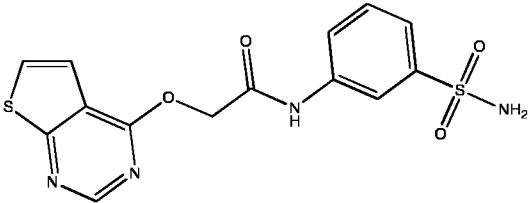
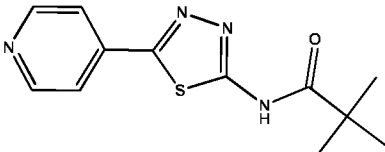
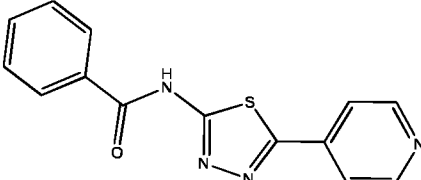
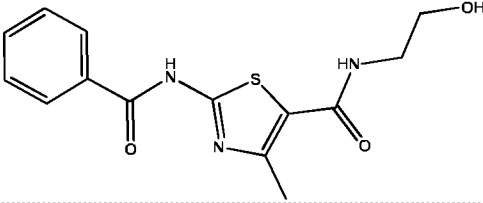
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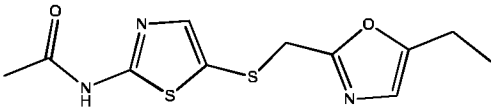
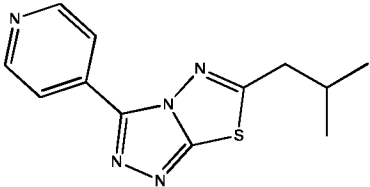
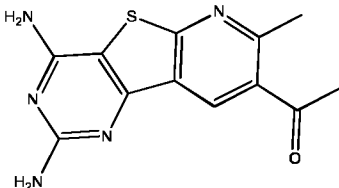
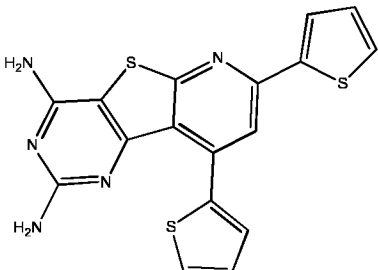
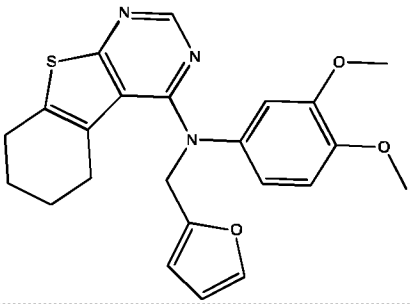
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371	 <chem>Fc1cc(F)cc(Nc2nc3ccccc3nc2)cc1SCC(=O)NCC4OCCO4</chem>
372	 <chem>Cc1ccc(cc1)n2nn[nH]2SCC3=C(N4C=CC=C(C=C4)O3)C5=CC=C(C=C5)F</chem>
373	 <chem>Nc1nc2ccccc2n1SCC3=C(N4C=CC=C(C=C4)N3)C5=CC=C(C=C5)N</chem>
374	 <chem>Cc1c(C)c2nc3ccccc3n2sc1SCC4=C(N5C=CC=C(C=C5)N4)C6=CC=C(C=C6)N</chem>

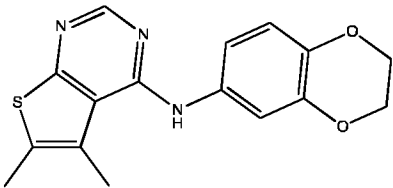
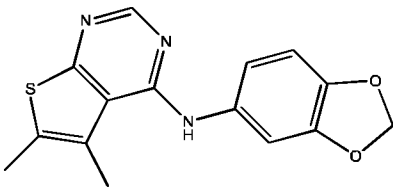
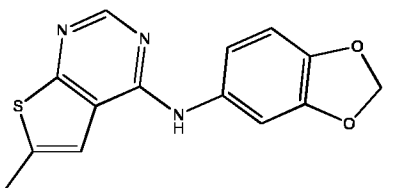
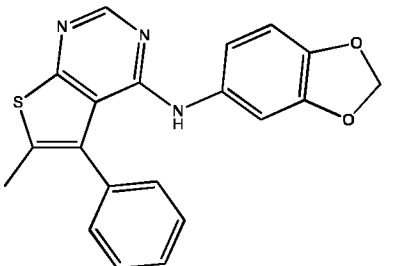
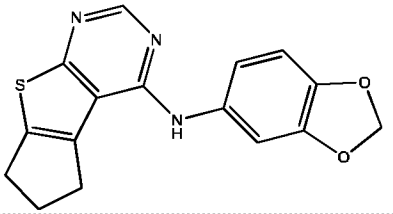
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376	 <chem>CCOC1=CC=C(C=C1)N2C(=O)C3=CC=CC=C3N=C2SCc4ccc(C#N)cc4</chem>
377	 <chem>Cc1nn[nH]c1SCc2nc3ccccc3o2</chem>
378	 <chem>c1ccccc1N2C3=CC=CC=C3N=N2SCc4nc5ccccc5o4</chem>
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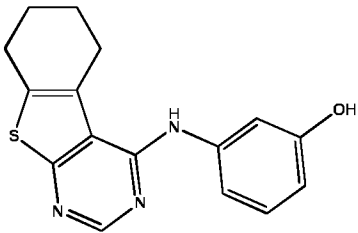
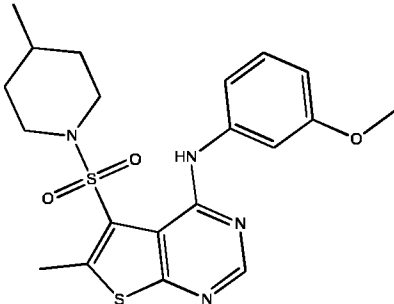
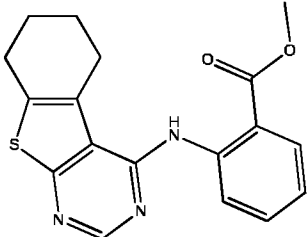
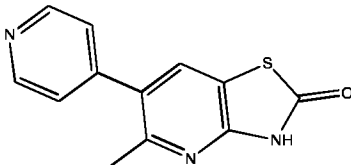
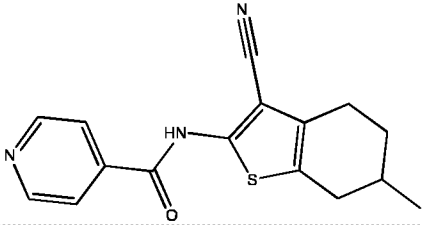
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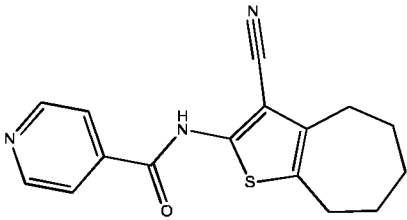
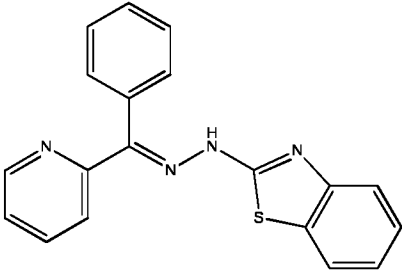
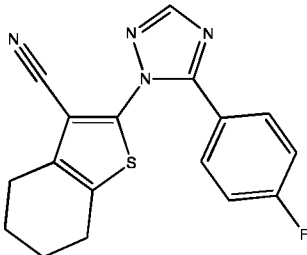
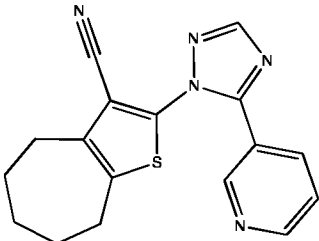
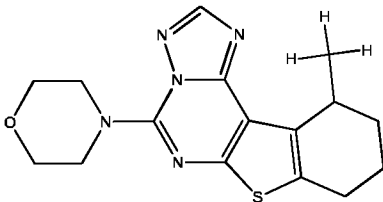
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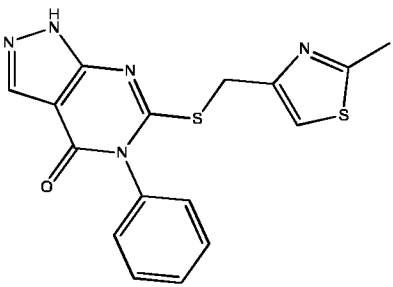
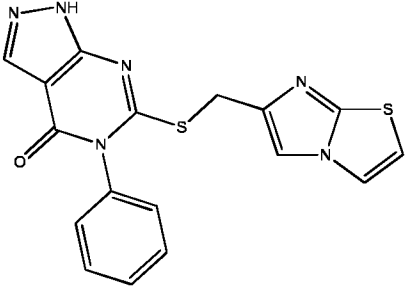
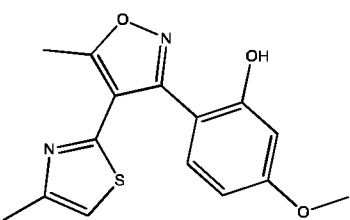
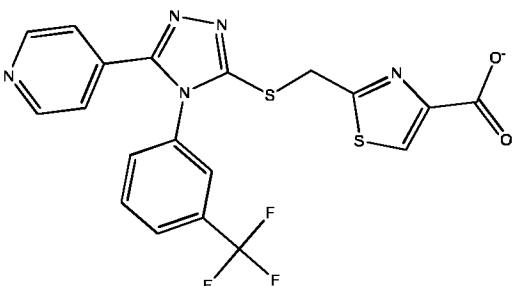
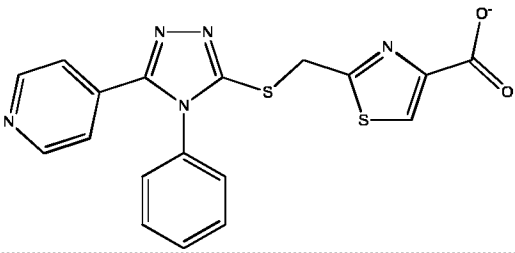
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391	 <chem>NC(=O)Nc1ccc(cc1)S(=O)(=O)Nc2cc3ccccc3n2Sc4ccccc4O2</chem>
392	 <chem>CC(C)(C)C(=O)Nc1sc2nc3ccccc3n2s1</chem>
393	 <chem>c1ccc(cc1)C(=O)Nc2sc3ccccc3n2</chem>
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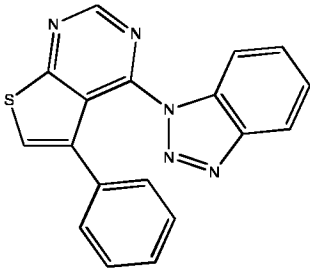
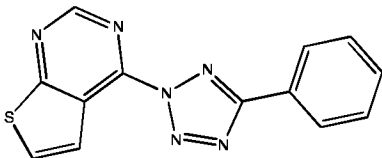
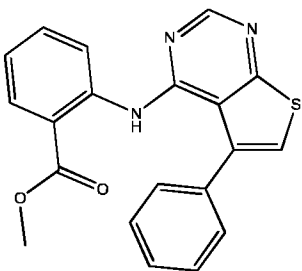
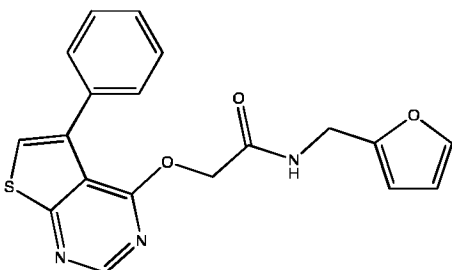
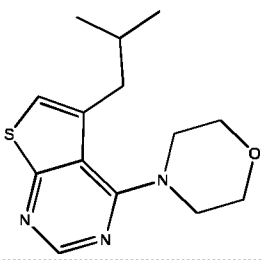
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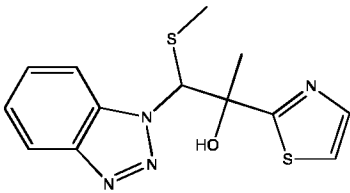
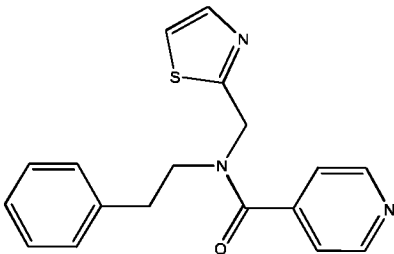
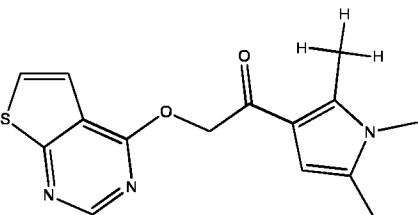
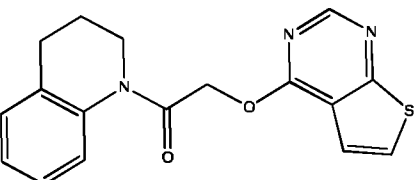
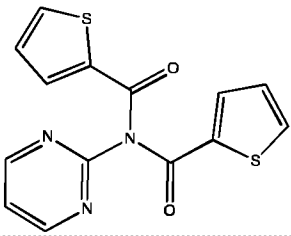
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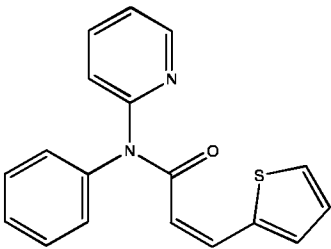
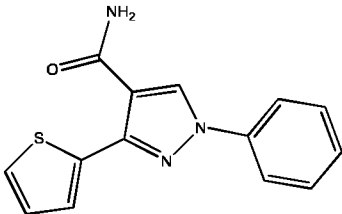
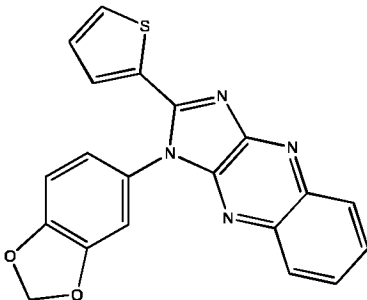
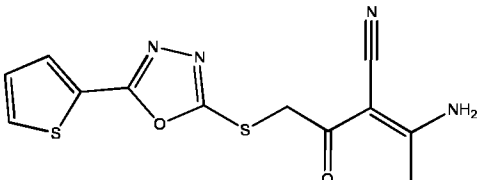
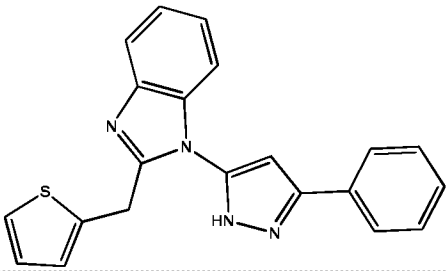
405	 <chem>Oc1ccc(Nc2nc3c(s2)C4CCCCC4c3)cc1</chem>
406	 <chem>COc1ccc(Nc2nc3c(s2)C(C)=C3S(=O)(=O)N4CCCC(C)C4)cc1</chem>
407	 <chem>COC(=O)c1ccccc1Nc2nc3c(s2)C4CCCCC4c3</chem>
408	 <chem>Cc1nc2c(s1)C(=O)N2c3ccncc3</chem>
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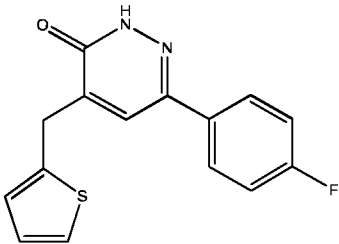
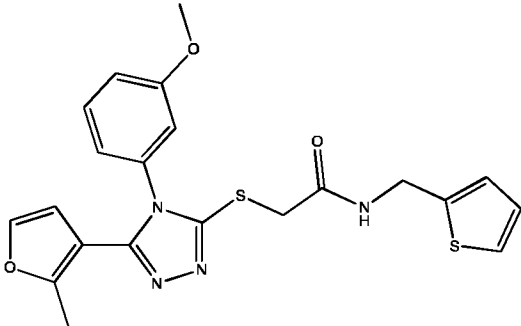
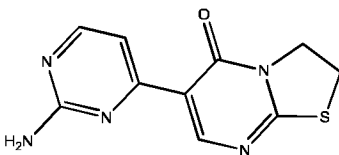
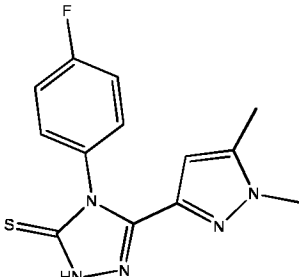
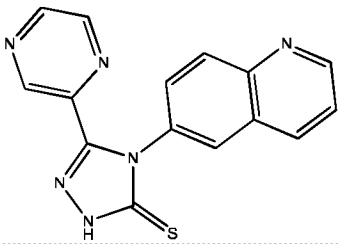
410	 <chem>N#Cc1ccc2sc(ccc2c1)C(=O)c3ccncc3</chem>
411	 <chem>c1ccc2nc(s2)NN=C(c3ccncc3)c4ccccc4</chem>
412	 <chem>Fc1ccc(cc1)-c2nc3ccn(c3n2)c4c5ccccc4s5C#N</chem>
413	 <chem>c1ccncc1-c2nc3ccn(c3n2)c4c5ccccc4s5C#N</chem>
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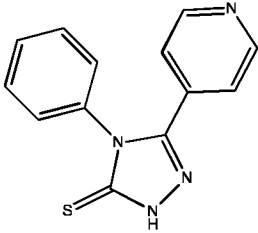
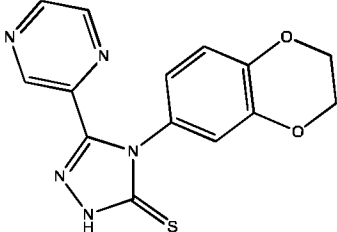
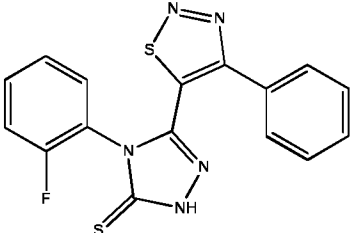
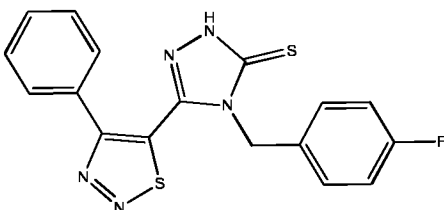
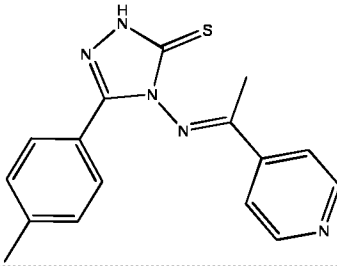
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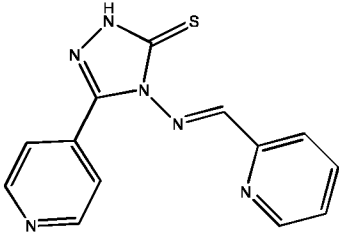
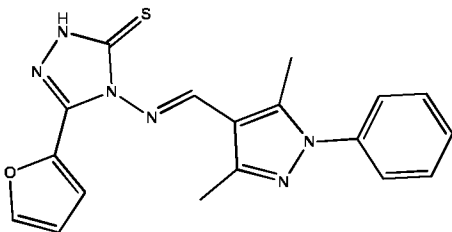
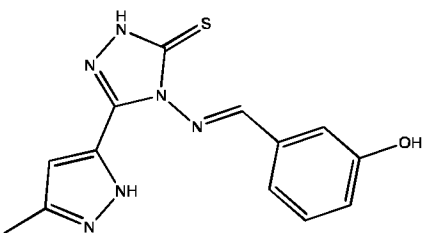
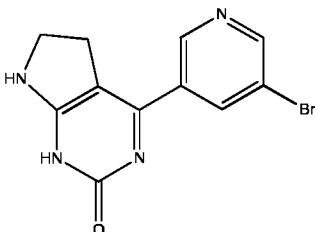
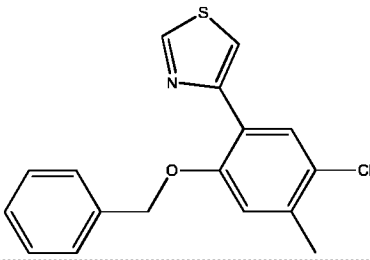
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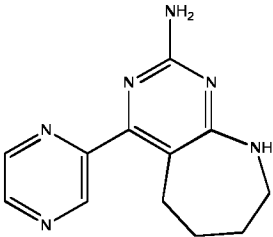
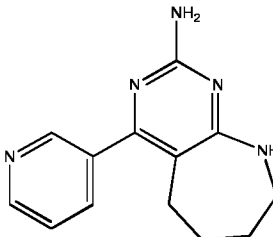
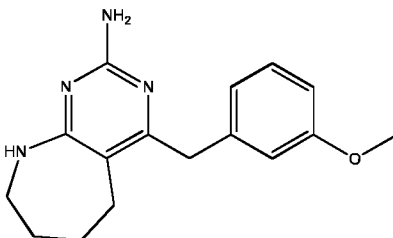
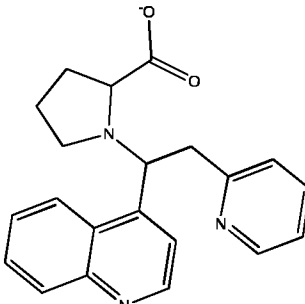
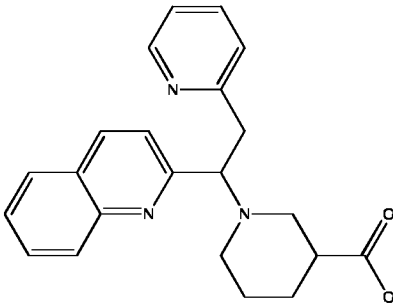
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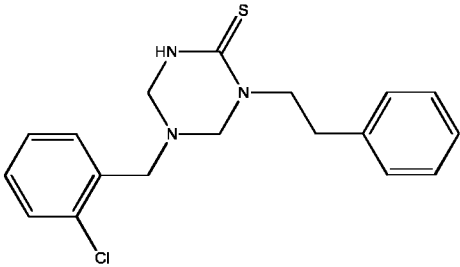
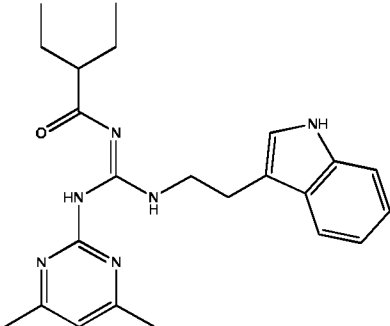
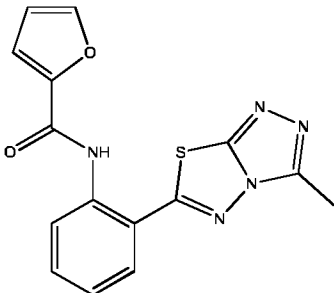
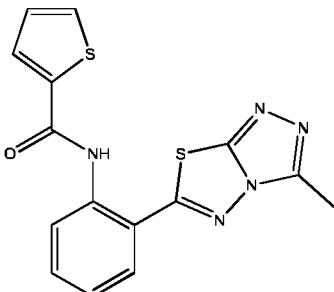
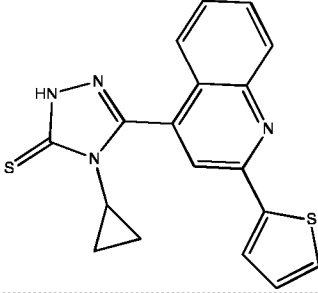
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431	 <chem>N#CC(=O)c1cnc(n1-c2ccsc2)-c3ccccc3</chem>
432	 <chem>c1ccc2c(c1)OCO2N3C4=CN=C5C(=N4)C(=CN3C5-c6ccsc6)C7=CC=CC=C7</chem>
433	 <chem>N#CC(=O)CCSC1=NC2=CC=CC=C2O1</chem>
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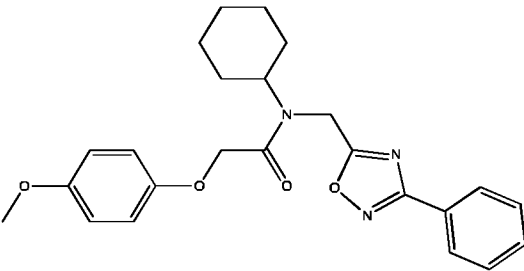
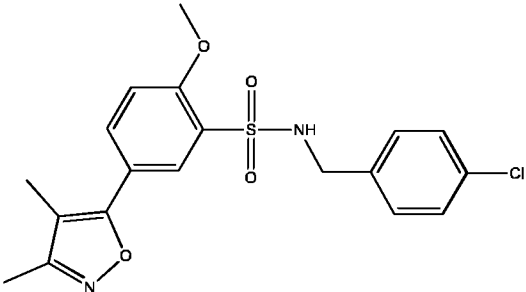
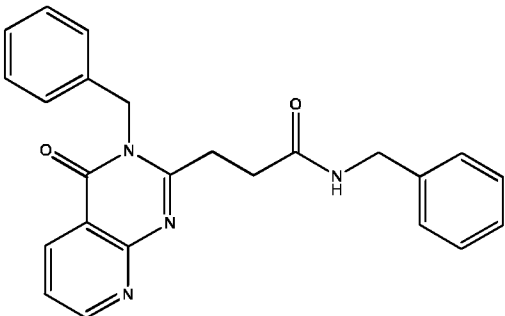
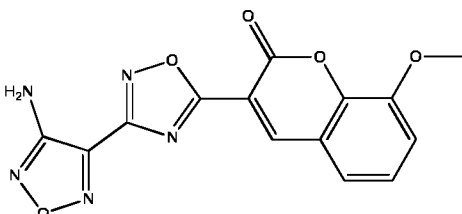
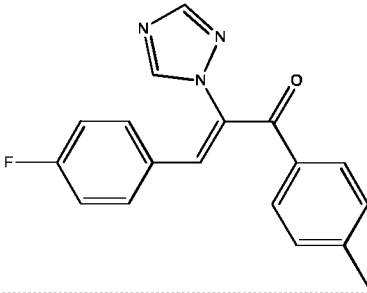
435	 <chem>O=C1NC(=O)C(=C(C1)Cc2ccsc2)C(=N1C=CC=C(C=C1)F)</chem>
436	 <chem>COc1ccccc1n2c(cnn2)SCCC(=O)NCCc3ccsc3</chem>
437	 <chem>Nc1ncnc2c1cnc2C3=CN4CCSC4=CN3C3=O</chem>
438	 <chem>Cc1cc(C)n(C)n1C2=NNC(=S)N2c3ccc(F)cc3</chem>
439	 <chem>C1=NC2=C(N1)C(=S)NC2c3cc4c(cc3)ncnc4</chem>

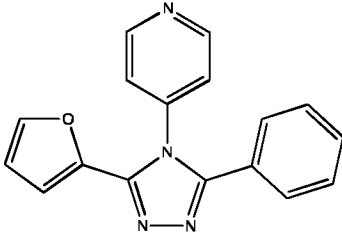
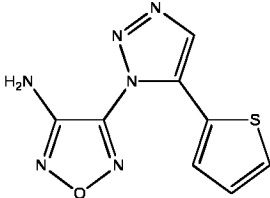
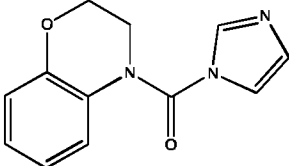
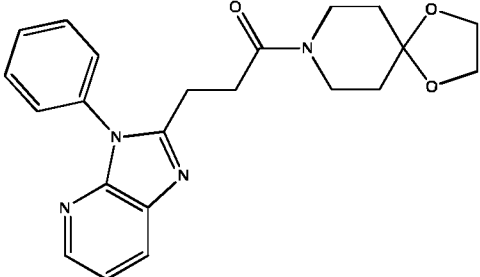
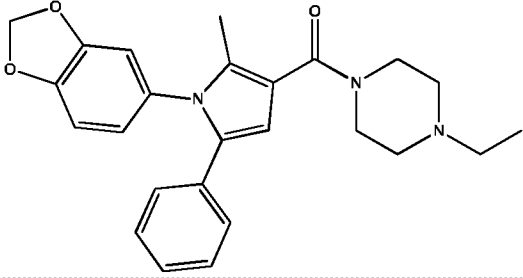
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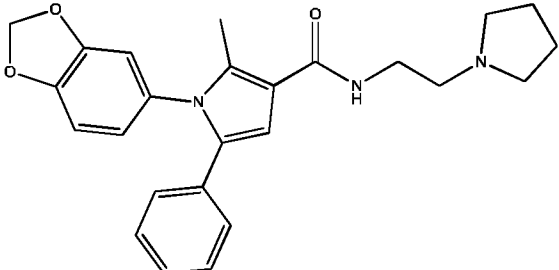
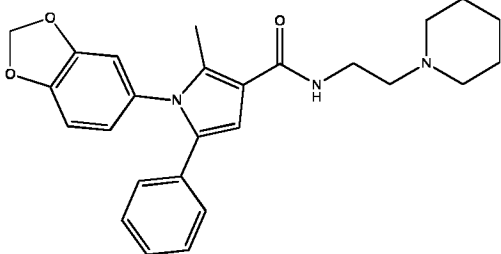
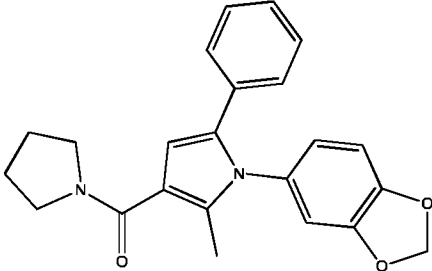
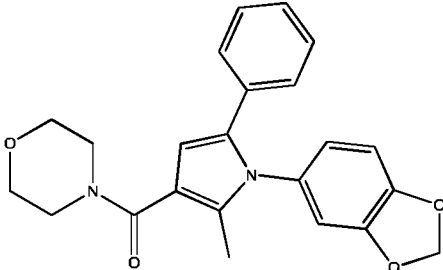
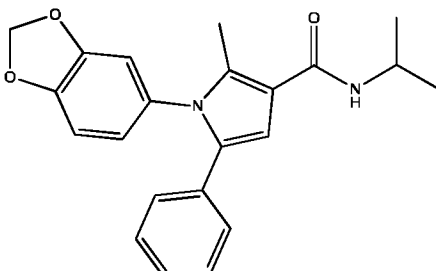
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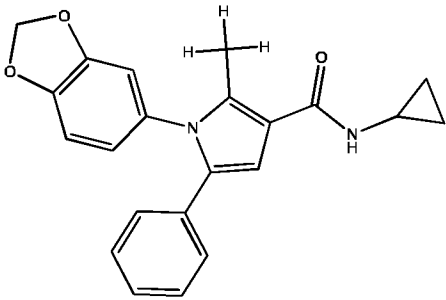
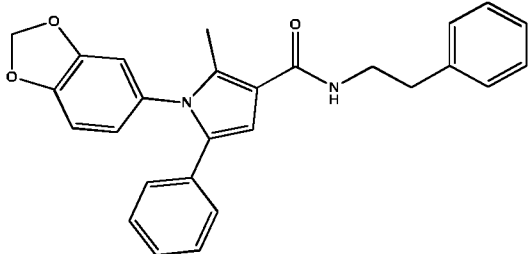
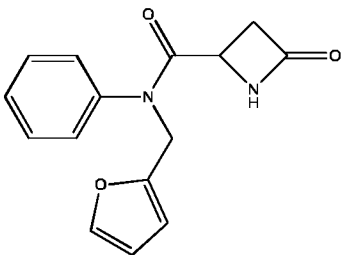
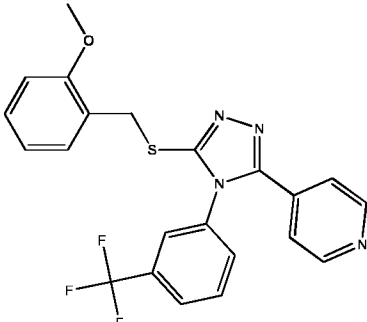
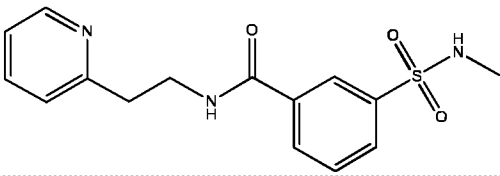
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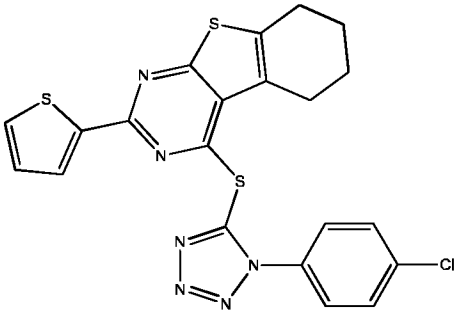
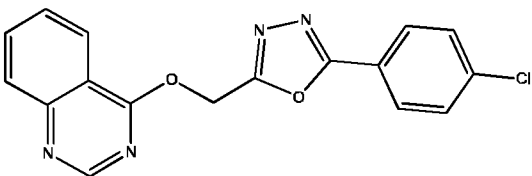
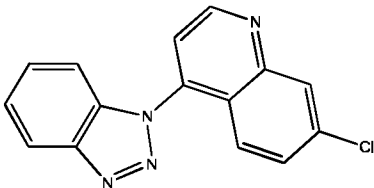
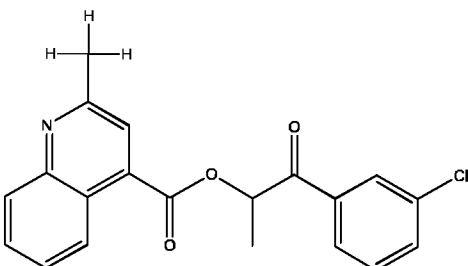
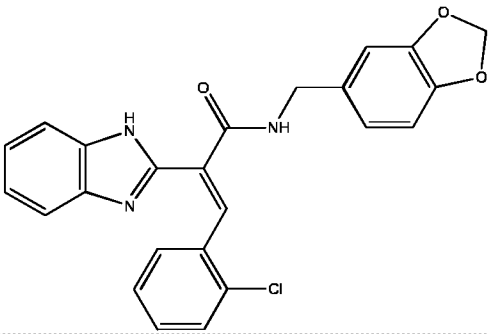
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456	 <chem>CC1=CN=C(NC(=O)N1)N2C=NC(=C2)CCN2CCN(CCN2C(=S)N)CCc3ccccc3</chem>
457	 <chem>c1ccoc1C(=O)Nc2ccccc2N3C=NC(=N3)SC4=CC=CC=C4C4=CC=CC=C4</chem>
458	 <chem>c1ccsc1C(=O)Nc2ccccc2N3C=NC(=N3)SC4=CC=CC=C4C4=CC=CC=C4</chem>
459	 <chem>C1CC1N2C=NC(=N2)C(=S)N3C=CC(=C3)N4C=CC(=C4)SC5=CC=CC=C5</chem>

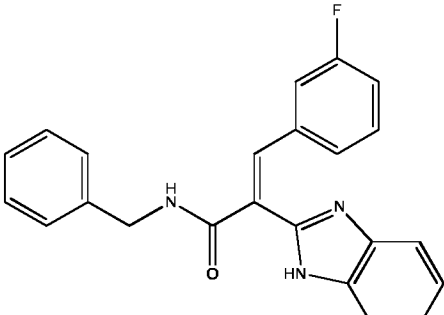
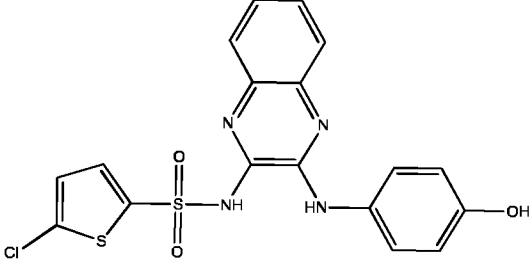
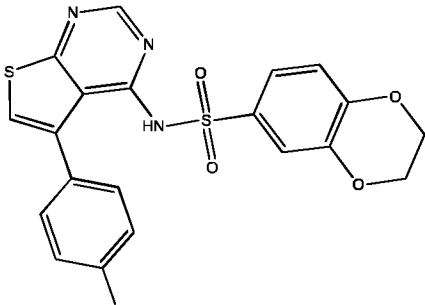
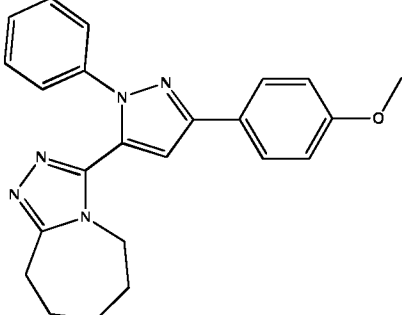
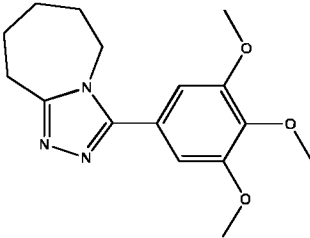
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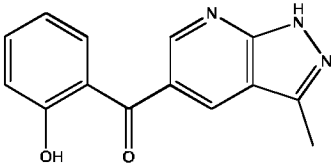
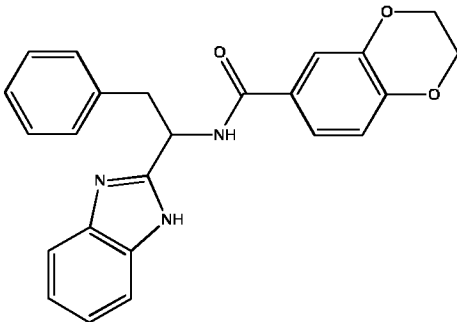
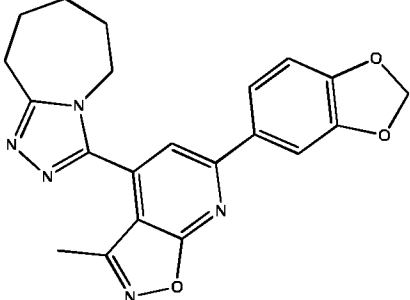
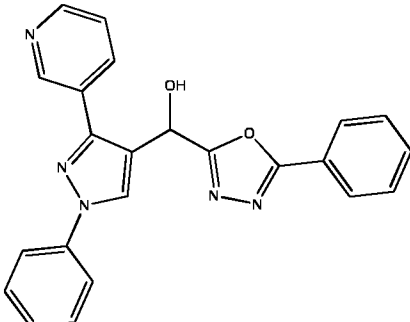
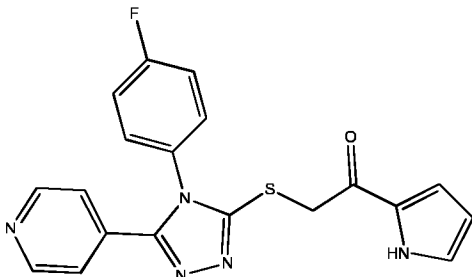
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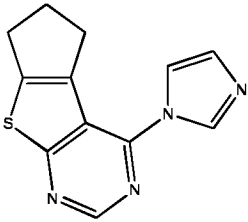
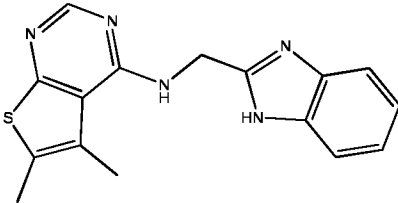
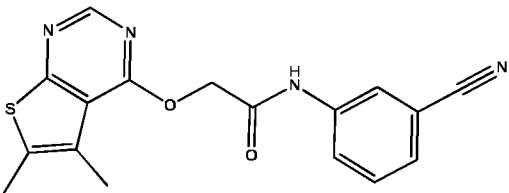
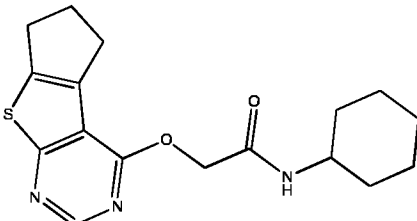
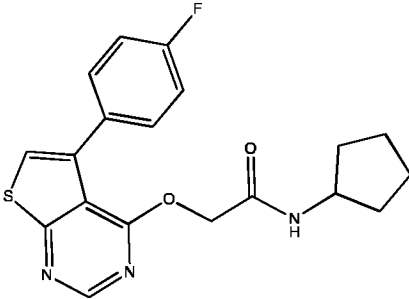
470	 <chem>CC1=C(C(=C(C=C1)C2=CC=CC=C2)C3=CC=C4C(=C(C=C3)OC5=CC=CC=C4O5)C(=O)NCCCN6CCCC6)C</chem>
471	 <chem>CC1=C(C(=C(C=C1)C2=CC=CC=C2)C3=CC=C4C(=C(C=C3)OC5=CC=CC=C4O5)C(=O)NCCCN6CCCCC6)C</chem>
472	 <chem>CC1=C(C(=C(C=C1)C2=CC=CC=C2)C(=O)N3CCCC3)N(C4=CC=C5C(=C(C=C4)OC6=CC=CC=C5O6))C</chem>
473	 <chem>CC1=C(C(=C(C=C1)C2=CC=CC=C2)C(=O)N3CCOCC3)N(C4=CC=C5C(=C(C=C4)OC6=CC=CC=C5O6))C</chem>
474	 <chem>CC1=C(C(=C(C=C1)C2=CC=CC=C2)C3=CC=C4C(=C(C=C3)OC5=CC=CC=C4O5)C(=O)N(C)C)C</chem>

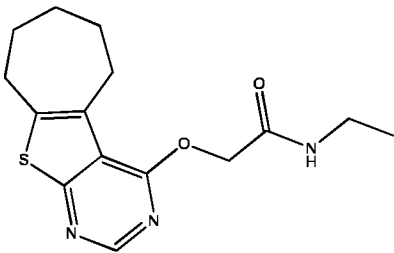
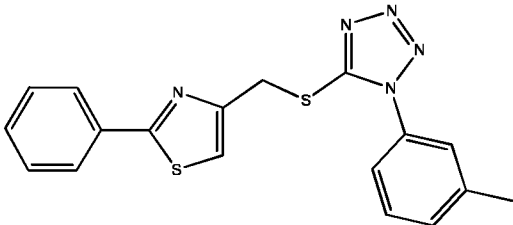
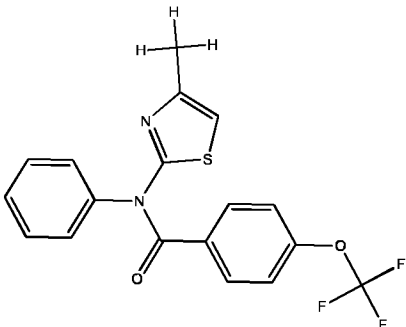
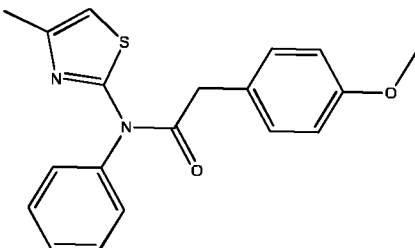
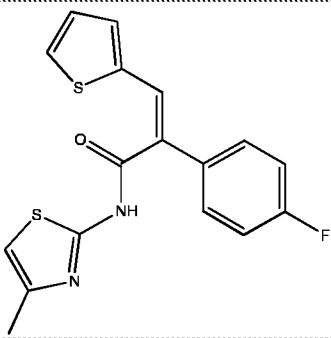
475	 <chem>C1CC1NC(=O)c2cc(C3=CC=CC=C3)c(N4C5=CC=CC=C5C6COC6)c24</chem>
476	 <chem>CC1=CC=C(C=C1)C(=O)NCCC2=CC=CC=C2</chem>
477	 <chem>O=C1CC(=O)N1C(=O)N(Cc2ccoc2)c3ccccc3</chem>
478	 <chem>C1=CC=C(C=C1)SC2=CC(=CC=C2)N3C(=NN=C3C4=CC=CC=C4C(F)(F)F)c5ccncc5</chem>
479	 <chem>CC(=O)NCCC1=CC=CC=C1S(=O)(=O)N</chem>

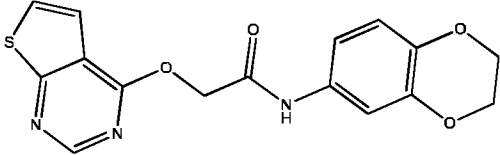
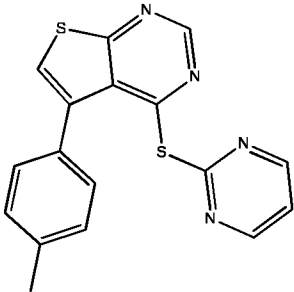
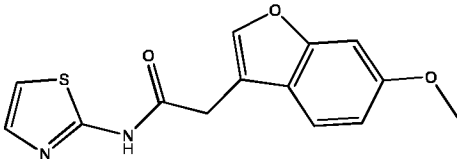
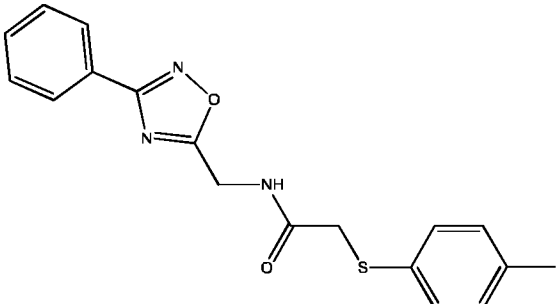
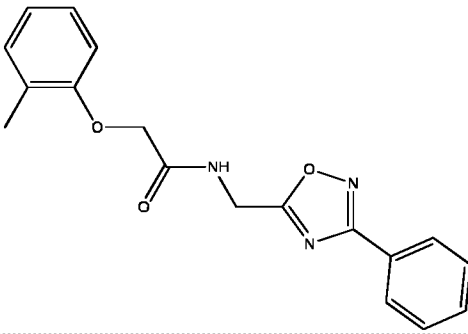
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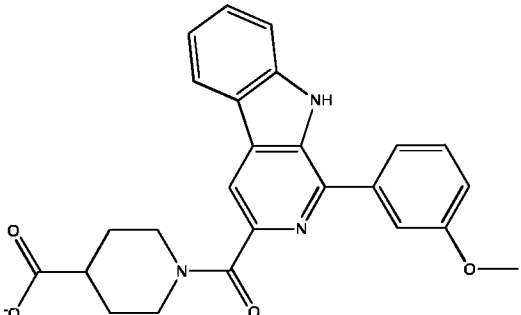
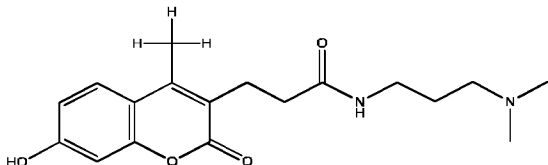
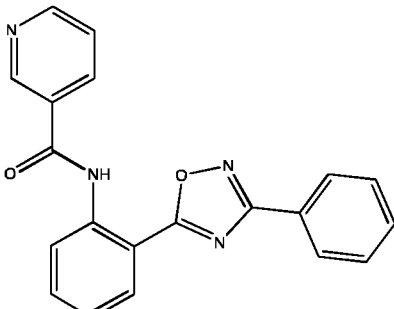
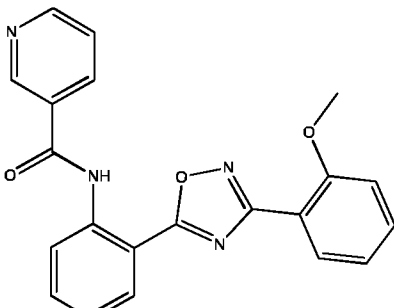
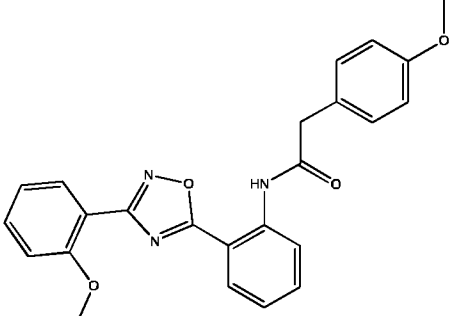
485	 <chem>Fc1ccc(cc1)/C=C/C(=O)NCCc2ccccc2c3c[nH]c4ccccc34</chem>
486	 <chem>Oc1ccc(cc1)Nc2nc3ccccc3n2NS(=O)(=O)c4ccc(Cl)cc4</chem>
487	 <chem>COc1ccc(cc1)NS(=O)(=O)Nc2c3ccccc3sc2n4cnc5c2cc(s5)C6=CC=CC=C6F</chem>
488	 <chem>COc1ccc(cc1)/C=C/c2nn(c2N3C4=CC=CC=C4N5C6=CC=CC=C6N35)C7=CC=CC=C7</chem>
489	 <chem>COc1ccc(cc1)/C=C/c2nnc2N3C4=CC=CC=C4N5C6=CC=CC=C6N35</chem>

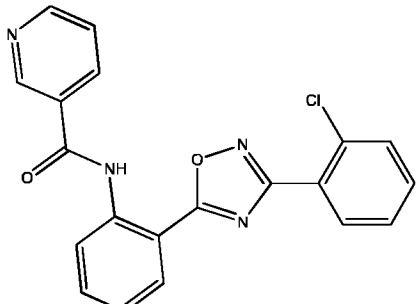
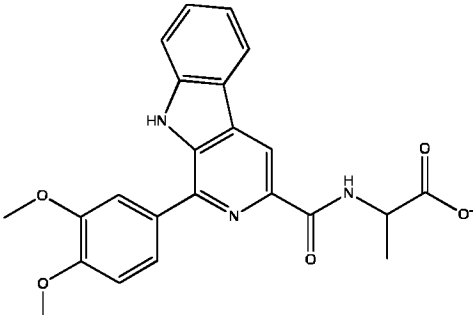
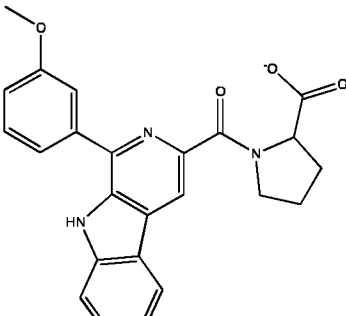
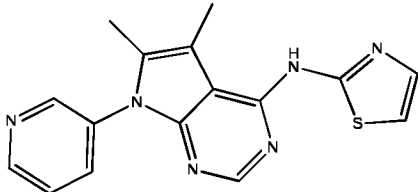
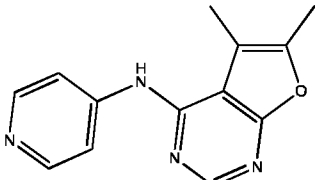
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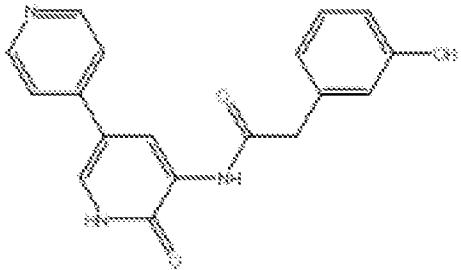
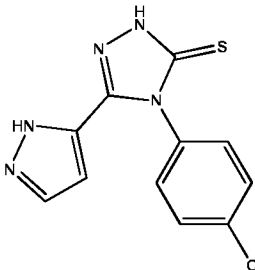
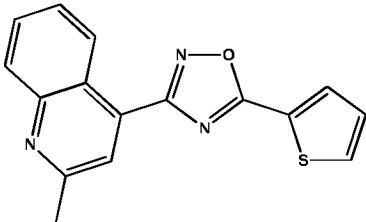
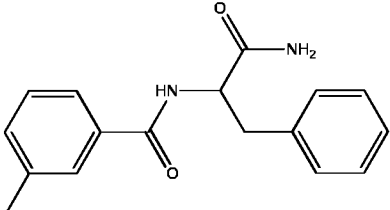
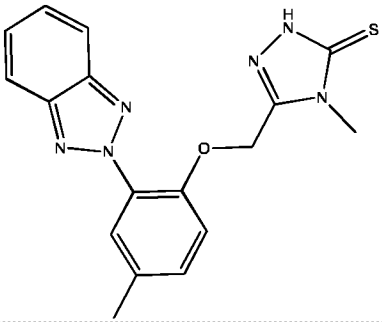
495	 <chem>C1=CN=C2C(=N1)SC(C2)C3=CC=CC=C3N4C=CC=C4</chem>
496	 <chem>C1=CN=C2C(=N1)SC(C2)C3=CC=CC=C3N4C=CC=C4N5C=CC=C5N6C=CC=C6N45</chem>
497	 <chem>C1=CN=C2C(=N1)SC(C2)C3=CC=CC=C3N4C=CC=C4N5C=CC=C5N45</chem>
498	 <chem>C1=CN=C2C(=N1)SC(C2)C3=CC=CC=C3N4C=CC=C4N5C=CC=C5N45</chem>
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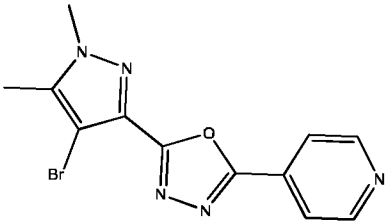
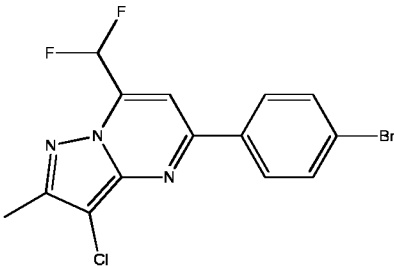
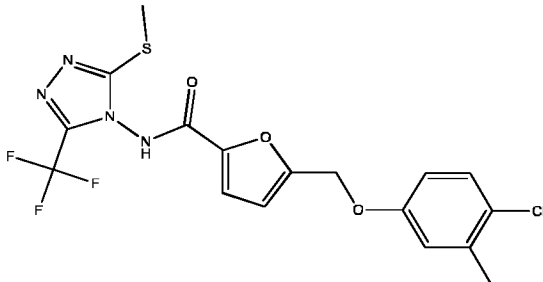
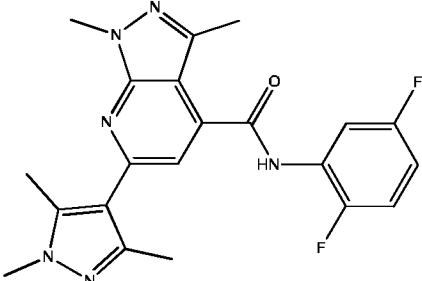
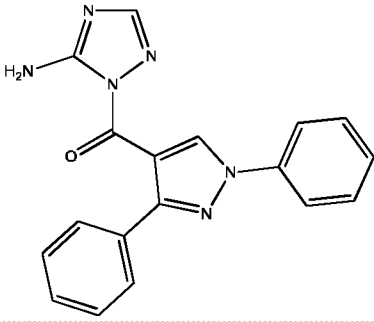
500	 <chem>CCNC(=O)COc1nc2nc3c(s1)CCCCC3</chem>
501	 <chem>Cc1ccc(cc1)n2ncnc2SCC3=CSC=C3c4ccccc4</chem>
502	 <chem>CC1(C)C=C(N1C(=O)c2ccc(OC(F)(F)F)cc2)c3ccccc3</chem>
503	 <chem>COc1ccc(cc1)CC(=O)N(c2ccccc2)c3nc(C)s3</chem>
504	 <chem>Cc1nc(C)s1NC(=O)C=Cc2cc(F)cc2</chem>

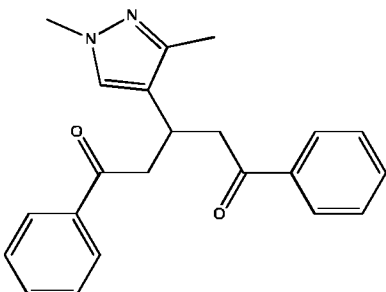
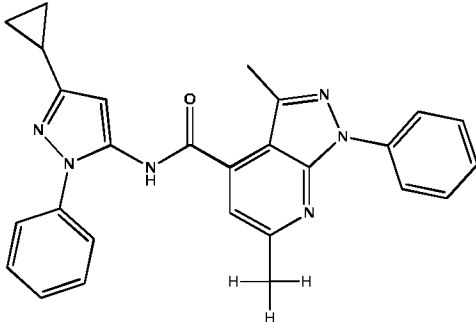
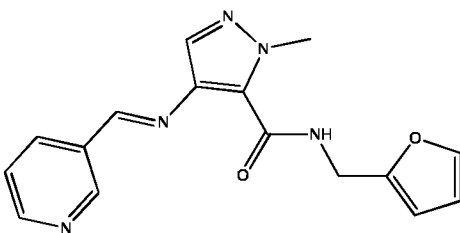
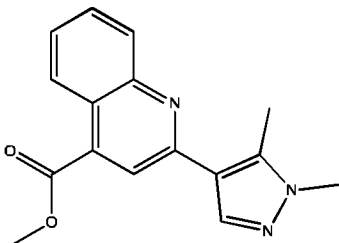
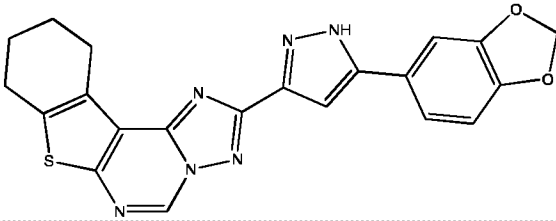
505	 <chem>C1=NC2=C(N1)SC=C2OCC(=O)Nc3ccc4c(c3)OCO4</chem>
506	 <chem>Cc1ccc(cc1)c2c3c(ncn3s2)S4=NC=CC=N4</chem>
507	 <chem>COC1=CC=C2C(=C1)OC(=C2)CC(=O)Nc3cc[nH]s3</chem>
508	 <chem>Cc1ccc(cc1)SCC(=O)NCc2nc3ccccc3o2</chem>
509	 <chem>Cc1ccccc1OCC(=O)NCC2=NC(=C3C=CC=CC3=N2)N=N3C=CC=CC3</chem>

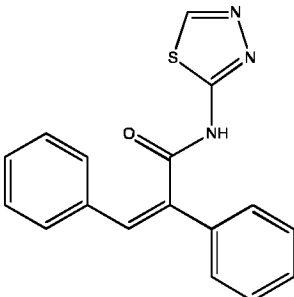
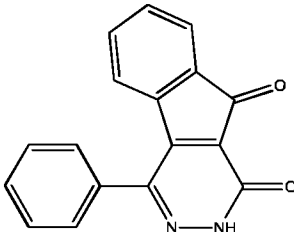
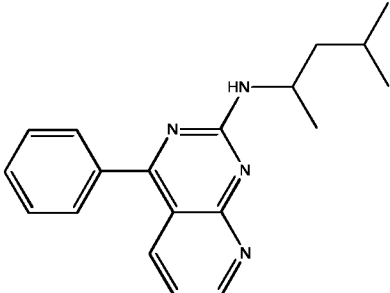
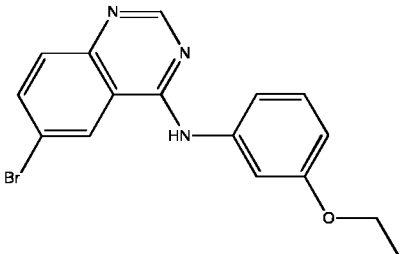
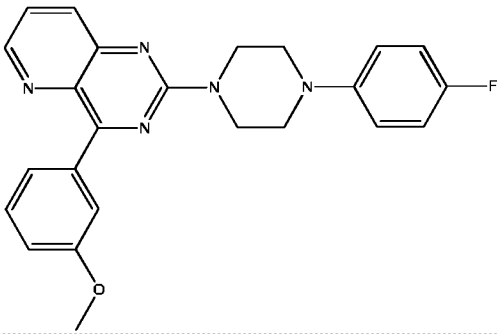
510	 <chem>COc1ccc(cc1)-c2nc3c(cc2c4ccccc4n3)C(=O)N5CCN(CC5)C(=O)[O-]</chem>
511	 <chem>CCN(C)CCNC(=O)CCC1=C(C)C(=O)Oc2cc(O)ccc12</chem>
512	 <chem>c1ccc(cc1)-c2nc3c(cc2o3)Nc4ccccc4C(=O)Nc5ccncc5</chem>
513	 <chem>COc1cccc(c1)-c2nc3c(cc2o3)Nc4ccccc4C(=O)Nc5ccncc5</chem>
514	 <chem>COc1ccc(cc1)-C(=O)Nc2ccccc2-c3nc4c(cc3o4)Nc5cc(OC)ccc5</chem>

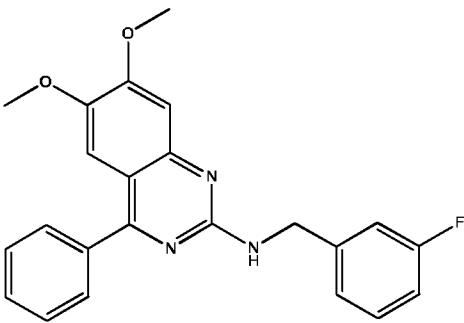
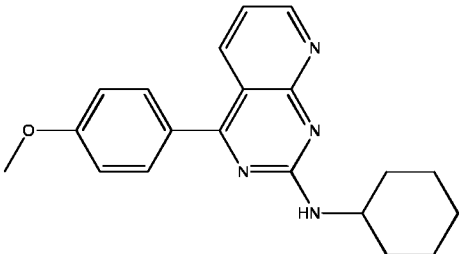
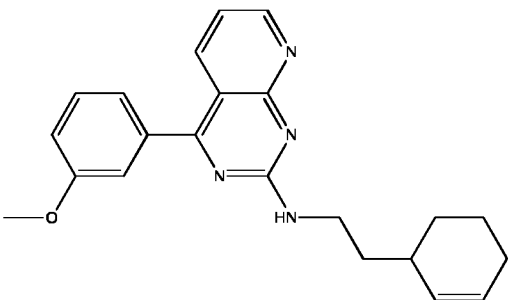
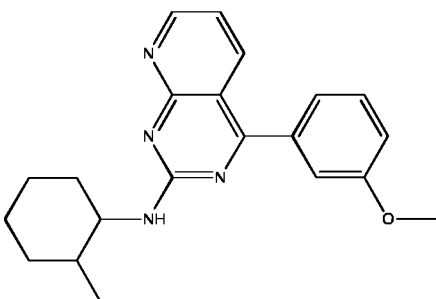
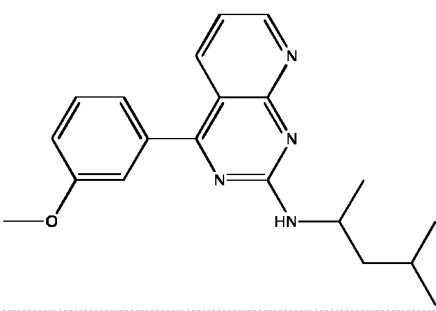
515	 <chem>N#Cc1ccc(cc1)C(=O)Nc2ccccc2c3nn(O)c4cc(Cl)ccc43</chem>
516	 <chem>COc1cc(OC)c(OC)cc1c2nc3c(c2)ccc4c3[nH]c5ccccc45C(=O)N[C@@H](C)C(=O)[O-]</chem>
517	 <chem>COc1ccc(cc1)c2nc3c(c2)ccc4c3[nH]c5ccccc45C(=O)N1CCCC1</chem>
518	 <chem>Cc1c(C)c2nc3cc(Nc4ccsc4)nc3n2c1c5cccnc5</chem>
519	 <chem>Cc1c2c(c1)oc3cc(Nc4cccnc4)nc3n2C</chem>

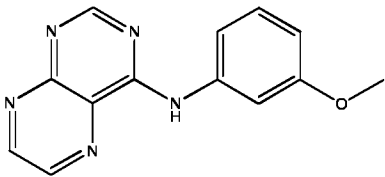
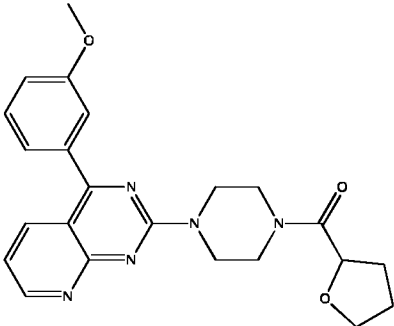
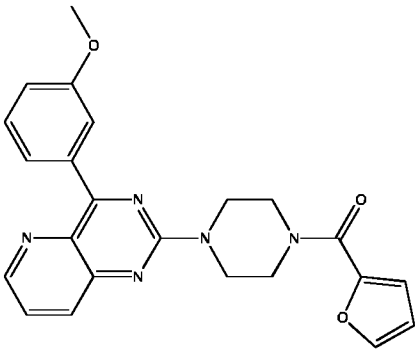
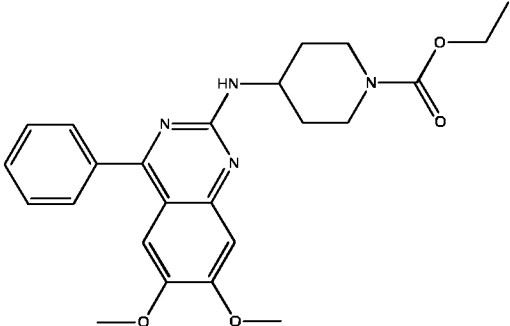
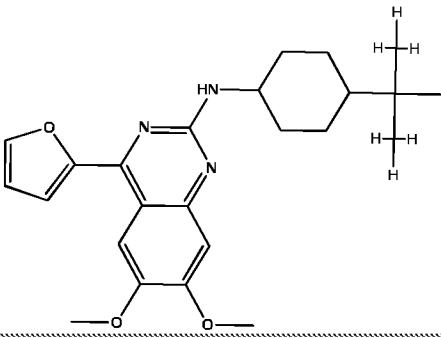
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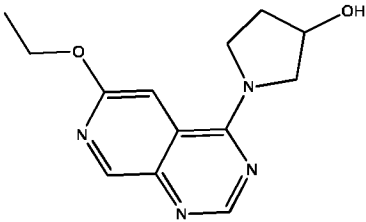
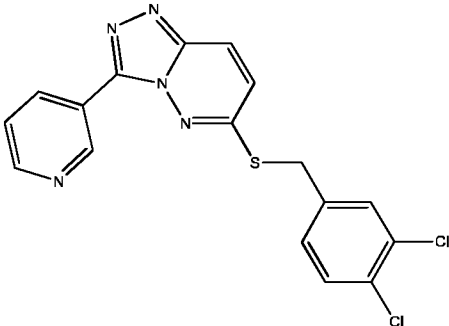
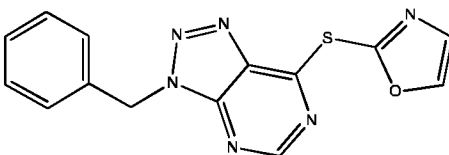
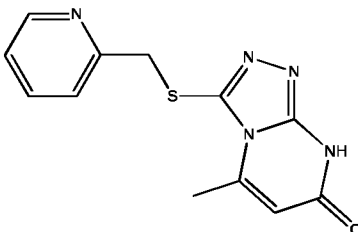
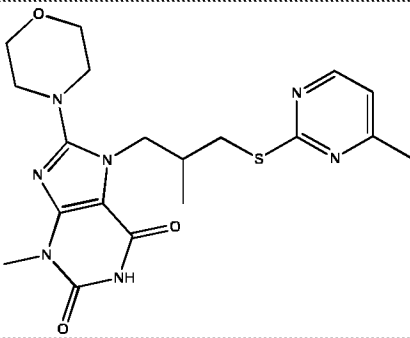
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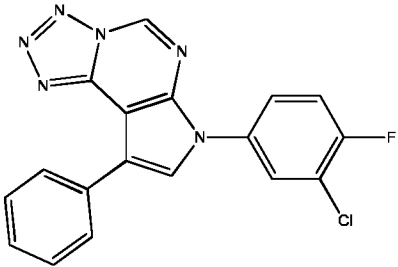
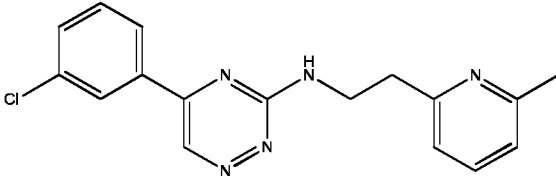
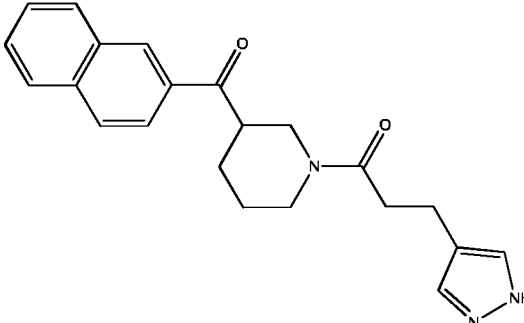
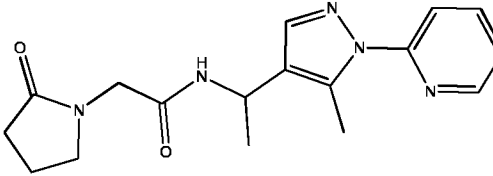
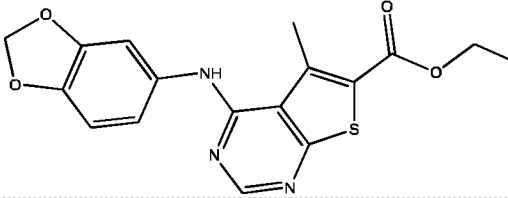
530	 <chem>Cc1nc(C)c(CCC(=O)c2ccccc2)c(CCC(=O)c3ccccc3)n1</chem>
531	 <chem>C1=CN(C2=CC=CC=C2)C=C1NC(=O)c3c(C4=CC=CC=C4)n(C5=CC=CC=C5)c(C6CC6)c3</chem>
532	 <chem>Cc1nc(C2=CC=CC=C2)C=C1NC(=O)NCCc3ccoc3</chem>
533	 <chem>Cc1nc(C2=CC=CC=C2)C=C1NC(=O)NCCc3ccoc3</chem>
534	 <chem>Cc1nc(C2=CC=CC=C2)C=C1NC(=O)NCCc3ccoc3</chem>

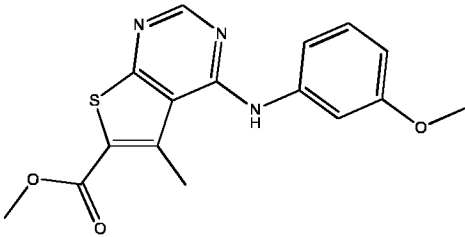
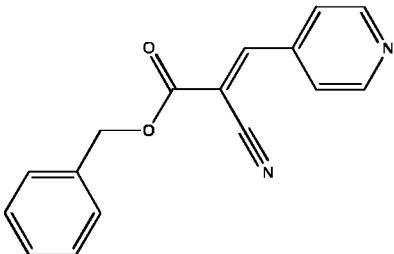
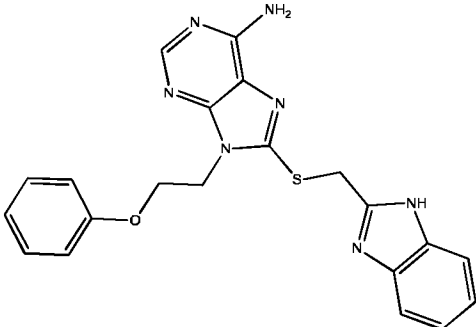
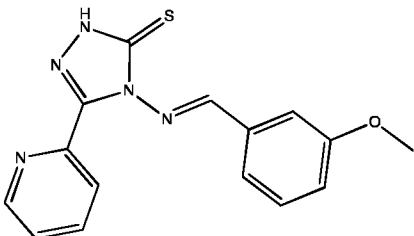
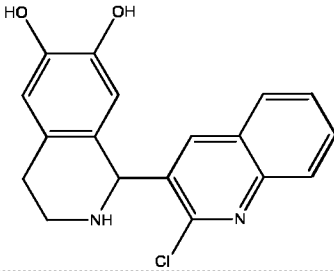
535	 <chem>O=C(C=Cc1ccccc1)C(c2ccccc2)NNc3nnsc3</chem>
536	 <chem>O=C1C(=O)C2=C(C1)c3ccccc3N2</chem>
537	 <chem>CC(C)CCNC1=NC2=CC=CC=C2N=C1c3ccccc3</chem>
538	 <chem>CCOC1=CC=C(C=C1)Nc2nc3cc(Br)ccc3n2</chem>
539	 <chem>COc1ccc(cc1)c2nc3ccncc3n2N4CCN(CC4)C5=CC=C(F)C=C5</chem>

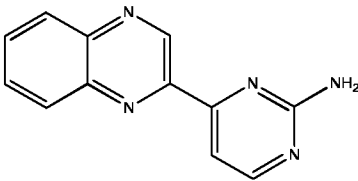
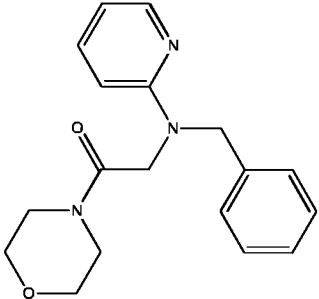
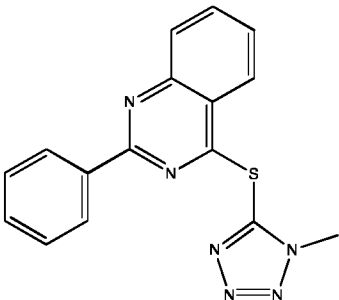
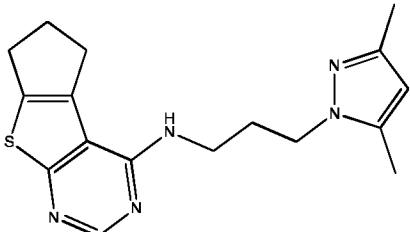
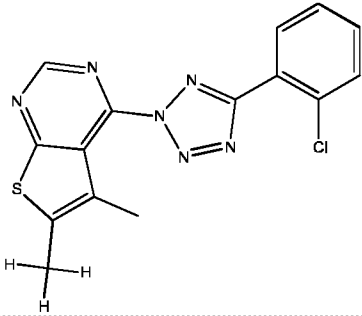
540	 <chem>COc1cc(OC)c(OC)cc1-c2nc(NCc3ccc(F)cc3)n(c2)c4ccccc4</chem>
541	 <chem>COc1ccc(cc1)-c2nc3ccccc3n2Nc4ccccc4</chem>
542	 <chem>COc1ccc(cc1)-c2nc3ccccc3n2NCCc4ccccc4</chem>
543	 <chem>COc1ccc(cc1)-c2nc3ccccc3n2NC4CCCCC4C</chem>
544	 <chem>COc1ccc(cc1)-c2nc3ccccc3n2NC(C)CC(C)C</chem>

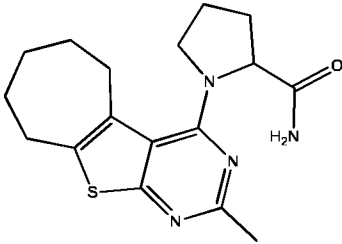
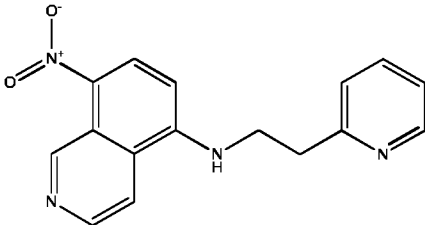
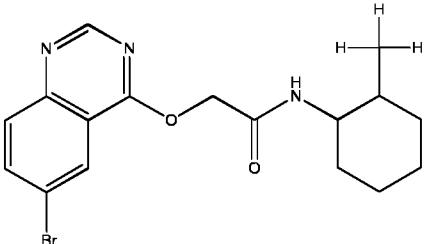
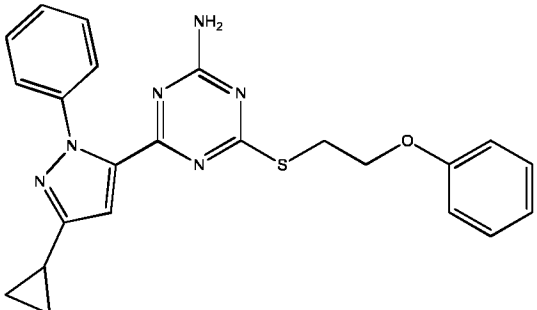
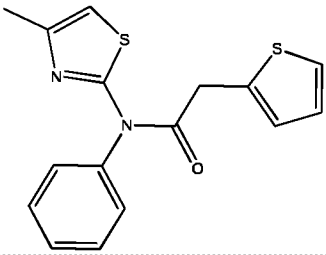
545	 <chem>COc1ccc(Nc2nc3ncnc3nc2)cc1</chem>
546	 <chem>COc1ccc(cc1)c2nc3ccncc3nc2N4CCNCC4C(=O)OCC5CCCC5</chem>
547	 <chem>COc1ccc(cc1)c2nc3ccncc3nc2N4CCNCC4C(=O)Oc5ccoc5</chem>
548	 <chem>COc1cc(OC)cc2c1nc3ccccc3nc2N4CCNCC4C(=O)OCC</chem>
549	 <chem>COc1cc(OC)cc2c1nc3ccccc3nc2N4CCNCC4C(=O)OCC</chem>

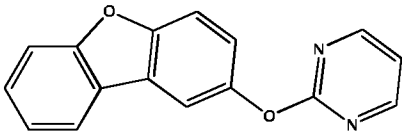
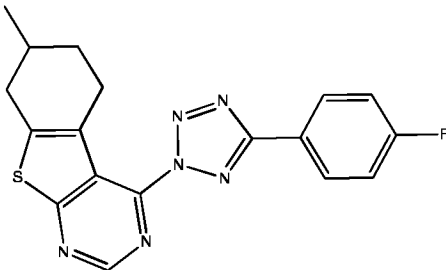
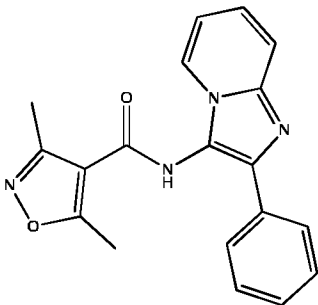
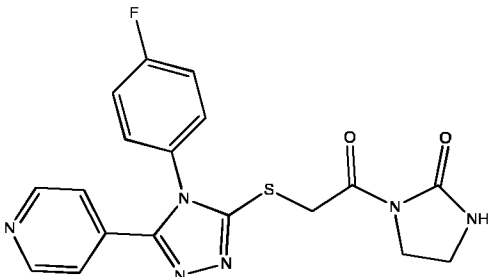
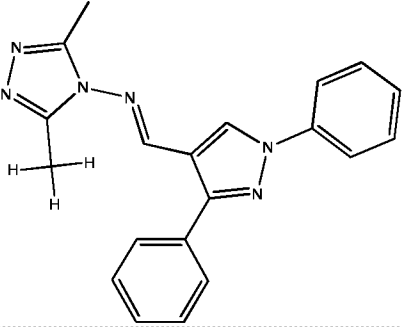
550	 <chem>CCOC1=CC2=C(N1)N=CN=C2CN(CCCO)CCO</chem>
551	 <chem>Clc1ccc(cc1Cl)CS2=CN3C(=N2)C(=N3)c4ccncc4</chem>
552	 <chem>c1ccoc1SC2=CN3C(=N2)C(=N3)CN(Cc4ccccc4)C5=CC=CC=C5</chem>
553	 <chem>Cc1cc(=O)[nH]c2c1n3c(nnn32)SCc4cccnc4</chem>
554	 <chem>Cc1ccnnc1SCC(C)CN2C(=N3C(=N2)C(=N3)C(=O)NC(=O)N2C)N4CCOCC4</chem>

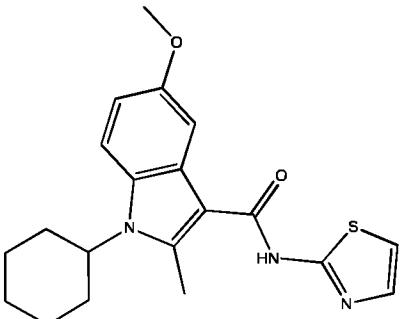
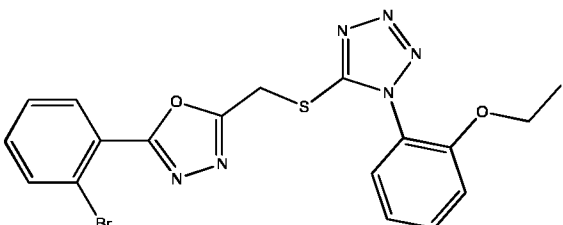
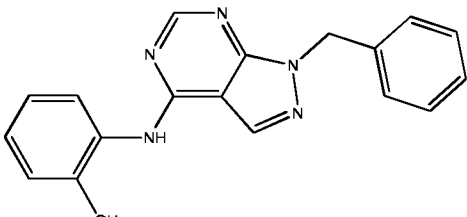
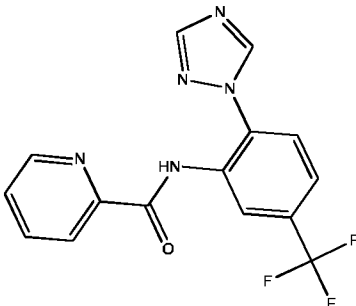
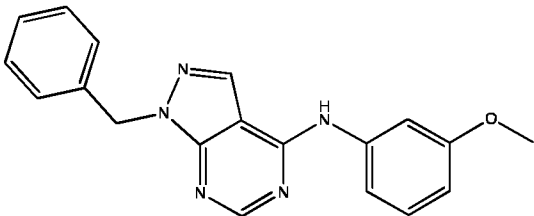
555	 <chem>c1ccc(cc1)c2cc3c(cc2n3)c4nn[nH]4c5ccc(F)c(Cl)c5</chem>
556	 <chem>Cc1ccncc1CCNC2=CN=C(N=C2C3=CC=CC=C3Cl)N</chem>
557	 <chem>c1ccc2cc(ccc2c1)C(=O)N3CCCCC3C(=O)NCCc4c[nH]c5c4n[nH]5</chem>
558	 <chem>CC1=C(C)C(=CN1C2=CC=CC=N2)CNC(=O)CN3CCCC3=O</chem>
559	 <chem>CCOC(=O)c1sc2c(c1)c3ncnc3c2c4ccc5c(c4)OCO5</chem>

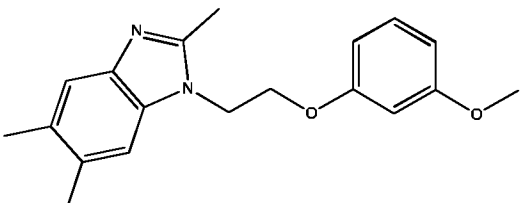
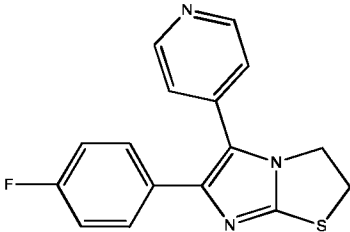
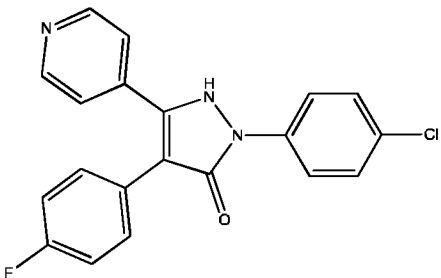
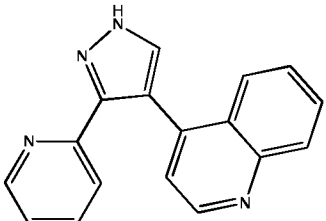
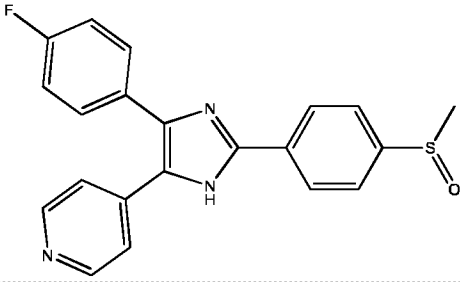
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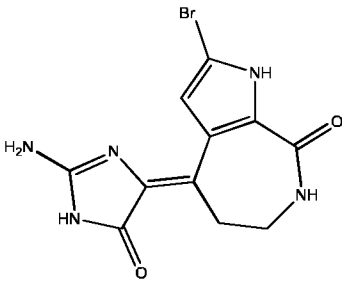
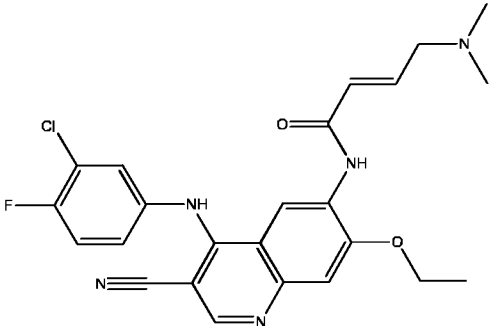
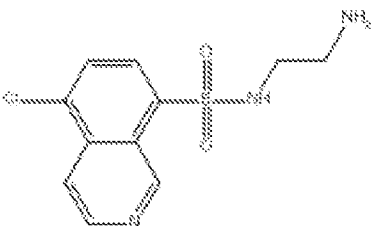
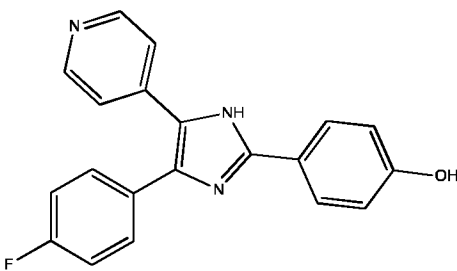
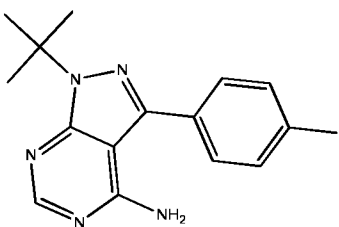
565	 <chem>Nc1ccnc2c1cnc3ccccc32</chem>
566	 <chem>c1ccccc1N(CC(=O)N2CCOCC2)c3ccncc3</chem>
567	 <chem>Cn1ccnc1S2C(=N3C(=N2)C(=C3)C4=CC=CC=C4)C5=CC=CC=C5</chem>
568	 <chem>Cc1cc(C)n(CCCCNc2cnc3c2sc4c3C=CC5CCCCC54)n1</chem>
569	 <chem>Cc1c(C2=CC=CC=C2N2C(=N3C(=N2)C(=C3)C4=CC=C(Cl)C=C4)N2)c3cnc4c3sc5c4cnc6c5cnc6</chem>

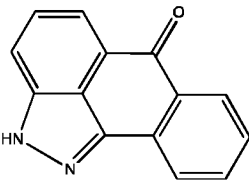
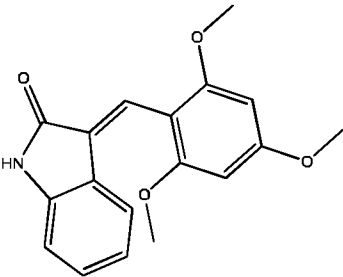
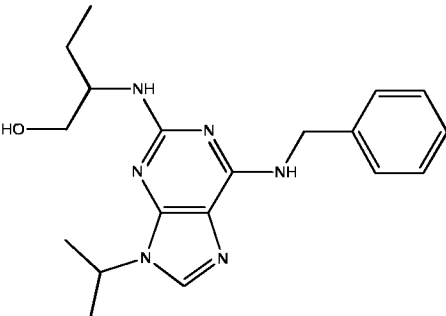
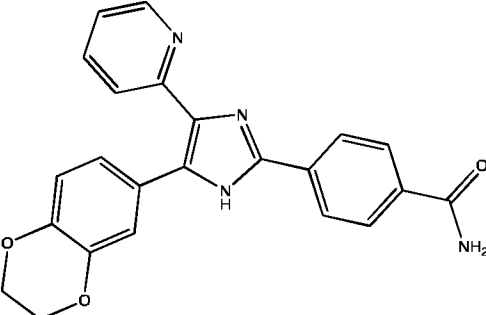
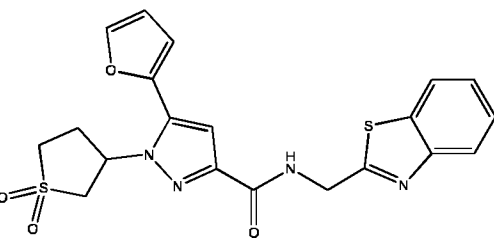
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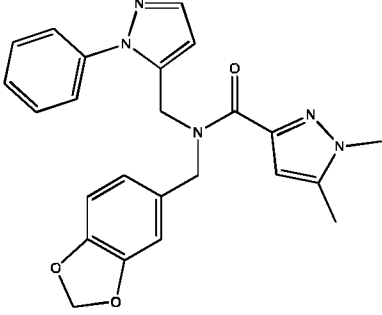
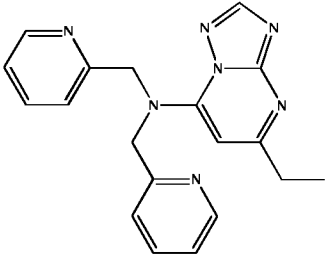
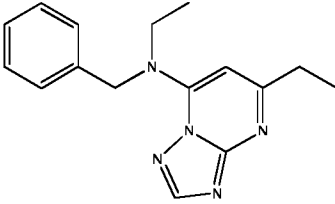
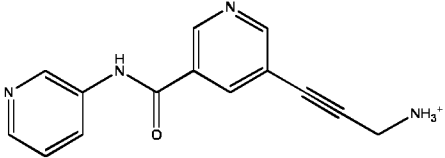
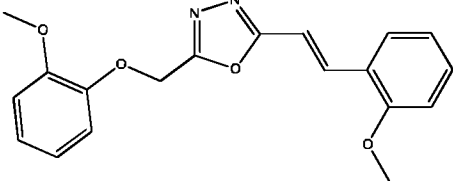
575	 <chem>c1ccc2c(c1)oc3cc(oc3cc2)Oc4ccncc4</chem>
576	 <chem>Cc1ccc2c(c1)sc3nc4nc(N5C=CN=C5C6C=CC(=C6)N=N=N6)cc32C7CCCCC7C8=CC=C(C=C8)F</chem>
577	 <chem>Cc1cc2nc3ccccc3n2c1C(=O)Nc4cc5c(nc4)oc(C)c5</chem>
578	 <chem>C1=CC=C(C=C1)N1C(=NN1)C2=CC=CC=C2FSCC(=O)N3C(=O)CCN3Cc4ccncc4</chem>
579	 <chem>Cc1cc2nnc(n2)N1C=CC(=C1)C(=O)N2C(=NN2)C3=CC=CC=C3</chem>

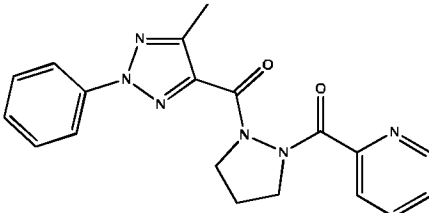
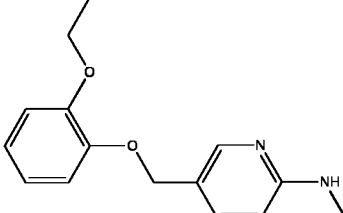
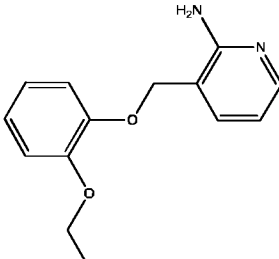
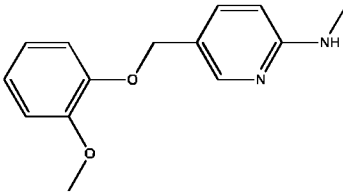
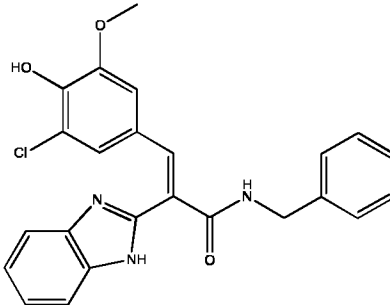
580	 <chem>COc1ccc2c(c1)c(c3ccccc3n2)C(=O)Nc4cc[nH]4</chem>
581	 <chem>CCOc1ccccc1N2C=NC=N2SCC3C=NC4C(=N3)OC(C4)c5ccccc5Br</chem>
582	 <chem>Nc1ccccc1N2C3=CC=CC=C3N(C2)c4cc(O)ccc4</chem>
583	 <chem>Nc1ccccc1N2C3=CC(=CC=C3C(F)(F)F)C=C2N(C3)c4cc[nH]4</chem>
584	 <chem>COc1ccc(Nc2cc3c(c2)c4ccccc4n3)cc1</chem>

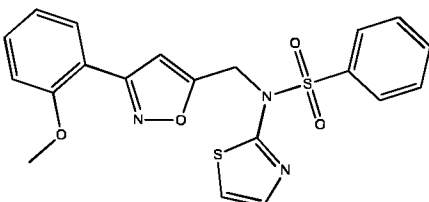
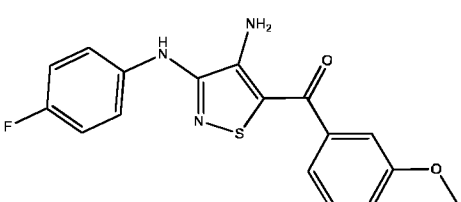
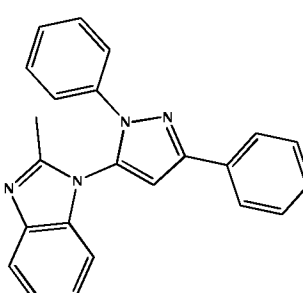
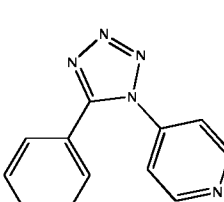
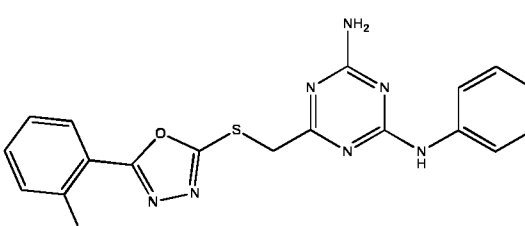
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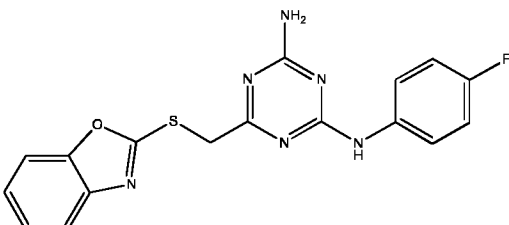
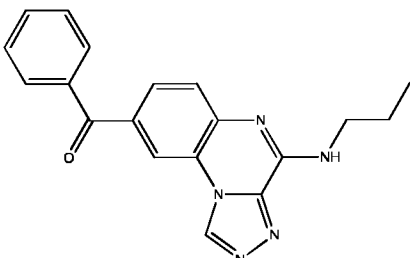
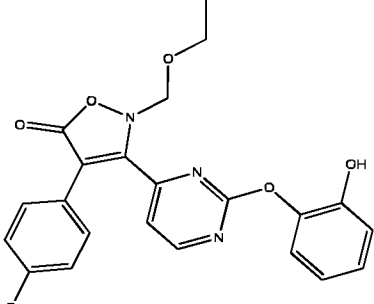
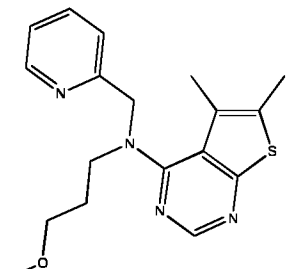
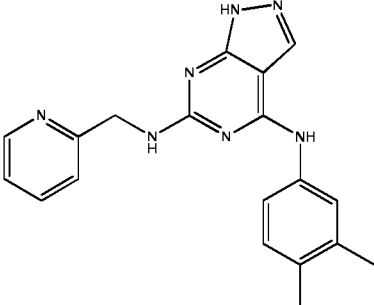
590	 <chem>Nc1nc(=O)[nH]c1C(=C2C(=CC(=C2)N)C(=O)NCC2)c3cc[nH]3Br</chem>
591	 <chem>CCOC1=CC=C2C(=C1)N=CC=C2C(=C3C(=CC(=C3)N#C)N=C4C(=CC(=C4)F)C(=C4)Cl)NC(=O)C=C[N+](C)(C)C</chem>
592	 <chem>NCCCNCC1(=O)C(=O)c2cc3cc[nH]c3cc2Cl</chem>
593	 <chem>Oc1ccc(cc1)c2nc3ccccc3n2c4cc(F)ccc4</chem>
594	 <chem>Cc1ccc(cc1)c2nc3c(ncn3C(C)(C)C)c4ncn42</chem>

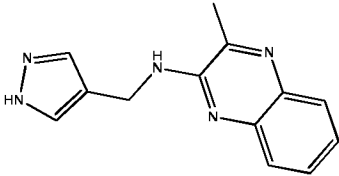
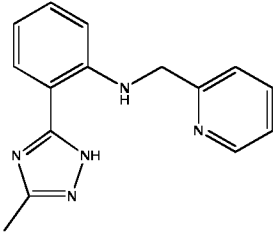
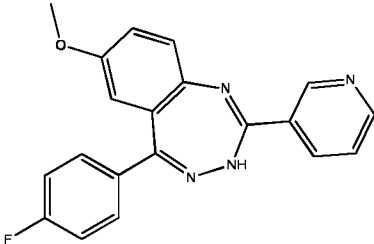
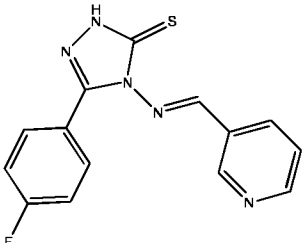
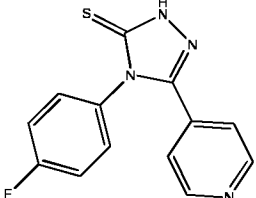
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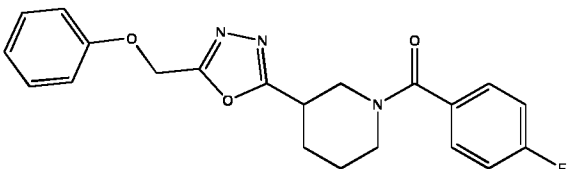
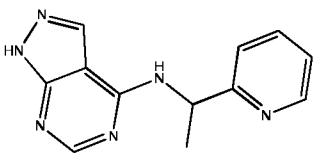
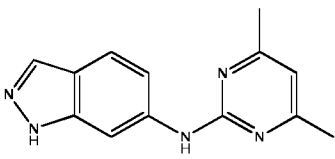
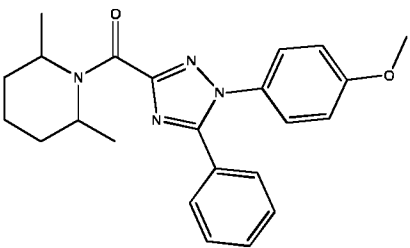
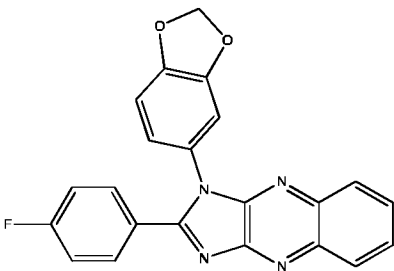
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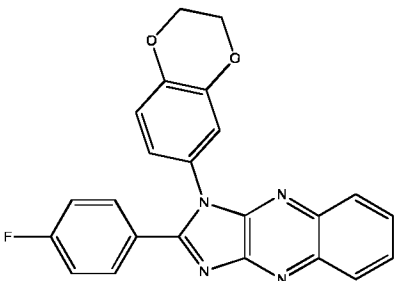
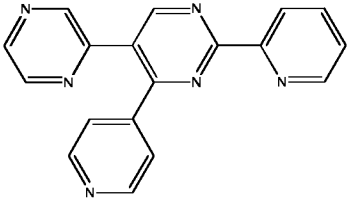
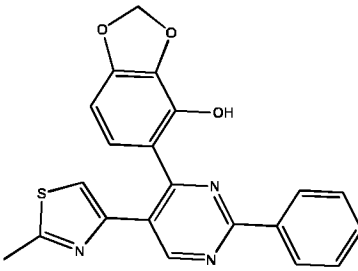
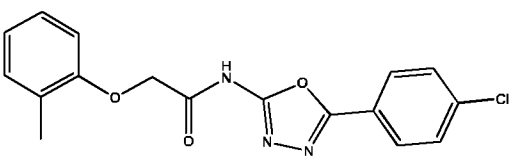
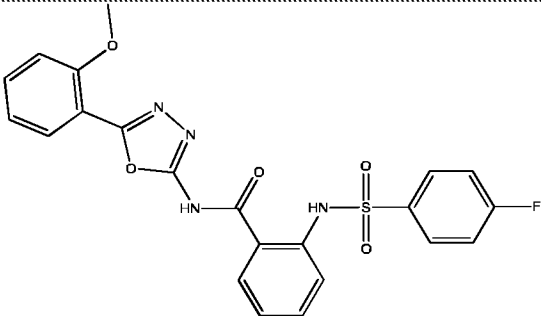
605	 <chem>CC1=CN=C(N1C(=O)N2CCCC2C(=O)C3=CC=CC=C3)C(=O)C4=CC=CC=C4</chem>
606	 <chem>CCOC1=CC=C(OC1CC2=CC=CC=C2N)C3=CC=CC=C3</chem>
607	 <chem>CCOC1=CC=C(OC1CC2=CC=CC=C2N)C3=CC=CC=C3</chem>
608	 <chem>COc1ccccc1OC1CC2=CC=CC=C2N)C3=CC=CC=C3</chem>
609	 <chem>COc1cc(Cl)cc(C=C(C1=CC2=C(N1)C=CC=C2)C(=O)NC3=CC=CC=C3)c1O</chem>

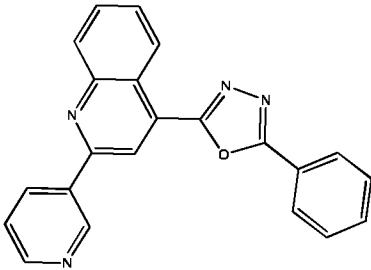
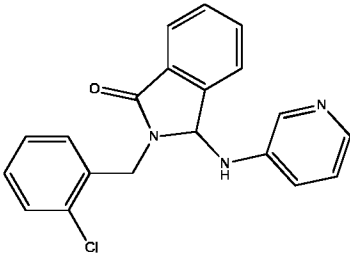
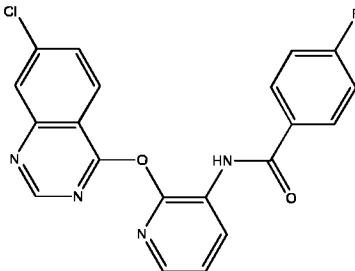
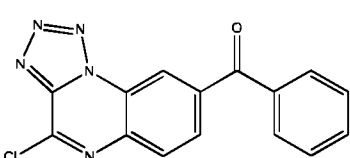
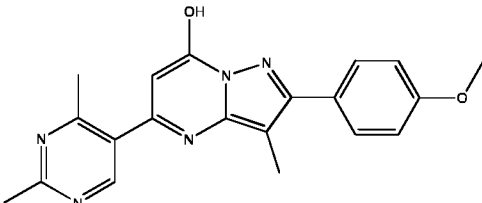
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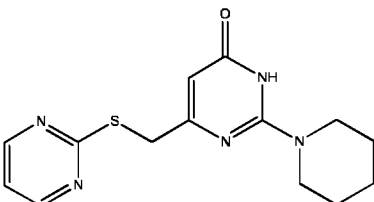
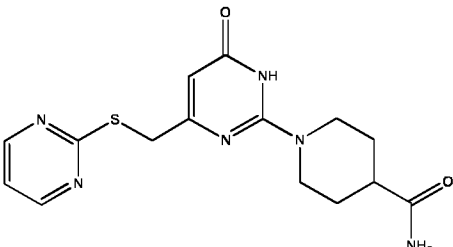
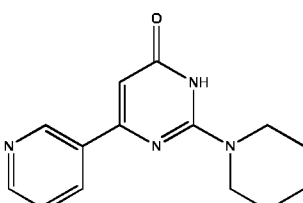
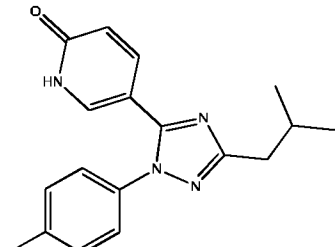
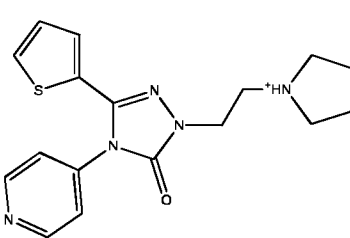
615	 <chem>Nc1nc(NC2=CC=C(C=C2)F)nc(CSC3c4ccccc4o3)c1</chem>
616	 <chem>CCCNc1nc2ccccc2n1C(=O)c3ccccc3</chem>
617	 <chem>Oc1ccccc1Oc2nc3ccccc3n2C4=C(C(=O)O4)c5cc(F)ccc5</chem>
618	 <chem>COCN(Cc1ccccn1)c2nc3sc(C)c3n2</chem>
619	 <chem>Cc1ccc(Nc2nc3c(ncn3)c4ccccc42)cc1NCc5ccccn5</chem>

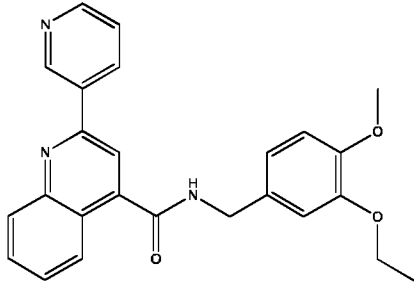
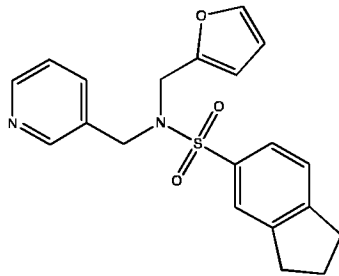
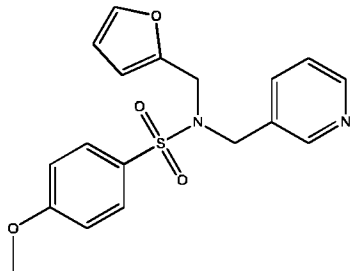
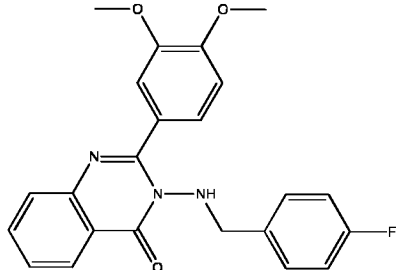
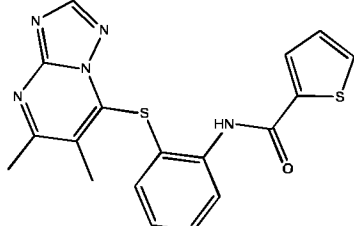
620	 <chem>Cc1nc2ccccc2n1CNc3cc[nH]3</chem>
621	 <chem>Cc1nc[nH]1C2=CC=C(C=C2)NCCc3ccncc3</chem>
622	 <chem>COc1ccc2nc3ccccc3n2c1C4=CC=C(C=C4)F</chem>
623	 <chem>C1=CC=C(C=C1)N2C(=S)N=C(N2)C3=CC=C(C=C3)F</chem>
624	 <chem>C1=CC=C(C=C1)N2C(=S)N=C(N2)C3=CC=C(C=C3)F</chem>

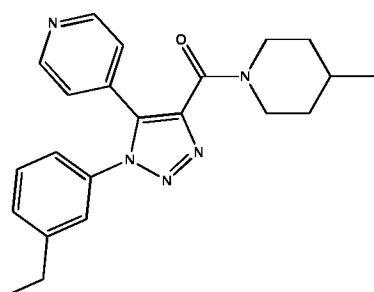
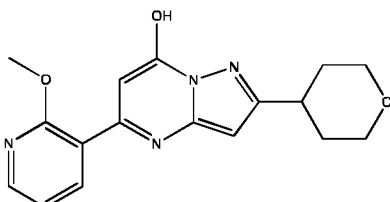
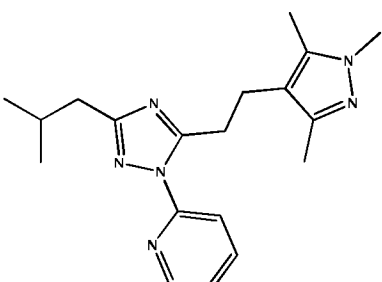
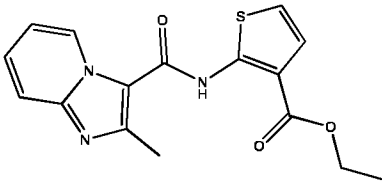
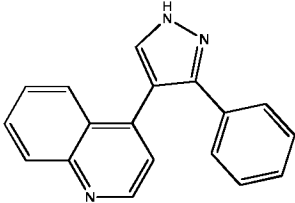
625	 <chem>COc1ccc(cc1)OCc2nnoc2C3CCN(CC3)C(=O)c4ccc(F)cc4</chem>
626	 <chem>CC(C)Nc1nc2c(ncn2)c1c3ccncc3</chem>
627	 <chem>Cc1nc(C)c(Nc2cc3c(cc2)nn3)nc1C</chem>
628	 <chem>COc1ccc(cc1)n2nc(C(=O)N3CCCCC3C)c2c4ccccc4</chem>
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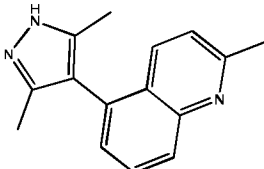
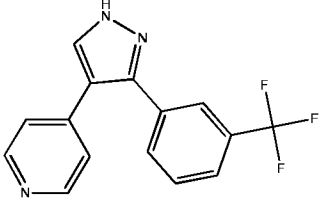
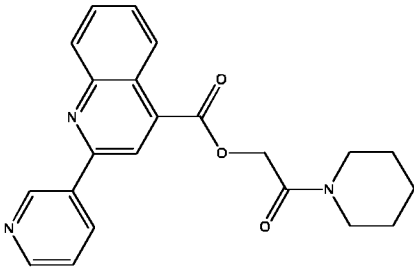
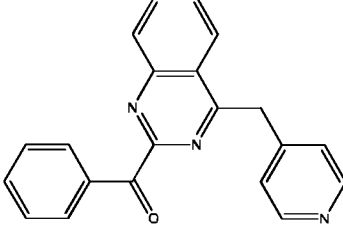
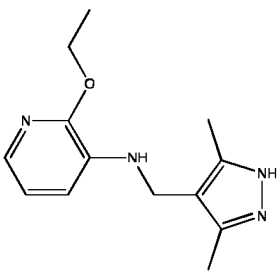
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631	 <chem>c1ccncc1c2nc3ccccc3n2c2nc4ccccc4n2</chem>
632	 <chem>Cc1ccsc1c2nc3ccccc3n2c2c4cc5ccccc5o4O</chem>
633	 <chem>COc1cccc(c1)OCC(=O)Nc1nnoc1-c2ccc(Cl)cc2</chem>
634	 <chem>COc1cccc(c1)c2nnoc2NC(=O)c3ccccc3NS(=O)(=O)c4ccc(F)cc4</chem>

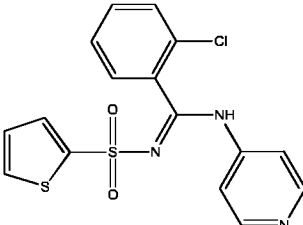
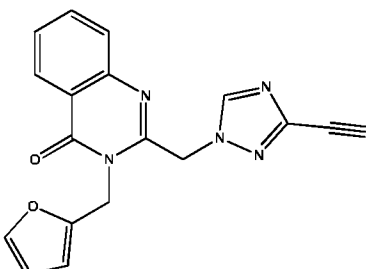
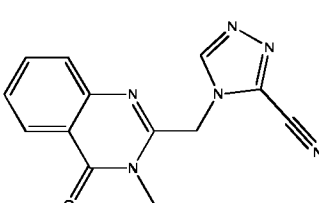
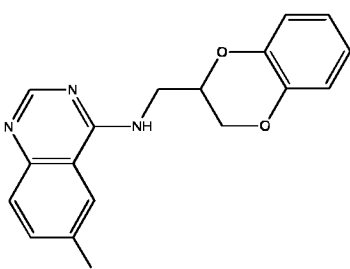
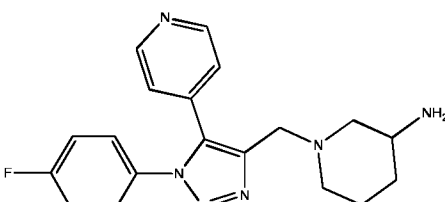
635	 <chem>c1ccc(cc1)-c2nc3cc(ccc3n2)-c4cccnc4</chem>
636	 <chem>Clc1ccc(cc1)CN2C(=O)c3ccccc3N2c4cccnc4</chem>
637	 <chem>Fc1ccc(cc1)C(=O)Nc2cc3ccccc3n2Oc4cc5ccccc5n4</chem>
638	 <chem>Clc1ccc(cc1)-c2cc3ccccc3n2-c4cc5ccccc5n4</chem>
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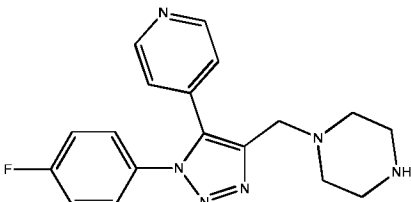
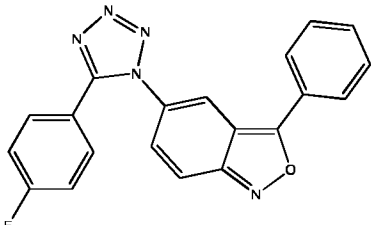
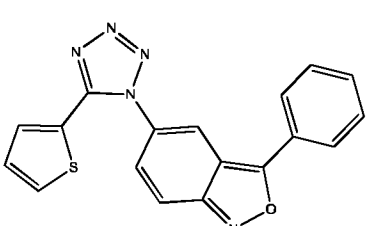
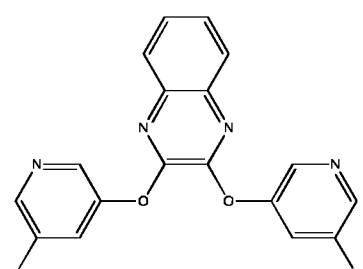
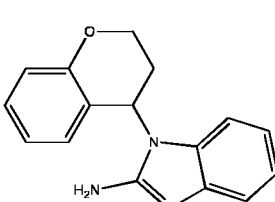
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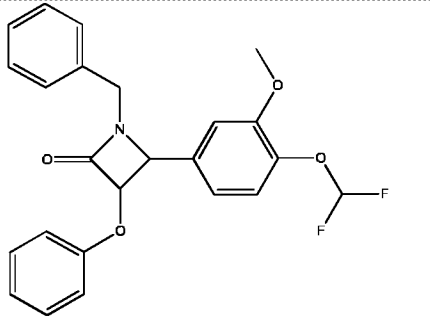
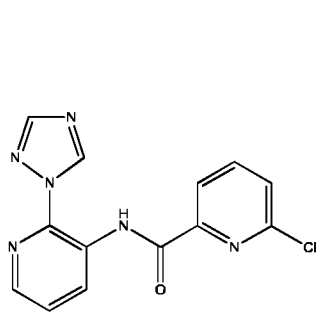
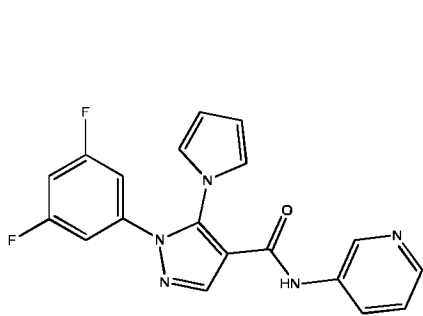
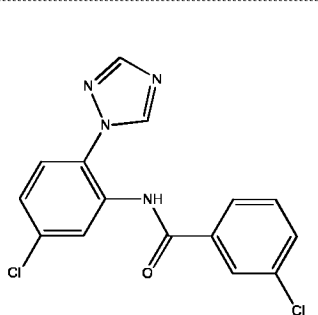
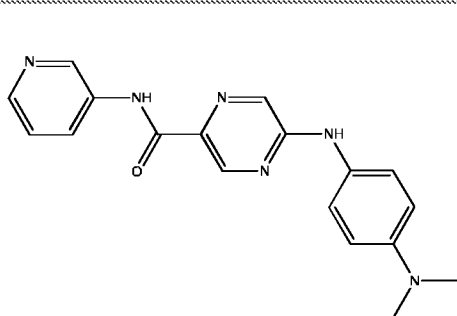
645	 <chem>COc1cc(OC)ccc1CN(C(=O)c2cc3ccccc3nc2c4ccncc4)Cc5ccc(OC)cc5</chem>
646	 <chem>O=C1C=CC=C(C=C1)S(=O)(=O)N(Cc2ccncc2)CC3C=CC=C3O</chem>
647	 <chem>COc1ccc(cc1)S(=O)(=O)N(Cc2ccncc2)CC3C=CC=C3O</chem>
648	 <chem>COc1cc(OC)ccc1C2=NC3=CC=CC=C3C(=O)N2NNCc4ccc(F)cc4</chem>
649	 <chem>CC1=C2N=CN=C2N3C=CC=C13SC(=O)Nc4ccc(cc4)SC5=CC=CC=C5S</chem>

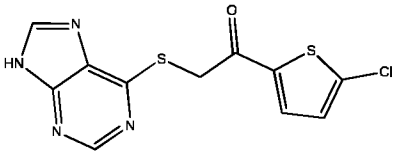
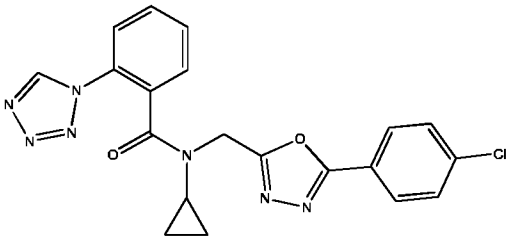
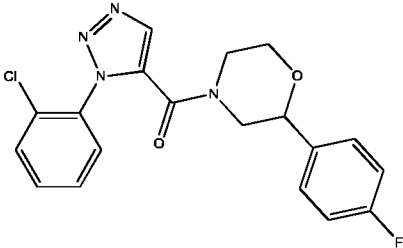
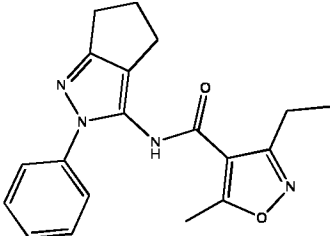
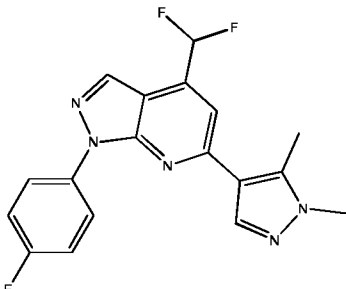
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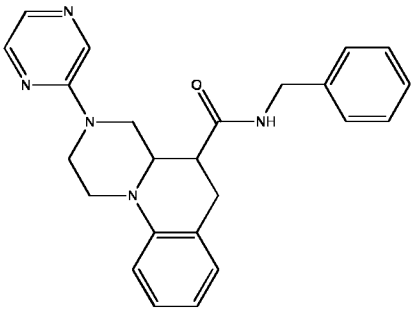
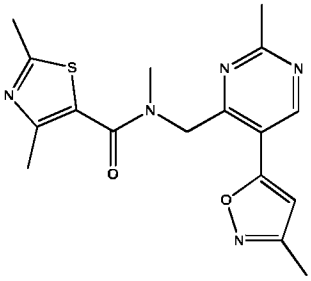
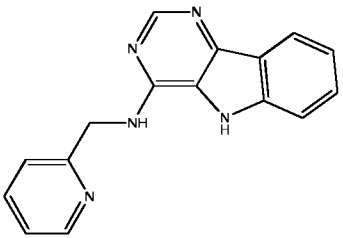
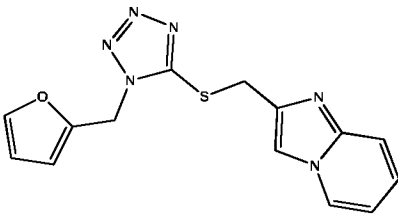
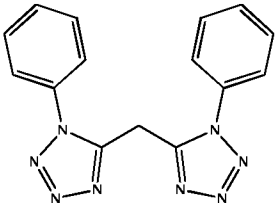
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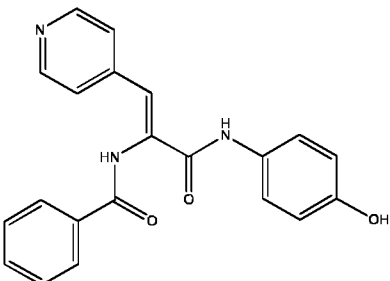
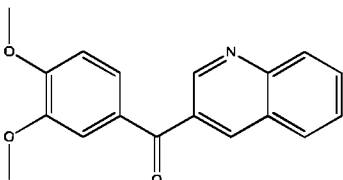
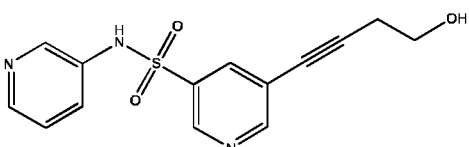
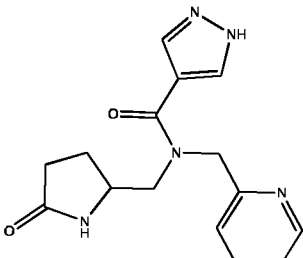
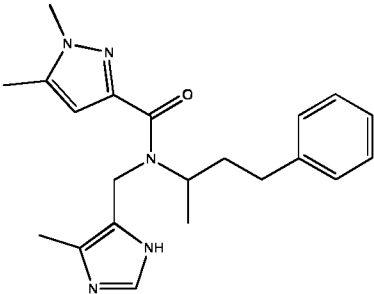
660	 <chem>O=S(=O)(c1ccsc1)C(=N)Nc2ccncc2c3ccccc3Cl</chem>
661	 <chem>N#Cc1nn(CCN2C(=O)c3ccccc3N2Cc4ccoc4)cnc1</chem>
662	 <chem>N#Cc1nn(CCN2C(=O)c3ccccc3N2Cc4ccoc4)cnc1</chem>
663	 <chem>N#Cc1nn(CCN2C(=O)c3ccccc3N2Cc4ccoc4)cnc1</chem>
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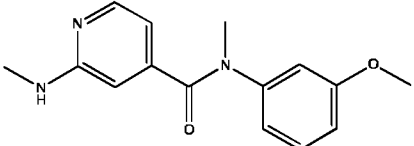
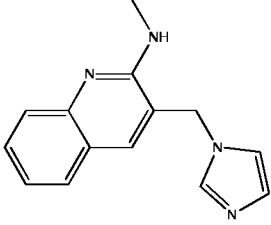
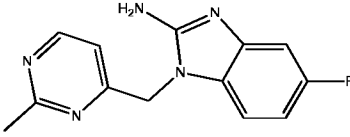
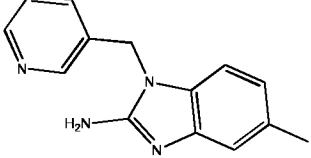
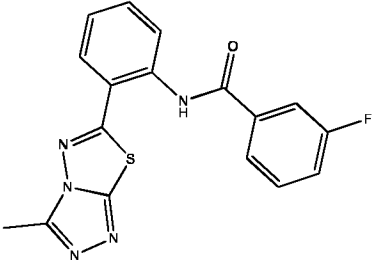
665	 <chem>Fc1ccc(cc1)n2nnnc2C3CCNCC3c4ccncc4</chem>
666	 <chem>Fc1ccc(cc1)n2nnnc2c3ccc4c(c3)ocn4Cc5ccccc5</chem>
667	 <chem>c1ccsc1n2nnnc2c3ccc4c(c3)ocn4Cc5ccccc5</chem>
668	 <chem>Clc1ccc(cc1)Oc2nnnc2Oc3ccc(Cl)cc3</chem>
669	 <chem>Nc1nn2c(c1)c3ccccc3n2C4CCOc5ccccc45</chem>

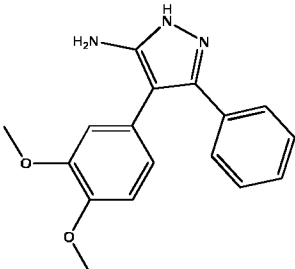
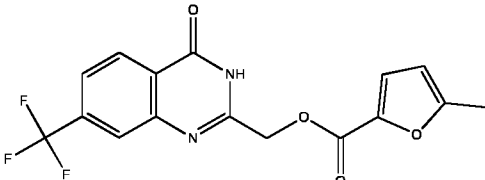
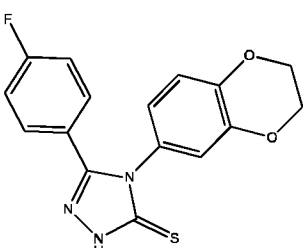
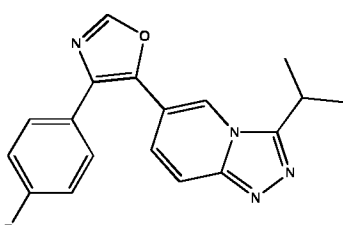
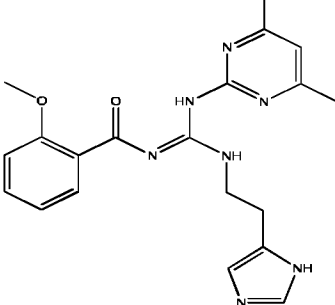
670	 <chem>COc1ccc(OC(F)F)cc1C2C(=O)N(Cc3ccccc3)C2Oc4ccccc4</chem>
671	 <chem>Clc1ccncc1C(=O)Nc2ccncc2n3ccncc3</chem>
672	 <chem>Fc1cc(F)cc(N2C(=O)Nc3ccncc3N2)c1C(=O)Nc4ccncc4</chem>
673	 <chem>Clc1ccncc1C(=O)Nc2ccncc2n3ccncc3</chem>
674	 <chem>CN(C)c1ccc(Nc2ccncc2C(=O)Nc3ccncc3)cc1</chem>

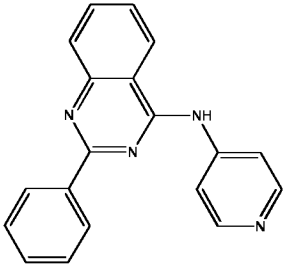
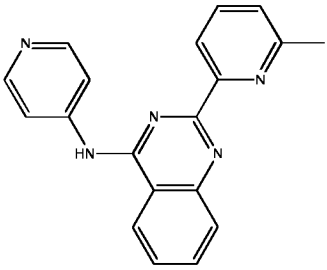
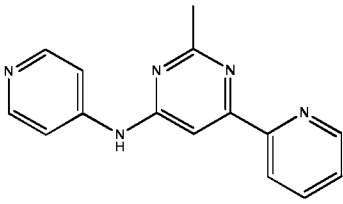
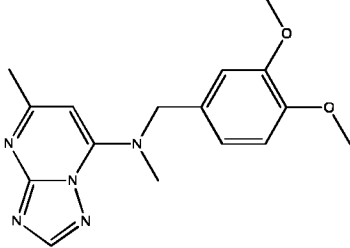
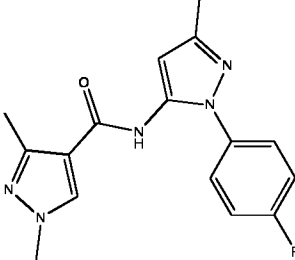
675	 <chem>C1=NC2=C(N1)N=CN=C2SCC(=O)c3cc(Cl)cs3</chem>
676	 <chem>C1=NN=C(N1)C(=O)N(C2CC2)Cc3nnoc3-c4ccc(Cl)cc4</chem>
677	 <chem>Clc1ccccc1n2nncc2C(=O)N3CCOC(C3)c4ccc(F)cc4</chem>
678	 <chem>CC1=C(C)ON=C1C(=O)Nc2c3ccccc3nn2</chem>
679	 <chem>Cc1nn(C)c(C2=CN3C(=CN=C2N3C(=O)C(F)F)c4ccc(F)cc4)c1</chem>

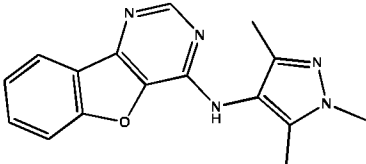
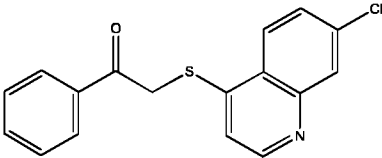
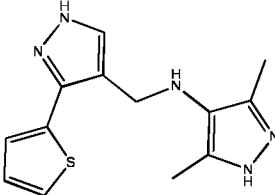
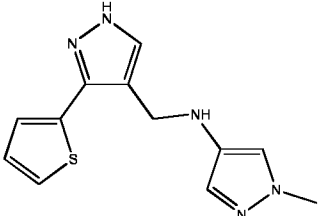
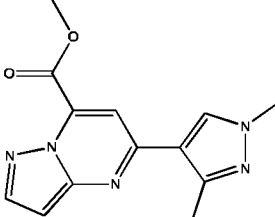
680	 <chem>O=C(NCc1ccccc1)C2C3Cc1ccccc1N2CCN3Cc4ccncc4</chem>
681	 <chem>Cc1cc(C)s(C(=O)NCC2=NC=CC(=C2)c3ccoc3n2)c1</chem>
682	 <chem>Nc1c2ccccc2c3c1cnc3Cc4ccncc4</chem>
683	 <chem>Cc1cc2c(c1)oc3ccccc3n2SC4=NN=CN4Cc5ccoc5</chem>
684	 <chem>c1ccccc1N2=NN=CC2Cc3nnnn3c4ccccc4N5=NN=CC5</chem>

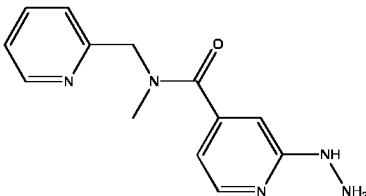
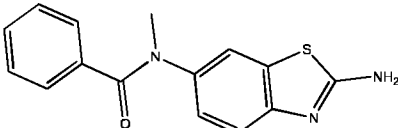
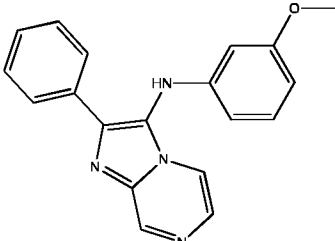
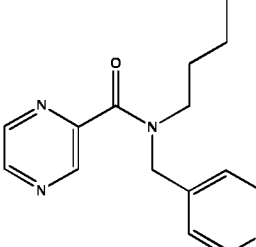
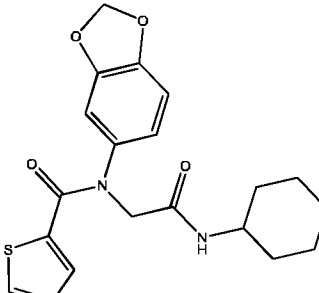
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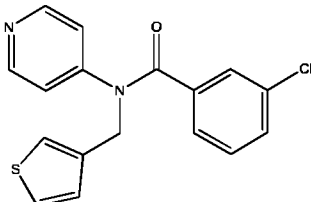
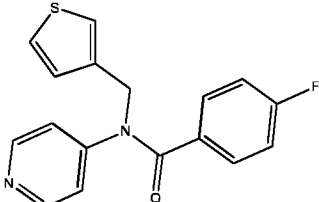
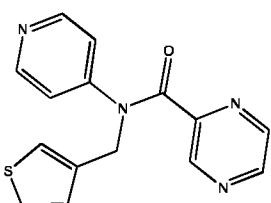
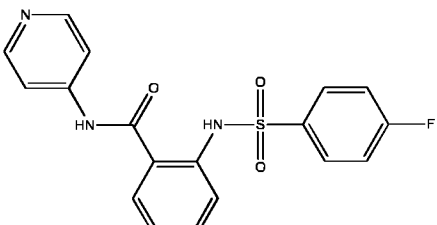
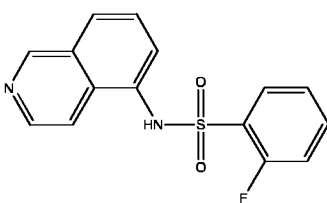
690	 <chem>CN(C)C(=O)c1ccncc1CN(C)c2ccc(OC)cc2</chem>
691	 <chem>CN1C=CN(C)C1Cc2c[nH]c3ccccc23</chem>
692	 <chem>Nc1ccncc1CN(C2=NC(=N)N2)Cc3ccncc3F</chem>
693	 <chem>Nc1ccncc1CN(C2=NC(=N)N2)Cc3cc(C)ccn3</chem>
694	 <chem>Cc1nn[nH]1Cc2cc(ccc2NC(=O)c3ccc(F)cc3)n4cnc(C)n4</chem>

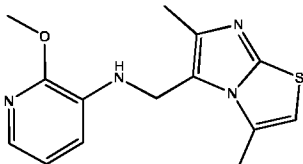
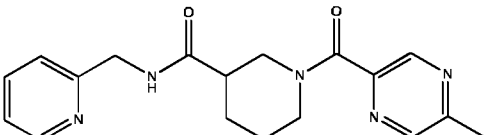
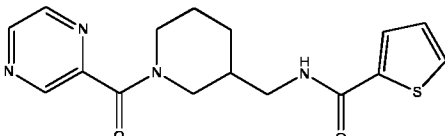
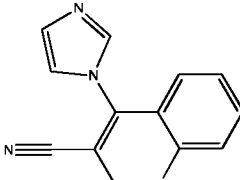
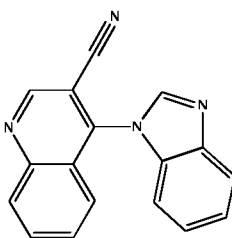
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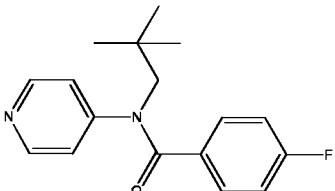
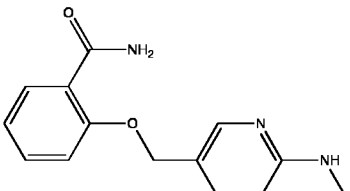
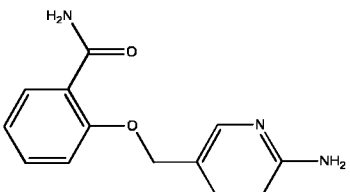
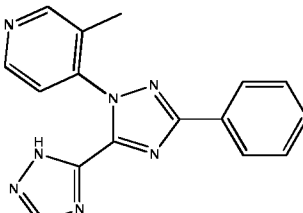
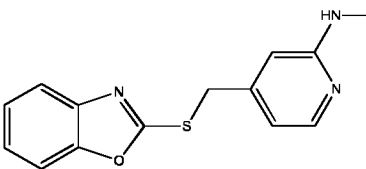
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701	 <chem>Cc1ccncc1c2nc3ccccc3n2Nc4cccnc4</chem>
702	 <chem>c1cccnc1c2nc3ccccc3n2Nc4cccnc4</chem>
703	 <chem>Cc1nc2nc3ncn3c2n1CN(C)Cc4cc(OC)cc(OC)c4</chem>
704	 <chem>Cc1nc2nc3ncn3c2n1CN(C)Cc4ccc(F)cc4</chem>

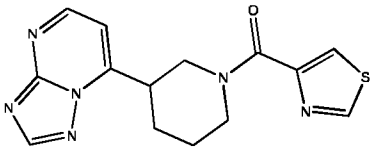
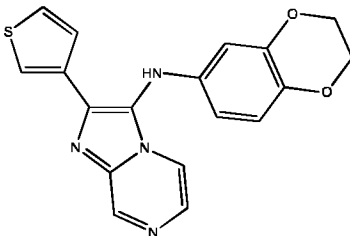
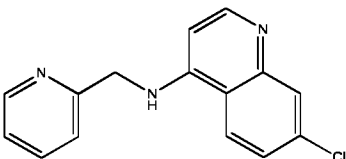
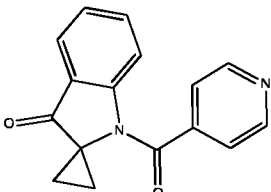
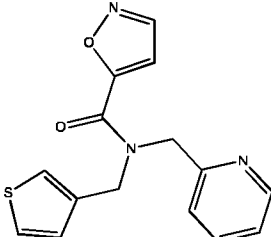
705	 <chem>Cc1nc(C)c(Nc2c3ccccc3oc2)n1</chem>
706	 <chem>Clc1ccc2cc(NC(=O)c3ccccc3)ccn2</chem>
707	 <chem>Cc1nc(C)c(NCc2c3ccccc3n2)n1-c4ccsc4</chem>
708	 <chem>Cc1nc(NCc2c3ccccc3n2)n1-c4ccsc4</chem>
709	 <chem>Cc1nc(C)c(Nc2c3cc4c(n2)ncn3C(=O)OC)c4</chem>

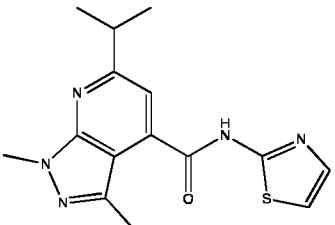
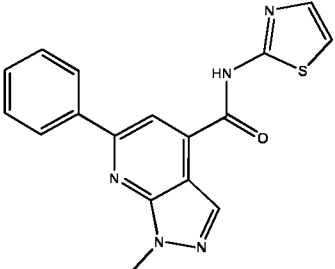
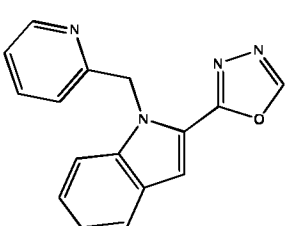
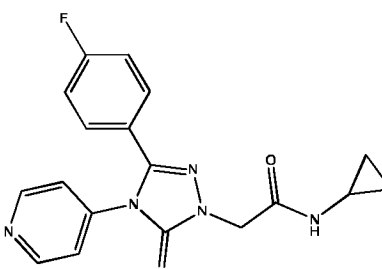
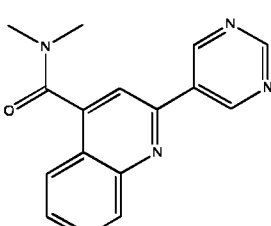
715	 <chem>CN(C)Cc1ccccn1C(=O)c2cc(N)ccn2</chem>
716	 <chem>NC1=NC2=CC=C(C=C2S1)N(C(=O)c3ccccc3)c4ccccc4</chem>
717	 <chem>COc1ccc(Nc2nc3ccncc3n2c4ccccc4)cc1</chem>
718	 <chem>CCCN(Cc1cccnc1)C(=O)c2ccncc2</chem>
719	 <chem>O=C1C=CC(S1)C(=O)N(Cc2ccccc22O1)c3ccccc3</chem>

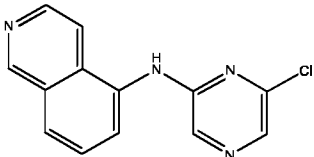
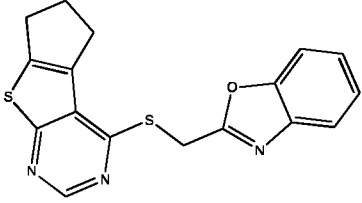
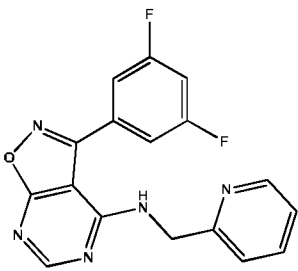
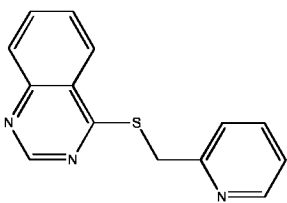
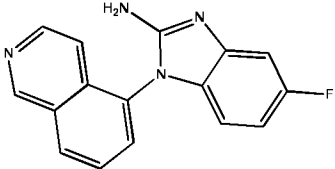
720	 <chem>Clc1ccc(cc1)C(=O)N(Cc2ccsc2)c3ccncc3</chem>
721	 <chem>Fc1ccc(cc1)C(=O)N(Cc2ccsc2)c3ccncc3</chem>
722	 <chem>c1ccncc1N(Cc2ccsc2)C(=O)c3c[nH]cn3</chem>
723	 <chem>Fc1ccc(cc1)S(=O)(=O)Nc2ccccc2C(=O)Nc3ccncc3</chem>
724	 <chem>Fc1ccccc1S(=O)(=O)Nc2cc3ccncc3cc2Nc4c5ccncc5cc4</chem>

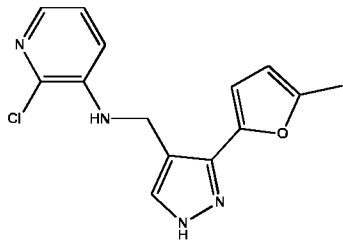
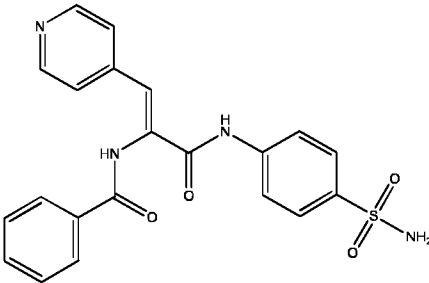
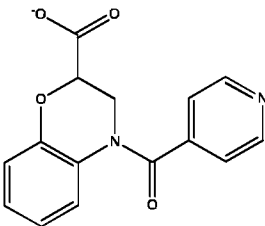
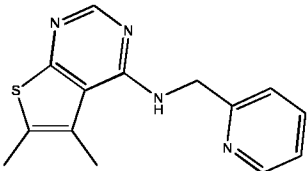
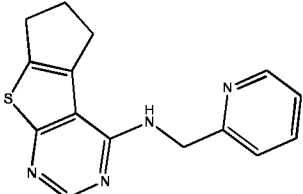
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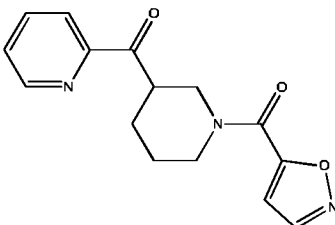
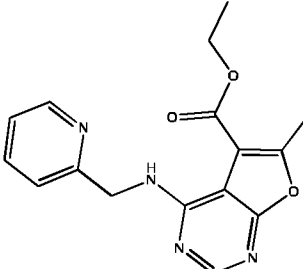
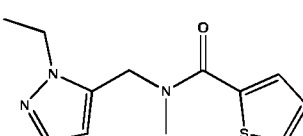
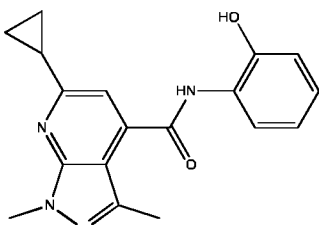
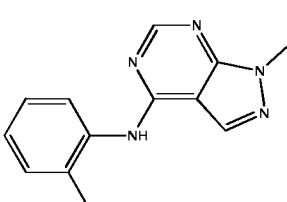
730	 <chem>CC(C)(C)CN(c1ccncc1)C(=O)c2ccc(F)cc2</chem>
731	 <chem>CCNc1ccncc1COc2ccccc2C(=O)N</chem>
732	 <chem>Nc1ccncc1COc2ccccc2C(=O)N</chem>
733	 <chem>Cc1ccncc1N1=NC2=CC=CC=C2N=C1N3C=NC=C3</chem>
734	 <chem>CNc1ccncc1CCSc2c3ccccc3o2</chem>

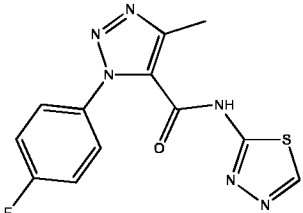
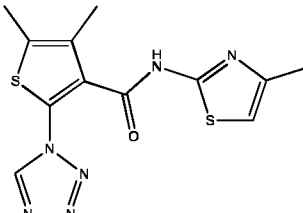
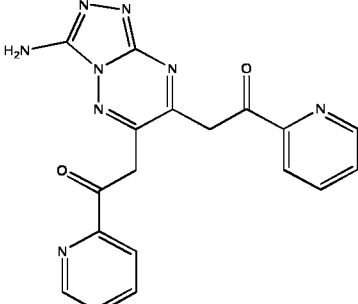
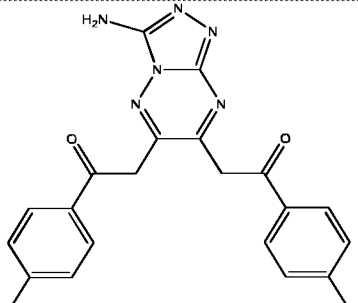
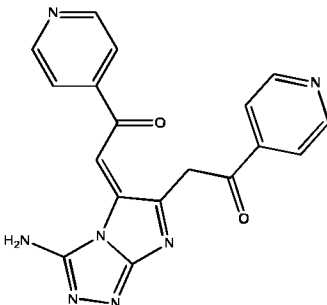
735	 <chem>c1cc[nH]c1C2CCN(CC2)C(=O)c3cc[nH]3</chem>
736	 <chem>c1cc[nH]c1-c2cc[nH]n2Nc3ccc4c(c3)OCO4</chem>
737	 <chem>c1cc[nH]c1-c2nc3ccccc3n2Nc4ccncc4</chem>
738	 <chem>O=C1C2CCN(C2)C1C(=O)c3ccncc3</chem>
739	 <chem>c1cc[nH]c1C(=O)Nc2cc[nH]n2</chem>

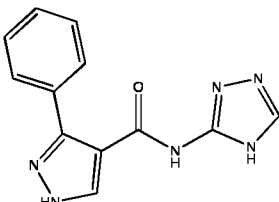
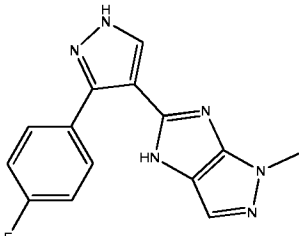
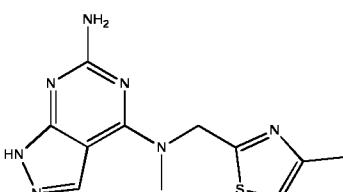
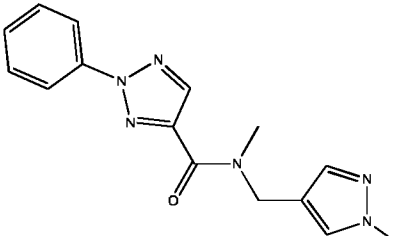
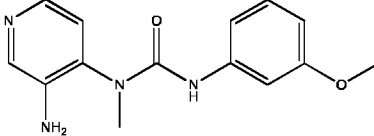
740	 <chem>CC(C)c1nc2c(nc1n2)C(C)=CNC(=O)c3ccsc3</chem>
741	 <chem>c1ccccc1c2nc3c(nc2n3)C(=C)C(=O)NC4=CC=CS4</chem>
742	 <chem>c1ccc2c(c1)c3c(nc2n3)C=C(C4=CC=CC=C4)C5=CC=CC=N5C6=CC=CC=N6</chem>
743	 <chem>Fc1ccc(cc1)c2nc3c(nc2n3)C(=O)N(CCC4CC4)C5=CC=CC=N5</chem>
744	 <chem>CN(C)C(=O)c1c2c(nc1n2)C(=C)C3=CC=CC=C3C4=CC=CC=N4</chem>

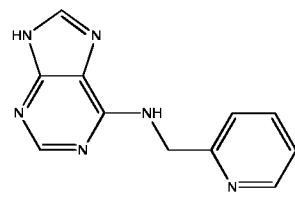
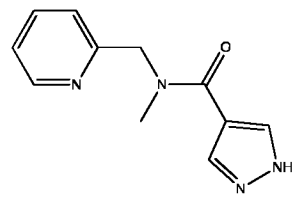
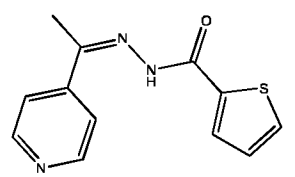
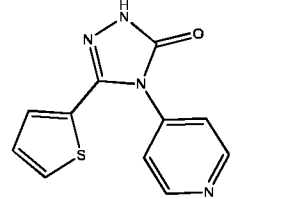
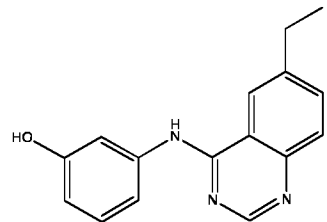
745	 <chem>Clc1ccncc1Nc2ccc3ccncc3c2</chem>
746	 <chem>c1ccc2c(c1)oc(CSc3c4c(c5ccncc35)C6=CC=CC=C6S6)n2</chem>
747	 <chem>Cc1cccnc1NC2=C3C(=C(C=C3)OC2=N)C4=CC(=CC=C4)F</chem>
748	 <chem>c1ccc2c(c1)nc(CSc3ccncc3)cc2</chem>
749	 <chem>Nc1nc2cc(F)ccc2n1C3=CC=CC=C3N4=CC=CC=C4</chem>

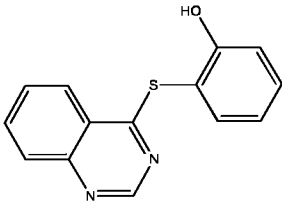
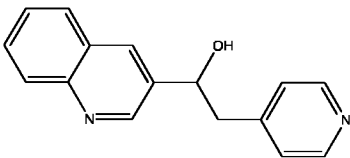
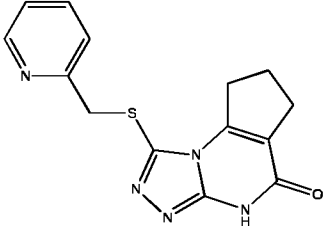
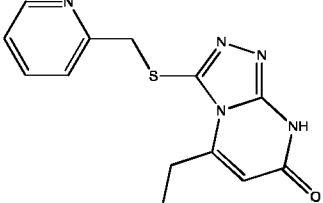
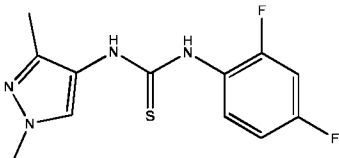
750	 <chem>Cc1cc(oc1)-c2nc3c(c[nH]3)CNc4cc(Cl)nc4</chem>
751	 <chem>NC(=O)S(=O)(=O)c1ccc(NC(=O)C(=Cc2ccncc2)NC(=O)c3ccccc3)cc1</chem>
752	 <chem>C1=CC=C2C(=C1)OC(C(=O)O)CN(C2)C(=O)c3ccncc3</chem>
753	 <chem>Cc1c2c(c3c1sc4c3ncnc45c2ccccc5N)NCC6=CC=CC=N6</chem>
754	 <chem>C1=CC=C2C(=C1)S3C(=C2)N=CN=C3C4C(C1)CC5C4=CC=CC5NCC6=CC=CC=N6</chem>

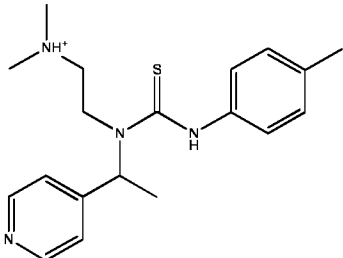
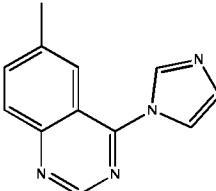
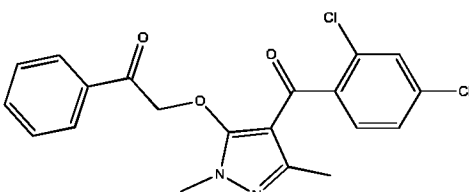
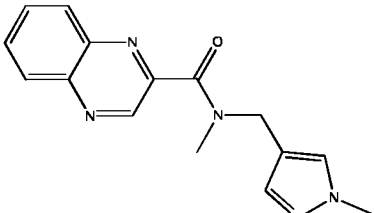
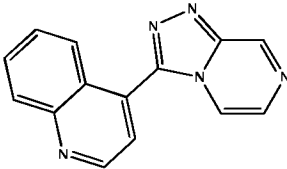
755	 <chem>O=C(c1ccncc1)C2CCN(C2)C(=O)c3ccoc3</chem>
756	 <chem>CCOC(=O)c1c2c(c1)nc3ccn3c2NCCc4ccncc4</chem>
757	 <chem>CCN(C)CCc1ccncc1C(=O)c2ccsc2</chem>
758	 <chem>CC1=CN(C2=CC=CC=C2C(=O)N1)C3=CC=CC=C3C4C3</chem>
759	 <chem>Oc1cccc(Nc2nc3c(ncn3C2)c4ccccc41)c5ccccc5</chem>

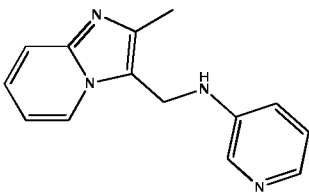
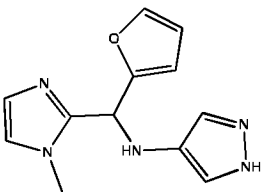
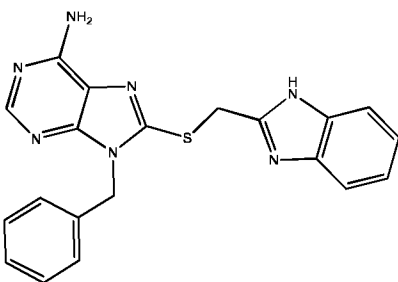
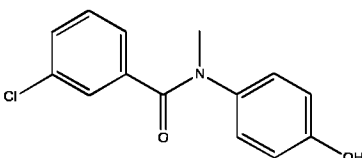
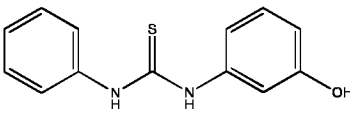
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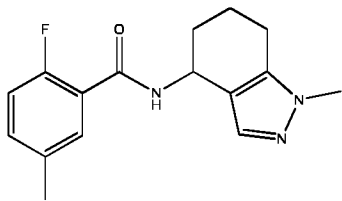
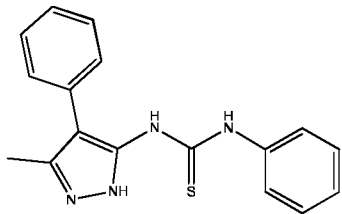
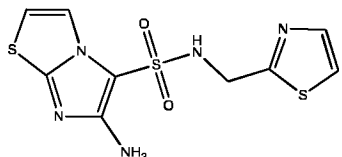
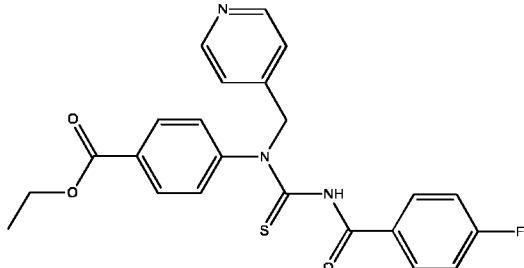
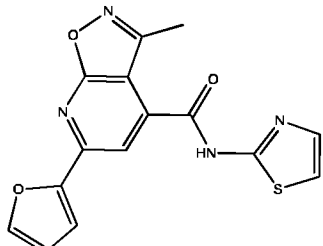
765	 <chem>c1ccc(cc1)-c2nc3cc[nH]c3n2C(=O)NC4=NC=CN4</chem>
766	 <chem>Fc1ccc(cc1)-c2nc3cc[nH]c3n2-c4c[nH]c5c4n(C)c[nH]5</chem>
767	 <chem>Cc1cc[nH]c2c1nc(N)n(C)cn2CC3=CN=C(S)C3C</chem>
768	 <chem>c1ccc(cc1)-n2nc3cc[nH]c3n2C(=O)N(C)CC4=CN=C(NC)C4</chem>
769	 <chem>Cc1cc(N)ncn1C(=O)NC2=CC=C(OC)C=C2</chem>

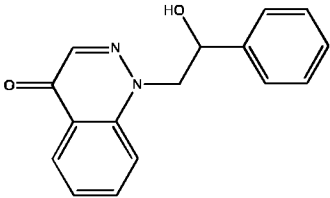
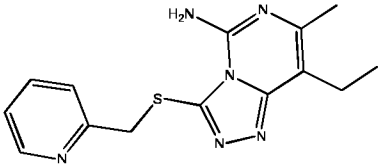
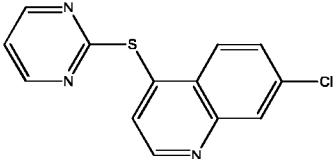
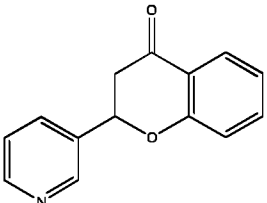
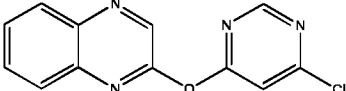
770	 <chem>Nc1nc2ncnc2n1NCc3cccnc3</chem>
771	 <chem>CN(Cc1cccnc1)C(=O)c2c[nH]c2</chem>
772	 <chem>C=C(NC(=O)c1ccsc1)c2cccnc2</chem>
773	 <chem>O=C1N=C(NC2=CC=CC=C2)N1c3ccsc3</chem>
774	 <chem>CC1=CC=C2C(=C1)N=CN=C2NC3=CC=C(O)C=C3</chem>

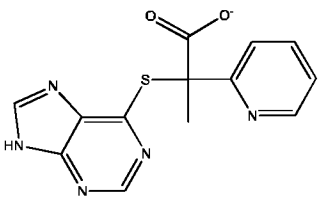
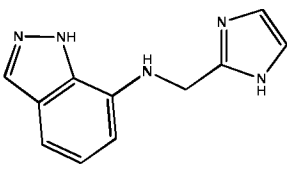
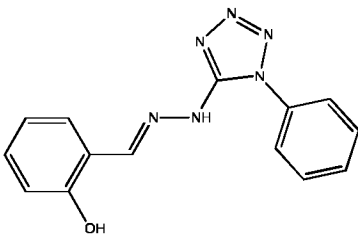
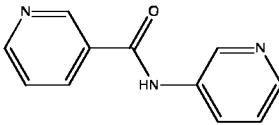
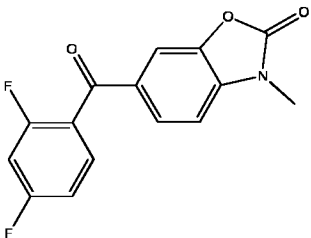
775	 <chem>Oc1ccccc1S2=NC3=CC=CC=C3N=C2</chem>
776	 <chem>OCC1=CC=CC=C1N=C2C=CC3=CC=CC=C3N=C21</chem>
777	 <chem>O=C1C=CC2=C1N3C(=N2)N=CN3SCC4=CC=CC=N4</chem>
778	 <chem>CCC1=CC(=O)N2C(=C1)N3C(=N2)N=CN3SCC4=CC=CC=N4</chem>
779	 <chem>C1=CN2C(=N1)N=CN2NC(=S)NC3=CC(=CC=C3F)F</chem>

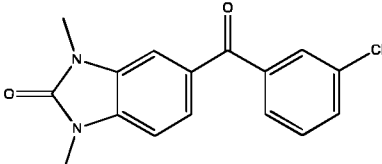
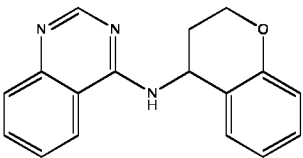
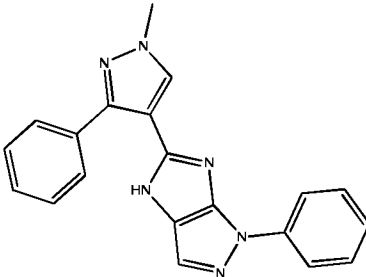
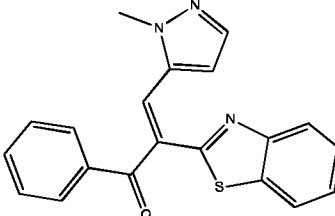
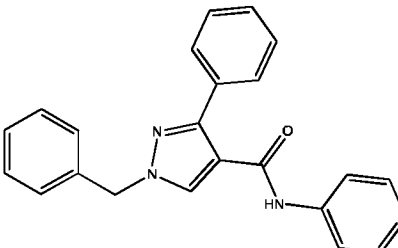
780	 <chem>CN(C)CCN(Cc1cccnc1)C(=S)Nc2ccc(C)cc2</chem>
781	 <chem>Cc1ccc(cc1)-c2nc3ccccc3n2-c4ncn4</chem>
782	 <chem>Cc1nn(C)c(C(=O)Oc2ccccc2)c1C(=O)c3cc(Cl)cc(Cl)c3</chem>
783	 <chem>Cc1nn(C)c1CCN(C)C(=O)c2cc3ccccc3nc2</chem>
784	 <chem>c1ccc2c(c1)nc(Cc3nn4cnc5ccncc45)n2</chem>

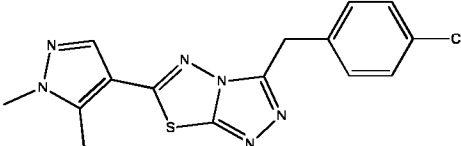
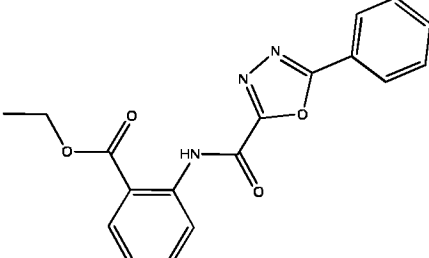
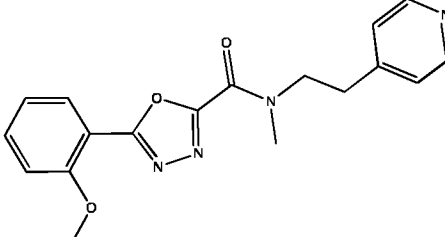
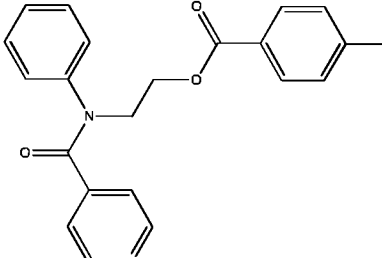
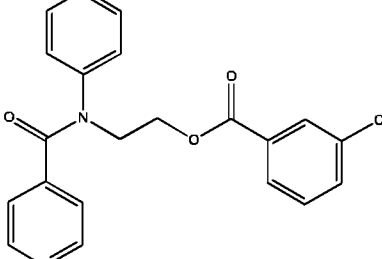
785	 <chem>Cc1nc2ccccc2n1CCNc3ccncc3</chem>
786	 <chem>Cn1cc[nH]1C(C2=CC=CC=O2)CNc3cc[nH]3</chem>
787	 <chem>Nc1nc2nc3c(ncn3Cc4ccccc4)c2n1SCCc5c[nH]c6ccccc56</chem>
788	 <chem>Oc1ccc(NC(=O)c2ccc(Cl)cc2)cc1</chem>
789	 <chem>Oc1ccc(NC(=S)Nc2ccccc2)cc1</chem>

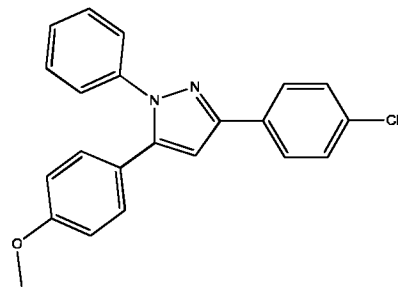
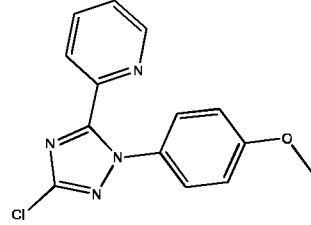
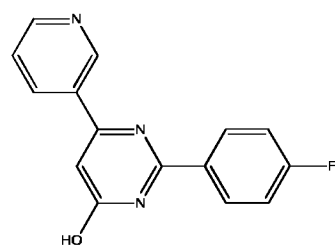
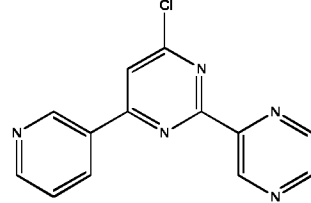
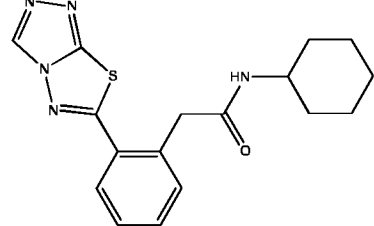
790	 <chem>Cn1cnc2ccccc2n1C(=O)Nc3ccc(F)cc3</chem>
791	 <chem>Cc1n[nH]c(c1)SC(=O)Nc2ccccc2</chem>
792	 <chem>Nc1nc2sc[nH]2c(S(=O)(=O)NCc3cc[nH]s3)n1</chem>
793	 <chem>CCOC(=O)c1ccc(NCc2ccncc2)cc1C(=O)Nc3ccc(F)cc3</chem>
794	 <chem>Cc1nc2ocn2c(c1)C(=O)Nc3cc[nH]s3c4ccoc4</chem>

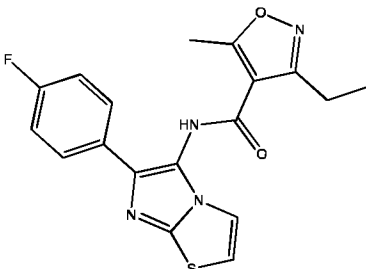
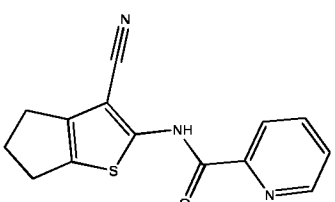
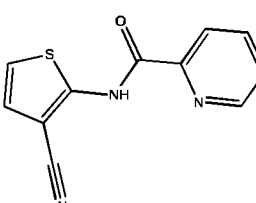
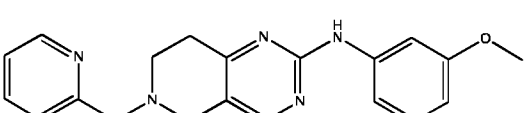
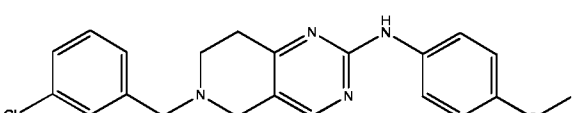
795	 <chem>O=C1C=CN(C(C1)c2ccccc2)C(O)c3ccccc3</chem>
796	 <chem>CC1=C(C)N2C(=N1)N=CN2SCC3=CC=CC=N3</chem>
797	 <chem>Clc1ccc2nc3ccccc3nc2c1SC4=CC=CC=N4</chem>
798	 <chem>O=C1C(=O)c2ccccc2O(C1)c3ccncc3</chem>
799	 <chem>Clc1ccncc1Oc2nc3ccccc3nc2</chem>

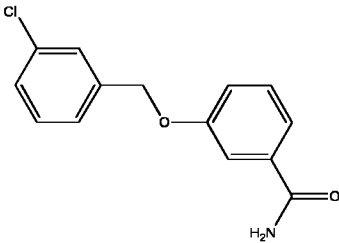
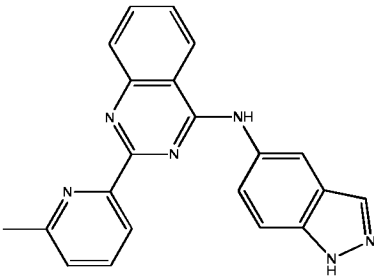
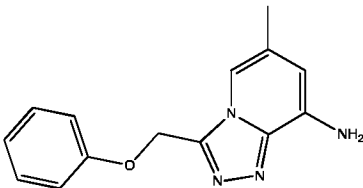
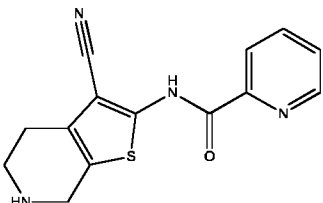
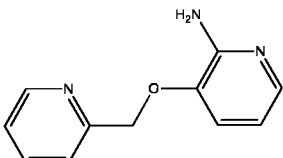
800	 <chem>CC(C(=O)[O-])SC1=NC2=NC=CC=C2N1c1ccncc1</chem>
801	 <chem>C1=CN=CN1CCNC2=NC3=CC=CC=C3N2</chem>
802	 <chem>Oc1ccccc1C=NN2C(=NN=N)N2c3ccccc3</chem>
803	 <chem>c1ccncc1C(=O)Nc2ccncc2</chem>
804	 <chem>CN1C(=O)Oc2ccc(cc21)C(=O)c3cc(F)cc(F)c3</chem>

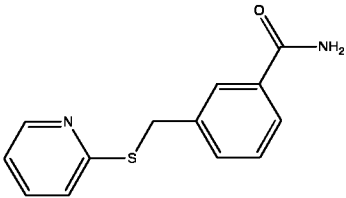
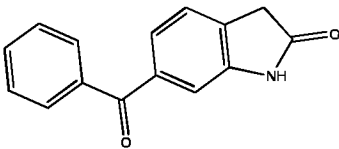
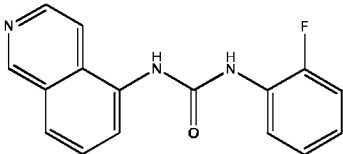
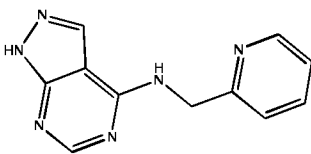
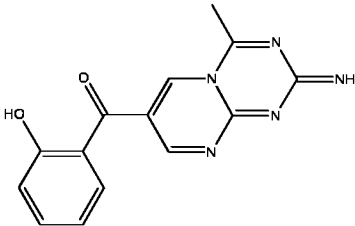
805	 <chem>CN1C(=O)c2ccc(cc2N1C)C(=O)c3ccc(Cl)cc3</chem>
806	 <chem>c1ccc2c(c1)cnc3c2cnc3Nc4c5ccccc5c6ccccc6OCC4</chem>
807	 <chem>CN1C=NC2=C1C(=C2)c3ccccc3N4C=CC5=C4N=CN=C5</chem>
808	 <chem>CN1C=NC2=C1C(=C2)c3ccccc3N4C=CC5=C4N=CC5</chem>
809	 <chem>c1ccc2c(c1)cnc3c2cnc3Nc4c5ccccc5c6ccccc6OCC4</chem>

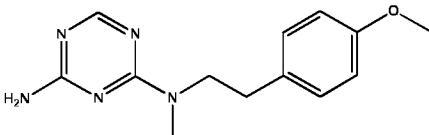
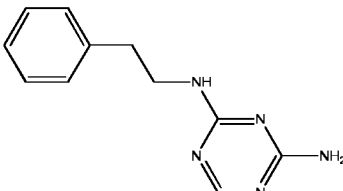
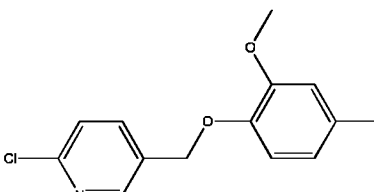
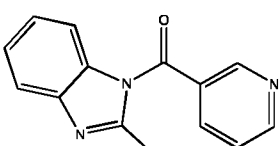
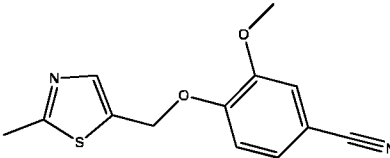
810	 <chem>CN1C=NC(C)=C1-c2nn[nH]2Cc3ccc(Cl)cc3</chem>
811	 <chem>CCOC(=O)c1ccccc1NC(=O)c2nn[nH]2c3ccccc3</chem>
812	 <chem>COc1cccc(c1)-c2nn[nH]2C(=O)N(C)CCc3ccncc3</chem>
813	 <chem>O=C(c1ccccn1)N(Cc2ccccc2)CCOC(=O)c3ccc(F)cc3</chem>
814	 <chem>O=C(c1ccccn1)N(Cc2ccccc2)CCOC(=O)c3cc(Cl)ccc3</chem>

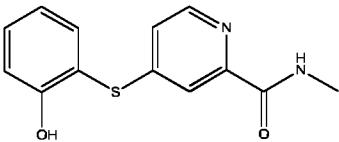
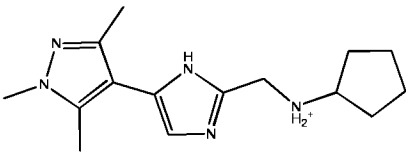
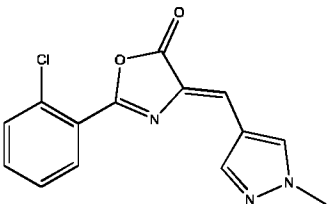
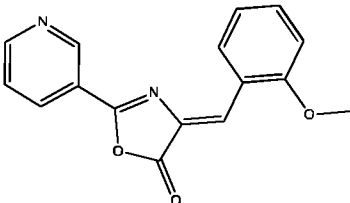
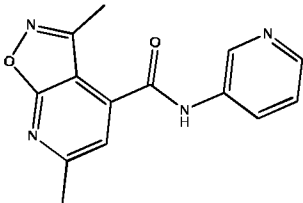
815	 <chem>COc1ccc(cc1)c2cc(Cc3ccc(Cl)cc3)nn2c4ccccc4</chem>
816	 <chem>COc1ccc(cc1)n2cc(Cl)nn2c3ccncc3</chem>
817	 <chem>Oc1cc(Cc2cc(F)cc2)nn(Cc3ccncc3)c1</chem>
818	 <chem>Clc1cc(Cc2ccncc2)nn(Cc3ccncc3)c1</chem>
819	 <chem>CC(=O)Nc1ccccc1C2=C3C=NC=N3SC2=C4C=NC=N4</chem>

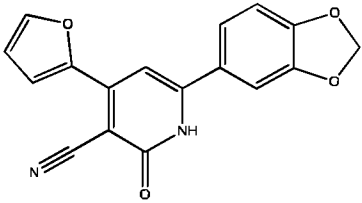
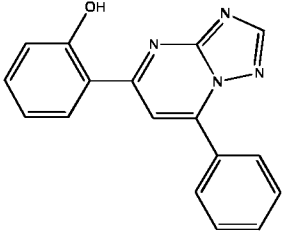
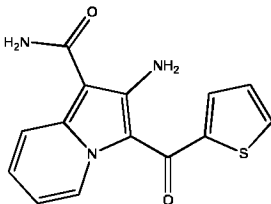
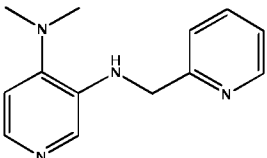
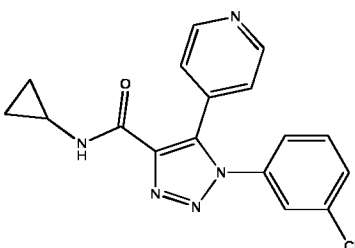
820	 <chem>CC1=C(C)OC(=N1)C(=O)Nc2nc3ccsc3n2-c4ccc(F)cc4</chem>
821	 <chem>N#Cc1c2ccccc2s1NC(=O)c3ccccn3</chem>
822	 <chem>N#Cc1cc(s1)NC(=O)c2ccccn2</chem>
823	 <chem>COC1=CC=C(C=C1)Nc2nc3cc4c(n2)CCN(CC4)Cc5cccnc5</chem>
824	 <chem>COC1=CC=C(C=C1)Nc2nc3cc4c(n2)CCN(CC4)Cc5ccc(Cl)cc5</chem>

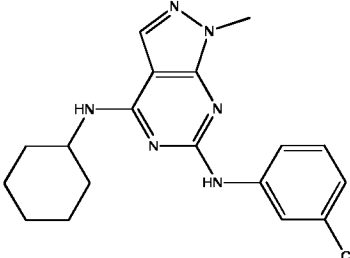
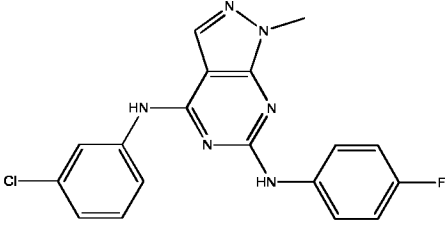
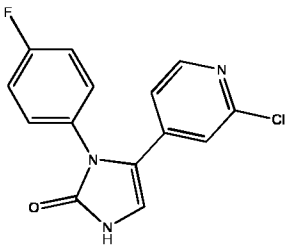
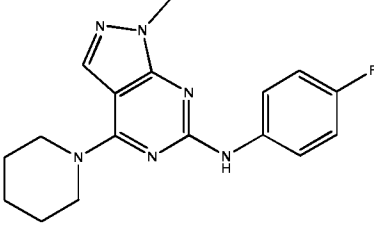
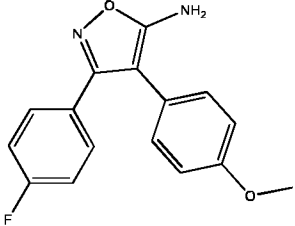
825	 <chem>NC(=O)c1ccc(OCCc2ccc(Cl)cc2)cc1</chem>
826	 <chem>Cc1ccc2nc3c(ncn3c2Nc4ccc5c(c4)nn[nH]5)cc1</chem>
827	 <chem>Cc1cc(N)nc2c1nnc2COCc3ccccc3</chem>
828	 <chem>N#Cc1c2c(s1)ccc3c2cnc3C(=O)Nc4cccnc4</chem>
829	 <chem>Nc1ccncc1OCC2=CC=CC=N2</chem>

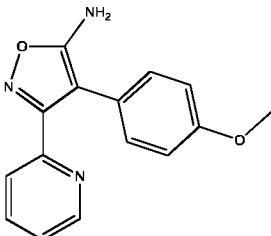
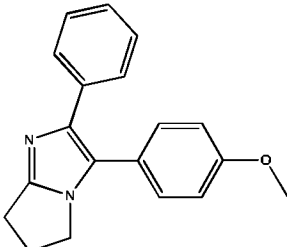
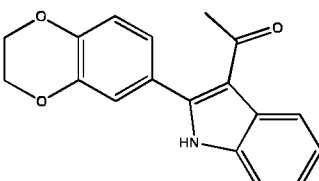
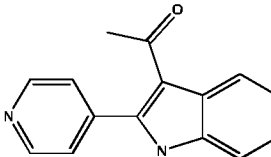
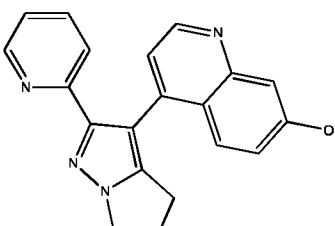
830	 <chem>NC(=O)c1ccc(cc1)CSc2ccncc2</chem>
831	 <chem>O=C1c2ccccc2C(=O)c3ccc4c(c3)ccc5[nH]c(=O)[nH]45</chem>
832	 <chem>Fc1ccccc1NC(=O)Nc2ccc3ncncc23</chem>
833	 <chem>c1ccc2ncncc2n1NCc3ccccn3</chem>
834	 <chem>Oc1ccccc1C(=O)c2cc3ncnc3nc2C4=NC(=N)C(=N)N4</chem>

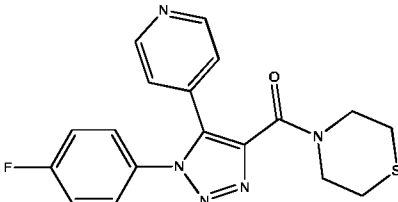
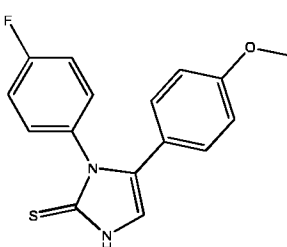
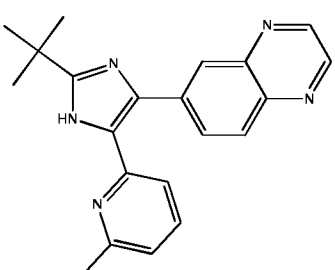
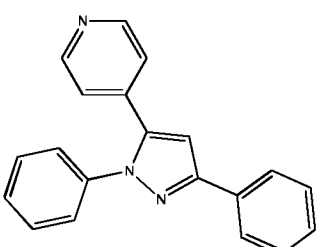
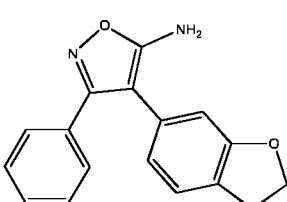
835	 <chem>CN(C)CCc1ccc(OC)cc1Nc2ncnc(N)c2</chem>
836	 <chem>Nc1ncnc(NC2=CC=CC=C2)nc1</chem>
837	 <chem>COc1ccc(cc1)OCc2cc(Cl)ncn2</chem>
838	 <chem>Cc1c2ccccc2n1C(=O)c3ccncc3</chem>
839	 <chem>COc1cc(C#N)ccc1OCc2ccsc2C</chem>

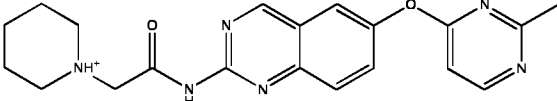
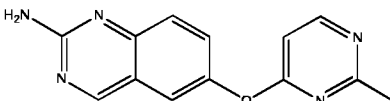
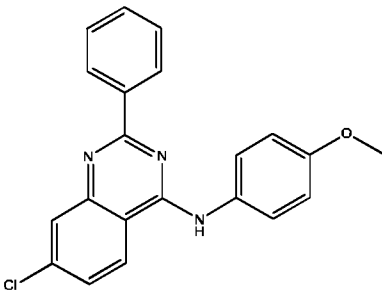
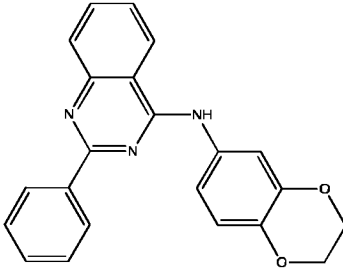
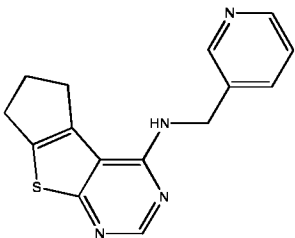
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841	 <chem>CN1C=NC2=C1C(=C(C)N2)CCN3CCCC3</chem>
842	 <chem>CN1C=NC2=C1C(=C(C)N2)C=C3C(=O)OC(=N3)c4ccccc4Cl</chem>
843	 <chem>COc1ccccc1C=C2C(=O)OC(=N2)c3cccnc3</chem>
844	 <chem>CN1C=NC2=C1C(=C(C)N2)C(=O)Nc3cccnc3</chem>

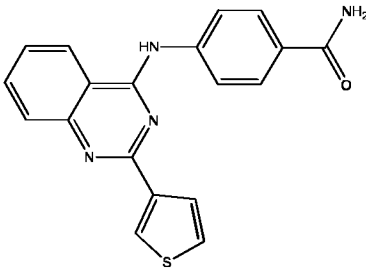
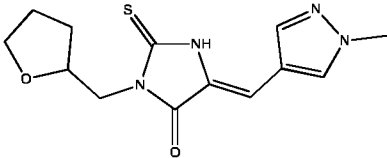
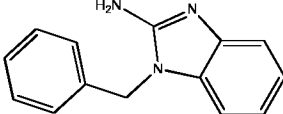
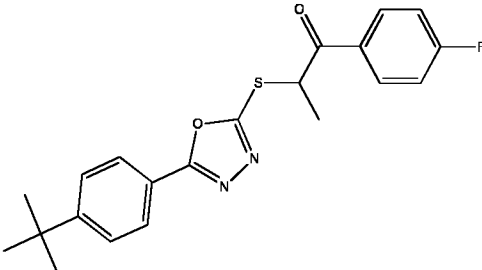
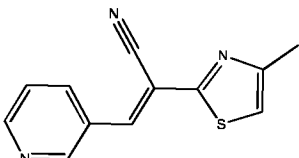
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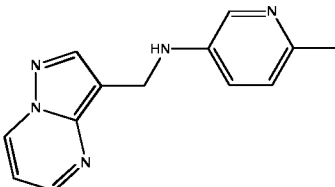
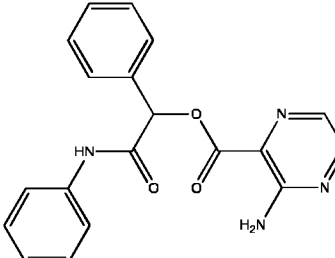
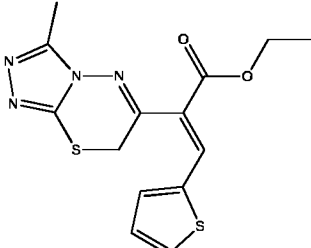
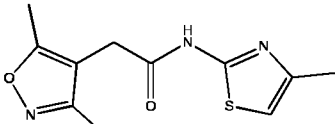
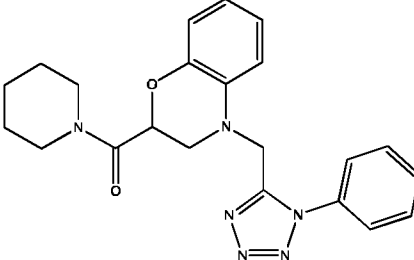
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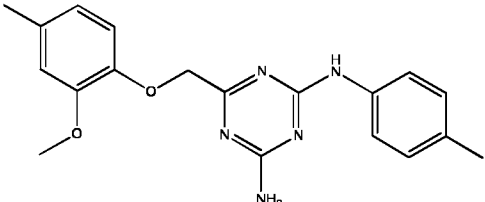
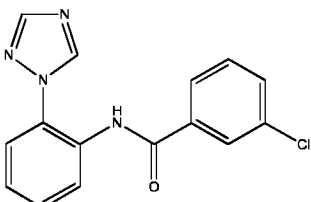
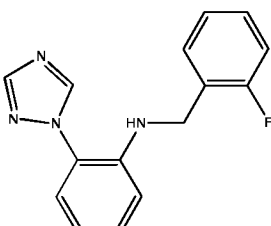
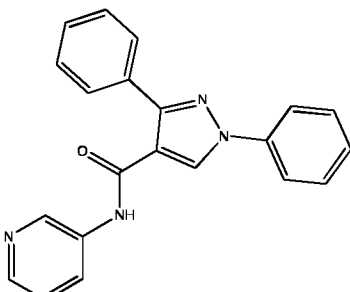
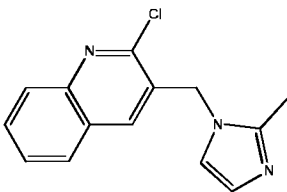
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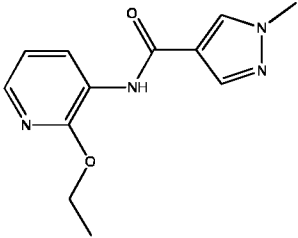
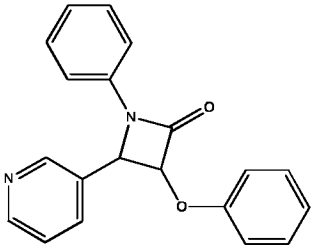
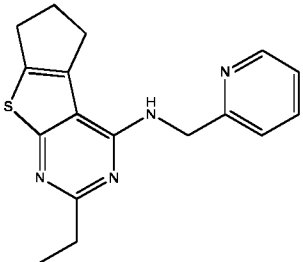
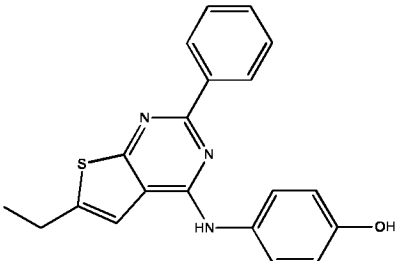
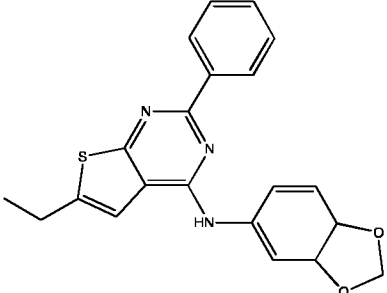
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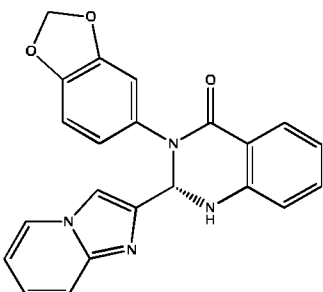
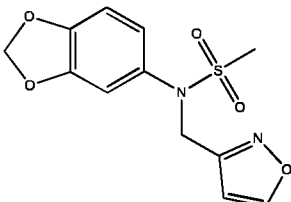
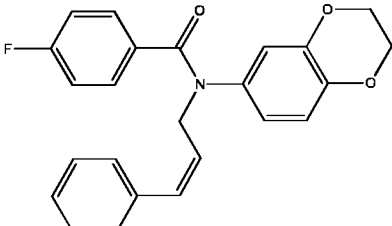
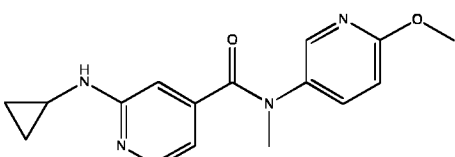
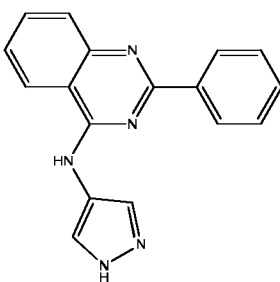
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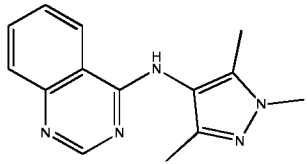
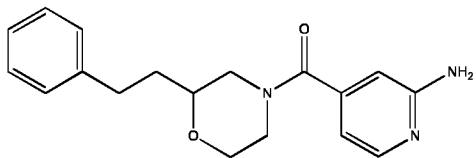
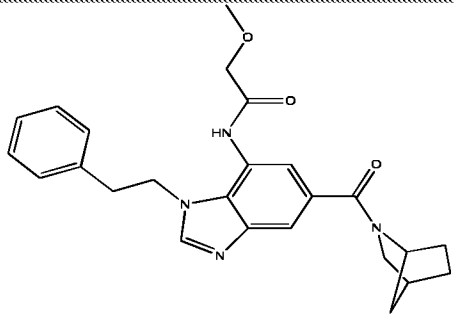
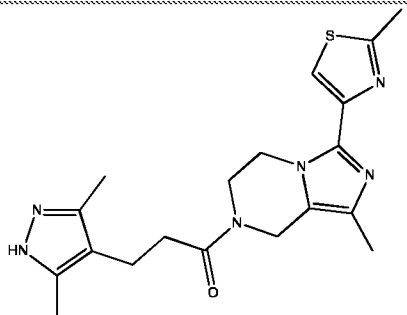
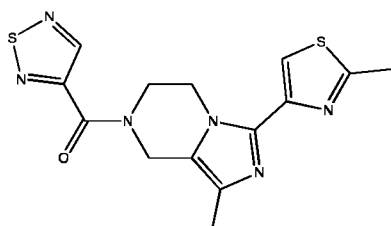
870	 <chem>NC(=O)c1ccc(Nc2nc3ccccc3nc2c4ccsc4)cc1</chem>
871	 <chem>Cc1cc(C=C2C(=O)NC(S2)CC3CCO3)nn1</chem>
872	 <chem>Nc1nc2ccccc2n1Cc3ccccc3</chem>
873	 <chem>CC(C)C(=O)c1ccc(F)cc1SC2=NC3=CC=C(C(C)(C)C)C=N3O2</chem>
874	 <chem>Cc1ccsc1C(=C2C#N)C=C2c3ccncc3</chem>

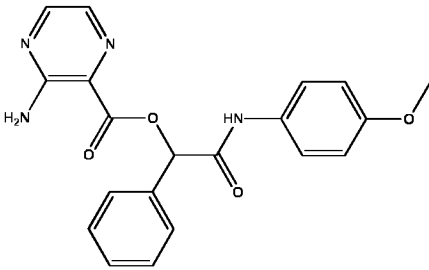
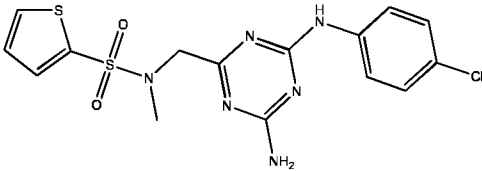
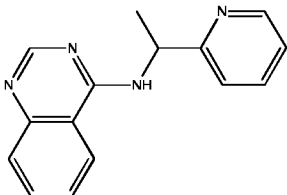
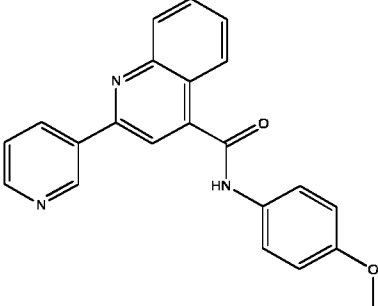
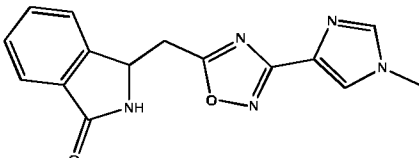
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876	 <chem>Nc1ccnc(C(=O)OC(C(=O)Nc2ccccc2)c3ccccc3)c1</chem>
877	 <chem>CCOC(=O)C1=C(C2SC3=NC4=C(N3)N=CN=C4S2)C=C5C=CC=C5S1</chem>
878	 <chem>Cc1ccsc1NC(=O)CC2=C(C)ON=N2</chem>
879	 <chem>c1ccc(cc1)n2ncnc2CN3CCc4c(c3)oc5ccccc45C(=O)N6CCCCC6</chem>

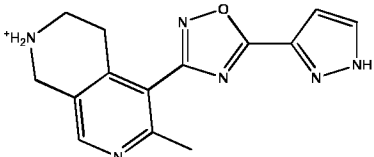
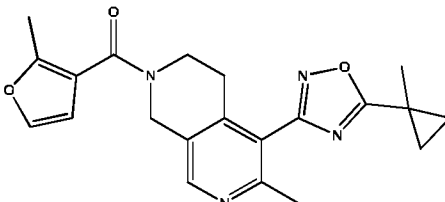
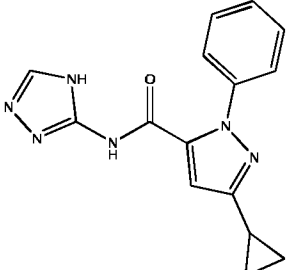
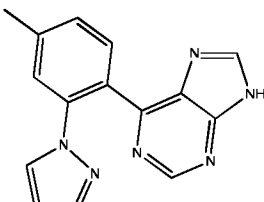
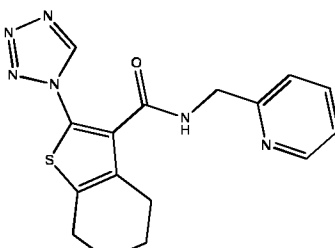
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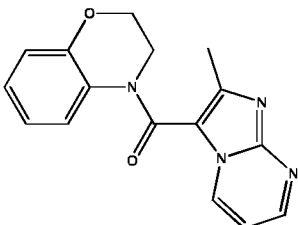
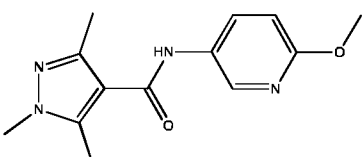
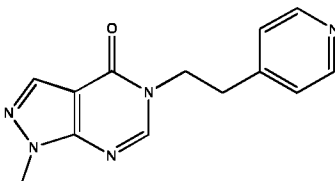
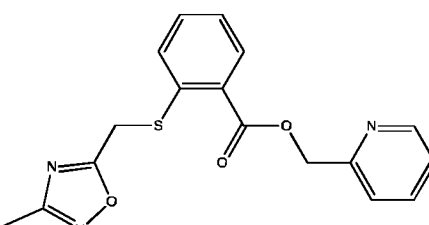
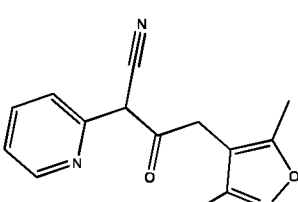
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886	 <chem>c1ccccc1N2C(=O)C(c3ccncc3)C2Oc4ccccc4</chem>
887	 <chem>CCc1cc2nc(NCc3ccncc3)c4sc5c2ccccc5n14</chem>
888	 <chem>CCc1cc2nc(Nc3ccc(O)cc3)c4c(c1)sc5c2c(c4)nc6ccccc6n5</chem>
889	 <chem>CCc1cc2nc(Nc3ccc4c(c3)OCO4)c4c(c1)sc5c2c(c4)nc6ccccc6n5</chem>

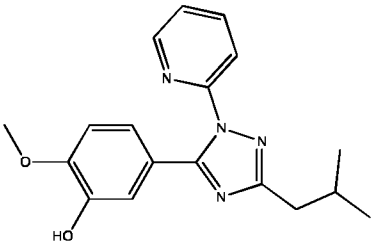
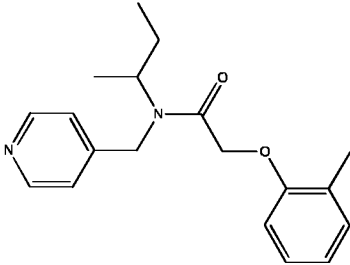
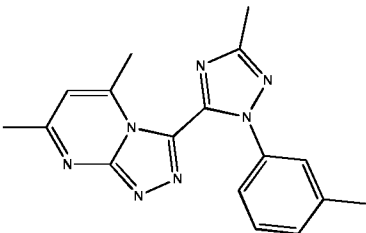
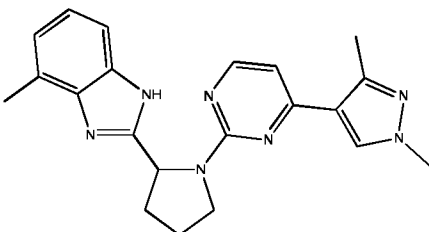
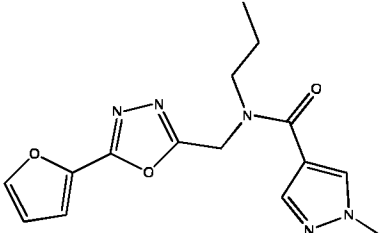
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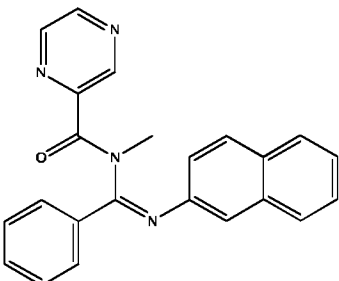
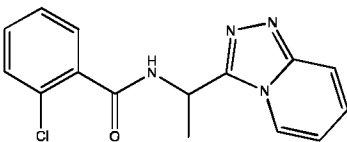
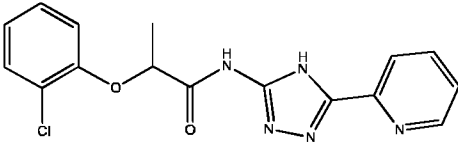
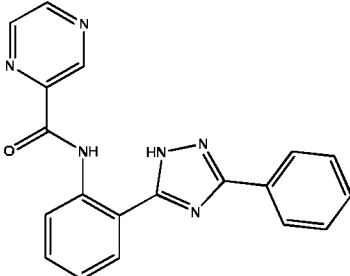
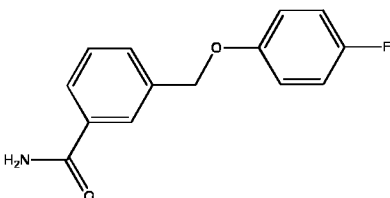
895	 <chem>CN1C=NC(C)=N1NC2=NC=CC=C3C=NC=N23</chem>
896	 <chem>NC1=CC=C(C=C1)C(=O)N2CCOC(CC2)Cc3ccccc3</chem>
897	 <chem>O=C1C(=C(C=C1)C(=O)N2C3CC4C(C3)CC4N2)C(=C(C=C1)NC(=O)CO)C5=CC=CC=C5</chem>
898	 <chem>CN1C=NC(C)=N1CCC(=O)N2CCN(C2)CC3=C(C)N=CN3C4=CC=CC=C4S</chem>
899	 <chem>CN1C=NC(C)=N1CC2(CCN(C2)C3=CC=CC=C3S)C4=CC=CC=C4S</chem>

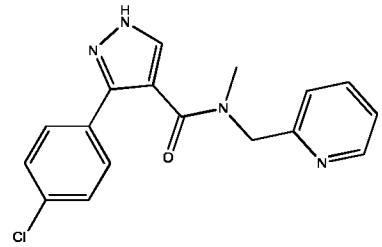
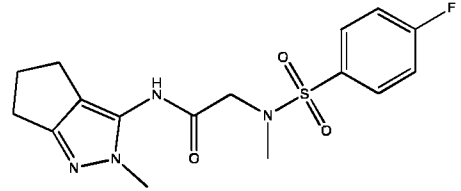
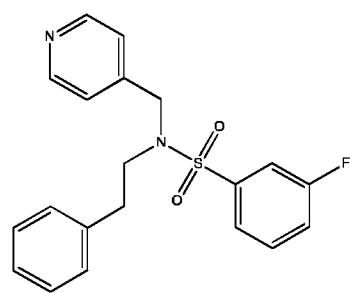
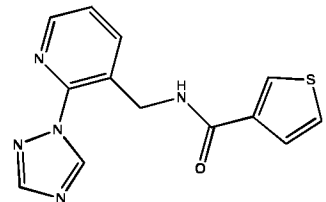
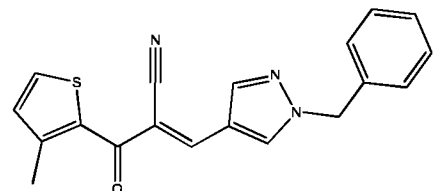
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901	 <chem>CN1C(S(=O)(=O)c2ccsc2)CCc3nc(N)cnc3Nc4ccc(Cl)cc4</chem>
902	 <chem>Cc1cccnc1NC2=CN3C=CC=CC=C3N2</chem>
903	 <chem>COc1ccc(NC(=O)c2c3ccccc3nc2c4cccnc4)cc1</chem>
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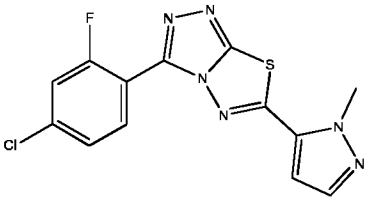
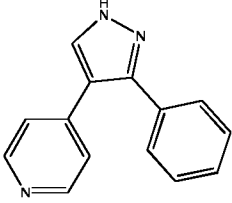
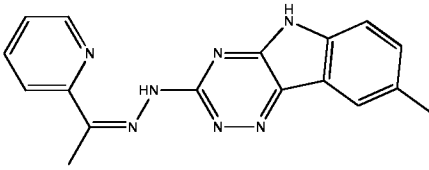
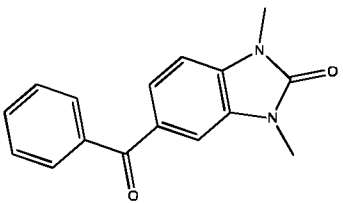
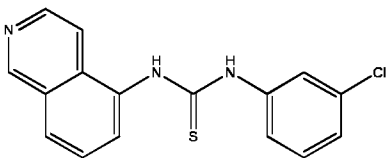
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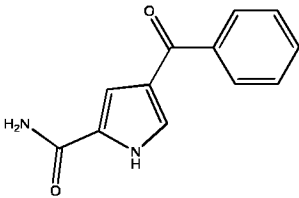
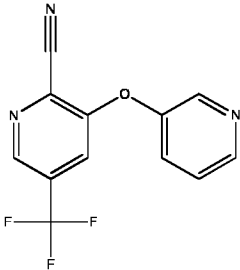
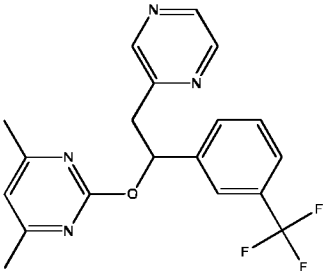
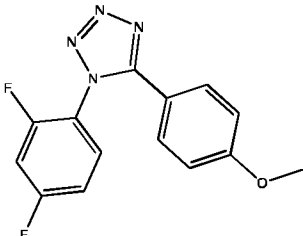
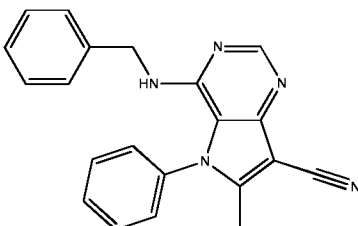
910	 <chem>Cc1nc2ccncc2n1C(=O)N3Cc4ccccc4O3</chem>
911	 <chem>COc1ccncc1NC(=O)c2c(C)n(C)c(C)n2</chem>
912	 <chem>Cn1c2ccncc2c(=O)n1CCCc3ccncc3</chem>
913	 <chem>Cc1nc2ccncc2o1SC(=O)c3ccccc3C(=O)OCc4ccncc4</chem>
914	 <chem>Cc1nc2ccncc2o1CC(=O)C(C#N)c3ccncc3</chem>

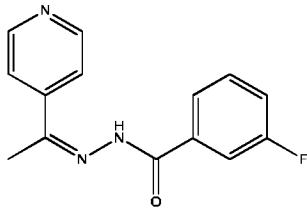
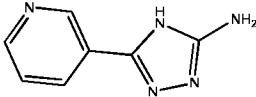
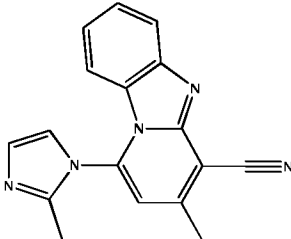
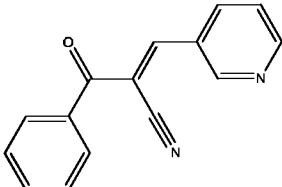
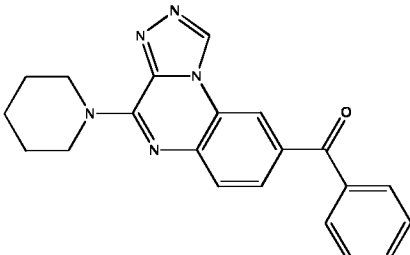
915	 <chem>CC(C)CN1=NC=C(N1c2ccc(OC)cc2)c3ccncc3</chem>
916	 <chem>CC1=CC=C(C=C1)COCC(=O)N(CC)CC2=CC=CC=N2</chem>
917	 <chem>CC1=CC=C(C=C1)N1C=NC2=C(N1)C=NC2C3=NC=CC=C3C</chem>
918	 <chem>CC1=CC=C(C=C1)N1C=NC2=C(N1)C=NC2C3=NC=CC=C3C</chem>
919	 <chem>CC1=CC=C(C=C1)N1C=NC2=C(N1)C=NC2C3=NC=CC=C3C</chem>

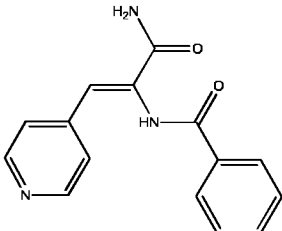
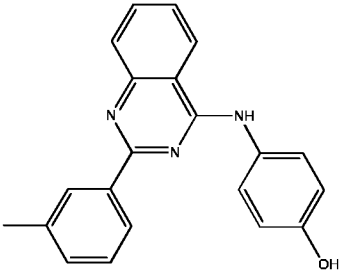
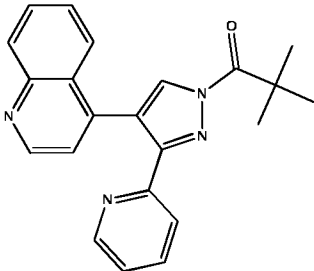
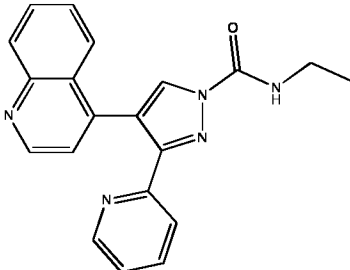
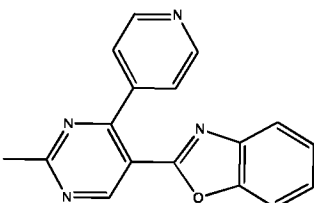
920	 <chem>CN(C(=O)c1ccncc1)C(=N)c2ccc3ccccc3c2</chem>
921	 <chem>CC1=CN2C(=N1)C=CC=C2NC(=O)c3cc(Cl)ccc3</chem>
922	 <chem>CC(=O)Nc1nn[nH]1C2=CC=CC=N2COc3cc(Cl)ccc3</chem>
923	 <chem>c1ccc(cc1)-c2nn[nH]2-c3ccccc3NC(=O)c4ccncc4</chem>
924	 <chem>NC(=O)c1ccc(cc1)COc2ccc(F)cc2</chem>

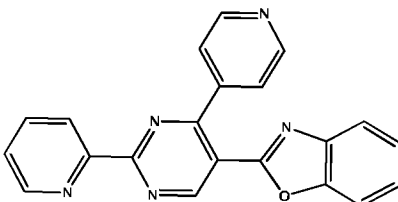
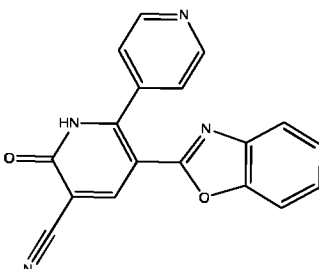
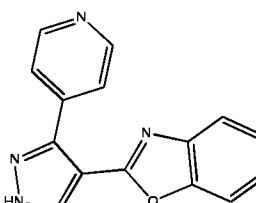
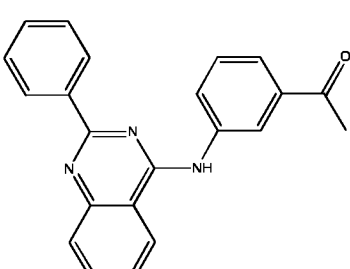
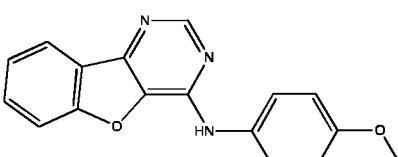
925	 <chem>CCN(C)Cc1ccncc1C(=O)c2c[nH]c3cc(Cl)ccc32</chem>
926	 <chem>CN1C=NC2CCCC12NC(=O)CN(C)CS(=O)(=O)c3ccc(F)cc3</chem>
927	 <chem>CN(C)CCc1ccccc1NS(=O)(=O)c2ccc(F)cc2</chem>
928	 <chem>c1cc[nH]c1CNC(=O)c2ccsc2</chem>
929	 <chem>Cc1ccsc1C(=O)C#N/C=C/c2c[nH]c3ccccc32</chem>

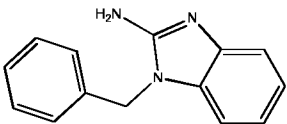
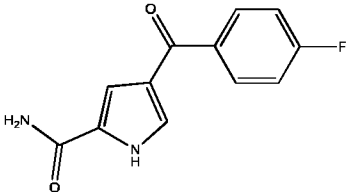
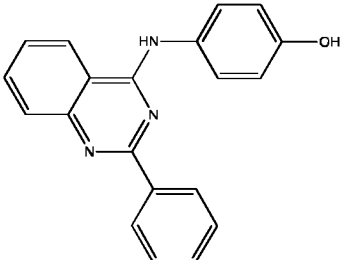
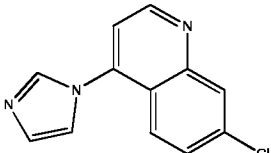
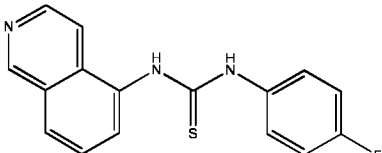
930	 <chem>Fc1cc(Cl)ccc1-c1nn[nH]s1-c1cc[nH]n1C</chem>
931	 <chem>c1ccc(cc1)-c2nc[nH]2-c3ccncc3</chem>
932	 <chem>Cc1ccncc1=N=Nc1nn[nH]s1-c1ccc2c(c1)[nH]cnc2C</chem>
933	 <chem>Cn1c(=O)[nH]c2cc(C(=O)c3ccccc3)ccc21C</chem>
934	 <chem>Cn1c[nH]c1-c1ccncc1C(=O)Nc2ccc(Cl)cc2</chem>

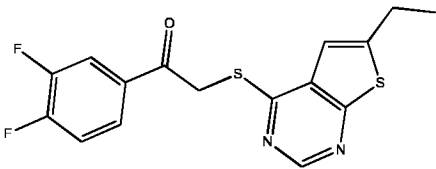
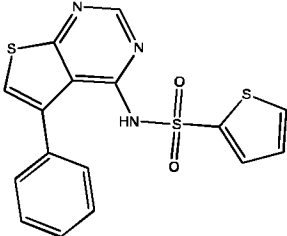
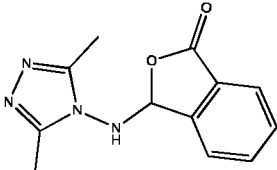
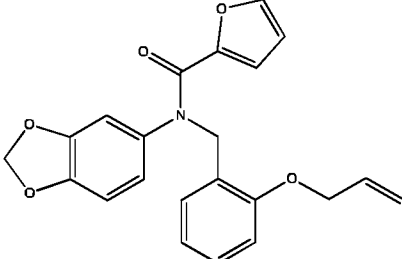
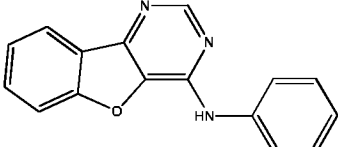
935	 <chem>O=C(N)c1cc(C(=O)c2ccccc2)c[nH]1</chem>
936	 <chem>N#Cc1cc(OC2=CC=CC=N2)nc(C(F)(F)F)n1</chem>
937	 <chem>CC1=CC(=C(C)N=C1OC2C(C=CC2)N3C=CC=CC=C3C(F)(F)F)CC4=CC=CC=N4</chem>
938	 <chem>COc1ccc(cc1C2=NN=N2N3C=CC(=C3)F)F</chem>
939	 <chem>Cc1c(C#N)c2c(c1n(C2)c3ccccc3)nc4ccccc4Nc5ccccc5</chem>

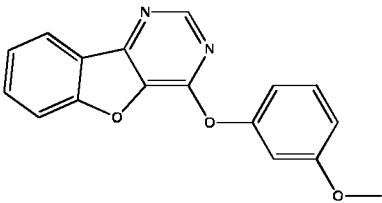
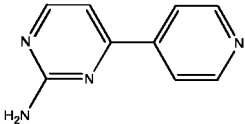
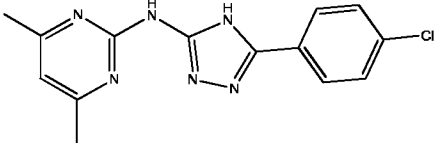
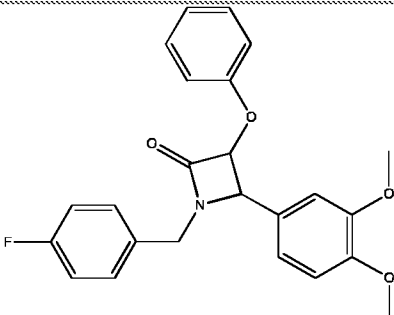
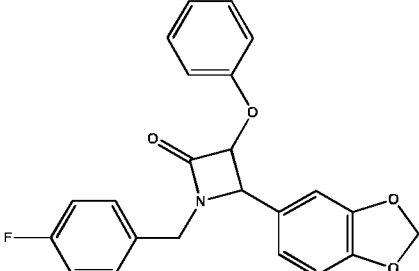
940	 <chem>CC(=N)Nc1ccc(F)cc1C(=O)Nc2ccncc2</chem>
941	 <chem>Nc1nn[nH]c1-c2ccncc2</chem>
942	 <chem>Cc1c(C#N)c2c(c1)n3ccccc3n2N4C=CN=C4</chem>
943	 <chem>N#CC(=Cc1ccncc1)C(=O)c2ccccc2</chem>
944	 <chem>O=C(c1ccc2c(c1)c3ccnnc3n2)C(=O)c4ccccc4N5CCCCC5</chem>

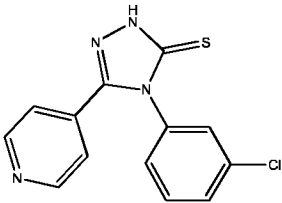
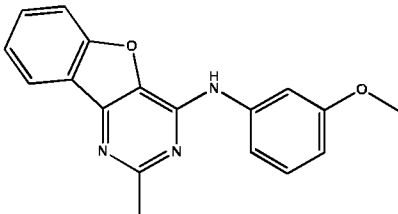
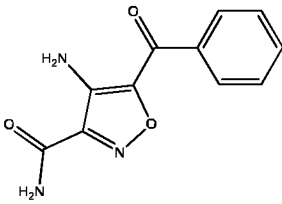
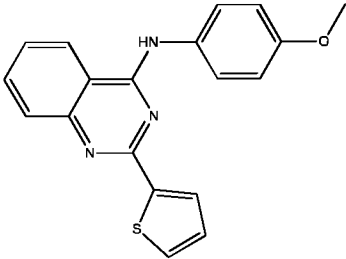
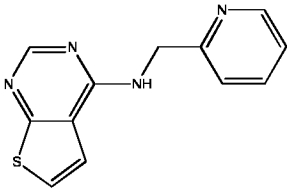
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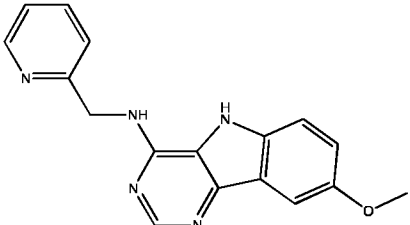
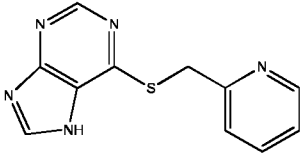
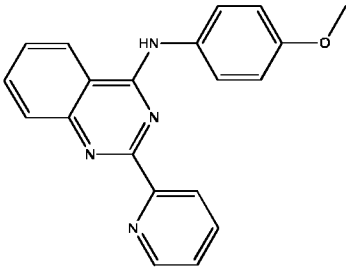
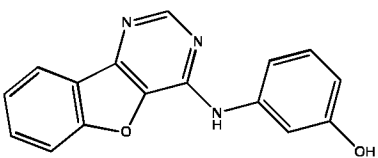
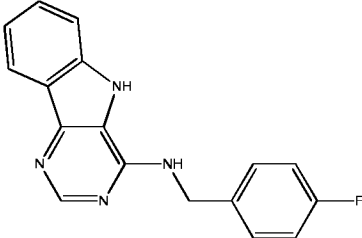
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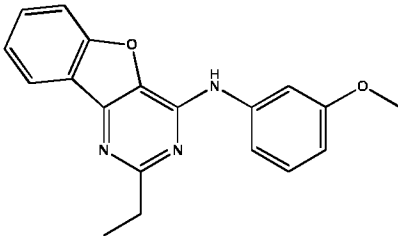
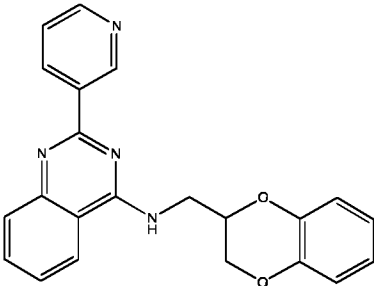
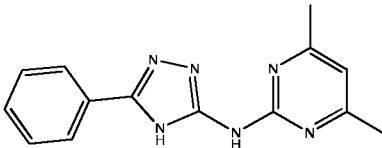
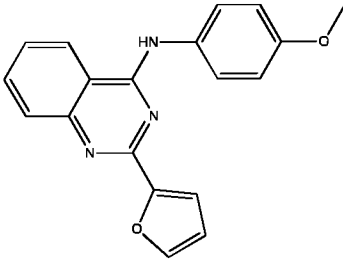
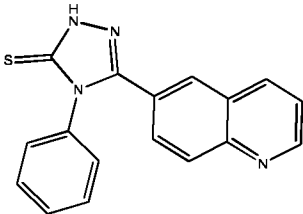
955	 <chem>Nc1nc2ccccc2n1CCc3ccccc3</chem>
956	 <chem>NCC(=O)c1cc(C(=O)c2ccc(F)cc2)c[nH]1</chem>
957	 <chem>Oc1ccc(Nc2nc3ccccc3nc2-c4ccccc4)cc1</chem>
958	 <chem>Clc1ccc2c(c1)c3ccncc3n2C4C=CN=C4</chem>
959	 <chem>Fc1ccc(NC(=S)Nc2ccc3ccncc3cc2)cc1</chem>

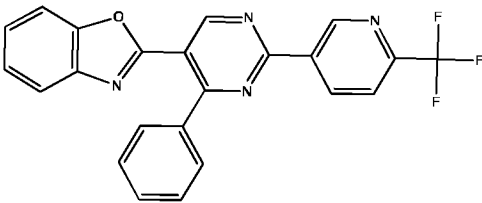
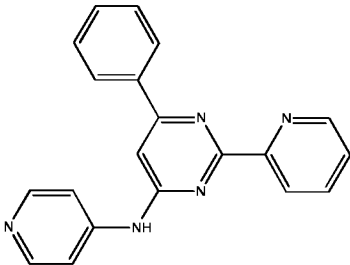
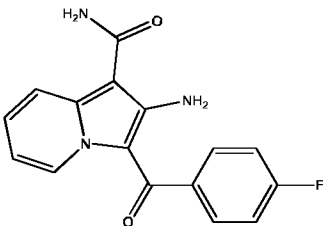
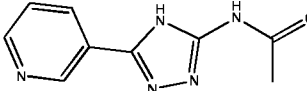
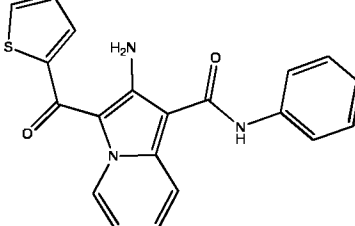
960	 <chem>CCc1cc2ncnc2s1SCC(=O)c3cc(F)cc(F)c3</chem>
961	 <chem>c1cc2nc3cc(s3)cc(NC(=O)S4=CC=CC=C4S2)c1-c5ccccc5</chem>
962	 <chem>Cc1nc(C)n(C)c1NC2C(=O)Oc3ccccc23</chem>
963	 <chem>C=CCOc1ccccc1CN(C(=O)c2ccoc2)c3ccc4c(c3)OCO4</chem>
964	 <chem>c1ccc(cc1)Nc2nc3cc4ccccc4oc3cc2</chem>

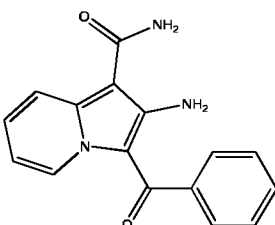
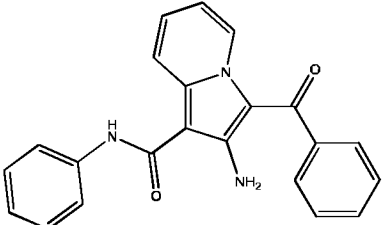
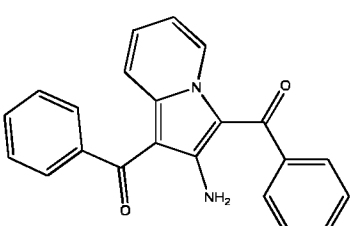
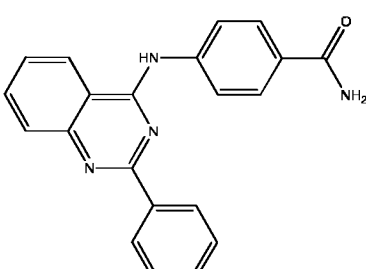
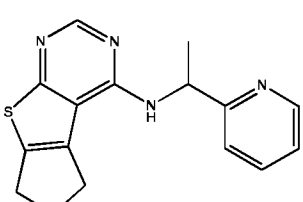
965	 <chem>COc1ccc(Oc2nc3ccccc3o2)cc1</chem>
966	 <chem>Nc1nc(NC2=CC=CC=N2)ncn1</chem>
967	 <chem>Cc1nc(C)c(NC2=NC=CC(=C2)C3=CC=C(C=C3)Cl)nc1</chem>
968	 <chem>COc1cc(OC)ccc1C2C(=O)N(Cc3ccc(F)cc3)C2Oc4ccccc4</chem>
969	 <chem>c1ccc2c(c1)OCO2C3C(=O)N(Cc4ccc(F)cc4)C3Oc5ccccc5</chem>

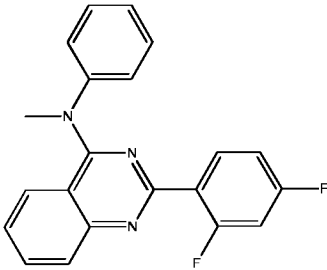
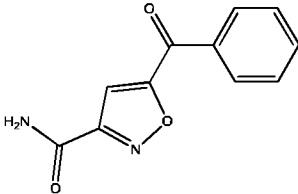
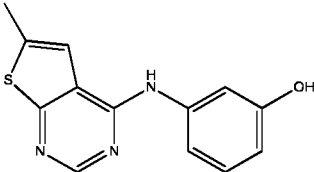
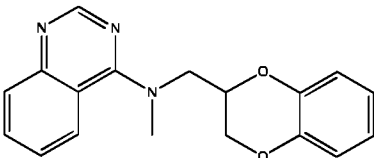
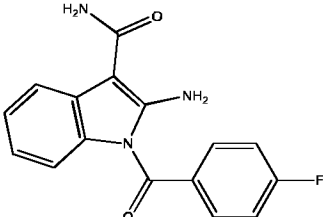
970	 <chem>C1=NC(=C(C=C1)N2C(=N1C(=N2)C(=S1)C3=CC=CC=C3Cl)C4=CC=CC=N4</chem>
971	 <chem>COc1ccc(Nc2nc3ccccc3oc2C)c(C)c1</chem>
972	 <chem>NC(=O)c1nc2ccccc2o1C(=O)N</chem>
973	 <chem>COc1ccc(Nc2nc3ccccc3n2C4=CC=CC=S4)cc1</chem>
974	 <chem>C1=CC=C(C=C1N2C(=N3C=CC(=N3)SC2=N1)NC4=CC=CC=N4</chem>

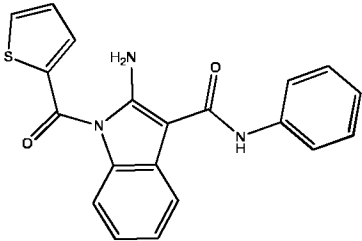
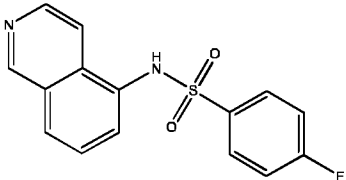
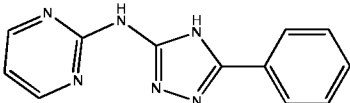
975	 <chem>COc1ccc2c(c1)c3c(c2)ncn3NCc4ccncc4</chem>
976	 <chem>c1ccncc1SCc2ncnc3[nH]cnc23</chem>
977	 <chem>COc1ccc(cc1)NC2=NC(=C(NC3=CC=CC=C3)N=C2C4=CC=CC=C4</chem>
978	 <chem>Oc1ccc(cc1)NC2=NC(=C3C=C2Oc4ccccc43</chem>
979	 <chem>Fc1ccc(cc1)NC2=NC(=C3C=C2Nc4ccccc43</chem>

980	 <chem>CCc1nc2c(nc1O2)Nc3ccc(OC)cc3</chem>
981	 <chem>c1ccc2c(c1)c(c3ccncc3)nc2NCC4OCc5ccccc4O5</chem>
982	 <chem>Cc1nc2nc(Nc3cnc(C)c3)nn2C4=CC=CC=C4</chem>
983	 <chem>COc1ccc(Nc2c3ccccc3nc2C4=CC=CC=C4O4)cc1</chem>
984	 <chem>c1ccc2c(c1)c(c3nn[nH]3)nc2Cc4ccc5ncncc45</chem>

985	 <chem>c1ccc2nc3c(cc12)c4ccccc4n3c5cc6cc(C(F)(F)F)ccn6</chem>
986	 <chem>c1ccc2nc3c(cc12)c4ccccc4n3c5cc6cc(Nc7ccncc7)ccn6</chem>
987	 <chem>Nc1ccc(cc1)C(=O)c2c3c(ccc4c3ncc5ccccc45)c(c2)C(=O)N</chem>
988	 <chem>CC(=O)Nc1nc2c(ncn2c1c3ccncc3)C4=CC=CC=N4</chem>
989	 <chem>Nc1c2c(ccc3c2ncc4ccccc34)C(=O)c5ccsc5C1=CC=CC=N1C(=O)Nc2ccccc2</chem>

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995	 <chem>CN(C1=NC2=CC=CC=C2N=C1C3=CC=C(C=C3)F)C4=CC=C(C=C4)F</chem>
996	 <chem>NC(=O)c1nc2oc(cc12)C(=O)c3ccccc3</chem>
997	 <chem>Cc1c2sc3ncnc3c2c(s1)Nc4ccc(O)cc4</chem>
998	 <chem>CN(C1=NC2=CC=CC=C2N=C1)CC3Cc4ccccc4Oc3ccccc33</chem>
999	 <chem>Nc1c2c(nc3ccccc13)C(=O)N2C(=O)c4ccc(F)cc4</chem>

1000	
1001	
1002	

According to a further aspect of the invention, there is provided a compound of any one of formulae (IA)-(IH) for use as a casein kinase 1 delta (CK1δ) inhibitor in the treatment of a neurodegenerative disorder, such as tauopathies.

5

According to a further aspect of the invention, there is provided a compound of formula 1-37, 39-53, 55-137, 139-160, 162-211, 213-242, 244-249, 251-272, 274-285, 287-372, 374-377, 379-414, 416-440, 442-457, 459-466, 468-479, 481-495, 497-532, 534-543, 545-570, 572-576, 578, 581-584, 586, 588-599, 603-628, 630-635, 637-646, 650-657, 659-661, 663-677, 679, 681-683, 686-702, 704-725, 727-746, 748-750, 752-756, 758-759, 761-768, 770-777, 779-782, 784-788, 780-801, 804-805, 807-823, 825-838, 840-860, 862-866, 868-870, 872, 875, 881-882, 885-886, 888-890, 894-894, 904-905, 931, 933, 935, 941, 946-958, 964-1000 and 1002 or a pharmaceutically acceptable salt or solvate thereof for use as a casein kinase 1 delta (CK1δ) inhibitor in the treatment of a neurodegenerative disorder, such as tauopathies.

15

Compounds of formula 1-1002 are either commercially available or may be prepared in accordance with known synthetic procedures.

According to a further aspect of the invention there is provided a pharmaceutical

- 5 composition comprising any one of the compounds of formulae (IA)-(IH) for use in the treatment of a neurodegenerative disorder, such as tauopathies.

The pharmaceutical compositions of the invention may comprise, in addition to one of the above substances, a pharmaceutically acceptable excipient, carrier, buffer, stabiliser or
10 other materials well known to those skilled in the art. Such materials should be non-toxic and should not interfere with the efficacy of the active ingredient. The precise nature of the carrier or other material may depend on the route of administration, e. g. oral, intravenous, cutaneous or subcutaneous, nasal, intramuscular, intraperitoneal routes.

- 15 Pharmaceutical compositions for oral administration may be in tablet, capsule, powder or liquid form. A tablet may include a solid carrier such as gelatin or an adjuvant.

Liquid pharmaceutical compositions generally include a liquid carrier such as water, petroleum, animal or vegetable oils, mineral oil or synthetic oil.

- 20 Physiological saline solution, dextrose or other saccharide solution or glycols such as ethylene glycol, propylene glycol or polyethylene glycol may be included.

- For intravenous, cutaneous or subcutaneous injection, or injection at the site of affliction,
25 the active ingredient will be in the form of a parenterally acceptable aqueous solution which is pyrogen-free and has suitable pH, isotonicity and stability. Those of relevant skill in the art are well able to prepare suitable solutions using, for example, isotonic vehicles such as Sodium Chloride Injection, Ringer's Injection, Lactated Ringer's Injection. Preservatives, stabilisers, buffers, antioxidants and/or other additives may be included,
30 as required.

- The compounds of formulae (IA)-(IH) are believed to be casein kinase 1 delta (CK1δ) inhibitors. Certain compounds of formulae (IA)-(IH) have inhibitory activity of greater than 5%, in particular greater than 10%, more particularly greater than 25%, yet more
35 particularly greater than 50%, especially greater than 75%, such as greater than 90%. Such compounds may be useful in the treatment in neurodegenerative disorders such as

tauopathies. Tauopathies are conditions which are characterised by neurofibrillary tangles or aggregates of the tau protein. Tauopathies are a recognised class of conditions known to those skilled in the art and include Alzheimer's disease, frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), progressive supranuclear palsy (PSP), Pick's disease, corticobasal degeneration, multisystem atrophy (MSA), neurobasal degeneration with iron accumulation, type 1 (Hallervorden-Spatz), argyrophilic grain dementia, Down's syndrome, diffuse neurofibrillary tangles with calcification, dementia pugilistica, Gerstmann-Straussler-Scheinker disease, myotonic dystrophy, Niemann-Pick disease type C, progressive subcortical gliosis, prion protein cerebral amyloid angiopathy, tangle only dementia, postencephalitic parkinsonism, subacute sclerosing panencephalitis, Creutzfeldt-Jakob disease, amyotrophic lateral sclerosis/parkinsonism-dementia complex, non-Guamanian motor neuron disease with neurofibrillary tangles/dementia, and Parkinson's disease. The intracellular tau deposits are usually neuronal or glial and are filamentous and generally in a hyperphosphorylated state as compared to the level of phosphorylation in tau from control human brain. In the case of AD, this hyperphosphorylated tau is often referred to a paired helical filament tau (PHF) tau because it is derived from the PHF. In one embodiment, the tauopathy comprises Alzheimer's disease.

According to a further aspect of the invention, there is provided a method of treating a neurodegenerative disorder, such as tauopathies, which comprises administering a therapeutically effective amount of a compound of formulae (IA)-(IH).

Biological Data

CK1δ Inhibition Assay

The compounds of the invention may be tested for inhibition of casein kinase 1 delta (CK1δ) in accordance with the assay protocols described in US 2010/0152157, EP 1,636,375 or Hanger *et al* (2007) J. Biol. Chem. 282, 23645-23654. In particular, the assay was conducted in accordance with the following protocol :

Reaction Buffer:

Base Reaction buffer; 20 mM Hepes (pH 7.5), 10 mM MgCl₂, 1 mM EGTA, 0.02% Brij35, 0.02 mg/ml BSA, 0.1 mM Na₃VO₄, 2 mM DTT, 1% DMSO

It should be noted that required cofactors are added individually to each kinase reaction.

Reaction Procedure:

1. Prepare indicated substrate in freshly prepared Base Reaction Buffer as described above
2. Deliver any required cofactors to the substrate solution
- 5 3. Deliver indicated kinase into the substrate solution and gently mix
4. Deliver compounds in DMSO into the kinase reaction mixture
5. Deliver ³³P-ATP (specific activity 0.01 µCi/µl final) into the reaction mixture to initiate the reaction
6. Incubate kinase reaction for 120 min. at room temperature
- 10 7. Reactions are spotted onto P81 ion exchange paper (Whatman # 3698-915)
8. Wash filters extensively in 0.75% Phosphoric acid

Kinase information:

CK1δ - Genbank Accession # NP_620693

- 15 Recombinant human full-length construct. GST-tagged, expressed in insect cells.

Final concentration in assay = 4 nM

Substrate: CK1tide

Substrate sequence: [KRRRAL[pS]VASLPGL]

Final substrate concentration in assay = 20 µM

- 20 It should be noted that no additional cofactors are added to the reaction mixture.

Compounds 10, 25, 30, 42, 45, 205, 223, 240, 281-282, 288, 314, 321, 324-325, 336, 374, 391, 405, 439, 465, 506, 512, 567, 583, 611-616, 619, 623-624, 626, 631, 633, 639-640, 646, 654, 656, 660-661, 663, 668, 670, 672, 675-677, 682-683, 696-697, 700, 705-706, 717, 723, 727, 730, 736-737, 740, 748, 753-754, 756, 759, 761, 765-766, 768, 770, 780, 790, 797, 784, 808-810, 819-820, 822-823, 825, 830, 832-834, 842, 844, 847, 851, 856, 859-860, 863, 868-870, 872, 875, 881-882, 885-886, 888-890, 894, 931, 933, 935, 941, 946-958, 964-1000 and 1002 were tested in the CK1δ inhibition assay and exhibited inhibition of greater than 5%.

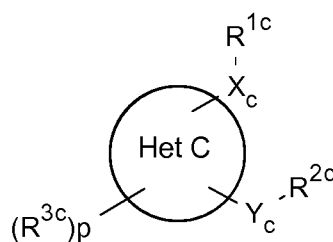
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In particular, compounds 10, 42, 45, 205, 240, 324-325, 405, 654, 656, 682, 700, 754, 766, 847, 856, 859, 863, 894, 931, 947-949, 951-952, 954, 964, 967, 972, 978-979, 986-987, 990, 997 and 999 exhibited inhibition of greater than 50%.

- 35 Yet more particularly, compounds 10, 324, 654, 856, 859, 931, 947, 952, 987, 990 and 999 exhibited inhibition of greater than 90%.

CLAIMS

1. A pharmaceutical composition comprising a compound of formula (IC) or a pharmaceutically acceptable salt or solvate thereof:



(IC)

wherein

“Het C” represents a 6 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is optionally fused to one or more (e.g.

1-3) further rings to form a polycyclic ring system comprising up to 4 rings;

X_c and Y_c independently represent a bond, $-C(R^{7c})(R^{8c})-$, $(CH_2)_2$, $-O-$, $-S-$, $-CH_2-O-$, $-$

$(CH_2)_2-O-$, NR^{6c} , $-N(R^{6c})-C(R^{7c})(R^{8c})-$, $-N(R^{6c})-(CH_2)_2-$, $-N(R^{6c})-(CH_2)_3-$, $-CH_2-N(R^{6c})-(CH_2)_2-$, $-N(R^{6c})-CO-$, $-CH_2-NH-CO-(CH_2)_2-$, $-N(R^{6c})-CO-CH_2-$, $-CO-N(R^{6c})-CH_2-$, $=N-$, $-C(H)(CN)-$, $-C(=N-NH-COC_{1-6} \text{ alkyl})-$, $-CH=C(R^{6c})-CO-$, $=CH-$, $-N=CH-$, $-N=C(Me)-$, $-C(R^{6c})=CH-$, $-NH-$

$CO-C(=CH-\text{heteroaryl})-$, $-C=C(Me)_2-$, $-CH=CH-CO-N(R^{6c})-$, $-CH=C(R^{6c})-NH-CO-$, $-CH=C(R^{6c})-CO-O-CH_2-$, $-CS-S-CH_2-$, $-NH-CS-NH-$, $-NH-CS-NH-CH_2-$, $-NH-CS-NH-(CH_2)_2-$

, $-CH_2-N(CSNH_2)-CH_2-$, $-S-CH_2-$, $-S-(CH_2)_2-O-$, SO_2 , $-NH-SO_2-$, $-CH_2-NH-SO_2-$, CO , $-CH_2-CO-$, $-(CH_2)_2-CO-$, $-O-CH_2-CO-$, $-(CH_2)_2-CO-$, COO , $-COO-C(R^{6c})(R^{7c})CO-$, $-CH=C(R^{5c})-CONH-CH_2-$, $-CO-CH_2-N(R^{6c})-CO-$, $-CO-CH_2-C(R^{6c})-CH_2-CO-$, $-CO-CH_2-N(R^{6c})-CH_2-$, $-$

$CO-NH-N=C(R^{7c})-$, $-S-CH_2-CO-$, $-S-CH_2-CO-N(R^{6c})-$, $-S-CH_2-CO-N(R^{6c})-CH_2-$, $-SO_2-N(R^{6c})-C(R^{7c})(R^{8c})-CONH-$, $-SO_2-N(R^{6c})-CH(-CH_2-\text{aryl})-CONH-CH_2-$, $-CH(-S-C_{1-6} \text{ alkyl})-C(Me)(OH)-$, $-CH_2-C(R^{6c})(OH)-$, $-C(OH)(CH(Me)(C_{3-8} \text{ cycloalkyl}))CH_2-$, $-C(OH)(R^{6c})CH_2-$, $-CH(Me)-NH-CO-CH_2-$, $-CO-N(R^{6c})-CH_2-$, $-CO-N(R^{6c})-CH_2-CH_2-$, $-CO-N(R^{6c})-CH_2-CH_2-$

$CO-NH-CH_2-$, $-CO-NH-C(-CONH_2)=CH-$, $-CO-NH-CH(-CONH_2)-CH_2-$, $-CH_2-C(H)(Me)-CH_2-S-$, $-O-CH_2-CO-NH-$, $-CH_2-N(R^{6c})-CO-CH_2-O-$, $-N(R^{6c})-CO-CH_2-O-$, $-C(H)(-CH_2-\text{aryl})-$, $-C(H)(-CH_2-\text{heteroaryl})-$, $-C(NH-\text{aryl})=N-N=CH-$, $-C(NH-\text{aryl})=N-N=CH-$, $-NH-N=C(-\text{aryl})-$, $-NH-N=C(-\text{aryl})-CO-$, $-NH-C(=N-CO-C_{1-6} \text{ alkyl})-NH-(CH_2)_2-$, $-C(-NH-\text{aryl})=N-N=CH-$, $-NH-C(-NH-\text{aryl})=N-CONH-$, $-C(=CH-\text{aryl})-CONH-CH_2-$, $-CH=C(R^{6c})-CONH-$, $-CH(-CH_2-\text{aryl})-$

$NH-CO-$ or $-CH(OH)-$, wherein said aryl or heteroaryl groups of X_c and Y_c may be optionally substituted by one or more halogen, C_{1-6} alkyl, C_{1-6} alkoxy, NO_2 or hydroxyl groups;

R^{5c} represents hydrogen, C₁₋₆ alkyl or cyano;

R^{6c} represents hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, cyano, C₃₋₈ cycloalkyl, -CH₂-C₃₋₈ cycloalkyl, aryl, heteroaryl, -C₁₋₆ alkylene-aryl, -CO-aryl, -CO-heteroaryl or -C(R^{7c})(R^{8c})-heteroaryl, wherein said aryl groups of R^{6c} may be optionally substituted by one or more

5 halogen or C₁₋₆ alkoxy groups;

R^{7c} and R^{8c} independently represent hydrogen or C₁₋₆ alkyl;

R^{1c} and R^{2c} independently represent aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1c} and R^{2c} may be substituted by one or more (e.g. 1, 2 or 3) R^{4c} groups;

10 R^{4c} represents halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, 15 cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{4c} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{4c} may be optionally substituted by one or more hydroxyl, amino, 20 cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;

p represents an integer from 0 to 3;

R^{3c} represents halogen, haloC₁₋₆ alkyl, C₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -S-C₁₋₆ alkyl, -CH₂-S-C₁₋₆ alkyl, -S-C₂₋₆ alkynyl, amino, cyano, NO₂, =O, =S, -SO₂-C₁₋₆ alkyl, -CONH₂, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -NH-C₁₋₆ alkyl, -NH-CO-C₁₋₆ alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, 25 C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH, -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein said aryl, heterocyclyl or heteroaryl groups of R^{3c} may be optionally substituted by one or more (e.g. 1, 2 or 3) R^{4c} groups and 30 wherein said C₁₋₆ alkyl groups of R^{3c} may be optionally substituted by one or more hydroxyl groups;

with the proviso that the compound is other than compound number 161, 648, 658, 680, 726, 824, 867, 880, 892, 896, 901, 903, 906, 928 and 944.

2. A pharmaceutical composition as defined in claim 1, wherein Het C represents a 6 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is optionally fused to one further ring, such as a phenyl ring.

5 3. A pharmaceutical composition as defined in claim 2, wherein Het C represents pyridinyl, pyrimidinyl or quinazolinyl, such as quinazolinyl.

4. A pharmaceutical composition as defined in any one of claims 1 to 3, wherein X_c and Y_c independently represent a bond or NR^{6c} , such as NH.

10

5. A pharmaceutical composition as defined in claim 4, wherein one of X_c and Y_c represents a bond and the other represents NH.

6. A pharmaceutical composition as defined in any one of claims 1 to 5, wherein R^{1c} and R^{2c} independently represent aryl (e.g. phenyl), bicyclic heterocyclyl (e.g. benzodioxinyl), monocyclic heteroaryl (e.g. pyridinyl, pyrazolyl or thiophenyl) or bicyclic heteroaryl ring system (e.g. benzoxazolyl), wherein R^{1c} and R^{2c} may be substituted by one or more (e.g. 1) R^{4c} groups selected from hydroxyl, C_{1-6} alkoxy (e.g. methoxy) or $-CONH_2$.

15

7. A pharmaceutical composition as defined in claim 6, wherein R^{1c} and R^{2c} independently represent aryl (e.g. phenyl) or monocyclic heteroaryl (e.g. pyridinyl, pyrazolyl or thiophenyl) wherein R^{1c} and R^{2c} may be substituted by one or more (e.g. 1) R^{4c} groups selected from hydroxyl, C_{1-6} alkoxy (e.g. methoxy) or $-CONH_2$.

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8. A pharmaceutical composition as defined in claim 7, wherein R^{1c} and R^{2c} independently represent unsubstituted aryl (e.g. phenyl) or unsubstituted monocyclic heteroaryl (e.g. pyridinyl or pyrazolyl).

25

9. A pharmaceutical composition as defined in any one of claims 1 to 8, wherein p represents an integer from 0 to 2, such as 0.

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10. A pharmaceutical composition as defined in any one of claims 1 to 8, wherein R^{3c} represents $=O$, cyano or a monocyclic heteroaryl ring system (e.g. pyridinyl).

11. A pharmaceutical composition as defined in any one of claims 1 to 10, wherein the compound of formula (IC) is selected from any of compounds:

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43, 46, 49, 147, 152, 154, 178-181, 183-184, 294-295, 305, 329, 339-341, 366, 370-371, 376, 435, 455, 459, 462, 486, 520, 539-543, 546-549, 556-557, 567, 631-632, 640-642, 645, 657, 661, 668, 671, 674, 681, 700-702, 727, 735, 755, 817-818, 823, 826, 845 or 865-866, 868, 870, 888-890, 894, 946, 949-951, 953, 957, 973, 977, 981, 983, 985-986, 993 and 995 as described herein or a pharmaceutically acceptable salt or solvate thereof.

12. A pharmaceutical composition as defined in claim 11, wherein the compound of formula (IC) is selected from any of compounds:

2-Phenyl-N-(pyridin-4-yl)quinazolin-4-amine (Compound 700);

10 N-(2,3-Dihydro-1,4-benzodioxin-6-yl)-2-phenylquinazolin-4-amine (Compound 868);

4-[[2-(Thiophen-3-yl)quinazolin-4-yl]amino]benzamide (Compound 870);

2-Phenyl-N-(1H-pyrazol-4-yl)quinazolin-4-amine (Compound 894);

2-[2-Methyl-4-(pyridin-4-yl)pyrimidin-5-yl]-1,3-benzoxazole (Compound 949);

2-[2-(Pyridin-2-yl)-4-(pyridin-4-yl)pyrimidin-5-yl]-1,3-benzoxazole (Compound 950);

15 5-(1,3-Benzoxazol-2-yl)-2-oxo-6-(pyridin-4-yl)-1,2-dihydropyridine-3-carbonitrile (Compound 951);

4-[(2-Phenylquinazolin-4-yl)amino]phenol (Compound 957);

N-(4-Methoxyphenyl)-2-(thiophen-2-yl)quinazolin-4-amine (Compound 973);

N-(4-Methoxyphenyl)-2-(pyridin-2-yl)quinazolin-4-amine (Compound 977);

20 6-Phenyl-2-(pyridin-2-yl)-N-(pyridin-4-yl)pyrimidin-4-amine (Compound 986); and

4-[(2-Phenylquinazolin-4-yl)amino]benzamide (Compound 993);

or a pharmaceutically acceptable salt or solvate thereof.

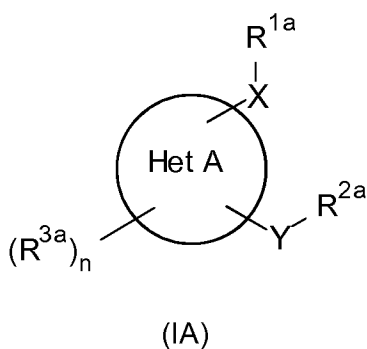
13. A pharmaceutical composition as defined in claim 12, wherein the compound of formula (IC) is selected from any of compounds:

2-Phenyl-N-(pyridin-4-yl)quinazolin-4-amine (Compound 700); and

2-Phenyl-N-(1H-pyrazol-4-yl)quinazolin-4-amine (Compound 894);

or a pharmaceutically acceptable salt or solvate thereof.

30 14. A pharmaceutical composition comprising a compound of formula (IA) or a pharmaceutically acceptable salt or solvate thereof:



wherein

“Het A” represents a 4 or 5 membered heterocyclic ring system containing 1 to 3

- 5 heteroatoms selected from O, N or S, wherein said ring system is optionally fused to one or more (e.g. 1-3) further rings to form a polycyclic ring system comprising up to 4 rings; X and Y independently represent a bond, $-\text{C}(\text{R}^{7a})(\text{R}^{8a})-$, $(\text{CH}_2)_2$, $-\text{O}-$, $-\text{S}-$, $-\text{CH}_2-\text{O}-$, $-(\text{CH}_2)_2-\text{O}-$, NR^{6a} , $-\text{N}(\text{R}^{6a})-\text{C}(\text{R}^{7a})(\text{R}^{8a})-$, $-\text{N}(\text{R}^{6a})-(\text{CH}_2)_2-$, $-\text{N}(\text{R}^{6a})-(\text{CH}_2)_3-$, $-\text{CH}_2-\text{N}(\text{R}^{6a})-(\text{CH}_2)_2-$, $-\text{N}(\text{R}^{6a})-\text{CO}-$, $-\text{CH}_2-\text{NH}-\text{CO}-(\text{CH}_2)_2-$, $-\text{N}(\text{R}^{6a})-\text{CO}-\text{CH}_2-$, $-\text{N}(\text{R}^{6a})-\text{CO}-(\text{CH}_2)_2-$, $-\text{CO}-\text{N}(\text{R}^{6a})-\text{CH}_2-$, $=\text{N}-$, $-\text{C}(\text{H})(\text{CN})-$, $-\text{C}(=\text{N}-\text{NH}-\text{COC}_{1-6} \text{ alkyl})-$, $-\text{CH}=\text{C}(\text{R}^{6a})-\text{CO}-$, $=\text{CH}-$, $-\text{CH}=\text{CH}-$, $=\text{CH}-\text{CO}-$, $-\text{N}=\text{CH}-$, $-\text{N}=\text{C}(\text{Me})-$, $-\text{C}(\text{R}^{6a})=\text{CH}-$, $-\text{NH}-\text{N}=\text{C}(\text{H})-$, $-\text{NH}-\text{CO}-\text{C}(=\text{CH}-\text{heteroaryl})-$, $-\text{C}=\text{C}(\text{Me})_2-$, $-\text{CH}=\text{CH}-\text{CO}-\text{N}(\text{R}^{6a})-$, $-\text{CH}=\text{C}(\text{R}^{6a})-\text{NH}-\text{CO}-$, $-\text{CH}=\text{C}(\text{R}^{6a})-\text{CO}-\text{O}-\text{CH}_2-$, $-\text{CS}-\text{S}-\text{CH}_2-$, $-\text{NH}-\text{CS}-\text{NH}-$, $-\text{NH}-\text{CS}-\text{NH}-\text{CH}_2-$, $-\text{NH}-\text{CS}-\text{NH}-(\text{CH}_2)_2-$, $-\text{CH}_2-\text{N}(\text{CSNH}_2)-\text{CH}_2-$, $-\text{S}-\text{CH}_2-$, $-\text{S}-(\text{CH}_2)_2-\text{O}-$, SO_2 , $-\text{NH}-\text{SO}_2-$, $-\text{CH}_2-\text{N}(\text{R}^{6a})-\text{SO}_2-$, CO , $-\text{CH}_2-\text{CO}-$, $-(\text{CH}_2)_2-\text{CO}-$, $-\text{O}-\text{CH}_2-\text{CO}-$, $-(\text{CH}_2)_2-\text{CO}-$, COO , $-\text{COO}-\text{C}(\text{R}^{7a})\text{CO}-$, $-\text{CH}=\text{C}(\text{R}^{5a})-\text{CONH}-\text{CH}_2-$, $-\text{CO}-\text{CH}_2-\text{N}(\text{R}^{6a})-\text{CO}-$, $-\text{CO}-\text{CH}_2-\text{C}(\text{R}^{6a})-\text{CH}_2-\text{CO}-$, $-\text{CO}-\text{CH}_2-\text{N}(\text{R}^{6a})-\text{CH}_2-$, $-\text{CO}-\text{NH}-\text{N}=\text{C}(\text{R}^{7a})-$, $-\text{S}-\text{CH}_2-\text{CO}-$, $-\text{S}-\text{CH}_2-\text{CO}-\text{N}(\text{R}^{6a})-$, $-\text{S}-\text{CH}_2-\text{CO}-\text{N}(\text{R}^{6a})-\text{CH}_2-$, $-\text{SO}_2-\text{N}(\text{R}^{6a})-\text{C}(\text{R}^{7a})(\text{R}^{8a})-\text{CONH}-$, $-\text{SO}_2-\text{N}(\text{R}^{6a})-\text{CH}(-\text{CH}_2-\text{aryl})-\text{CONH}-\text{CH}_2-$, $-\text{CH}(-\text{S}-\text{C}_{1-6} \text{ alkyl})-\text{C}(\text{Me})(\text{OH})-$, $-\text{CH}_2-\text{C}(\text{R}^{6a})(\text{OH})-$, $-\text{C}(\text{OH})(\text{CH}(\text{Me})(\text{C}_{3-8} \text{ cycloalkyl}))-\text{CH}_2-$, $-\text{C}(\text{OH})(\text{R}^{6a})-\text{CH}_2-$, $-\text{CH}(\text{Me})-\text{NH}-\text{CO}-\text{CH}_2-$, $-\text{CO}-\text{N}(\text{R}^{6a})-\text{CH}_2-$, $-\text{CO}-\text{N}(\text{R}^{6a})-\text{CH}_2-\text{CH}_2-$, $-\text{CO}-\text{N}(\text{R}^{6a})-\text{CH}_2-\text{CH}_2-\text{CO}-\text{NH}-\text{CH}_2-$, $-\text{CO}-\text{NH}-\text{C}(-\text{CONH}_2)=\text{CH}-$, $-\text{CO}-\text{NH}-\text{CH}(-\text{CONH}_2)-\text{CH}_2-$, $-\text{CH}_2-\text{C}(\text{H})(\text{Me})-\text{CH}_2-\text{S}-$, $-\text{O}-\text{CH}_2-\text{CO}-\text{NH}-$, $-\text{CH}_2-\text{N}(\text{R}^{6a})-\text{CO}-\text{CH}_2-\text{O}-$, $-\text{N}(\text{R}^{6a})-\text{CO}-\text{CH}_2-\text{O}-$, $-\text{C}(\text{H})(-\text{CH}_2-\text{aryl})-$, $-\text{C}(\text{H})(-\text{CH}_2-\text{heteroaryl})-$, $-\text{C}(\text{NH}-\text{aryl})=\text{N}-\text{N}=\text{CH}-$, $-\text{C}(\text{NH}-\text{aryl})=\text{N}-\text{N}=\text{CH}-$, $-\text{NH}-\text{N}=\text{C}(-\text{aryl})-$, $-\text{NH}-\text{N}=\text{C}(-\text{aryl})-\text{CO}-$, $-\text{NH}-\text{C}(=\text{N}-\text{CO}-\text{C}_{1-6} \text{ alkyl})-\text{NH}-(\text{CH}_2)_2-$, $-\text{C}(-\text{NH}-\text{aryl})=\text{N}-\text{N}=\text{CH}-$, $-\text{NH}-\text{C}(-\text{NH}-\text{aryl})=\text{N}-\text{CONH}-$, $-\text{C}(=\text{CH}-\text{aryl})-\text{CONH}-\text{CH}_2-$, $-\text{CH}=\text{C}(\text{R}^{6a})-\text{CONH}-$, $-\text{CH}(-\text{CH}_2-\text{aryl})-\text{NH}-\text{CO}-$ or $-\text{CH}(\text{OH})-$,
- 10
15
20
25

wherein said aryl or heteroaryl groups of X and Y may be optionally substituted by one or more halogen, C_{1-6} alkyl, C_{1-6} alkoxy, NO_2 or hydroxyl groups;

R^{5a} represents hydrogen, C_{1-6} alkyl or cyano;

R^{6a} represents hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, cyano, C_{3-8} cycloalkyl, $-\text{CH}_2-\text{C}_{3-8}$

- 30 cycloalkyl, aryl, heteroaryl, $-\text{C}_{1-6}$ alkylene-aryl, $-\text{CO}-\text{aryl}$, $-\text{CO}-\text{heteroaryl}$ or $-\text{C}(\text{R}^{7a})(\text{R}^{8a})-$

heteroaryl, wherein said aryl groups of R^{6a} may be optionally substituted by one or more halogen or C₁₋₆ alkoxy groups;

R^{7a} and R^{8a} independently represent hydrogen or C₁₋₆ alkyl;

R^{1a} and R^{2a} independently represent aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic

- 5 heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1a} and R^{2a} may be substituted by one or more (e.g. 1, 2 or 3) R^{4a} groups;

R^{4a} represents halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-

- 10 NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-aryl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, -NH-aryl, -NH-SO₂-aryl, aryl or

- 15 heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{4a} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{4a} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;

- 20 n represents an integer from 0 to 3;

R^{3a} represents halogen, haloC₁₋₆ alkyl, C₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -S-C₁₋₆ alkyl, -CH₂-S-C₁₋₆ alkyl, -S-C₂₋₆ alkynyl, amino, cyano, NO₂, =O, =S, -SO₂-C₁₋₆ alkyl, -CONH₂, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -NH-C₁₋₆ alkyl, -NH-CO-C₁₋₆ alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH,

- 25 -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein said aryl, heterocyclyl or heteroaryl groups of R^{3a} may be optionally substituted by one or more (e.g. 1, 2 or 3) R^{4a} groups and wherein said C₁₋₆ alkyl groups of R^{3a} may be optionally substituted by one or more

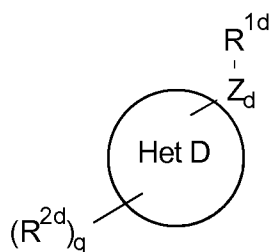
- 30 hydroxyl groups;

with the proviso that the compound is other than compound number 38, 138, 212, 243, 378, 415, 441, 480, 577, 579, 580, 587-589, 593, 598, 600, 629, 636, 678, 684, 747, 760, 802, 861, 871, 873, 879, 883, 897-899, 904-905, 907, 909, 915, 917-919, 922-923, 925, 929-930, 938-939, 961.

15. A pharmaceutical composition as defined in claim 14, wherein the compound of formula (IA) is selected from any of compounds:

1, 4-17, 19-25, 36-37, 39-40, 42, 44-45, 52, 61, 71-76, 80-83, 86-91, 93-97, 102-107, 110-112, 114, 117-122, 139-143, 149-151, 153, 158-160, 163-170, 174-177, 185-197, 200, 202-203, 208-209, 211, 213-221, 223-224, 226, 228-229, 232, 234, 237-240, 256, 261-264, 267-268, 270, 272, 275-283, 296, 304, 313, 319, 321-323, 326-328, 332, 334-335, 342-345, 350, 356, 361-365, 367-369, 372, 377, 379, 383, 393, 398, 403, 406, 412-413, 416-423, 431-432, 434, 436, 438-440, 442-447, 460, 463, 465-466, 468-476, 478, 481, 487-488, 492-494, 499, 501, 506, 508-510, 512-515, 517-518, 521-522, 525, 527-529, 531-532, 534, 551-552, 554-555, 558, 562-563, 569, 573, 576, 578, 581-582, 584, 586, 599, 604-605, 610-614, 617, 619, 623-625, 628, 630, 633-635, 639, 643-644, 650-652, 654, 656, 664-667, 670, 672, 676-677, 679, 683, 695, 697-698, 704, 707-708, 710, 714, 717, 733, 736, 741-743, 750, 761-766, 768, 773, 782, 787, 791, 794, 807, 809-812, 815-816, 820, 841-843, 846, 849-856, 859-860, 862-864, 931, 947-948, 967, 970, 982, 984, 989, 991-992, 1000 and 1002 as described herein or a pharmaceutically acceptable salt or solvate thereof.

16. A pharmaceutical composition comprising a compound of formula (ID) or a pharmaceutically acceptable salt or solvate thereof:



(ID)

wherein

"Het D" represents a 6 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is fused to one or more (e.g. 1-3)

further rings to form a polycyclic ring system comprising up to 4 rings;

Z_d represents a bond, $-C(R^{7d})(R^{8d})-$, $-(CH_2)-C(R^{7d})(R^{8d})-$, $-O-$, $-S-$, $-CH_2-O-$, $-(CH_2)_2-O-$, NR^{6d} , $-N(R^{6d})-C(R^{7d})(R^{8d})-$, $-N(R^{6d})-(CH_2)_2-$, $-N(R^{6d})-(CH_2)_3-$, $-CH_2-N(R^{6d})-(CH_2)_2-$, $-N(R^{6d})-CO-$, $-CH_2-NH-CO-(CH_2)_2-$, $-N(R^{6d})-CO-CH_2-$, $-CO-N(R^{6d})-CH_2-$, $=N-$, $-C(H)(CN)-$, $-C(=N-NH-COC_{1-6} \text{ alkyl})-$, $-CH=C(R^{6d})-CO-$, $=CH-$, $-N=CH-$, $-N=C(Me)-$, $-C(R^{6d})=CH-$, $-NH-CO-C(=CH-\text{heteroaryl})-$, $-C=C(Me)_2-$, $-CH=CH-CO-N(R^{6d})-$, $-CH=C(R^{6d})-NH-CO-$, $-CO-O-CH_2-$, $-CH=C(R^{6d})-CO-O-CH_2-$, $-CS-S-CH_2-$, $-NH-CO-NH-$, $-NH-CS-NH-$, $-NH-CS-NH-CH_2-$, $-NH-$

- CS-NH-(CH₂)₂-, -CH₂-N(CSNH₂)-CH₂-, -S-CH₂-, -S-(CH₂)₂-O-, SO₂-, -NH-SO₂-, -CH₂-NH-SO₂-, CO-, -CH₂-CO-, -(CH₂)₂-CO-, -O-CH₂-CO-, -(CH₂)₂-CO-, COO-, -COO-C(R^{7d})CO-, -CH=C(R^{5d})-CONH-CH₂-, -CO-CH₂-N(R^{6d})-CO-, -CO-CH₂-C(R^{6d})-CH₂-CO-, -CO-CH₂-N(R^{6d})-CH₂-, -CO-NH-N=C(R^{7d})-, -S-CH₂-CO-, -S-CH₂-CO-N(R^{6d})-, -S-CH₂-CO-N(R^{6d})-CH₂-, -SO₂-N(R^{6d})-C(R^{7d})(R^{8d})-CONH-, -SO₂-N(R^{6d})-CH(-CH₂-aryl)-CONH-CH₂-, -CH(-S-C₁₋₆ alkyl)-C(Me)(OH)-, -CH₂-C(R^{6d})(OH)-, -C(OH)(CH(Me)(C₃₋₈ cycloalkyl))-CH₂-, -C(OH)(R^{6d})-CH₂-, -CH(Me)-NH-CO-CH₂-, -CO-N(R^{6d})-CH₂-, -CO-N(R^{6d})-CH₂-CH₂-, -CO-N(R^{6d})-CH₂-CH₂-CO-NH-CH₂-, -CO-NH-C(-CONH₂)=CH-, -CO-NH-CH(-CONH₂)-CH₂-, -CH₂-C(H)(Me)-CH₂-S-, -O-CH₂-CO-NH-, -CH₂-N(R^{6d})-CO-CH₂-O-, -N(R^{6d})-CO-CH₂-O-, -C(H)(-CH₂-aryl)-, -C(H)(-CH₂-heteroaryl)-, -C(NH-aryl)=N-N=CH-, -C(NH-aryl)=N-N=CH-, -NH-N=C(-aryl)-, -NH-N=C(-aryl)-CO-, -NH-C(=N-CO-C₁₋₆ alkyl)-NH-(CH₂)₂-, -C(-NH-aryl)=N-N=CH-, -NH-C(-NH-aryl)=N-CONH-, -C(=CH-aryl)-CONH-CH₂-, -CH=C(R^{6d})-CONH-, -CH(-CH₂-aryl)-NH-CO- or -CH(OH)-, wherein said aryl or heteroaryl groups of Z_d may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, NO₂ or hydroxyl groups;
- R^{5d} represents hydrogen, C₁₋₆ alkyl or cyano;
- R^{6d} represents hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, cyano, C₃₋₈ cycloalkyl, -CH₂-C₃₋₈ cycloalkyl, aryl, heteroaryl, -C₁₋₆ alkylene-aryl, -CO-aryl, -CO-heteroaryl or -C(R^{7d})(R^{8d})-heteroaryl, wherein said aryl groups of R^{6d} may be optionally substituted by one or more halogen or C₁₋₆ alkoxy groups;
- R^{7d} and R^{8d} independently represent hydrogen or C₁₋₆ alkyl;
- R^{1d} represents aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1d} may be substituted by one or more (e.g. 1, 2 or 3) R^{4d} groups;
- R^{4d} represents halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{4d} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{4d} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;

q represents an integer from 0 to 3;

R^{2d} represents halogen, halo C_{1-6} alkyl, C_{1-6} alkyl, hydroxyl, C_{1-6} alkoxy, -S- C_{1-6} alkyl, -CH₂-S- C_{1-6} alkyl, -S- C_{2-6} alkynyl, amino, cyano, NO₂, =O, =S, =NH, -SO₂- C_{1-6} alkyl, -CONH₂, -CO- C_{1-6} alkyl, -COO- C_{1-6} alkyl, -NH- C_{1-6} alkyl, -NH-CO- C_{1-6} alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C_{1-6} alkyl, -CO-NH- C_{1-6} alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH, -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH- C_{1-6} alkyl, wherein said C_{1-6} alkyl groups of R^{2d} may be optionally substituted by one or more hydroxyl groups;

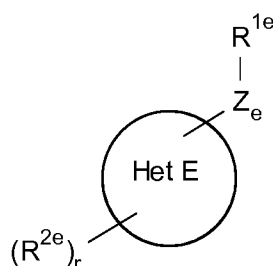
with the proviso that the compound is other than compound number 273, 286, 467, 533,

544, 571, 591, 662, 783, 795, 806, 884, 887, 895, 902, 908, 921, 932, 934, 942, 959-960 and 1001.

17. A pharmaceutical composition as defined in claim 16, wherein the compound of formula (ID) is selected from any of compounds:

29, 34, 41, 65-70, 92, 109, 116, 126, 130-137, 162, 182, 231, 246, 252-255, 258, 274, 290-293, 297-298, 317-318, 330-331, 347-349, 352, 450-454, 483, 536-538, 545, 550, 564-565, 572, 620, 637, 655, 663, 675, 682, 686, 691, 696, 706, 711, 724, 728-729, 737, 744-745, 748, 752, 774-776, 781, 797-799, 832, 834, 954, 958, 964-965, 971, 974-976, 978-980, 994 or 997-998 as described herein or a pharmaceutically acceptable salt or solvate thereof.

18. A pharmaceutical composition comprising a compound of formula (IE) or a pharmaceutically acceptable salt or solvate thereof:



(IE)

wherein

"Het E" represents a 6 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S;

Z_e represents a bond, -C(R^{7e})(R^{8e})-, (CH₂)₂, -O-, -S-, -CH₂-O-, -(CH₂)₂-O-, NR^{6e}, -N(R^{6e})-

C(R^{7e})(R^{8e})-, -N(R^{6e})-(CH₂)₂-, -N(R^{6e})-(CH₂)₃-, -CH₂-N(R^{6e})-(CH₂)₂-, -N(R^{6e})-CO-, -CH₂-NH-

- CO-(CH₂)₂-, -N(R^{6e})-CO-CH₂-, -CO-N(R^{6e})-CH₂-, =N-, -C(H)(CN)-, -C(=N-NH-COC₁₋₆ alkyl)-, -C(R^{6e})=N-NH-CO-, -CH=C(R^{6e})-CO-, =CH-, -N=CH-, -N=C(Me)-, -C(R^{6e})=CH-, -NH-CO-C(=CH-heteroaryl)-, -C=C(Me)₂-, -CH=CH-CO-N(R^{6e})-, -CH=C(R^{6e})-NH-CO-, -CH=C(R^{6e})-CO-O-CH₂-, -CS-S-CH₂-, -NH-CS-NH-, -N(R^{6e})-CO-N(R^{7e})-, -NH-CS-N(R^{6e})-CH(R^{7e})-, -CO-NH-CS-N(R^{6e})-, -NH-CS-NH-(CH₂)₂-, -CH₂-N(CSNH₂)-CH₂-, -S-CH₂-, -S-(CH₂)₂-O-, SO₂-, -NH-SO₂-, -CH₂-N(R^{6e})-SO₂-, CO-, -CH₂-CO-, -(CH₂)₂-CO-, -O-CH₂-CO-, -(CH₂)₂-CO-, COO-, -COO-C(R^{7e})CO-, -CH=C(R^{5e})-CONH-CH₂-, -CO-CH₂-N(R^{6e})-CO-, -CO-CH₂-C(R^{6e})-CH₂-CO-, -C(R^{6e})-CO-CH₂-, -CO-CH₂-N(R^{6e})-CH₂-, -CO-NH-N=C(R^{7e})-, -S-CH₂-CO-, -S-CH₂-CO-N(R^{6e})-, -S-CH₂-CO-N(R^{6e})-CH₂-, -SO₂-N(R^{6e})-C(R^{7e})(R^{8e})-CONH-
- 10 , -SO₂-N(R^{6e})-CH(-CH₂-aryl)-CONH-CH₂-, -CH(-S-C₁₋₆ alkyl)-C(Me)(OH)-, -CH₂-C(R^{6e})(OH)-, -C(OH)(CH(Me)(C₃₋₈ cycloalkyl))-CH₂-, -C(OH)(R^{6e})-CH₂-, -CH(Me)-NH-CO-CH₂-, -CO-N(R^{6e})-CH₂-, -CO-N(R^{6e})-CH₂-CH₂-, -CO-N(R^{6e})-CH₂-CH₂-O-CO-, -CO-N(R^{6e})-CH₂-CH₂-CO-NH-CH₂-, -CO-NH-C(-CONH₂)=CH-, -CO-NH-CH(-CONH₂)-CH₂-, -CH₂-C(H)(Me)-CH₂-S-, -O-CH₂-CO-NH-, -CH₂-N(R^{6e})-CO-CH₂-O-, -N(R^{6e})-CO-CH₂-O-, -C(H)(-
- 15 CH₂-aryl)-, -C(H)(-CH₂-heteroaryl)-, -C(NH-aryl)=N-N=CH-, -C(NH-aryl)=N-N=CH-, -NH-N=C(-aryl)-, -NH-C(R^{6e})=N-SO₂-, -NH-N=C(-aryl)-CO-, -NH-C(=N-CO)(R^{6e})-, -NH-C(=N-CO-C₁₋₆ alkyl)-NH-(CH₂)₂-, -C(-NH-aryl)=N-N=CH-, -NH-C(-NH-aryl)=N-CONH-, -C(=CH-aryl)-CONH-CH₂-, -CH=C(R^{6e})-CONH-, -CH(-CH₂-aryl)-NH-CO- or -CH(OH)-, wherein said aryl or heteroaryl groups of Z_e may be optionally substituted by one or more halogen,
- 20 C₁₋₆ alkyl, C₁₋₆ alkoxy, NO₂ or hydroxyl groups;
- R^{5e} represents hydrogen, C₁₋₆ alkyl or cyano;
- R^{6e} represents hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkylamino, cyano, C₃₋₈ cycloalkyl, -CH₂-C₃₋₈ cycloalkyl, aryl, heteroaryl, -C₁₋₆ alkylene-aryl, -C₁₋₆ alkylene-heteroaryl, -NH-CO-aryl, -CO-aryl, -CO-heteroaryl or -C(R^{7e})(R^{8e})-heteroaryl, wherein said aryl groups of R^{6e}
- 25 may be optionally substituted by one or more halogen or C₁₋₆ alkoxy groups;
- R^{7e} and R^{8e} independently represent hydrogen or C₁₋₆ alkyl;
- R^{1e} represents aryl, C₃₋₈ cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or bicyclic heteroaryl ring system, wherein R^{1d} may be substituted by one or more (e.g. 1, 2 or 3) R^{4e} groups;
- 30 R^{4e} represents halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -SO₂NH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -NH-NH₂, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -
- 35 SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -

CH₂-O-CO-aryl, -O-aryl, -CO-NH-aryl, -NH-SO₂-aryl, -NH-CO-heteroaryl, -NH-C₁₋₄ alkylene-heteroaryl, -NH-CO-CH₂-aryl, aryl or heteroaryl groups, wherein said C₁₋₆ alkynyl, aryl, heterocyclyl or heteroaryl groups of R^{4e} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{4e} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;

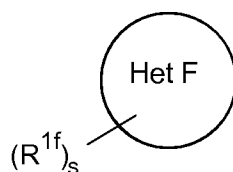
r represents an integer from 0 to 3;

R^{2e} represents halogen, haloC₁₋₆ alkyl, C₁₋₆ alkyl, C₁₋₆ alkynyl, hydroxyl, C₁₋₆ alkoxy, -S-C₁₋₆ alkyl, -CH₂-S-C₁₋₆ alkyl, -S-C₂₋₆ alkynyl, amino, cyano, NO₂, =O, =S, -SO₂-C₁₋₆ alkyl, -CONH₂, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -NH-C₁₋₆ alkyl, -NH-CO-C₁₋₆ alkyl, -NH-CO-CH=CH-CH₂-N(Me)₂, C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH, -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, wherein said C₁₋₆ alkyl or C₁₋₆ alkynyl, groups of R^{2e} may be optionally substituted by one or more hydroxyl or alkylamino groups; with the proviso that the compound is other than compound number 250, 647, 685, 751, 769, 803, 874, 876, 893, 900, 911, 913-914, 916, 920, 927, 936-937, 940, 943 and 945.

19. A pharmaceutical composition as defined in claim 18, wherein the compound of formula (IE) is selected from any of compounds:

18, 50, 55-56, 62, 77, 85, 108, 115, 144, 146, 148, 198-199, 201, 222, 230, 245, 247, 251, 265, 284, 287, 300, 306, 337-338, 346, 381-382, 392, 426, 429-430, 479, 561, 566, 583, 603, 606-608, 621-622, 646, 659-660, 687-688, 690, 699, 715, 718, 720-723, 730-732, 739, 771-772, 780, 793, 813-814, 822, 829-830, 835-837, 840, 848, 885-886, 941, 966 or 988 as described herein or a pharmaceutically acceptable salt or solvate thereof.

20. A pharmaceutical composition comprising a compound of formula (IF) or a pharmaceutically acceptable salt or solvate thereof:



(IF)

wherein

"Het F" represents a heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S, wherein said ring system is fused to one or more (e.g. 1-3) further rings to form a polycyclic ring system comprising up to 4 rings;

R^{1f} represents halogen, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, C_{3-8} cycloalkyl, halo C_{1-6} alkyl, hydroxyl, C_{1-6} alkoxy, $-O-C_{1-6}$ alkenyl, halo C_{1-6} alkoxy, $-COOH$, $-CO-C_{1-6}$ alkyl, $-COO-C_{1-6}$ alkyl, $-CONH_2$, $-CH_2-CONH_2$, $-NH-C_{1-6}$ alkyl, $-NH-C_{2-6}$ alkenyl, $-NH-CO-C_{1-6}$ alkyl, $-CO-NH-C_{1-6}$ alkyl, $-O-CH_2-CO-NH-C_{1-6}$ alkyl, $-CH_2-CH_2-CO-NH-C_{1-6}$ alkyl, $-S-C_{1-6}$ alkyl, $-SO-C_{1-6}$ alkyl, $-SO_2-C_{1-6}$ alkyl, $-SO_2-NH-C_{1-6}$ alkyl, $-S-CH_2-CO-C_{2-6}$ alkenyl, $-SO_2-OH$, amino, cyano, NO_2 , $=O$, $-CO-NH-(CH_2)_2-OMe$, $-NH-C_{3-8}$ cycloalkyl, wherein said C_{1-6} alkyl or C_{2-6} alkenyl groups of R^{1f} may be optionally substituted by one or more hydroxyl, amino, cyano, C_{1-6} alkoxy, $CONH_2$ or $-COO-C_{1-6}$ alkyl groups;

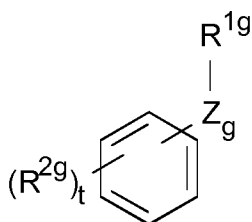
s represents an integer from 1 to 3;

with the proviso that the compound is other than compound number 592 or 595.

21. A pharmaceutical composition as defined in claim 20, wherein the compound of formula (IF) is selected from any of compounds:

53, 79, 124-125, 205, 289, 299, 301-302, 353-355, 397, 500 or 511 as described herein or a pharmaceutically acceptable salt or solvate thereof.

22. A pharmaceutical composition comprising a compound of formula (IG) or a pharmaceutically acceptable salt or solvate thereof:



(IG)

wherein

Z_g represents a bond, $-C(R^{7g})(R^{8g})-$, $(CH_2)_2$, $-O-$, $-S-$, $-CH_2-O-$, $-(CH_2)_2-O-$, NR^{6g} , $-N(R^{6g})-C(R^{7g})(R^{8g})-$, $-N(R^{6g})-(CH_2)_2-$, $-N(R^{6g})-(CH_2)_3-$, $-CH_2-N(R^{6g})-(CH_2)_2-$, $-N(R^{6g})-CO-$, $-CH_2-NH-CO-(CH_2)_2-$, $-N(R^{6g})-CO-CH_2-$, $=N-$, $-C(H)(CN)-$, $-C(=N-NH-COC_{1-6} \text{ alkyl})-$, $-CH=C(R^{6g})-CO-$, $=CH-$, $-N=CH-$, $-N=C(Me)-$, $-C(R^{6g})=CH-$, $-NH-CO-C(=CH-\text{heteroaryl})-$, $-C=C(Me)_2-$, $-CH=CH-CO-N(R^{6g})-$, $-CH=C(R^{6g})-NH-CO-$, $-CH=C(R^{6g})-CO-O-CH_2-$, $-CS-S-CH_2-$, $-NH-CS-NH-$, $-NH-CS-NH-CH_2-$, $-NH-CS-NH-(CH_2)_2-$, $-CH_2-N(CSNH_2)-CH_2-$, $-S-CH_2-$, $-S-(CH_2)_2-O-$, SO_2 , $-NH-SO_2-$, $-CH_2-NH-SO_2-$, CO , $-CH_2-CO-$, $-(CH_2)_2-CO-$, $-O-CH_2-CO-$, $-(CH_2)_2-CO-$, $COO-$, $-COO-C(R^{7g})CO-$, $-CH=C(R^{5g})-CONH-CH_2-$, $-CO-CH_2-N(R^{6g})-CO-$, $-CO-CH_2-C(R^{6g})-CH_2-CO-$, $-CO-CH_2-N(R^{6g})-CH_2-$, $-CO-NH-N=C(R^{7g})-$, $-S-C(R^{6g})(R^{7g})-CO-$, $-S-CH_2-CO-$

- $N(R^{6g})-$, $-S-CH_2-CO-N(R^{6g})-CH_2-$, $-SO_2-N(R^{6g})-C(R^{7g})(R^{8g})-CONH-$, $-SO_2-N(R^{6g})-CH(-CH_2-$
 aryl)- $CONH-CH_2-$, $-CH(-S-C_{1-6} \text{ alkyl})-C(Me)(OH)-$, $-CH_2-C(R^{6g})(OH)-$, $-C(OH)(CH(Me)(C_{3-8}$
 cycloalkyl))- CH_2- , $-C(OH)(R^{6g})-CH_2-$, $-CH(Me)-NH-CO-CH_2-$, $-CO-N(R^{6g})-CH_2-$, $-CO-$
 $N(R^{6g})-CH_2-CH_2-$, $-CO-N(R^{6g})-CH_2-CH_2-CO-NH-CH_2-$, $-CO-NH-C(-CONH_2)=CH-$, $-CO-NH-$
 5 $CH(-CONH_2)-CH_2-$, $-CH_2-C(H)(Me)-CH_2-S-$, $-O-CH_2-CO-NH-$, $-CH_2-N(R^{6g})-CO-CH_2-O-$, $-$
 $N(R^{6g})-CO-CH_2-O-$, $-C(H)(-CH_2-aryl)-$, $-C(H)(-CH_2-heteroaryl)-$, $-C(NH-aryl)=N-N=CH-$, $-$
 $C(NH-aryl)=N-N=CH-$, $-NH-N=C(-aryl)-$, $-NH-N=C(-aryl)-CO-$, $-NH-C(=N-CO-C_{1-6} \text{ alkyl})-$
 $NH-(CH_2)_2-$, $-C(-NH-aryl)=N-N=CH-$, $-NH-C(-NH-aryl)=N-CONH-$, $-C(=CH-aryl)-CONH-$
 CH_2- , $-CH=C(R^{6g})-CONH-$, $-CH(-CH_2-aryl)-NH-CO-$ or $-CH(OH)-$, wherein said aryl or
 10 heteroaryl groups of Z_g may be optionally substituted by one or more halogen, C_{1-6} alkyl,
 C_{1-6} alkoxy, NO_2 or hydroxyl groups;
 R^{5g} represents hydrogen, C_{1-6} alkyl or cyano;
 R^{6g} represents hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, cyano, C_{3-8} cycloalkyl, $-CH_2-C_{3-8}$
 cycloalkyl, aryl, heteroaryl, $-C_{1-6}$ alkylene-aryl, $-CO-aryl$, $-CO-heteroaryl$ or $-C(R^{7g})(R^{8g})-$
 15 heteroaryl, wherein said aryl groups of R^{6g} may be optionally substituted by one or more
 halogen or C_{1-6} alkoxy groups;
 R^{7g} and R^{8g} independently represent hydrogen or C_{1-6} alkyl;
 R^{1g} represents aryl, C_{3-8} cycloalkyl, monocyclic or bicyclic heterocyclyl or a monocyclic or
 bicyclic heteroaryl ring system, wherein R^{1g} may be substituted by one or more (e.g. 1, 2
 20 or 3) R^{4g} groups;
 R^{4g} represents halogen, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, C_{3-8} cycloalkyl, halo C_{1-6} alkyl,
 hydroxyl, C_{1-6} alkoxy, $-O-C_{1-6}$ alkenyl, halo C_{1-6} alkoxy, $-COOH$, $-CO-C_{1-6}$ alkyl, $-COO-C_{1-6}$
 alkyl, $-CONH_2$, $-CH_2-CONH_2$, $-NH-C_{1-6}$ alkyl, $-NH-C_{2-6}$ alkenyl, $-NH-CO-C_{1-6}$ alkyl, $-CO-$
 $NH-C_{1-6}$ alkyl, $-O-CH_2-CO-NH-C_{1-6}$ alkyl, $-CH_2-CH_2-CO-NH-C_{1-6}$ alkyl, $-S-C_{1-6}$ alkyl, $-SO-C_{1-}$
 25 $_6$ alkyl, $-SO_2-C_{1-6}$ alkyl, $-SO_2-NH-C_{1-6}$ alkyl, $-S-CH_2-CO-C_{2-6}$ alkenyl, $-SO_2-OH$, amino,
 cyano, NO_2 , $=O$, $-CO-NH-(CH_2)_2-OMe$, $-NH-C_{3-8}$ cycloalkyl, $-CO-heterocyclyl$, $-CO-$
 heteroaryl, $-COO-(CH_2)_2-heterocyclyl$, $-OCH_2-aryl$, $-OCH_2-heteroaryl$, $-CH_2-O-CO-aryl$, $-$
 $O-aryl$, $-NH-CO-heteroaryl$, $-NH-CO-CH_2-aryl$, aryl or heteroaryl groups, wherein said aryl,
 heterocyclyl or heteroaryl groups of R^{4g} may be optionally substituted by one or more
 30 halogen, C_{1-6} alkyl, C_{1-6} alkoxy, $=S$ or hydroxyl groups and wherein said C_{1-6} alkyl or C_{2-6}
 alkenyl groups of R^{4g} may be optionally substituted by one or more hydroxyl, amino,
 cyano, C_{1-6} alkoxy, $CONH_2$ or $-COO-C_{1-6}$ alkyl groups;
 t represents an integer from 0 to 3;
 R^{2g} represents halogen, halo C_{1-6} alkyl, C_{1-6} alkyl, hydroxyl, C_{1-6} alkoxy, $-S-C_{1-6}$ alkyl, $-CH_2-$
 35 $S-C_{1-6}$ alkyl, $-S-C_{2-6}$ alkynyl, amino, cyano, NO_2 , $=O$, $=S$, $-SO_2-C_{1-6}$ alkyl, $-CONH_2$, $-CO-C_{1-}$
 $_6$ alkyl, $-COO-C_{1-6}$ alkyl, $-NH-C_{1-6}$ alkyl, $-NH-CO-C_{1-6}$ alkyl, $-NH-CO-CH=CH-CH_2-N(Me)_2$,

C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -CO-NH-CH(Me)-COOH, -S-CH₂-CO-N(Et)₂, -NH-(CH₂)₂-OH, -NH-(CH₂)₃-OH, -NH-CH(Et)-CH₂-OH, -CO-NH-(CH₂)₃-OH, -CH(CH₂OH)₂ or -S-CH₂-CO-NH-CO-NH-C₁₋₆ alkyl, wherein said C₁₋₆ alkyl groups of R^{2g} may be optionally substituted by one or more hydroxyl groups;

- 5 with the proviso that the compound is other than compound number 789, 839 and 924.
In one embodiment, the compound of formula (IG) is selected from any of compounds: 98-101, 248, 257, 259-260, 266, 271, 380, 394, 449, 461, 464, 477, 502-504, 523, 530, 535, 574, 673, 713, 779, 788, 825, 881-882, 935, 956, 968, 972 or 996 as described herein or a pharmaceutically acceptable salt or solvate thereof.

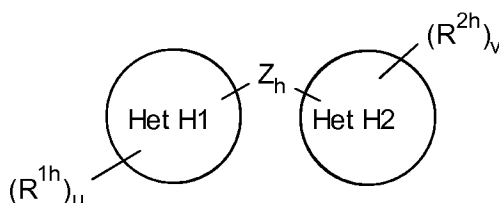
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23. A pharmaceutical composition as defined in claim 22, wherein the compound of formula (IG) is selected from any of compounds:

98, 101, 248, 257, 259-260, 266, 271, 380, 394 or 530 as described herein or a pharmaceutically acceptable salt or solvate thereof.

15

24. A pharmaceutical composition comprising a compound of formula (IH) or a pharmaceutically acceptable salt or solvate thereof:



(IH)

20 wherein

"Het H1" and "Het H2" independently represent a 5 membered heterocyclic ring system containing 1 to 3 heteroatoms selected from O, N or S;

Z_h represents a bond, -C(R^{7h})(R^{8h})-, (CH₂)₂, -O-, -S-, -CH₂-O-, -(CH₂)₂-O-, NR^{6h}, -N(R^{6h})-C(R^{6h})(R^{7h})-, -N(R^{6h})-(CH₂)₂-, -N(R^{6h})-(CH₂)₃-, -CH₂-N(R^{6h})-(CH₂)₂-, -N(R^{6h})-CO-, -CH₂-NH-CO-(CH₂)₂-, -N(R^{6h})-CO-CH₂-, =N-, -C(H)(CN)-, -C(=N-NH-COC₁₋₆ alkyl)-, -CH=C(R^{6h})-CO-, =CH-, -N=CH-, -N=C(Me)-, -C(R^{6h})=CH-, -NH-CO-C(=CH-heteroaryl)-, -C=C(Me)₂-, -CH=CH-CO-N(R^{6h})-, -CH=C(R^{6h})-NH-CO-, -CH=C(R^{6h})-CO-O-CH₂-, -CS-S-CH₂-, -NH-CS-NH-, -NH-CS-NH-CH₂-, -NH-CS-NH-(CH₂)₂-, -CH₂-N(CSNH₂)-CH₂-, -S-CH₂-, -S-(CH₂)₂-O-, SO₂-, -NH-SO₂-, -CH₂-NH-SO₂-, CO-, -CH₂-CO-, -(CH₂)₂-CO-, -O-CH₂-CO-, -(CH₂)₂-CO-, COO-, -COO-C(R^{7h})CO-, -CH=C(R^{5h})-CONH-CH₂-, -CO-CH₂-N(R^{6h})-CO-, -CO-CH₂-C(R^{6h})-CH₂-CO-, -CO-CH₂-N(R^{6h})-CH₂-, -CO-NH-N=C(R^{7h})-, -S-CH₂-CO-, -S-CH₂-CO-N(R^{6h})-, -S-CH₂-CO-N(R^{6h})-CH₂-, -SO₂-N(R^{6h})-C(R^{7h})(R^{8h})-CONH-, -SO₂-N(R^{6h})-CH(-CH₂-aryl)-

30

- CONH-CH₂-, -CH(-S-C₁₋₆ alkyl)-C(Me)(OH)-, -CH₂-C(R^{6h})(OH)-, -C(OH)(CH(Me)(C₃₋₈ cycloalkyl))-CH₂-, -C(OH)(R^{6h})-CH₂-, -CH(Me)-NH-CO-CH₂-, -CO-N(R^{6h})-CH₂-, -CO-N(R^{6h})-CH₂-CH₂-, -CO-N(R^{6h})-CH₂-CH₂-CO-NH-CH₂-, -CO-NH-C(-CONH₂)=CH-, -CO-NH-CH(-CONH₂)-CH₂-, -CH₂-C(H)(Me)-CH₂-S-, -O-CH₂-CO-NH-, -CH₂-N(R^{6h})-CO-CH₂-O-, -N(R^{6h})-CO-CH₂-O-, -C(H)(-CH₂-aryl)-, -C(H)(-CH₂-heteroaryl)-, -C(NH-aryl)=N-N=CH-, -C(NH-aryl)=N-N=CH-, -NH-N=C(-aryl)-, -NH-N=C(-aryl)-CO-, -NH-C(=N-CO-C₁₋₆ alkyl)-NH-(CH₂)₂-, -C(-NH-aryl)=N-N=CH-, -NH-C(-NH-aryl)=N-CONH-, -C(=CH-aryl)-CONH-CH₂-, -CH=C(R^{6h})-CONH-, -CH(-CH₂-aryl)-NH-CO- or -CH(OH)-, wherein said aryl or heteroaryl groups of Z_h may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, NO₂ or hydroxyl groups;
- R^{5h} represents hydrogen, C₁₋₆ alkyl or cyano;
- R^{6h} represents hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, cyano, C₃₋₈ cycloalkyl, -CH₂-C₃₋₈ cycloalkyl, aryl, heteroaryl, -C₁₋₆ alkylene-aryl, -CO-aryl, -CO-heteroaryl or -C(R^{7h})(R^{8h})-heteroaryl, wherein said aryl groups of R^{6h} may be optionally substituted by one or more halogen or C₁₋₆ alkoxy groups;
- R^{7h} and R^{8h} independently represent hydrogen or C₁₋₆ alkyl;
- R^{1h} and R^{2h} independently represent halogen, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₈ cycloalkyl, haloC₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, -O-C₁₋₆ alkenyl, haloC₁₋₆ alkoxy, -COOH, -CO-C₁₋₆ alkyl, -COO-C₁₋₆ alkyl, -CONH₂, -CH₂-CONH₂, -NH-C₁₋₆ alkyl, -NH-C₂₋₆ alkenyl, -NH-CO-C₁₋₆ alkyl, -CO-NH-C₁₋₆ alkyl, -O-CH₂-CO-NH-C₁₋₆ alkyl, -CH₂-CH₂-CO-NH-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -SO-C₁₋₆ alkyl, -SO₂-C₁₋₆ alkyl, -SO₂-NH-C₁₋₆ alkyl, -S-CH₂-CO-C₂₋₆ alkenyl, -SO₂-OH, amino, cyano, NO₂, =O, -CO-NH-(CH₂)₂-OMe, -NH-C₃₋₈ cycloalkyl, -CO-heterocyclyl, -CO-heteroaryl, -COO-(CH₂)₂-heterocyclyl, -OCH₂-aryl, -OCH₂-heteroaryl, -CH₂-O-CO-aryl, -O-aryl, -NH-CO-heteroaryl, -NH-CO-CH₂-aryl, aryl or heteroaryl groups, wherein said aryl, heterocyclyl or heteroaryl groups of R^{1h} and R^{2h} may be optionally substituted by one or more halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, =S or hydroxyl groups and wherein said C₁₋₆ alkyl or C₂₋₆ alkenyl groups of R^{1h} and R^{2h} may be optionally substituted by one or more hydroxyl, amino, cyano, C₁₋₆ alkoxy, CONH₂ or -COO-C₁₋₆ alkyl groups;
- u and v independently represent an integer from 0 to 3;
- with the proviso that the compound is other than compound number 757 and 878.

25. A pharmaceutical composition as defined in claim 24, wherein the compound of formula (IH) is selected from any of compounds:

- 35 395, 433, 689 or 786 as described herein or a pharmaceutically acceptable salt or solvate thereof.

26. A compound of formula (IA), (IC), (ID), (IE), (IF), (IG) or (IH) as defined in any one of claims 1 to 25 for use in therapy.

5 27. A compound of formula formula (IA), (IC), (ID), (IE), (IF), (IG) or (IH) as defined in any one of claims 1 to 25 for use as a casein kinase delta (CK1δ) inhibitor in the treatment of a neurodegenerative disorder, such as tauopathies.

28. A compound as defined in claim 27, wherein the tauopathy is selected from
10 Alzheimer's disease, frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), progressive supranuclear palsy (PSP), Pick's disease, corticobasal degeneration, multisystem atrophy (MSA), neurobasal degeneration with iron accumulation, type 1 (Hallervorden-Spatz), argyrophilic grain dementia, Down's syndrome, diffuse neurofibrillary tangles with calcification, dementia pugilistica,
15 Gerstmann-Straussler-Scheinker disease, myotonic dystrophy, Niemann-Pick disease type C, progressive subcortical gliosis, prion protein cerebral amyloid angiopathy, tangle only dementia, postencephalitic parkinsonism, subacute sclerosing panencephalitis, Creutzfeldt-Jakob disease, amyotrophic lateral sclerosis/parkinsonism-dementia complex, non-Guamanian motor neuron disease with neurofibrillary tangles/dementia, and
20 Parkinson's disease.

29. A compound as defined in claim 27 or claim 28, wherein the tauopathy comprises Alzheimer's disease.