High-throughput virtual screening of novel CHK1 inhibitors

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Check point kinase 1 (Chk1) is an essential protein in G2 phase checkpoint arrest, which cancer cells need to sustain the cell cycle and prevent cell death. Chk1 inhibitors have been shown to eliminate the S and G2 checkpoints and change the DNA repair pathway, resulting in immature mitotic progression, mitotic catastrophe, and cell death. Normal cells remain in the G1 phase to repair DNA damage as a result of p53 and are less affected by the deletion of the S and G2 checkpoints. Due of its function in this research we have tried to target CHK1 to identify potent CHK1 inhibitors by employing computer aided drug design. Million Molecules Database, Natural Product Database, NCI Database has been screened and three molecules has been identified by structure-based virtual screening followed by filtering for various drug likeness, ADME, toxicity, Molecular docking. Our research work resulted in lead molecules that have shown strong binding affinity with effective ADME properties, low toxicity, and high stability.

Graphical Abstract:



Key words: ewing sarcoma, CHK1, CHK1 inhibitors

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INTRODUCTION

Numerous anticancer treatments induce DNA damage and activate cell cycle checkpoints, giving cancer cells time to repair their DNA and recover [1]. As potential therapeutic targets, these checkpoints have been the subject of extensive research, and Chk1 inhibitors have emerged as fascinating novel therapeutic drugs [2]. Through inactivation of p53 or Rb or amplification of proto-oncogenes, cancer cells usually lack one or more genes for G1 checkpoint regulation (cyclins and CDKs). Chk1 inhibitors that inhibit the remaining checkpoints, S and G2, ought to render cancer cells more susceptible to anticancer therapies, such as c-radiation or DNA-damaging drugs [3-5]. Chk1 was initially recognized as a regulator of the G2/M checkpoint, but it has now been demonstrated to serve other roles in replication fork stability, origin firing, and homologous recombination. Inhibition of these systems can greatly increase the sensitivity of cells to specific antimetabolites [6,7]. Inhibition of CHK-1 is particularly effective in cancer cells devoid of p53 [8]. Consequently, the selective efficacy of CHK-1 inhibitors in combination with cytotoxic, such as DNA-damaging chemicals, is a significant advantage of these medications as cancer therapy [9-11]. Even if several small molecule-based CHK-1 inhibitors are undergoing clinical testing, there is always the possibility of identifying novel CHK1 inhibitors. Using computer-assisted drug design, we have attempted to identify effective CHK1 inhibitors in this study. Million Compounds Database, Natural Product Database, NCI Database has been examined and three molecules has been found by structure-based virtual screening followed by filtering for various drug Likeness, ADME, toxicity, Molecular docking. Our research led to the development of lead compounds with high binding affinity, efficient ADME characteristics, low toxicity, and high stability.

MATERIALS AND METHODS

Identification of Hits

For the Identification of Hit molecules; Million Molecules Database, Natural Product database and NCI Database available at RASPD were screened by following RASPD protocol [12]. A cut off was set at -7.0 Kcal/mol. Those molecules have successfully passed the cut off they were taken for further studies.

Filtering Hits based on Drug Likeness

Properties

Drug-likeness properties were evaluated by using Swiss ADME server [13]. To exclude molecules that are incompatible with pharmacokinetics parameters Lipinski's rule of five, Ghose rule, Veber rule, Muegge rule was applied. The molecules those have passed all these rules and having "Drug Like" properties were taken for further studies [14-17].

Lead Optimization

Docking:

To understand the molecular level interaction and get accurate poses Molecular Docking was carried out by using Auto Dock Vina implemented in AMDock [18,19]. The Crystal Structure of CHK1 was obtained from RCSB- Protein Data Bank (PDB After the Screening and removing the duplicate molecule a total id: 1nvq, resolution: 2.00 Å [20,21]. The crystal structure was freed from water molecules, Co-Factors, ions and covalent ligand by using the Dock-prep procedure implemented in the UCSF Chimera program [22]. Charges were computed, polar hydrogen atoms were subsequently added. As no active site was mentioned so we preferred for bind docking. The grid box centred in (X=5.062639, Y=6.464194, Z=16.857611) based on the active sites of the protein (CYS87, ALA36, LEU15, GLY16, GLU91, LEU137, GLU85, VAL23, LYS38, SER147, ASN135) [21,23]. Grid box centre points and dimensions were set to target the substrate binding-binding pocket of the protein. The best docked pose was selected based on its binding energy score and significant interactions in Active sites. Based on the ΔG , the best result was subjected to ADME and Toxicity.

ADME:

The Pharmacokinetic profile was checked by using Swiss Lead Optimization ADME, Pre-ADMET, vnnadmet [13,24,25]. Parameters such as Solubility (LogS), Water solubility (mg/ml), Solubility Class, SKlogS buffer, Bioavailability, GI Absorption, Human Intestinal The docking was carried out to find the most suitable Confirmation Absorption (HIA %), Madin-Darby Canine Kidney (MDCK), of the molecule that can bind with CHK1 with lowest being Caco-2 Permeability, Skin permeability (logKp) (cm/s), Partition energy. Out of all 51 drug like molecules, top 35 molecules were Coefficient (LogP), Distribution Coefficient (logD), BBB taken for further studies based on their binding energy and (Cbrain/Cblood), BBB, Pgp Inhibition, P-gp Substrate, Plasma chemical interactions. The Molecular Docking Results of all the protein binding (%PPB), Human Liver Microsomes (HLM), 53 molecules along with SMILEs and binding energy has been CYP1A2 inhibitor, CYP3A4 inhibitor, CYP3A4 Substrate, reported in Table 1. CYP2D6 inhibitor, CYP2D6 substrate, CYP2C9 inhibitor, CYP2C19 inhibitor were selected for the studies. Those molecules have shown proper pharmacokinetic profile taken for The reason behind the failure of lead molecules in the Clinical trial further studies.

Toxicity:

was carried out by using Pre-ADMET, vnnadmet and lazar [24-

26]. Toxicity parameters such Acute Oral Toxicity, Human Ether-a-Go-Related Gene Inhibition, Liver Toxicity: Cytotoxicity, Mitochondrial Toxicity, Acute algae toxicity, AMES, Carcinogenicity (Mouse), Carcinogenicity(Rat), Carcinogenicity (Rodent), Acute daphina toxicity, hERG Blocker

Honey Bee Toxicity, Acute fish toxicity (medaka), Acute fish toxicity (minnow), Ames TA100 (-S9), Ames TA1535 (-S9), Biodegradation, MRTD (mg/day) were predicted. Only nontoxic molecules have been reported as therapeutic potential for CHK1 inhibitors.

RESULTS AND DISCUSSION

Identification of Hits

3313 unique hit molecules were found that are binding with the receptor having binding affinity less than -7.0 Kcal/mol which were taken for further studies..

Filtering Hits based on Drug Likeness Properties

To get lead like molecule Swiss ADME server was used to calculate all the hits in multiple batches. Microsoft Excel was employed for process and analysis of the data generated by Swiss ADME. Out of 3313 hit molecules only 51 Molecules Obeyed multiple drug likeness Rules such as Lipinski rule, Ghose rule, Veber rule, Muegge rule. Among them 2010 Molecules obeyed Lipinski Rule of 5 followed by 1775 molecules obeyed Veber rule, 1710 Molecules obeyed Egan rule, 1507 molecules obeyed Muegge rule, and 51 molecules obeyed Ghose rule.

Docking:

ADME:

are low Poor ADME properties. To eliminate such molecules which having poor pharmacokinetic profile Insilco Pharmacokinetics study was conducted. Out of 35, only 17 molecules have passed all Toxicity causes 30% of lead candidates to fail. The toxicity study the criteria of ADME Profile. A detail view has shown in Table 2.

Tab. 1. Docking Results	Molecule Id	SMILE	Binding Energy
	ZINC12132957	Cc1cc(=O)c(c2n1-c3ccccc3S[C@H](C2)c4ccccn4)C(=O)NC[C@H]5COCCO5	-10.1
	ZINC20600602	c1ccc(cc1)c2c3ccccc3c(=O)n(n2)CC(=O)N[C@@H]4CCCN(C4)c5ncccn5	-10.1
	ZINC12516005	Cc1cc(n(n1)c2nc3c(n2CCCc4ccccc4)c(=O)n(c(=O)n3C)CC(=O)C)C	-9
	ZINC01056864	c1ccc2c(c1)CCN(C2)C(=O)c3cnn4c3nc(cc4C(F)(F)F)c5cccs5	-8.9
	ZINC01056864	c1ccc2c(c1)CCN(C2)C(=O)c3cnn4c3nc(cc4C(F)(F)F)c5cccs5	-8.9
	ZINC11840098	Cc1cc(n(n1)c2cccc(c2)C(=O)NC[C@H]3Cc4cc(ccc4O3)c5ccc(nn5)OC)C	-8.8
	ZINC14992739	CCOC(=O)[C@@H]1CCCCN1C(=O)c2cc(cc(c2)n3cnnn3)c4cc(ccc4OC)Cl	-8.8
	ZINC11784547	COc1ccc2c(c1)[nH]c(n2)CCNC(=0)CC[C@@]3(CCC(=0)N3)Cc4ccc(cc4)Cl	-8.6
	ZINC00945916	Cn1c2cccc2nc1SCC(=O)N/N=C/c3ccc(cc3)OCc4ccccc4	-8.5
	ZINC12034833	CN(Cc1nc2ccccc2s1)C(=O)C[C@]3(CC(=O)N(C3=O)C4CC4)c5ccc(cc5)OC	-8.4

ZINC14885414 Cctccc(n1)2cccc2(c)P(I)03IXN(=)DCXN(C)(P0(P0)(ACS(=A))(ACS(=A)) 8.3 ZINC14733310 Cctccc(n1)2ccc(c)P(I)(-0)(C)CAIRCAACCA(P)(P)(F)Excco5 8.1 ZINC1235676 Cctcc(c)II(I)(HH)2CXN(C)(C)(C)CO23ccc4(c)I)(CCCCA 8.1 ZINC1235676 CCCCCL(ccc(c)IN(C)(-0)C3CCACCC2)CCCCA 8.1 ZINC1235670 CCCCCL(ccc(c)IN(C)(-0)C3CCACCC2)Aanna)AccCAC(F)(F)F)Excco5 8.1 ZINC123620 Ctccccc1(I)C2CCacc(C2)(H)+I)(O)(C)(-I)(F)F)F(P)(P)N 8 ZINC123620 Ctccccc1(C)C2CCaC(C)(Z)(H)+I)(C)(D)(C)(F)F)F(C)N 8 ZINC123620 Ctccccc1(C)C2CCaC(C)(Q)H)I(C)(D)(C)(F)F)F(C)N 8 ZINC123620 Ctccccc1(C)(D)(Z)(C)(Q)(Q)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)	ZINC12447659	Cc1ccc(cc1)C2=NN(c3nc4c(n3[C@@H]2C)c(=O)n(c(=O)n4C)C)[C@@H]5CCS(=O)(=O)C5	-8.3
2INC1473310 Cc1ccc(c1)2cc(c2)[c-0] 6.31 2INC01216760 cc1ccc(c1)[N(H+)2CCN(C2)[c-0] 6.11 2INC01253930 CC0c1cc(c1)[N(H+)2CCN(C2)[c-0] 6.11 2INC14885974 C[C0H][c1cccs1]N(C)[C)=0] 6.11 2INC14885974 C[C0H][c1cccs1]N(C)[C)=0] 6.11 2INC19259509 c1ccc(c1C)[CCCC(C)[C)[F][F][C][O]N(C) 6.11 2INC12038520 c1cccc(c1)[CCCC](C)[C][F][F][C][C]N(C) 6.31 2INC12038520 c1cccc(c1)[CCC][C][F][F][C][C]]N(C) 6.31 2INC12038520 CC1cccc(c1)2c3:cc(c1)N(C)[C][C][F][F][C]]N(C) 6.31 2INC12434790 CCN[CCC1:cccn1][C][C][C][C][C][C][C][C][C][C][C][C][C]	ZINC14885414	Cc1ccc(nc1)c2ccc3c(c2)C[C@H](O3)CNC(=O)CCN(C)[C@@H]4CCS(=O)(=O)C4	-8.3
2INC01216760 c1ccc(cc1)C(NH+12CCN(C2)C)C-03cmA(-3nc(cc4C(F)(F)F)-5ccco5) -8.1 2INC0285380 CC001cccc(c1)N(C)(C)O(2cc(c(c2))SCCA4(cc3)CCC4 -8.1 2INC1885974 C1CGEHI(C)C)O(2cc(c(c2))SCDA4CS(C)CCC4) -8.1 2INC19774479 c1ccc(c1)O(2cc(c(c2))C(C))(C)(P)(F)(F)(F)(C)ON -8 2INC12038520 c1ccc(c1)O(2cc(c2)(C)(-0)(C)(H)(P)(C)(C)(D)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)	ZINC14733310	Cc1ccc(s1)c2cc(cc(c2)S(=O)(=O)N3CCOCC3)C(=O)N(C)Cc4nccn4C	-8.3
ZINC28539380CCC0c1ccc(c1)N(C=0)Csc2nc(c2)CpC0c2ccc4(c3)CCCC49.81ZINC1885974C[CQH][c1cccc1)(C1C(C2)C1C-0)C3cndc4CccC4C4[P[F]F]C5Ccco59.81ZINC108925969c1ccc(c1)Oc2ccc(c2)[N+1]-0](D-1)[C[F]F]C1-0]N.8ZINC1039620c1ccc-2(c1)Oc2ccc(c2)[N+1]-0](D-1)[C[F]F]F]C1-0]N.8ZINC1239620c1ccc-2(c1)Oc2ccc(c2)[N+1]-0](C-0]N[CC0CC4CccC4).8ZINC12464790CCN(CCn1cccn1]C1-0]C[CQH]2C[-0]NCCN[N+1]2C3ccc4ccc4c3.8ZINC14530440COc1cccc1[C]=0]Z(CH]12(C]]N(C1)O(C2)CC4cccC4).8ZINC14530440COc1cccc1[C]=0]Z(C(H)1]C3C3cccc3]C(C)D[NC[C]C4cccc4C4].8ZINC12461790CCn1ccc1[C]=0]Z(C(H)1]C3C3cccc3]C(C)D[NC[C]C4cccc4C4].8ZINC1246104Cc1ccccc1[Q=@]Z(C(H)N]C2=O[C3cccc3]C(C)D[NC[C4cccc4C5].8ZINC1245157C1ccc(c1)]Z(C(H)]Z(C)C]C3cccc3]C(C)D[NC[C4cccc4C5].8ZINC1245157C1ccc(c1)]Z(CN(C2)C[-0]C3cnnd-3]C(c4C)D[NCCC0.8ZINC1245157C1ccc(c1)]Z(CN(C2)C[-0]C3cnnd-3]C(c4C)D[NCCC0.8ZINC1295050C1ccc(c1)]Z(CN(C2)C[-0]C3cnnd-3]C(c4C)D[NCCC0.8ZINC1295050C1ccc(c1)]Z(CN(C2)C[-0]C3cnnd-3]C(c4C)D[NCCC0.8ZINC1295050C1ccc(c1)]Z(CN(C2)C(C)[C][C]]=]S(C-0)O[N(C)C4cccc452.8ZINC1295051C1ccc(c1)]Z(CN(C2)C[C][C]]=]S(C-0)O[N(C]C4cccc452.8ZINC1295051C1ccc(c1)[Z][D]]=[D]]Z(C1)[C][D]]Z(C1)[C][D]]Z(C1)[C]][D]]Z(C1)[C]]Z	ZINC01216760	c1ccc(cc1)C[NH+]2CCN(CC2)C(=O)c3cnn4c3nc(cc4C(F)(F)F)c5ccco5	-8.1
2INC1485574 C[C@H][c1ccc1]N(C)C(-0)2cc(cc(2)Rann3)c4ccc5c4ncc5 8.1 2INC19774779 c1ccc(c1)(C)2CcC(2)[-0)3cnn43n(c4cc(f)[F]F)F5ccc5) 8.1 2INC10395503 C1cccc-2)[c1]C3-2ccc(c3]C[NH+]4CCC[C@H][(C])N(C)COC) 8 2INC12038620 C1cccc-2)[c1]C3-2ccc(c3]C[NH+]4CCC[C@H][(C])NCCCO) 8 2INC1453040 CCN(CCn1ccn1)C[-0)C[C@H][CC])NCCN(CN(C3)Ccccccc4c3) 8 2INC1453040 CCn1ccc(c1)c2:n([C])P(I/C)[P(I/C)]NCCOC3)CCC6ACccc4 8 2INC14730488 CN(C)[C-0)c1c2c(n)I/C)[P(I/E)[C2]NACCOC3CccC6C5C4]CI 8 2INC14730489 CN(C)[C-0)c1c2c(n)I/C)[P(I/E)[C2]NACCOC3CccC6C4CC5 8 2INC14730589 CC1cccc(c1)P2CCI(PO)I/C2)C(C3CccnC3C4Ccc4C6 8 2INC14987901 c1ccc(c1)P2CCI(C)P(I/C)P(I/C)ACccccc6C4CC5] 8 2INC1208505 c1ccc(c1)P2CCI(C)P(I/C)P(I/C)ACccccc6C4CC4C7] 8 2INC1208507 c1ccc(c1)N2CD(C)C(C)C)C)P(I/C)Accccc4C5CC5 8 2INC1208507 CC1CCCC(I/N+2)[CCC)C(C)C)C)P(I/C)Accccc4C5CC5 8 2INC1208507 CC1CCCC(I/N+2)[CCC)C(C)C)C)P(I/C)Accccc4C5CC5 8 2INC1208507 CC1CCCC(I/N+2)[CCC)C)C(C)C)C(I/C)P(I/C)CC4CcccC4C5C5 8 2INC120757	ZINC02859380	CCOc1ccc(cc1)NC(=O)CSc2nnc(n2C)COc3ccc4c(c3)CCCC4	-8.1
ZINC19774479 c1ccc(c1)C[NH+]2CCN(C2)C[-0)c3cnn43nc(cc4C[F][F]F]c5ccc05 8.1 ZINC0952569 c1ccc/c1]Dc2ccc(c2][H[=D]D)C[F][F]F]C[=D)N 8 ZINC10358620 c1ccc-2c1]Dc2ccc(c2][NH]CCD[CC]P]I[C4]DSCcn(D)NCCCO 8 ZINC1444790 CCN(CCn1cccn1](C=D)C[P]I]ZC[D]NCCN(IC]/C2/c3ccc(c3D)CCdCcccc43 8 ZINC1453844 COC1ccccc(1)c2-23nc([InH+]2](DP]H4CCOC4]CCN(IC]/C2/c3ccc(c3C4)CI 8 ZINC1453850 CCN(CC(1)C[-D)C2(C][P]H2[C1]NCCC04]CCN(IC]/C3/c3ccc62(C5C4)CI 8 ZINC14740689 CN(IC)C[-D)C2(C][P]H2[C2]NCC04]CCN(C3)Ccc62(C5C4)CI 8 ZINC14740689 CN(IC)C=D)C2(C][P]H2[C2]NCC04]CCC4CccC5C4 8 ZINC14740689 C1cccc(c1)2(Carc(1)2(CC1)C)NC2C0Cc3Ccc63)CI(D)N(C2C0Cc3Ccc53)CI 8 ZINC104880502 c1cccc(c1)2(CAC1)2(C1)C)C3cccc3)CIN(IC]CC4Cccc53 8 ZINC10483139 CCOCCC[O]IC12C1(INH)2CCC(C2)C)C]C3ccn423)CCA(C2)[CP]NC2CC03 8 ZINC10483139 CCOCCC(INH+2][C2P]H1[CCC]C3ccc3]CA(IC)C2]C4cccc45Ccc53 8 ZINC10453144 CC11[C0PH1]ZCCN(C2)[C0]C3ccn423]CCA(C2)[CP]N(C2)C4cccc45]CCC3]C 8 ZINC10453159 CC11CCCC1][C0PH1]CCC]C3cc1]C2CC3]C[C0PH1[CC2]A4cccc42]CCA]C1 8 ZINC1453551 CC11CCC1][C0PH1	ZINC14885974	C[C@H](c1cccs1)N(C)C(=O)c2cc(cc(c2)n3cnnn3)c4cccc5c4nccc5	-8.1
ZINC08925969ctcc(cc1)02ccc(c2)(PI(F)F)C(=0)N.8ZINC1208520c1ccc-2c1(C3-2ccc(c3)C(MPH)4CCC(Q=MI)(C4)N5cc(n5)C(=0)NCCCO.8ZINC12464790CCN(CCn1ccn1)C(=0)C(CM)2C(-C)C3ccc(cc3)OC64cccc4.8ZINC14530440C0c1cccc(1)2c1an(I(n+1)2)[C@H]4CCO4)CCN(C3)Cc5cc6(cc5C1)OC06.8ZINC14530440C0c1cccc(1)2c1an(I(n)C3ccccc3)C(CM)4COC2>ccc(cc5C4)CC.8ZINC1470689CNC(C)C(-D)c1c2c1(n1)C(-C3)Ccccc)C3(CC)ON(C)Cc4cccs4.8ZINC12401040Cc1ccccc1]0a2(m2)CC(=0)N3cCCCC3C(mC)C2>ccc(cc5C4)CC.8ZINC1245157Cc1ccccc1]0a2(m2)CC(=0)N3cCccC3C+QCCC4.8ZINC1245157Cc1ccccc1]0a2(m2)CC(=0)N3cCccC3C+QCCC4.8ZINC1473339CCCCC(=0)LC2(n)PI(C2)C(=0)N3cCccC3C+QCCC4.8ZINC1473339CCCCC(=0)LC2(n)PI(C2)C(=0)N3cCccC3C+QCC4.8ZINC1473339CCCCC(=0)LC2L2(n)PI(D)C2)C3cccca3)C(C)ON(CCC0.8ZINC1473339CCCCC(=0)LC2L2(n)PI(D)CC1CC2CccC3C+QCCCC4.8ZINC1473339CCCCC(=0)LC2L2(n)PI(D)C2)CC2(ccc4C+Scccc5.8ZINC1473339CCCCC(=0)LC2L2(n)PI(C2)(C2)(C2)(-0)Acsmcc4C4CF)[F)F)C5ccc5.8ZINC1473339CCCCC(C1)C(2)PI(C2)(C2)(C2)(C1)(C2)(C2)(C2)(C2)(C2)(C2)(C2)(C2)(C2)(C2	ZINC19774479	c1ccc(cc1)C[NH+]2CCN(CC2)C(=O)c3cnn4c3nc(cc4C(F)(F)F)c5ccco5	-8.1
2INC12038620 ctccc-2(c1)Cc3c2ccc(c3)C(NH+4)CCC(C@PH](C4)N5cC(onS)C(=0)NCCCO -8 2INC12038620 CCCCCCC1Cc2cc(c1)C(-0)C(CC)(-C/-C/CcCcccc(c2)C)CCA -8 2INC14538250 CCCN1Ccc1(c1)C(-0)C(CP)[2(C)ONCCCO)(CN(C1)C5Cc5cc(c5C)C)CCO -8 2INC14538250 CCCN1c2cc(c1)L2:AnI((InH)+2)[CP)H[CCC)AdcCOC4SCCC(C5C)C]CI -8 2INC14730689 CN(C)C[C)C)L2:C(n1)]C(-3Cccccc)C(C)(2)Cdc4ccc5C4CCCC)C]CI -8 2INC14730689 CN(C)C[C)C)L2:C(n1)]C(-3Cccccc)C]C(O)N(C)Cc4cccsC4)CI -8 2INC14730689 CN(C)C[C)C)L2:C(n1)]C(-3Cccccc3)C(C)O)N(C)Cc4cccsC4)CI -8 2INC14987901 CLCccc(c1)N2CCN(C2)(C)C)C(C4cccc4)C(C)ONCCCO -8 2INC149887901 CLCccc(c1)N2CN(C)C)(C)C)C3Cn4CCC4(F)(F)F)Sccccc5 -8 2INC14987901 CLCCC(C)N+1]CCN(C)C)(C)C)C3Cn4CCC4(F)(F)F)Sccccc5 -8 2INC14987901 CCCCC(C)N+2](C)(P)H]3CCD)(C)C4Ccccc4Sccc5 -8 2INC14987901 CCCCCC(N+2)[C)(P)H]3CCN(C)C)C4Ccccc4Sccc5 -8 2INC14987901 CCCCCC(C)N+2)[C(P)H]3CCN(C)C)CAccccc5C)(1 -8 2INC14987901 CCCCCCC(N+2)[C)(P)H]2CN(C)C)CAccccc5C)(1 -8 2INC1495315 CCCN(C)CCCC)N+2][CP]H]3CCN(C)C)O)CN(C)C-0]Cccccc5C)(1 -7	ZINC08925969	c1cc(cc(c1)Oc2ccc(cc2[N+](=O)[O-])C(F)(F)F)C(=O)N	-8
2INC00955034 CS[=0](=0]c1ccc2c1c1]sc(n2)NC[=0]/C=C/c3ccc1cc3)OCc4ccccc4 -8 2INC12464790 CCN(CCn1ccn1)C=0)C[C@H]ZC(=0)NCCN(H12)C3cccccc4ccc4C3 -8 2INC143530440 CC0c1cccc(1)C2c3n(c[n1)H-12)CGCH]CCOVACSCcc(cc5C4CIC) -8 2INC1435305 CCn1c12c2(n1)C[-0)NC2C0C0C3C(C[@H](CC2)N4CC0C5ccc(cc5C4CIC) -8 2INC14746689 CN(C)C[=0]c1ccc(c1)PC(m2)C5Ccc(m3)CC1=0)N(C)Cc4ccsc4 -8 2INC1245157 Cc1ccccc(1)PC(m2)C2(C=0)NC2Cc5CF]64Cncc4 -8 2INC1245157 Cc1cccc(c1)PC(m2)C2(C=0)NC2Cc5CF]64Cncc4 -8 2INC1245157 Cc1ccc(c1)N2CN(C2)(C=0)Scaccn3)CCN(2)C4ccsc45Csc55 -8 2INC1345169 CCC0C(-0)1C22(n]H12CCCC(C)(C)C)C10C3Cncd3)CCAC(C)(F)[F]Sccc55 -8 2INC1363801 CCC0C(-0)12C2(n]H12CC2(csc32C2(-0)n(n3)C4CC5cccc5C5)C1 -8 2INC1393801 CCC0C(C)12C2(n]H12CC2(csc32C2(-0)n(n3)C4c5cccc45)Cc2 -8 2INC1393801 CCC0(C(m2)H12C)CM3(CGH]12(C0)C10)N(C)C4cccc4)C1 -8 2INC1393801 CCCN(C(1CC0C1)C02Ccccc2)C)(N(C)CQH13(CC03)C(-0)Acccc4)C1 -8 2INC1203076 CCN(C(1Cccc1)C1)CM14)ZCCC)(C)C)(M14(C)C0)C(C)C4cccc4)C1 -79 2INC1203077 CC1(CCC0)C10C2ccc2)CC)(N(C)CQH13(CC03)C)(-0)Acccn10AC1	ZINC12038620	c1ccc-2c(c1)Cc3c2ccc(c3)C[NH+]4CCC[C@@H](C4)n5cc(nn5)C(=O)NCCCO	-8
ZINC12464790 CCN(CCn1cccn1)C(=0)C(C@H]2C(=0)NCCN(H+]2C3ccc4ccccc4SC)OC06 -8 ZINC14530440 COC1cccc(1)C2AIn([HH+]2)C(@H]4CCOC4)CCN(G)C5cc6c(cCSC)OC06 -8 ZINC14538250 CCn1c2c((n1)C(=0)N3CCOCG)C(Q)C(C)C4cccc6C)CCCCSC)OC06 -8 ZINC1470689 CN(C)C([-0)C122c)(C)C3CCCG)C(Q)C(C)C4cccc6S4C)C -8 ZINC12401004 Cc1cccc(c1)@Q)2(CC(=0)N(C2=0)C3CccG)AC(C)(Q)(C)C4cccc64 -8 ZINC1245157 Cc1ccc(c1)D2C1/Q(C)(Q)(C)C4CCCC3H)(4C(0n4)C(=0)NCCCC -8 ZINC025602 c1ccc(c1)D2CCN(C)(Q)(-0)C3CcnA3C)(C4(F)(F)F)Scccco5 -8 ZINC1373139 CCCOCC(N)H+12CCN(C2)(C-0)C3CnA43n(c4C4(F)(F)F)Scccco5 -8 ZINC1373139 CCCOCC(N)H+12CCN(C2)(C-0)C3CnA43n(c4C4(F)(F)F)Scccco5 -8 ZINC137377 CCC0CCC(N)H+12CCN(C2)(C)(-0)C3C(C)(C)(C)(C)(-0)C4CcccC4S)(C1) -8 ZINC1303789 CCCN(Cc1cccn1)[C@H]3CCCO3)(C-0)C4CccccAS(C1) -8 ZINC1305079 CC1(CCC1)C0C2cccc2)CC)(C)(C)(@H]3CCCO3)(C-0)ActoscccAS(C1) -8 ZINC123757 C1c1cccc12Cn(N)C1/CC2)CN(C1/CC@H]3CCCO3)(C-0)ActoscccAS(C1) -7 ZINC130579 CC1(CCC1)C0C2/CC2)CN(C1/CC@H]3CCCO3)(C-0)ActoscccAS(C1) -7 ZINC1237957 C1c1(CCC1)C02/CC2)CN(C1/C@H]3CCC	ZINC00955034	CS(=O)(=O)c1ccc2c(c1)sc(n2)NC(=O)/C=C/c3ccc(cc3)OCc4ccccc4	-8
ZINC14530440 COC1cccc(1)c2c3n(c[nH+]2][C@H]4CC0C4)CN(C3)cCsccc6C5C4)C1 -8 ZINC14538250 CCn1c2c(n1)(C=0)N3CC0CC3)C(@H](C2)N4CC05cscc(c5C4)C1 -8 ZINC14740689 CN(C)C(=0)c1c2c(n1)C3ccccc3)C(C@H](C2)C4ccn5c4ccc5C4)C1 -8 ZINC1245157 Cc1cccc(1)@2[2(C(=0)N(C2=0)C3Ccccn3)C(C=0)N(C)C4ccsc4 -8 ZINC02504256 c1ccc(cc1)D2C(NC2)C(=0)C3Cn4C3n(C4C4(F)(F)F)5Ccco5 -8 ZINC03606020 c1ccc(cc1)C(NH+]2CN(C2)C(=0)C3Cn4C3n(C4C4(F)(F)F)5Ccco5 -8 ZINC1458301 CCOCCC(ND+12)C(Q)C1(C2)C(=0)C3Cn4C3n(C4C4(F)(F)F)5Cccc5 -8 ZINC14584144 CC11[C@H]2CC+C([C@H]1CC2Cs(C3C2(C=0)n(n3)C4C5cccc45C4(F)(T) -8 ZINC1458511 CC0C(C(ND+12)[C@H]1CC2Cs(C3C2(C=0)n(n3)C4C5cccc45C4(F)(T) -8 ZINC14584144 CC11[[C@H]2CC-C1[C@H]1CC2Cs(C3C2(C)[0)Acm5c4mcc45 -8 ZINC1458515 CC0C1(C0C1)C02ccccc2C)CN(C[C@H]3CCC03)C(=0)Acm5c4mcc5 -8 ZINC1230378 CC11cccc10[M+12]CQ](M]40C0C3)C(=0)Acm5c4mcc45 -8 ZINC12300378 CC11cccc10[M+12]CQ](M]3CC03)C(=0)Acm5c4mcc45 -7.9 ZINC12300378 CC11cccc10[M+12]CCQ](N](C1C@H]3CCC03)C(=0)Acm5c4mcc45 -7.9 ZINC12300378 CC11cccc10[M+12]CCQ](N](C1C@H]3CCC03)C(ZINC12464790	CCN(CCn1cccn1)C(=O)C[C@H]2C(=O)NCC[NH+]2Cc3ccc4ccccc4c3	-8
ZINC14538250 CCCn1c2c((n1)C(=0)N3CC0CC3)C(Q#)I(C2)N4CC02sccc(c2S(4)CI -8 ZINC14740689 CN(C)C(=0)L12c1(n1)C3ccccc3)C((2)N(C)C4ccnc54ccc4 -8 ZINC145157 Cc1cccc(1)P2(C)Q)N(C2=0)N(C)C4ccnc54ccc4 -8 ZINC14987901 c1ccc(cc1)P2(C)Q)N(C)C4)O(N2C00)CCC0 -8 ZINC02504256 c1ccc(cc1)P2CN(C2)C(-0)C3cnn42an(c4C4(F)(F)F)Sccc55 -8 ZINC03880620 c1ccc(cc1)N2CN(C2)C(-0)C3cnn42an(c4C4(F)(F)F)Sccc55 -8 ZINC14933139 CC0CC(NH2+I)COMCC2)C(-0)C3cnn42an(c4C4(F)(F)F)Sccc55 -8 ZINC1493814 CC01(CC(H)12CC)C(C)C)C)C)C10C1CaC(m3)CAC5cccc5C4)C1 -8 ZINC14954144 CC01(CC(H)2C)C-C(ICQ@H)12CC3(CM)3C(C)C)ON(C)OAccccc4DSccc05 -8 ZINC12036079 CC01(CCC1)DC2cccc2COC)CN(C(C@H)3C(CC3)C(-0)Acn5Acncc5 -8 ZINC12036079 CC1(CCC1)DC2cccc2COC)CN(C(C@H)3CCC03)C(-0)Acn5Acncc5 -7.9 ZINC12300378 CC1(CCC1)D12CC2C(C)CN(C)C(Q)H)3CCC03)C(-0)Acn5Acncc5 -7.9 ZINC12278958 C11cccc1)D12(P)(I)C2P)N2CC32c(CC3)C)C)C0CCCCC -7.9 ZINC12278958 C11cccc1)D12(P)(I)CC1)C12CC2CCC)C)CCCCCCCCCCCCCCCCCCCCCC	ZINC14530440	COc1cccc(c1)c2c3n(c([nH+]2)[C@H]4CCOC4)CCN(C3)Cc5cc6c(cc5Cl)OCO6	-8
ZINC14740689 CN(C)C(=0)c1c2c(n(n1)Cc3ccccc3)CCN(C2)C4ccnc54cccc5 -8 ZINC1204104 Cc1ccccc1[Q@]2(C(=0)N(C2=0)C4ccnc3)C(=0)N(C)C4cccs4 -8 ZINC12045157 Cc1cccc(c1)2(C(n)2)C(-C)C(-C)(C)C4ccnc3)C(-C)N(C)C0 -8 ZINC14987901 c1ccc(c1)2CCCN(C2)C(-0)3cnn43n(c4C4(F)(F)F)F)Sccco5 -8 ZINC05680620 c1ccc(c1)2(CN(C1)C)C(-0)3cnn43n(c4C4(F)(F)F)Sccco5 -8 ZINC14733139 CCCOC(C)0)122C(n(n1)C3ccccn3)CCN(C)C2C4ccccc4Sccco5 -8 ZINC14733139 CCCOC(C)NH1/2CCX(ICC2)(-0)3cnn43n(c4C4(F)(F)F)Sccco5 -8 ZINC14733139 CCCOC(C)NH1/2CCX(ICC2)(-0)3cnn43n(c4C4(F)(F)F)Sccco5 -8 ZINC14733139 CCCOC(C)NH1/2CCX(ICC2)(-0)140(C)C4ccccc4Sccco5(A)(1 -8 ZINC1473539 CCOI(CC1(DCH)1/2CC3(CCC3)(C)D)(C)0/2CCCC3CCC4)(C) -8 ZINC12306079 CCIC(CCC1(CC2)(C)C)(C)(C)H1/3CCC03)(C)O)(C4ccccc4)(C2 -8 ZINC12303078 CC1(CCC1)(DC2/CCCC)(C)C(C)H1/3CCC03)(C)O)(C4ccccc4)(C2 -7.9 ZINC12303078 CC1ccccc1C10n(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(ZINC14538250	CCn1c2c(c(n1)C(=O)N3CCOCC3)C[C@H](CC2)N4CCOc5ccc(cc5C4)Cl	-8
ZINC12041004 CC1ccccc1[C@@]2[CC(=0)N(C2=0)C3cccnc3)CC(=0)N(C)Cc4ccsc4 -8 ZINC01245157 CC1cccc(c1)n2C(nnc3CC(=0)Nc3ccccc3F)C4cnnc4 -8 ZINC01245167 c1cccc(c1)2CC(NL+3)CCC(C)(H)(C)Nc4ccnc4(-D)NCCCO -8 ZINC02504256 c1cccc(c1)N2C(N(C2)C(=0)c3cnn43n(cc4C(F)(F)F)C5cccs5 -8 ZINC04680620 c1cccc(c1)N2C(N(C2)C(=0)c3cnn43n(cc4C(F)(F)F)C5cccs5 -8 ZINC1493139 CCOC(=0)t2C(n(n1)C3ccccn3)CN(C)C2)C4ccccc4c5ccco5 -8 ZINC14954144 CCC1[[C@H]2CC=C[[C@H]1C2)CN3C[C@H][C]CH]3C(=0)OC)NC(=0)c4ccccc4n5cccn5)C -8 ZINC14954144 CCC1[C@H]2CC=C[[C@H]1C2)CN3C[C@H]3C(C3)C(=0)C4cnc5c4ccc5 -8 ZINC14954144 CCC1[C@H]2CC=C[[C@H]1C2)CN3C[C@H]3CCC3)C(=0)c4cnc5c4ccc5 -8 ZINC12037267 CCC1(CC1(C1)C2/CC2)CN(C]C@H]3CCC03)C(=0)c4cnc5c4ccc5 -8 ZINC12306378 CC1(CCC1)C02ccc(c2)C)N(C]C@H]3CCC03)C(=0)c4cccn4C2 -7.9 ZINC12278958 Cn1cc(c1)D(2)C1/C02/CC(C2)CN(C]C@H]3CCC03)C(=0)C4cccn4C3 -7.9 ZINC12278958 Cn1cc(c1)C1/C02/CC(C2)CN(C]C@H]4CCC04)CC0/C05CC5 -7.8 ZINC1256779 CCICcccn12/C(M]2/CE(=0)N/CCCacccc2)CO/C0CC -7.8 ZINC1257898 Cn1ccc(c1)D/C(C)@N/CCCacccc2)CO/C0CC </td <td>ZINC14740689</td> <td>CN(C)C(=O)c1c2c(n(n1)Cc3ccccc3)CCN(C2)Cc4ccnc5c4cccc5</td> <td>-8</td>	ZINC14740689	CN(C)C(=O)c1c2c(n(n1)Cc3ccccc3)CCN(C2)Cc4ccnc5c4cccc5	-8
ZINC01245157 Cc1ccc(c1)n2CC(C2)(NH+]3CCC(C2)H(C3)n4cc(nn4)C(-D)NCCCO -8 ZINC14987901 c1ccc(c1)c2ccc(c2)C(NH+]3CCC(C2)H(C3)n4cc(nn4)C(-D)NCCCO -8 ZINC02504256 c1ccc(c1)N2CCN(C2)C(-D)c3cn4c3n(c4C(F)[F)[F)5cccc55 -8 ZINC03806020 c1ccc(c1)(NH+]2CCN(C2)C(-D)c3cn4c3n(c4C(F)[F)[F)5cccc55 -8 ZINC14733139 CCOC(C0)c1c2c(n10)C2Ccccc3c2c3c2(-D)(nc3)C4Cc5cccc54)C1 -8 ZINC14954144 CCC1([C0]H]2CC=C([C0]H]1CC2Cc3c2c3c2)CN(C3CCCC3)C(-D)C4cnccc4c45cccc5) -8 ZINC12037267 CC0c1cccc(c1)C2Cccc3C2)CN(C3CCCC3)C(-D)C4cnccc4c45cccc5) -8 ZINC12037267 CC0c1cccc1)C0C2cccc2)CN(C3CCC3)C(-D)C4cnccc4c3C2 -8 ZINC12037267 CC1(C0C1)C0C2cc(cc2OC)CN(C1C0@H]3CCC03)C(-D)C4ccccc4)C2 -8 ZINC1203767 CC1cccc1c1Cn(n2]C@H]3CCC03)C(-D)C4ccccc4)C2 -7.9 ZINC1203778 CC1(C0C1)C0C2cccc2OC)CN(C1C0@H]3CCC03)C(-D)C4ccccc4)C2 -7.9 ZINC1203779 CC1cccc1c1Cn(n2]C@H]3CCC03)C(-D)C4ccccc4)C2 -7.9 ZINC1278978 Cn1ccc(1)C0(1)C02cc(c2)C)CN(C1C@H]3CCC03)C(-D)C4ccccc4) -7.9 ZINC1278979 CC1cccc1n2[C0]H]CCC0A)C(C0C)C3ccccc3)CCCCCC -7.9 ZINC1278958 Cn1ccc(c1n1)C(C)C)ACCCC2)C(C0)CC	ZINC12041004	Cc1ccccc1[C@@]2(CC(=O)N(C2=O)Cc3cccnc3)CC(=O)N(C)Cc4ccsc4	-8
ZINC14987901 c1ccc(cc1)c2ccc(c2)C[NH+]3CCC[C@H](C3)n4cc(nn4)C(=0)NCCC0 -8 ZINC02504256 c1ccc(cc1)N2CCN(CC2)C(=0)c3cnn4c3nc(cc4C(F)(F)F)c5ccco5 -8 ZINC08680620 c1ccc(cc1)C[NH+]2CCN(CC2)C(=0)c3cnn4c3nc(cc4C(F)(F)F)c5ccco5 -8 ZINC14733139 CCC0C(=0)c1c2c(n(n1)Cc3ccccn3)CCN(C2)C4cccc4c5ccco5 -8 ZINC14973143 CCC0(CC[NH2+][C@H]1CC2)CAS(CC4)C(C4CCC4)C(C0)CAccccc4)CCC -8 ZINC14954144 CCC1([C@H]2CC-C([C@H]1C2)CAS(CG4)C[CH]3C(=0)OCNC(=0)C4ccccc4)Sccco5)C -8 ZINC14975395 CCO1ccc(c10C2cccs2)CN(C1CC0C4)CC1)C0C4ccccc4)C2 -8 ZINC12036079 CCC1(C0C1)C0c2cc(cc2)CO/N(C[C@H]3CCC03)C(=0)c4cnfnsc4ncc5 -7.9 ZINC1230378 Cc1ccccc12Cn(n+2]C@H]3CCC03)C(=0)c4cnfn4C)C -7.9 ZINC12300378 Cc1ccccc1[C@H]2CCC2]C(PN[C]C@H]3CCC03)C(=0)c4ccnfn4C)C -7.9 ZINC1230759 Cf1ccccc1Nh+]2CCC[C2]CNN[C[C@H]3CCC03)C(=0)c4ccnfn4C)C -7.9 ZINC1230759 Cf1cccc1NhC]C1=0)A2CC03Ccc1cc32)CO/CC4cccc4 -7.9 ZINC12450755 C[C[C@H](C1CC0]C2]CC1]0N1C3Cccc(c12)CC1]CC4cccc4C4O/CD/CDC0C -7.8 ZINC145075 C[C1cccc1]NLC]C(=0)N2CC03Ccc1C3)OC1C4cccc4A -7.8 ZINC145075 CC1cccc1[n1D]C1[O]	ZINC01245157	Cc1ccc(cc1)n2c(nnc2SCC(=O)Nc3ccccc3F)c4ccncc4	-8
ZINC02504256 c1ccc(c1)N2CCN(C2)C(=0)c3cnn4c3nc(cc4C(F)(F)F)c5ccco5 -8 ZINC08680620 c1ccc(c1)C(NH+]2CN(C2)C(=0)c3cnn4c3nc(cc4C(F)(F)F)c5ccco5 -8 ZINC14733139 CCO0CC(=0)L12C((n)L)C3ccccn3)CN(C2)Cc4ccccc45ccco5 -8 ZINC12038301 CCO0CCC(NH2+][C@@H]1C2Cacsc3c2(=0)n(cn3)Cc4c5cccco5C4)C1 -8 ZINC12037267 CO1ccccc(c1O2@H]1C2CAS(c2O)C(=0)c4cnn5c4nccc5 -8 ZINC12037267 CC01(CCC1(C02C2)CC2)CN(C1C@H]3CCCO3)C(=0)c4cn5c4nccc5 -8 ZINC12030727 CC11(CC01)C02c2c(c2C2)CN(C1C@H]3CCCO3)C(=0)c4cn5nc4ncc5 -8 ZINC12030738 CC11(CC01)C02c2c(c2C2)CN(C1C@H]3CCCO3)C(=0)c4cn5nccn5n4 -8 ZINC12300378 CC1ccccc1C[NH+]2CCC(C2)CN(C1C@H]3CCCO3)C(=0)c4ccfn4C)C -7.9 ZINC12300378 CC1ccccc1C[NH+]2CCC(C2)CN(C1C@H]3CCCO3)C(=0)c4ccfn4C)C -7.9 ZINC12300378 CC1ccccc1C[NH+]2CCC(C2)CN(C1C@H]3CCCO3)C(=0)c4ccfn4C)C -7.9 ZINC12278958 CC1ccccc1C[NH+]2CCC(C2)CN(C1C@H]3CCCO3)C(=0)c4ccfc40)CO)CO -7.9 ZINC12278958 CC1cccc1C1[NH+]2CCC(C2)CN(C1C@H]4CCO4)C(=0)C2CCCCC -7.9 ZINC12450779 CC1cccc1C1C0C1C0C0+]3CCCCC3)C(=0)CCCCCCCC)C3CCCC -7.8 ZINC12450759 CC1ccc(In1)C(C)(H)(C)	ZINC14987901	c1ccc(cc1)c2ccc(cc2)C[NH+]3CCC[C@H](C3)n4cc(nn4)C(=O)NCCCO	-8
ZINC08680620 c1ccc(c1)C[NH+]2CCN(C2)C[=0)c3cnn4c3nc(cc4C(F)(F)F)Fc5cccs5 -8 ZINC14733139 CCCOC(=0)c1c2c(n(n1)Cc3ccccn3)CCN(C2)Cc4ccccc4c5ccco5 -8 ZINC14053140 CCCOCCC(NH2+][C@@H]1CC)cc3cs2c2(=0)n(n3)C4Cc5ccccs5(4)C1 -8 ZINC14054144 CCC1[[C@H]2CC=([C@@H]1C2)CN3C[C@H][C[C@H]3C(=0)C)NC(=0)c4cccc4n5cccn5)C -8 ZINC12037267 CCC1ccc(c1OC2cccc2)CN(C3CCCC3)(C=0)c4nc5c4nccc4)C2 -8 ZINC12036079 CCC1(C0C1)C0c2cc(cc2OC)CN(C1C@H)3CCC03)(C=0)c4nc5n4ncccn5)C -8 ZINC12036079 CC1(C0C1)C0c2cc(cc2OC)CN(C1C@H]3CCC03)(C=0)c4nc5n4nccn5A1 -8 ZINC1203078 Cc1ccccc12(nH)=2CCC(C2)CN(C1C@H]3CCC03)(C=0)c4nc5n4nccn5A1 -8 ZINC1203078 Cc1ccccc12(nH)=2CCC(C2)CN(C1C@H]3CCC03)(C=0)c4nc5n4nc5A1 -7.9 ZINC1203078 Cc1ccccc12(nH)=2CCC(C2)CN(C1C@H]3CCC03)(C=0)c4ncfn4C2) -7.9 ZINC1278958 Cn1ncc(c=0)c21ccc2)C(C0(C1C@D)N2CC03cc(c0)C0C)CC -7.9 ZINC12450775 C[C@@H](1ccc31)N(C1(C)@D)C2c3ccn(c32)CD)C0C4ccncc4 -7.9 ZINC1455070 Cn1ccc(n1nn2)[C@H](3CCCC3](C=0)A(C1C)C0C)CC -7.8 ZINC2207794 Cc1cccc(n1nn2)[C@H](3CCCC3](C=0)A(C1C)C0C)C0C -7.8 ZINC2285769 Cc1ccc(n1n)	ZINC02504256	c1ccc(cc1)N2CCN(CC2)C(=O)c3cnn4c3nc(cc4C(F)(F)F)c5ccco5	-8
ZINC14733139 CCCOC(=0)c1c2c(n(n1)Cc3ccccn3)CCN(C2)Cc4cccc45cccc5) -8 ZINC12038301 CCCOCCC(NH2+][C@H]1CCC2c(s3c2c(=0)n(cn3)C4Cc5cccc5C4)C1 -8 ZINC12037267 CCC1([C@H]2CC-C([C@H]1C2)CN3C[C@H](C[C@H]3CCC0)C(=0)c4cccc4n5cccn5)C -8 ZINC12037267 CCC1(ccc1cncc1)[C@H]2CC3c(c(n)AC)C(=0)c4cccc4N2CC2A)C -8 ZINC12037267 CCCN(Cc1cncc1)[C@H]2CC3c(c(n)AC)C(=0)N(C)C4cccc4N2(2)C -8 ZINC12036079 CCC1(CC01)CO2cccc2OC)CN(C[C@H]3CCC03)(C=0)c4cccn4N2(C)C -79 ZINC12270677 CC1ccccc1C(NH+]2CCC(C2)CN(C[C@H]3CCC03)(C=0)c4cccn4N2(C)C -79 ZINC12270878 CC1cccc1C(NH+]2CCC(C2)CN(C[C@H]3CCC03)(C=0)c4cccn4AC)C -79 ZINC122708798 CC1cccc1C(NH+]2CCC(C2)CN(C[C@H]3CCC03)CC]0C4cccn4 -79 ZINC1278958 Cn1cc(c=0)2c1cccc2)(=0)N(C2c3ccn(c32)C)ClC4cccn4 -79 ZINC1278958 Cn1cc(c=0)2c1cccc2)(=0)N(C2c3ccn(c32)C)CC4cccn4 -79 ZINC12450775 C[C@@H](c1cccs1)N(C)(C=0)2Cc3ccn(c32)C)CC4cccn4 -79 ZINC14542466 Cc1cc(s(n1)C)(C=0)N2CCG2(cc(2)NAC)(C4CC04)C(=0)CC4cccc4)C -78 ZINC1455070 CC1ccc(n1n2)[C@H](S)CNC1)C)CC4cccc(c1/2)CC0C05 -7.8 ZINC22077949 Cc1cccc(n1n2)CC(C)(M](C)C	ZINC08680620	c1ccc(cc1)C[NH+]2CCN(CC2)C(=O)c3cnn4c3nc(cc4C(F)(F)F)c5cccs5	-8
ZINC12038301 CC0CCC[NH2+][C@@H]1CC2c(sc3c2c(=0)n(cn3)C4Cc5cccc5C4)C1 -8 ZINC14954144 CC1([C@H]2CC=C([C@@H]1C2)CN3C[C@H](C[@H]3C(=0)CNC(=0)c4cccc4h5cccn5)C -8 ZINC12037267 COc1ccc(c1OCc2cccs2)CN(C3CCCC3)C(=0)c4cnn5c4nccc5 -8 ZINC1203709 CC1(COC1)CO2ccccc2OC)CN(C[C@H]3CCC03)C(=0)c4cnn5c4nccc5 -8 ZINC12036079 CC1(COC1)CO2cccccc2OC)CN(C[C@H]3CCC03)C(=0)c4nc5nccn5n4 -8 ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cnc5nccn5n4 -7.9 ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cccc4 -7.9 ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cccn4 -7.9 ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cccn4 -7.9 ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cccn4 -7.9 ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cccn4 -7.9 ZINC1230579 CC1cccc1C10N2C[C@OH](CNC(C=0)C2Ccc3cc(c32)C)CCCCC0 -7.9 ZINC1454246 Cc1cqs(n1)C)C(=0)N2CC3cq(cc2)And0A)C0CC3Cccc3C0 -7.8 ZINC14525769 CC1cccc(InH+]C1)C2ccc3c(C2])N2(C)OC10C10 -7.8 ZINC1458515 Cc1cccc(In1C)C(C=0)N2CC3cq(nA	ZINC14733139	CCOC(=O)c1c2c(n(n1)Cc3ccccn3)CCN(C2)Cc4ccccc4c5ccco5	-8
ZINC14954144 CCC1{[C@H]2CC=C([C@@H]1C2)CN3C[C@H]4C[C@H]3C(=0)OCNC(=0)c4ccccc4n5cccn5)C	ZINC12038301	CCOCCC[NH2+][C@@H]1CCc2c(sc3c2c(=O)n(cn3)C4Cc5ccccc5C4)C1	-8
ZINC12037267 COC1ccc(c1OC2cccs2)CN(C3CCCC3)C(=0)c4cn5c4cncc5 -8 ZINC14753959 CCN(Cc1ccncc1)[C@H]2CCC3c((nn3C)C[=0)N(C)Cc4cccc4)C2 -8 ZINC12036079 CC1(COC1)CO2cc(cc2OC)CN(C[C@H]3CCC03)C(=0)c4nc5nccn5n4 -8 ZINC12279677 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4nc5nccn5n4 -7.9 ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cccn4C)C -7.9 ZINC1279057 CC1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cccn4A)C)C -7.9 ZINC12278958 Cn1cc(c=0)c2c1ccc2)C(=0)N(C23ccc(c3)C)C4cccc4A)OC)C5CC5 -7.9 ZINC12450775 C[C@@H](c1cccs1)N(C)C(=0)c2cc(cc(2)n3cnnn3)c4ccc(c40C)OC)OC -7.9 ZINC14542446 Cc1ccs(n1)C)C(=0)N2C[C@@H](CN(C)=0)C2C3cnn(c3)C)OCc4cncc4 -7.9 ZINC1455070 CN(Cc1ccccc3c(c2n1)OC03)CN(C[C@H]4CCC04)C(=0)C5Cccs5 -7.8 ZINC22077949 Cc1cccc(1n2c(nnn2)[C@H](3CCCC3)(CH)H+](C)[C@@H]4CCS)C0)[-0)C4 -7.8 ZINC2205759 CC1ccc(In1+]c1)c2ccc3c(c2)C[C@H](03)CNC=0)CC[NH+](C]CC@@H]4CCS)[-0)P(C)C -7.7 ZINC2825769 CC1cc(c0n1)C)CC(=0)N2CCC3c(cn2)N3C(=0)Acccc4C3)C -7.7 ZINC2833795 CS[=0)(=0)(C]C@@H](C=0)C(C2)CC2C)N3C(=0)N(C2)C5Csc5)S(C2) -7.7 ZINC2837	ZINC14954144	CC1([C@H]2CC=C([C@@H]1C2)CN3C[C@H](C[C@H]3C(=O)OC)NC(=O)c4ccccc4n5cccn5)C	-8
ZINC14753959 CCN(Cc1ccncc1)[C@H]2CCC3c(c(nA3C)C(=0)N(C)Cc4cccc4)C2 -8 ZINC12036079 CC1(COC1)COc2cc(cc2OC)(N(C)C@H]3CCCO3)C(=0)c4nc5nccn5n4 -8 ZINC12279677 Cc1ccccc1c2nc(nc2]C@H]3CCCN(3)C(=0)C4nc5nccr5 -7.9 ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C]C@H]3CCCO3)C(=0)c4cc(nn4C)C -7.9 ZINC12150749 CCNC(=0)c1cn(cc(=0)C)(=0)N2CCO3ccc(cc3C2)C)Cc4cccc4 -7.9 ZINC12278958 Cn1cc(c(=0)c2c1ccc2)C(=0)N(C3ccc(c(a3)OCc4ccco4)OC)C5CC5 -7.9 ZINC12450775 C[C@@H](c1cccs1)N(C)(=0)C2cc(cc(2)A3cnnn3)c4ccc(c(4OC)OC)OC -7.9 ZINC14542446 Cc1(sc(n1)C)(=0)N2CCO@eH](CN(C(=0)C2)C3cnn(c3)C)OCc4ccncc4 -7.9 ZINC145456070 CN(C)c1c(cc2ca3c(c2n1)OC03)CN(C[C@H]4CCC04)C(=0)C5CC55 -7.8 ZINC2077949 Cc1cccc(InH+]c1)C2cca3c(c2)[NH+](C)C4cc5c(c(c4)OC)OC05 -7.8 ZINC14885515 Cc1ccc(InH+]c1)C2cca3(c2)C[C@H](03)CNC(=0)CC(NH+](C]C@@H]4CCS(=0)(=0)C4 -7.8 ZINC2825769 COCCCN1C(=0)N2CCC3c1(nn3C4C4C4)C(=0)N(C)C5csn5)C2 -7.7 ZINC02833795 CS(=0)(=0)C(]C@H](C(=0)C(C(=0)N(C2=O)CCC0)C3cccc4C3C0) -7.6 ZINC0294396 CCOCC(=0)[C@H](CC[OM]2[CC(=0)N(C2=O)CC0)C3cccc4C3C0) -7.6 ZINC0294395	ZINC12037267	COc1ccc(cc1OCc2cccs2)CN(C3CCCC3)C(=O)c4cnn5c4nccc5	-8
ZINC12036079 CC11(COC1)CO2cc(cc22OC)CN(C[C@H]3CCCO3)C(=0)c4nc5ncccn5n4 -8 ZINC12279677 CC1ccccc12cnc(nc2[C@H]3CCCN(3)C(=0)[C@@H]4CCOC4)c5ccnc5 -7.9 ZINC12300378 CC1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCCO3)C(=0)c4cc(nn4C)C -7.9 ZINC12150749 CCNC(=0)c1cn(cc(1=0)C(=0)N2CCO3ccc(cc32)C)ICc4cccc4 -7.9 ZINC12278958 Cn1cc(c(=0)c2c1cccc2)C(=0)N(Cc3ccc(cc3)CC4Ccco4)OC)CSCC5 -7.9 ZINC1450775 C[C@@H](c1cccs1)N(C)C(=0)2ccc(cc(2)N3cnnn3)c4ccc(c4OC)OC)OC -7.9 ZINC1454246 Cc1c(sc(n1)C)C(=0)N2C[C@@H](CN(C(=0)C2)Cc3cnnc3)C)OCc4ccncc4 -7.9 ZINC14956070 CN(C)c1c(cc2c3c(cc2n1)OCO3)CN(C[C@H]4CCC04)C(=0)C5cccs5 -7.8 ZINC14885515 Cc1cccc(InH+]c1)2ccc3c(c2)C[C@H](03)CNC(=0)CC[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC2825769 COCCCN1(=0)2ccc(acc21=0)C(=0)3CCC(=0)3ccc(c3)c4cccc4)C3=0 -7.7 ZINC2833795 CS(=0)(=0)C[C@@H](C(=0)OC(c1ccccc1)2ccccc2)N3C(=0)c4cccc4C3=0 -7.7 ZINC2833795 CS(=0)(=0)C[C@@H](C)C(NH+](C)C2ccc(cc2)C -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)N(C)C(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3cccc30C -7.6 ZINC14879900 Cc1csc(n1)[C@H](C)N(C)C(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3cccc30C -7.6	ZINC14753959	CCN(Cc1ccncc1)[C@@H]2CCc3c(c(nn3C)C(=O)N(C)Cc4ccccc4)C2	-8
ZINC12279677 CC1ccccc12cnc(nc2[C@H]3CCCN(C3)C(=0)[C@@H]4CCOC4)c5ccncc5 -7.9 ZINC12300378 CC1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cc(nn4C)C -7.9 ZINC12150749 CCNC(=0)c1cn(cc(1=0)C(=0)N2CC0c3ccc(c32)C)lCc4cccc4 -7.9 ZINC12278958 Cn1cc(c(=0)c2c1ccc2)C(=0)N(Cc3ccc(c(a)OCc4ccco4)OC)C5CC5 -7.9 ZINC12450775 C[C@@H](c1cccs1)N(C)C(=0)c2cc(cc(2)n3cnnn3)c4ccc(c(c4OC)OC)OC -7.9 ZINC14542446 Cc1c(sc(n1)C)C(=0)N2C[C@@H](CN(C(=0)C2)Cc3cnn(c3)C)OCc4ccncc4 -7.9 ZINC14556070 CN(C)c1c(cc2c3c(cc2n1)OC03)CN(C[C@H]4CCC04)C(=0)C55Ccs5 -7.8 ZINC1485515 Cc1cccc(InH+]c1)c2ccc3c(c2)C[C@H](03)CNC(=0)CC[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC02825769 COCCCN1C(=0)N2CCC3c(cn1)C(C)ON2CC(=0)A(CC4C))A(C=0)N(C)C55ccs5)C2 -7.7 ZINC02833795 CS(=0)(=0)C[C@@H](C)O(C)(=0)C(C)C0C(=0)A(CC4C))A(C=0)C(C)C)A(C=0)A(CC4C))A(CC4C))A(C=0)A(CC4C))A(C=0)A(CC4C))A(CC4C))A(CC4C))A(C=0)A(CC4C))A(CC4C))A(CC4C)	ZINC12036079	CC1(COC1)COc2cc(ccc2OC)CN(C[C@@H]3CCCO3)C(=O)c4nc5ncccn5n4	-8
ZINC12300378 Cc1ccccc1C[NH+]2CCC(C2)CN(C[C@H]3CCC03)C(=0)c4cc(nn4C)C -7.9 ZINC12150749 CCNC(=0)c1cn(cc(c1=0)C(=0)N2CC03ccc(c32)C)lC4ccccc4 -7.9 ZINC12278958 Cn1cc(c(=0)c2c1cccc2)C(=0)N(C3ccc(c(3)OCc4ccco4)OC)C5CC5 -7.9 ZINC12450775 C[C@@H](c1cccs1)N(C)C(=0)c2cc(cc(2)n3cnnn3)c4ccc(c(4OC)OC)OC -7.9 ZINC14542446 Cc1c(sc(n1)C)C(=0)N2C[C@@H](CN(C(=0)C2)Cc3cnn(3)C)OCc4ccncc4 -7.9 ZINC14556070 CN(C)c1c(c2c23c(cc2n1)OC03)CN(C[C@H]4CCC04)C(=0)C55ccs5 -7.8 ZINC14885515 Cc1cccc(InH+]c1)c2ccc3c(c2)C[C@H](03)CNC(=0)CC[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC14885515 Cc1ccc(InH+]c1)c2ccc3c(c2)C1=0)C(C)OC1C=0)3ccc(c3)c4cccc4 -7.8 ZINC14885515 Cc1cc(con1)CC(=0)N2CCC3c(cn1)C(=0)OCC(=0)ACCCC3)cc4cc3)c4 -7.8 ZINC1483515 Cc1ccc(InH+]c1)c2ccc3c(c2)C1=0)C(C)OC1C=0)ACCC3)cc4cc3)c4 -7.8 ZINC1483515 Cc1cc(con1)CC(=0)N2CCC3c(c1)C1C(=0)N(C)C5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)C[C@@H](C)O(C)C1c2ccc(c2)N3C(=0)ACCC3)CC -7.7 ZINC14879900 Cc1csc(n1)[C@H](CN(C)C(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3cccc30C -7.6 ZINC19853115 COCCN(C1c1c2cc(c(c2n1N3CCOCC3)OC)C)C)C)C)C)C0C]C3cccc30C -7.6	ZINC12279677	Cc1ccccc1c2cnc(nc2[C@H]3CCCN(C3)C(=O)[C@@H]4CCOC4)c5ccncc5	-7.9
ZINC12150749 CCNC(=0)c1cn(cc(c1=0)C2(=0)N2CCO23ccc(cc32)C1)Cc4ccccc4 -7.9 ZINC12278958 Cn1cc(c(=0)c2c1ccc2)C(=0)N(Cc3ccc(cc3)OCc4ccco4)OC)C5CC5 -7.9 ZINC12450775 C[C@@H](c1cccs1)N(C)C(=0)c2cc(cc(2)n3cnnn3)c4ccc(c(c4OC)OC)OC -7.9 ZINC14542446 Cc1c(sc(n1)C)C(=0)N2C[C@@H](CN(C)=0)C2Cc3cnn(c3)C)OCc4ccncc4 -7.9 ZINC14556070 CN(C)c1c(c2cc3c(cc2n1)OC03)CN(C[C@H]4CCC04)C(=0)C5cccs5 -7.8 ZINC14885515 Cc1cccc(InH+]c1)c2ccc3c(c2)[C@H](03)CNC(=0)C2C(M+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC14541675 Cc1ccc(InH+]c1)c2ccc3c(c2)C1=0)C(=0)OCC(=0)c3ccc(c3)c4cccc4 -7.8 ZINC14541675 Cc1c(c(on1)C)CC(=0)N2CCC3c(n1)C2C()OCC[H+](C)C)C5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)C[C@@H](C)C(NH+](C)C2ccccc2)N3C(=0)Accccc4C3=0 -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)N(C)(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3ccccc3OC -7.6 ZINC1883115 COCCCN(C1c2c2cc(c2n1N3CCOCC3)OC)C(=0)[C@H]4CCC04 -7.6 ZINC1883115 COCCN(C1c2c2c(c(c2n1N3CCOCC3)OC)C)C=0)[C@H]4CCC04 -7.6 ZINC20995059 Cc1cccn2n1n(c2CN(C)C[C@@H](C)C[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC12300378	Cc1ccccc1C[NH+]2CCC(CC2)CN(C[C@H]3CCCO3)C(=O)c4cc(nn4C)C	-7.9
ZINC12278958 Cn1cc(c=0)c2c1ccc2)C(=0)N(Cc3ccc(c(3)OCc4ccco4)OC)C5CC5 -7.9 ZINC12450775 C[C@@H](c1cccs1)N(C)C(=0)c2cc(cc(2)n3cnnn3)c4ccc((c4OC)OC)OC -7.9 ZINC14542446 Cc1c(sc(n1)C)C(=0)N2C[C@@H](CN(C)=O)C2)Cc3cnn(c3)C)OCc4ccncc4 -7.9 ZINC14956070 CN(C)c1c(cc2cc3c(cc2n1)OCO3)CN(C[C@H]4CCCO4)C(=0)Cc5cccs5 -7.8 ZINC22077949 Cc1cccc(1n2c(nn2)[C@H](c3cccc3)[NH+](C)Cc4cc5c(c(c4)OC)OC05 -7.8 ZINC2825769 CC1cccc([nH+]c1)c2ccc3c(c2)[C@H](03)CNC(=0)CC(=0)c3ccc(c3)c4cccc4 -7.8 ZINC14541675 Cc1c(c(on1)C)C(=0)N2CCc3c(cn0)CC(=0)c3ccc(c3)c4cccc4 -7.8 ZINC2833795 CS(=0)(=0)CC[C@@H](C)=0)CC(=0)C3ccc(c2)N4C(=0)N(C)C5c5csn5)C2 -7.7 ZINC02833795 CS(=0)(=0)CC[C@@H](C)=0)C(c1ccccc1)N2CCc2)N3C(=0)c4cccc4C3=0 -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)(C)(C]@[2@@]2(CC(=0)N(C2=0)CCOC)c3ccccc3OC -7.6 ZINC1883115 COCCCN(C1c2c2c(c(c2n1N3CCOCC3)OC)C)C)(=0)[C@@H]4CCC04 -7.6 ZINC2995059 Cc1cccn2n1nc(c2CN(C)[C@@H](C)C[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC12150749	CCNC(=O)c1cn(cc(c1=O)C(=O)N2CCOc3ccc(cc3C2)Cl)Cc4ccccc4	-7.9
ZINC12450775 C[C@@H](c1cccs1)N(C)C(=0)c2cc(cc(2)n3cnnn3)c4ccc(c4OC)OC)OC -7.9 ZINC14542446 Cc1c(sc(n1)C)C(=0)N2C[C@@H](CN(C)=O)C2Cc3cnn(c3)C)OCc4ccncc4 -7.9 ZINC14556070 CN(C)c1c(cc2cc3c(cc2n1)OCO3)CN(C[C@H]4CCCO4)C(=0)Cc5cccs5 -7.8 ZINC22077949 Cc1cccc1n2c(nnn2)[C@H](c3cccc3)[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC14885515 Cc1cccc([nH+]c1)c2ccc3c(c2)C[O@H](O3)CNC(=0)CC[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC2825769 COCCCN1C(=0)N2CCc3c(cnn3CC4CC4)C(=0)N(C)C5cscn5)C2 -7.7 ZINC14541675 Cc1cc((on1)C)CC(=0)N2CCc3c(cnn3CC4CC4)C(=0)N(C)Cc5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)CC[C@@H](C)=0)C(C1ccccc1)N3C(C2C)N3C(=0)c4cccc4C3=0 -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)(C)(C]@[2@[2](CC(=0)N(C2=0)CCOC)c3cccc30C -7.6 ZINC1853115 COCCCN(C1c2c2c(c(c2nc1N3CCOCC3)OC)C)C)(=0)[C@@H]4CCC04 -7.6 ZINC195059 Cc1cccn2n1nc(c2CN(C)[C@@H](C)[NH+]3CCCC3)C](=0)N4CCOCC4 -7.6	ZINC12278958	Cn1cc(c(=O)c2c1cccc2)C(=O)N(Cc3ccc(c(c3)OCc4ccco4)OC)C5CC5	-7.9
ZINC14542446 Cc1c(sc(n1)C)C(=0)N2C[C@@H](CN(C(=0)C2)Cc3cnn(c3)C)OCc4ccncc4 -7.9 ZINC14956070 CN(C)c1c(c2cc3c(cc2n1)OCO3)CN(C[C@H]4CCCO4)C(=0)Cc5cccs5 -7.8 ZINC22077949 Cc1cccc1n2c(nnn2)[C@H](c3ccccc3)[NH+](C)Cc4cc5c(c(c4)OC)OCO5 -7.8 ZINC14885515 Cc1cccc([nH+]c1)c2ccc3c(c2)C[C@H](03)CNC(=0)CC[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC2825769 COCCCN1C(=0)c2ccc(c2C1=0)C(=0)OCC(=0)c3ccc(c3)c4ccccc4 -7.8 ZINC14541675 Cc1cc(on1)C)CC(=0)N2CCc3c(c(nn3CC4CC4)C(=0)N(C)Cc5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)CC[C@@H](C)O(C)C(=0)X2Cccccc2)N3C(=0)c4ccccc4C3=0 -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)N(C)C(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3ccccc30C -7.6 ZINC19853115 COCCCN(C1c2c2cc(cc2n1N3CCOCC3)OC)OC)C(=0)[C@H]4CCC04 -7.6 ZINC20995059 Cc1cccn2n1nc(c2CN(C)[C@@H](C)C[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC12450775	C[C@@H](c1cccs1)N(C)C(=O)c2cc(cc(c2)n3cnnn3)c4ccc(c(c4OC)OC)OC	-7.9
ZINC14956070 CN(C)c1c(cc2c3c(cc2n1)OCO3)CN(C[C@H]4CCC04)C(=0)Cc5ccc55 -7.8 ZINC22077949 Cc1cccc1n2c(nnn2)[C@H](c3cccc3)[NH+](C)Cc4cc5c(c(c4)OC)OCO5 -7.8 ZINC14885515 Cc1ccc([nH+]c1)c2ccc3c(c2)C[C@H](03)CNC(=0)CC[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC2825769 COCCCCN1C(=0)c2ccc(c2C1=0)C(=0)OCC(=0)c3ccc(c3)c4ccccc4 -7.8 ZINC14541675 Cc1cc(c0n1)C)CC(=0)N2CCc3c(c(nn3CC4CC4)C(=0)N(C)Cc5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)CC[C@@H](C)C0)C(=0)N2Ccccc(c2)C -7.7 ZINC0294396 CC0CCC(=0)[C@H]1CCC[NH+](C1)Cc2ccc(c2)C -7.6 ZINC14879900 Cc1csc(n1)[C@H](CN(C)(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3ccccc30C -7.6 ZINC19853115 COCCCN(C1c2c2cc((cc2nt1N3CC0CC3)OC)OC)C(=0)[C@@H]4CCC04 -7.6 ZINC20995059 Cc1cccn2ntn(c2CN(C)[C@@H](C)[NH+]3CCC3)C(=0)N4CC0CC4 -7.6	ZINC14542446	Cc1c(sc(n1)C)C(=O)N2C[C@@H](CN(C(=O)C2)Cc3cnn(c3)C)OCc4ccncc4	-7.9
ZINC22077949 Cc1cccc1n2c(nnn2)[C@H](c3cccc3)[NH+](C)Cc4cc5c(c(4)OC)OC05 -7.8 ZINC14885515 Cc1cccc(InH+]c1)c2ccc3c(c2)C[C@H](03)CNC(=0)CC[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC02825769 COCCCN1C(=0)c2ccc(cc2C1=0)C(=0)OCC(=0)c3ccc(cc3)c4ccccc4 -7.8 ZINC14541675 Cc1cc(on1)C)CC(=0)N2CCc3c(c(nn3CC4CC4)C(=0)N(C)Cc5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)CC[C@@H](C(=0)OC(1ccccc1)c2ccccc2)N3C(=0)c4cccc4C3=0 -7.7 ZINC0294396 CC0CC(=0)[C@H]1CCC[NH+](C1)Cc2ccc(cc2)C -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)N(C)(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3cccc30C -7.6 ZINC19853115 COCCCN(C1c2c2c(c(cc2nc1N3CCOCC3)OC)OC)C(=0)[C@@H]4CCC04 -7.6 ZINC20995059 Cc1cccn21nc(c2CN(C)[C@@H](C)[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC14956070	CN(C)c1c(cc2cc3c(cc2n1)OCO3)CN(C[C@H]4CCCO4)C(=O)Cc5cccs5	-7.8
ZINC14885515 Cc1ccc([nH+]c1)c2ccc3c(c2)C[@H](03)CNC(=0)CC[NH+](C)[C@@H]4CCS(=0)(=0)C4 -7.8 ZINC02825769 COCCCN1C(=0)c2ccc(cc2C1=0)C(=0)OCC(=0)c3ccc(cc3)c4ccccc4 -7.8 ZINC14541675 Cc1cc(on1)C)CC(=0)N2CCc3c(cnn3CC4CC4)C(=0)N(C)Cc5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)CC[C@@H](C(=0)OC(1ccccc1)c2cccc2)N3C(=0)c4cccc4C3=0 -7.7 ZINC0294396 CCOCC(=0)[C@H]1CCC[NH+](C1)Cc2ccc(cc2)C -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)N(C)(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3ccccc30C -7.6 ZINC19853115 COCCN(C1c2ccc(cc2nc1N3CCOCC3)OC)OC)(=0)[C@@H]4CCC04 -7.6 ZINC20995059 Cc1cccn2c1nc(c2CN(C)C[C@@H](C)[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC22077949	Cc1ccccc1n2c(nnn2)[C@H](c3ccccc3)[NH+](C)Cc4cc5c(c(c4)OC)OCO5	-7.8
ZINC02825769 COCCCN1C(=0)c2ccc(cc2C1=0)C(=0)OCC(=0)c3ccc(cc3)c4ccccc4 -7.8 ZINC14541675 Cc1c(c(on1)C)CC(=0)N2Ccc3c(c(nn3CC4CC4)C(=0)N(C)Cc5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)CC[C@@H](C(=0)OC(c1ccccc1)c2cccc2)N3C(=0)c4cccc4C3=0 -7.7 ZINC0294396 CCOCC(=0)[C@H]1CCC[NH+](C1)Cc2ccc(cc2)C -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)C)(C)(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3ccccc3OC -7.6 ZINC19853115 COCCN(Cc1cc2cc(cc2nc1N3CCOCC3)OC)OC)(=0)[C@@H]4CCCO4 -7.6 ZINC20995059 Cc1cccn2c1nc(c2CN(C)C[C@@H](C)C[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC14885515	Cc1ccc([nH+]c1)c2ccc3c(c2)C[C@H](O3)CNC(=O)CC[NH+](C)[C@@H]4CCS(=O)(=O)C4	-7.8
ZINC14541675 Cc1c(c(on1)C)CC(=0)N2CCc3c(c(nn3CC4CC4)C(=0)N(C)Cc5cscn5)C2 -7.7 ZINC02833795 CS(=0)(=0)CC[C@@H](C(=0)OC(c1ccccc1)c2cccc2)N3C(=0)c4cccc4C3=0 -7.7 ZINC0294396 CCOC(=0)[C@H](CC(NH+](C1)Cc2ccc(cc2)C -7.7 ZINC14879900 Cc1csc(n1)[C@H](C)N(C)C(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3ccccc30C -7.6 ZINC19853115 COCCN(Cc1cc2cc((cc2nc1N3CCOCC3)OC)OC)C(=0)[C@@H]4CCC04 -7.6 ZINC20995059 Cc1csccn2tnc(c2CN(C)C[C@@H](C)C[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC02825769	COCCCN1C(=0)c2ccc(cc2C1=0)C(=0)c3ccc(cc3)c4ccccc4	-7.8
ZINC02833795 CS(=0)(=0)CC[C@@H](C(=0)OC(c1ccccc1)v2cccc2)N3C(=0)c4cccc4C3=0 -7.7 ZINC0294396 CCOC(=0)[C@H](CC[NH+](C1)Cc2ccc(cc2)C -7.7 ZINC14879900 Cc1csc(n1)[C@H](CN(C)C(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3ccccc30C -7.6 ZINC19853115 COCCN(Cc1cc2cc((cc2nc1N3CCOCC3)OC)OC)C(=0)[C@@H]4CCCO4 -7.6 ZINC20995059 Cc1cscn2c1nc(c2CN(C)C[C@@H](C)C[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC14541675	Cc1c(c(on1)C)CC(=O)N2CCc3c(c(nn3CC4CC4)C(=O)N(C)Cc5cscn5)C2	-7.7
ZINC00294396 CCOC(=O)[C@H]1CCC[NH+](C1)Cc2ccc(c2)C -7.7 ZINC14879900 Cc1csc(n1)[C@H](CN(C)C(=O)C[C@@]2(CC(=O)N(C2=O)CCOC)c3ccccc3OC -7.6 ZINC19853115 COCCN(Cc1cc2cc(cc2nc1N3CCOCC3)OC)OC)C(=O)[C@@H]4CCCO4 -7.6 ZINC20995059 Cc1cccn2c1nc(c2CN(C)C[C@@H](C)C[NH+]3CCCC3)C(=O)N4CCOCC4 -7.6	ZINC02833795	CS(=O)(=O)CC[C@@H](C(=O)OC(c1ccccc1)c2ccccc2)N3C(=O)c4ccccc4C3=O	-7.7
ZINC14879900 Cc1csc(n1)[C@H](C)N(C)C(=0)C[C@@]2(CC(=0)N(C2=0)CCOC)c3ccccc3OC -7.6 ZINC19853115 COCCN(Cc1cc2cc(c(cc2nc1N3CCOCC3)OC)OC)C(=0)[C@@H]4CCCO4 -7.6 ZINC20995059 Cc1cccn2c1nc(c2CN(C)C[C@@H](C)C(NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC00294396	CCOC(=O)[C@H]1CCC[NH+](C1)Cc2ccc(cc2)C	-7.7
ZINC19853115 COCCN(Cc1cc2cc(c(cc2nc1N3CCOCC3)OC)OC)C(=0)[C@@H]4CCC04 -7.6 ZINC20995059 Cc1cccn2c1nc(c2CN(C)C[C@@H](C)C[NH+]3CCCC3)C(=0)N4CCOCC4 -7.6	ZINC14879900	Cc1csc(n1)[C@H](C)N(C)C(=O)C[C@@]2(CC(=O)N(C2=O)CCOC)c3ccccc3OC	-7.6
ZINC20995059 Cc1cccn2c1nc(c2CN(C)C[C@@H](C)C[NH+]3CCCC3)C(=O)N4CCOCC4 -7.6	ZINC19853115	COCCN(Cc1cc2cc(c(cc2nc1N3CCOCC3)OC)OC)C(=O)[C@@H]4CCCO4	-7.6
	ZINC20995059	Cc1cccn2c1nc(c2CN(C)C[C@@H](C)C[NH+]3CCCC3)C(=O)N4CCOCC4	-7.6



Fig. 1. CDK1-ZINC08925969 interaction depicted in Ribbon representation and 2D Depiction

Toxicity:

To be an effective drug compound, a highly biologically active lead molecule must possess low toxicity. In-silico Toxicity predictions are gaining acceptance in toxicological risk assessment. Out of 19 molecules, only 5 molecules have shown Non-Toxic properties (rows highlighted in Green) such as: Liver Toxicity: DILI, Mitochondrial Toxicity (MMP), Acute algae toxicity, AMES, Carcinogenicity (Mouse), Carcinogenicity (Rat), Carcinogenicity Likeness, ADME and Toxicity study has been taken for Molecular (Rodent), Acute daphina toxicity, in vitro hERG inhibition,



Fig. 2. CHK1- ZINC11784547 interaction depicted in Ribbon representation and 2D Depiction

Acute fish toxicity (medaka), Acute fish toxicity (minnow), Ames TA100 (+S9), Ames TA100 (-S9), Ames TA1535 (-S9). The Toxicity Prediction of the top 39 molecules listed Table 3.

Molecular Interaction Analysis:

To understand the molecular level interaction all, the top three molecules (ZINC08925969, ZINC11784547, and ZINC12516005) that have successfully passed all the Drug

Tab. 2. ADME Results	Zinc id	Solubility Class	GI Ab- sorp- tion	Human intestinal absorption (HIA %)	Madin-Darby Canine Kid- ney (MDCK)	Caco-2 Per- meability	Partition Coefficent (LogP)	Distribution Coefficient (logD)	BBB (Cbrain/ Cblood)	Pgp Inhibi- tion	P-gp Sub- strate	Plasma protein binding [%PPB]	Human Liver Microsomes (HLM)	CYP1A2 inhibitor	CYP3A4 inhibitor	CYP3A4 Substrate
	ZINC12464790	Soluble	High	92.131957	0.91684	37.1475	1.02	0.42643	No	Non	Yes	43.736916	Yes	No	No	Substrate
	ZINC14885414	Soluble	High	97.30467	0.16601	9.80078	2.4	0.07455	No	Non	Yes	64.319963	Yes	No	Yes	Weakly
	ZINC14538250	Soluble	High	97.428477	0.145629	50.5155	2.61	1.38984	Yes	Inhibitor	No	72.34835	Yes	No	Yes	Substrate
	ZINC14733310	Soluble	High	100	0.350966	21.713	2.29	2.18163	No	Non	Yes	93.160059	Yes	No	Yes	Substrate
	ZINC12036079	Soluble	High	99.446545	0.0747592	52.8658	2.22	1.5696	No	Inhibitor	Yes	69.966481	Yes	No	Yes	Substrate
	ZINC12041004	Soluble	High	99.229839	3.83683	30.5199	3.11	2.74565	No	Non	Yes	91.555344	Yes	No	Yes	Substrate
	ZINC01216760	Soluble	High	93.448984	0.404492	29.9402	2.27	1.53396	Yes	Inhibitor	Yes	46.438777	Yes	No	No	Substrate
	ZINC19774479	Soluble	High	97.585841	0.213209	38.3199	2.27	1.8019	Yes	Inhibitor	Yes	75.010224	Yes	No	No	Weakly
	ZINC12279677	Soluble	High	97.605255	2.37906	48.2635	3.41	2.82912	Yes	Non	Yes	87.991134	Yes	No	Yes	Substrate
	ZINC14753959	Soluble	High	97.380853	0.896182	53.2898	£	1.67318	Yes	Inhibitor	Yes	83.909847	Yes	No	Yes	Substrate
	ZINC12038620	Moderately soluble	High	89.753368	1.0062	19.2858	1.84	1.04455	No	Non	Yes	50.512485	Yes	No	No	Substrate
	ZINC14987901	Moderately soluble	High	89.32498	1.89877	18.9232	1.72	1.22128	No	Non	Yes	54.274299	No	No	No	Substrate
	ZINC14530440	Moderately soluble	High	97.475122	0.0586677	55.9159	3.39	3.06295	Yes	Inhibitor	Yes	84.471095	Yes	No	Yes	Substrate
	ZINC14740689	Moderately soluble	High	97.669741	0.0579102	50.5699	3.2	1.98879	Yes	Inhibitor	Yes	82.007294	Yes	No	Yes	Substrate
	ZINC02504256	Moderately soluble	High	97.586951	0.268624	37.2832	3.09	3.42467	Yes	Inhibitor	Yes	92.882846	Yes	No	Yes	Weakly
	ZINC12447659	Moderately soluble	High	99.602877	2.13039	1.37961	1.76	2.71327	No	Inhibitor	No	100	Yes	No	No	Substrate
	ZINC12516005	Moderately soluble	High	99.524021	0.0495903	24.3883	2.63	3.26059	No	Inhibitor	No	90.548132	Yes	No	Yes	Substrate
	ZINC12034833	Moderately soluble	High	99.621884	0.0971435	38.3776	3.27	2.69902	No	Non	Yes	89.055638	Yes	No	Yes	Substrate
	ZINC08925969	Moderately soluble	High	98.503336	0.0460023	21.3751	2.52	1.60789	No	Non	No	88.810932	Yes	Yes	Yes	Weakly
	ZINC14733139	Moderately soluble	High	97.750533	0.734869	38.443	3.44	2.56431	Yes	Inhibitor	Yes	83.690586	Yes	No	Yes	Substrate
	ZINC14954144	Moderately soluble	High	96.384572	0.0555437	25.3521	3.15	1.85147	Yes	Inhibitor	Yes	77.171736	Yes	No	Yes	Substrate
	ZINC12132957	Moderately soluble	High	97.448023	1.47904	25.884	2.81	2.54095	No	Non	Yes	83.753715	No	No	Yes	Substrate
	ZINC08680620	Moderately soluble	High	94.473155	0.190938	27.1701	2.83	1.98318	No	Non	Yes	72.27183	Yes	No	No	Substrate
	ZINC20600602	Moderately soluble	High	96.70851	1.25893	24.49	2.69	2.97726	No	Non	Yes	93.709467	Yes	No	Yes	Weakly
	ZINC11784547	Moderately soluble	High	91.29963	0.07203	17.3092	3.31	2.82744	No	Non	Yes	84.5226	No	Yes	Yes	Weakly
	ZINC01056864	Moderately soluble	High	97.831212	0.0614135	48.0599	4.13	3.8651	No	Inhibitor	Yes	93.822916	Yes	Yes	Yes	Weakly
	ZINC11840098	Moderately soluble	High	97.831212	0.0614135	48.0599	3.64	3.8651	No	Inhibitor	Yes	93.822916	Yes	No	Yes	Weakly
	ZINC12037267	Moderately soluble	High	98.650061	0.0901468	54.503	3.91	4.08286	No	Inhibitor	Yes	93.073048	No	No	Yes	Substrate
	ZINC12038301	Moderately soluble	High	94.346549	7.3874	23.5531	3.2	1.47678	No	Non	Yes	36.813913	Yes	No	Yes	Substrate
	ZINC01245157	Moderately soluble	High	96.772975	0.0985069	44.7343	3.7	4.7439	No	Inhibitor	No	99.446876	No	Yes	Yes	Weakly
	ZINC14992739	Moderately soluble	High	99.578491	0.0614725	22.5019	3.52	3.82613	No	Inhibitor	No	90.591818	Yes	Yes	Yes	Substrate
	ZINC14885974	Poorly soluble	High	98.571171	0.457832	37.013	3.92	4.2395	No	Inhibitor	Yes	92.200846	Yes	No	Yes	Substrate
	ZINC02859380	Poorly soluble	High	97.179052	20.0541	51.9786	3.92	5.40364	No	Inhibitor	No	96.692417	No	No	Yes	Substrate
	ZINC00945916	Poorly soluble	High	96.871525	0.86525	45.2023	4.07	5.64578	No	Inhibitor	No	96.895471	Yes	Yes	Yes	Substrate
	ZINC00955034	Poorly soluble	Low	97.149361	0.241538	19.746	4.33	4.69202	No	Inhibitor	No	100	Yes	No	Yes	Weakly

ults	ZINC ID	Acute Oral Toxicity	Human Ether-a- go-go-Related Gene Inhibition	Liver Toxicity: Cyto- toxicity	Mitochondrial Toxicity (MMP)	AMES	Carcinogenic- ity (Mouse)	Carcinoge- nicity(Rat)	Carcinogenicity (Rodent)	hERG Blocker	Honey bee Toxicity	Ames TA100 (+S9)	Ames TA100 (-S9)	Ames TA1535 (-S9)
	ZINC01056864	≡	Weak inhibitor	No	No	No	positive	negative	non-carcinogenic	Yes	Low HBT	positive	negative	negative
	ZINC12037267	≡	Weak inhibitor	No	No	No	negative	negative	carcinogenic	No	Low HBT	positive	negative	negative
	ZINC14733310	≡	Weak inhibitor	No	No	Yes	negative	negative	non-carcinogenic	Yes	Low HBT	positive	negative	negative
	ZINC12034833	≡	Strong inhibitor	No	No	No	negative	negative	non-carcinogenic	Yes	Low HBT	negative	negative	negative
	ZINC14992739	≡	Weak inhibitor	No	No	No	negative	negative	non-carcinogenic	Yes	Low HBT	positive	negative	negative
	ZINC12516005	≡	Weak inhibitor	No	No	No	negative	negative	non-carcinogenic	No	Low HBT	negative	negative	negative
	ZINC12036079	≡	Weak inhibitor	No	No	Yes	negative	positive	carcinogenic	Yes	Low HBT	positive	positive	negative
	ZINC12041004	≡	Weak inhibitor	No	No	No	negative	negative	non-carcinogenic	Yes	Low HBT	positive	negative	negative
	ZINC08925969	≡	Weak inhibitor	Yes	Yes	No	negative	negative	non-carcinogenic	No	Low HBT	negative	negative	negative
	ZINC11840098	≡	Weak inhibitor	No	No	Yes	negative	positive	non-carcinogenic	Yes	Low HBT	negative	negative	negative
	ZINC12132957	≡	Weak inhibitor	No	No	No	negative	negative	non-carcinogenic	Yes	Low HBT	positive	positive	negative
	ZINC14885414	≡	Weak inhibitor	No	No	Yes	negative	negative	non-carcinogenic	Yes	Low HBT	negative	negative	negative
	ZINC01245157	≡	Weak inhibitor	No	No	No	negative	positive	carcinogenic	No	Low HBT	negative	negative	negative
	ZINC20600602	≡	Strong inhibitor	No	No	No	negative	negative	non-carcinogenic	Yes	Low HBT	positive	negative	negative
	ZINC08680620	≡	Weak inhibitor	No	No	No	negative	positive	non-carcinogenic	Yes	Low HBT	positive	negative	negative
	ZINC12038301	≡	Weak inhibitor	No	No	No	negative	negative	carcinogenic	Yes	Low HBT	negative	positive	negative
	ZINC11784547	≡	Weak inhibitor	No	No	No	negative	negative	non-carcinogenic	No	Low HBT	negative	negative	negative

Tab. 3. Toxicity Resu

Interaction Analysis. All the molecules have been found that they **CONCLUSION** are effectively binding with the same amino acids present in the active site of CHK1 (CYS87, ALA36, LEU15, GLY16, GLU91, The identified molecules ZINC08925969, ZINC11784547, in ribbon representation and 2D Depiction in Figure 1-3.



Fig. 3. CHK1- ZINC12516005 interaction depicted in Ribbon representation and 2D Depiction

LEU137, GLU85, VAL23, LYS38, SER147, ASN135) and they ZINC11972241, and ZINC12516005 exhibit drug-like have formed sufficient Hydrogen bonds to make complex. The properties, ADME, and non-toxicity with strong binding energy interaction details of CHK1 all the molecules have been reported at the active site of CHK1 and interacting Key amino acid residues with stable hydrogen bonds and a thermodynamically favourable receptor-ligand interaction. Therefore, we wish to report that these compounds may be effective CHK1 inhibitors.

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DECLARATION OF INTERESTS

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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