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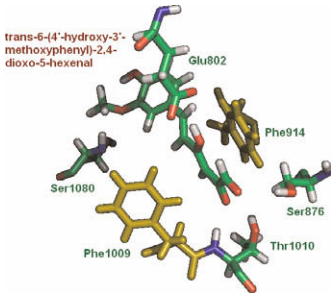
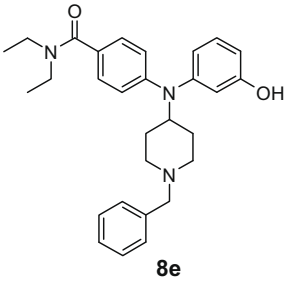
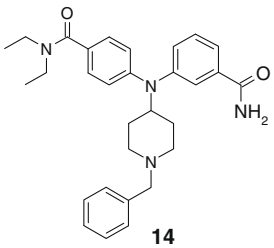
Contents

ARTICLES





8e



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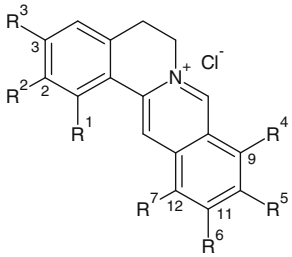
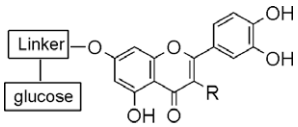
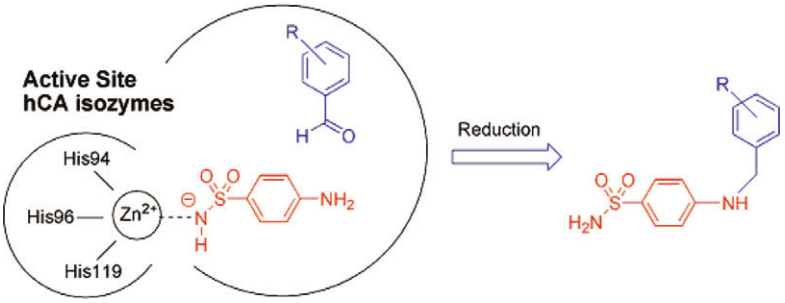
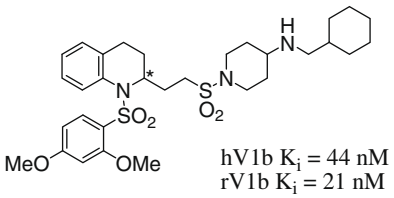


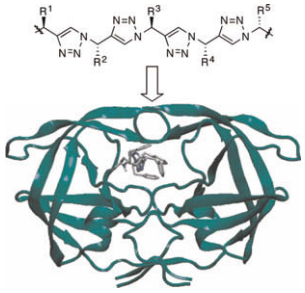


3a~f, R = OCH_3 or H

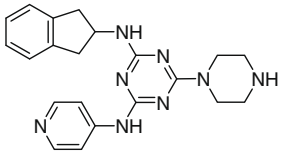




hV1b K_i = 44 nM
rV1b K_i = 21 nM

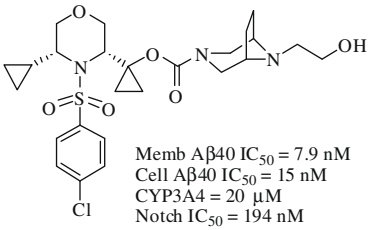


Design of nonpeptidic β-strand mimetics as protease inhibitors is reported.

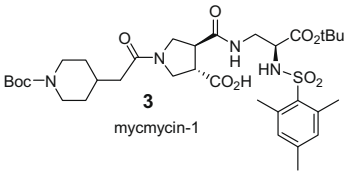


1A

A series of triazine and pyrimidine based ROCK inhibitors is described. An initial binding mode was established based on a homology model and the proposed interactions are consistent with the observed SAR. Compounds from the series are potent in a cell migration assay and possess a favorable kinase selectivity. In vivo activity was demonstrated for compound **1A** in a spontaneous hypertensive rat model.

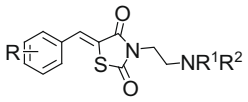


The design of a new class of *N*-arylsulfonamide γ-secretase inhibitors based on the introduction of a morpholine core is reported. Compounds devoid of CYP 3A liability and active orally in a Tg CRND8 mice model of Alzheimer's disease were obtained.

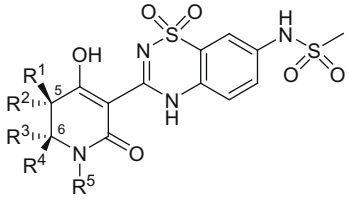


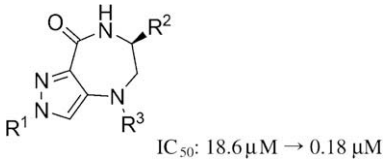
3
mycmycin-1

EOT (efficiency of transformation)	Myc–Max (% inhibition in FRET assay)
0.05	66%

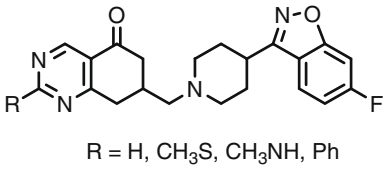


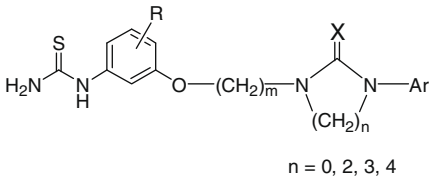
Preliminary structure–activity relationship studies of 3-(2-amino-ethyl)-5-(4-ethoxy-benzylidene)-thiazolidine-2,4-dione, a putative substrate-specific ERK1/2 inhibitor, is reported.



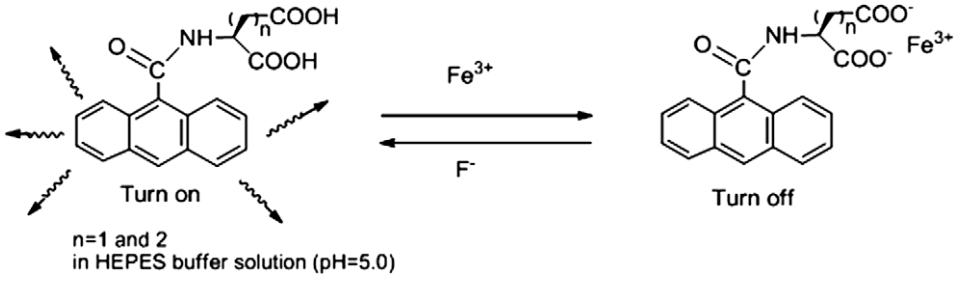


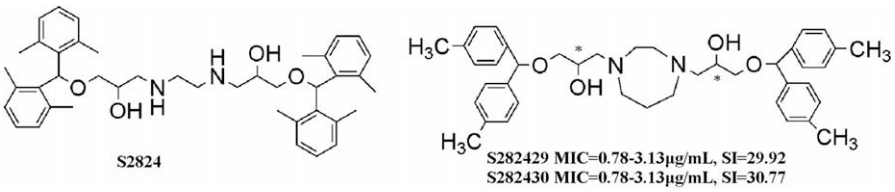
Novel and potent antagonists of $P2X_7$ receptors were developed through optimization of a weak lead compound identified from a potential privileged structure-based library.





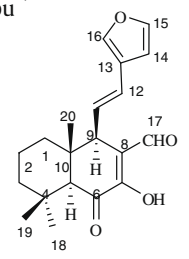
Synthesis and SAR for a series of novel arylthiourea derivatives as potent hepatitis C virus inhibitors are reported.



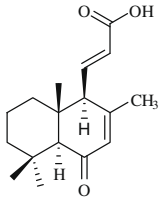


Thirty analogs of (*S*,*S*)-*N*,*N*′-bis-[3-(2,2′,6,6′-tetramethylbenzhydryloxy)-2-hydroxy-propyl]-ethylenediamine were synthesized and tested antituberculosis activity. Two compounds in this series showed highly active against drug-resistant strains.

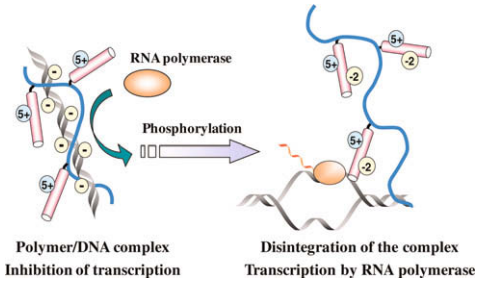
Phytochemical investigation of rhizomes of the *Hedychium spicatum* yielded two new labdane diterpenes (**1, 2**) along with six known compounds (**3–8**). Cytotoxic activity of the isolates was studied against THP-1 (human acute monocytic leukemia), HL-60 (human promyelocytic leukemia), A-375 (human malignant melanoma) and A-549 (human lung carcinoma) cell lines.

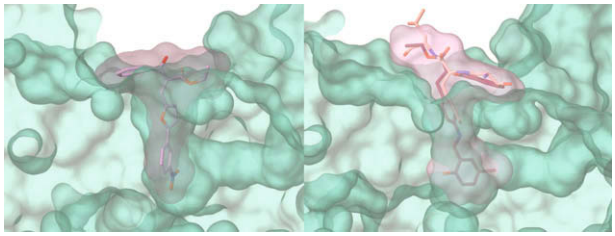


7-hydroxy hydichinal (1)

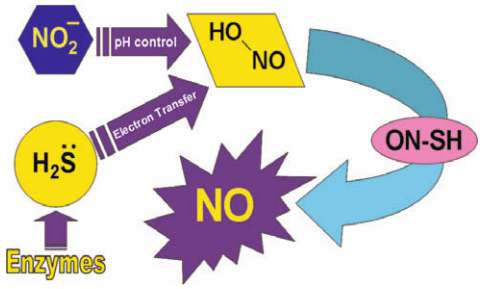


Spicatanoi cacid (2)

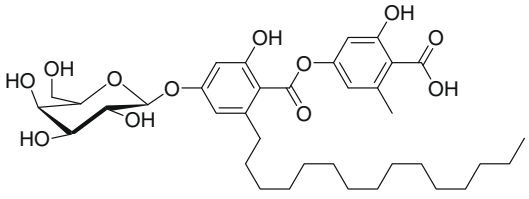




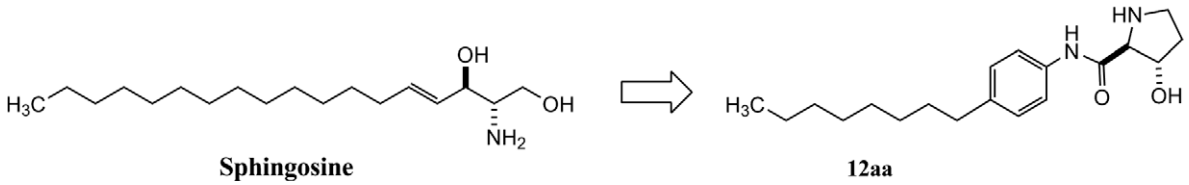
Two novel chemical scaffolds targeting the HIV-1 gp120 Phe43 cavity and able to interfere with gp120–CD4 protein–protein interactions were identified by structure-based in silico screening.



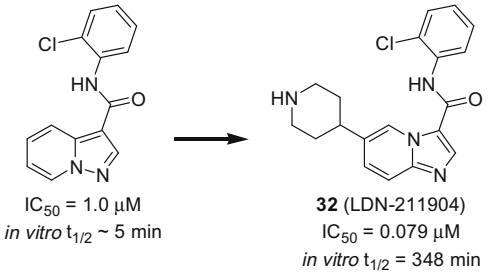
Hydrogen sulfide displays a role as cofactor of the nitrite in the NO release, which depends on the pH of the medium.

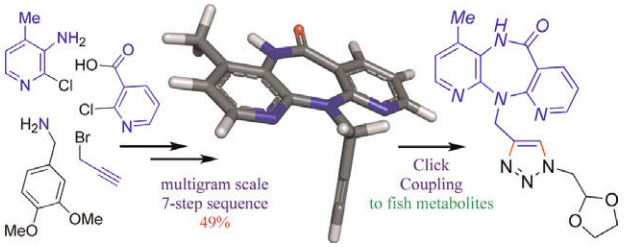


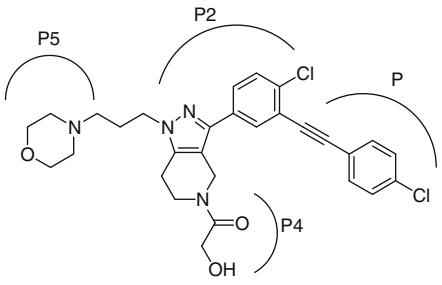
Bioassay-guided investigation on the EtOAc extract of cultures of the marine-derived fungus *Cosmospora* sp. SF-5060 afforded a potent tyrosine phosphatase 1B (PTP1B) inhibitory metabolite, aquastatin A.

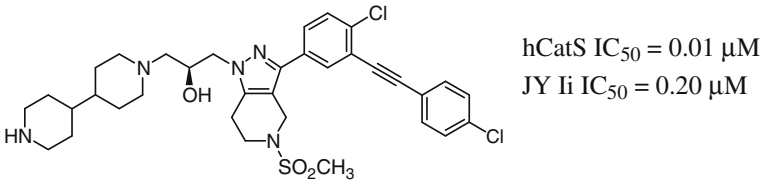


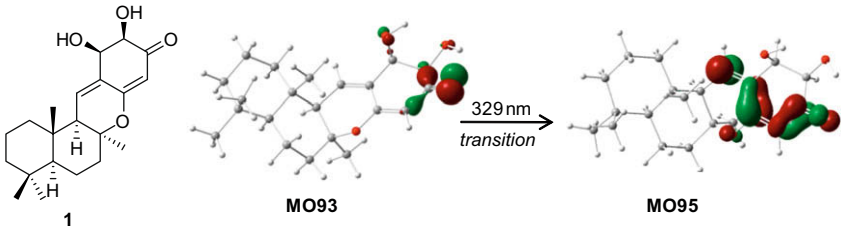
Potent and novel sphingosine kinase 1 (SK1) inhibitor (12aa) have been discovered through a series of modifications of sphingosine, the substrate of this enzyme.



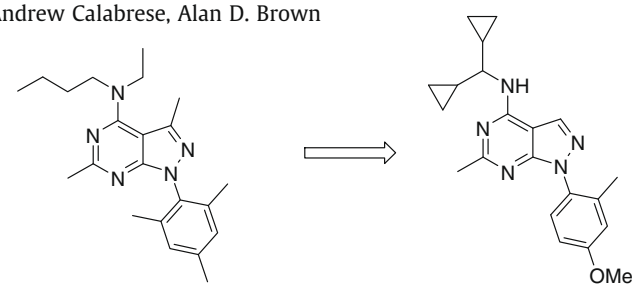




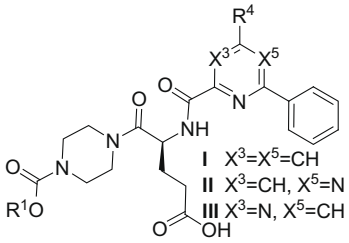




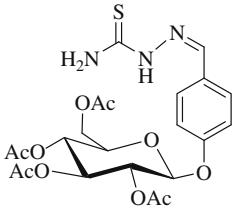
Puupehanol (**1**), a new sesquiterpene-dihydroquinone derivative, was isolated from the marine sponge *Hyrtios* sp., along with the known antifungal compounds puupehenone (**2**) and chloropuupehenone (**3**).



Balancing potency and metabolic stability in a target which favours lipophilic ligands is a considerable challenge. Here we describe two strategies employed to achieve this balance in a series of pyrazolopyrimidine CRF antagonists: moderation of lipophilicity, and incorporation of a metabolically stable lipophilic group.

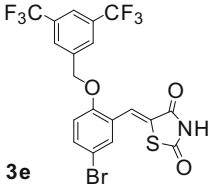


Piperazinyl-glutamate-pyrimidines were prepared with oxygen, nitrogen, and sulfur substitution at the 4-position (R^4) of the pyrimidine leading to highly potent $P2Y_{12}$ antagonists.



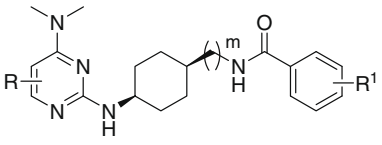
9a IC_{50}=0.31±0.12 μM

A series of 4-functionalized phenyl-*O*-β-D-glycosides were designed, synthesized and evaluated as tyrosinase inhibitors. Compound **9a** was found to be the most potent inhibitor.

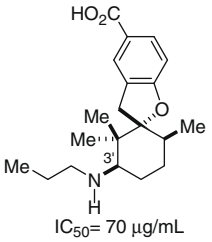


3e

Compound **3e** inhibited PTP1B, improved glucose tolerance, suppressed weight gain, and improved blood parameters in a mouse model system.

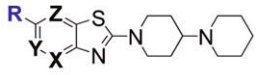


A series of pyrimidine analogues derived from ATC0175 were potent antagonists of human MCH-R1 in vitro with improved receptor selectivity. One example was shown to inhibit food intake and decrease body weight in a chronic study. However observed effect was most likely not due to interaction with the MCH-R1.



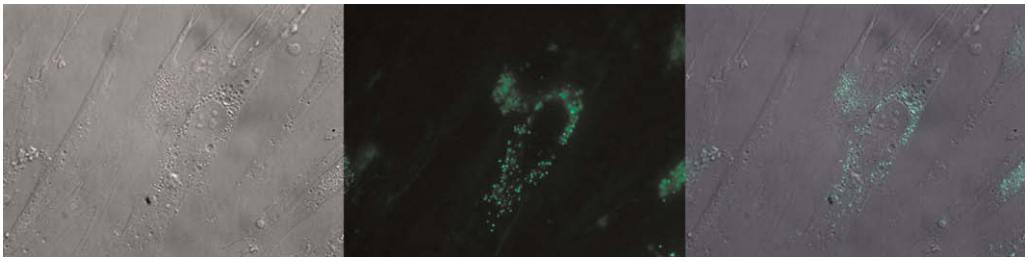
IC_{50}= 70 μg/mL

The synthesis of new analogs of K76-COOH, as complement inhibitors, employing filifolinol as staring material suggest that the nature and stereochemistry of the C3′ substituent may be important for the biological activity.

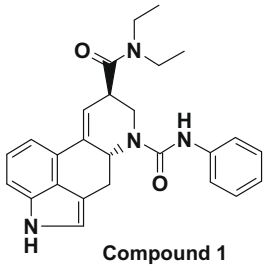


one of X, Y or Z is N and the other two of X, Y or Z are CH

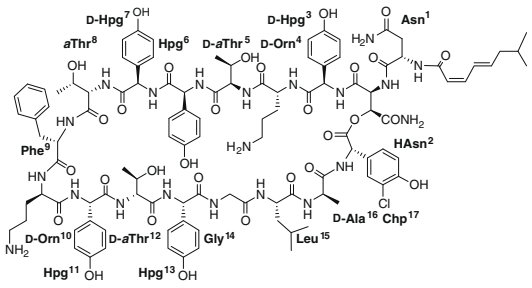
A series of 2-(1,4′-bipiperidine-1′-yl)thiazolopyridines was discovered as novel non-imidazole histamine H_3 receptor antagonists. The synthesis and structure–activity relationships for these new thiazolopyridine antagonists are described.

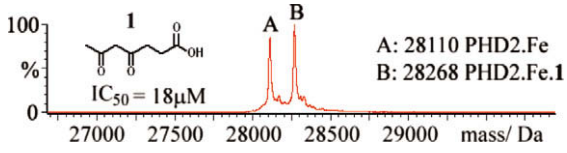


Modified PNAs enter cells and inhibit expression of huntingtin.

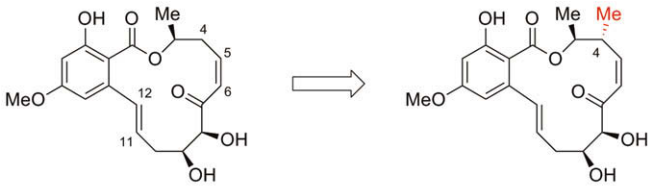


Compound 1

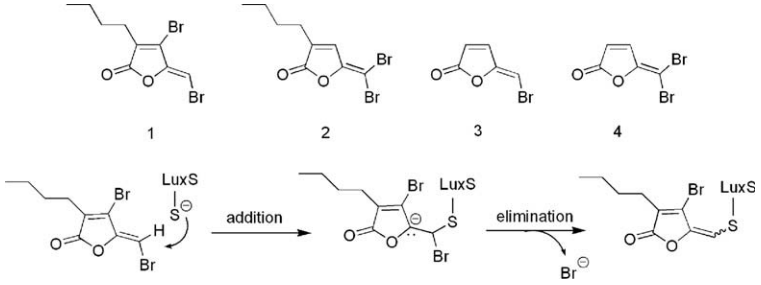


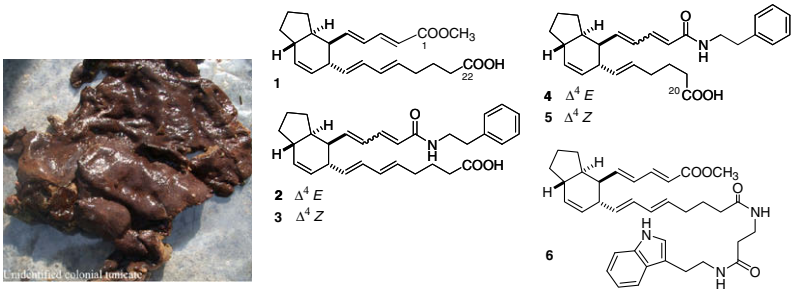


2-Oxoglutarate analogues were evaluated as inhibitors of the human oxygen sensing enzyme prolyl hydroxylase domain 2 and screened for binding by non-denaturing electrospray ionization mass spectrometry.

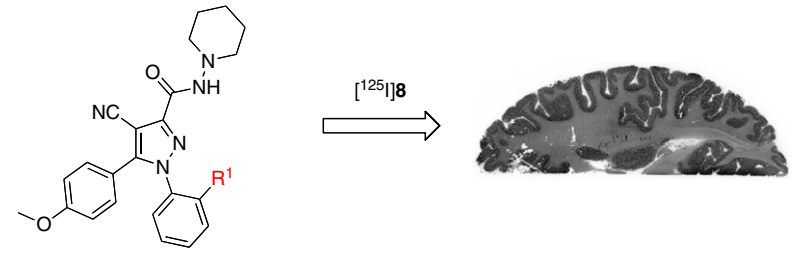


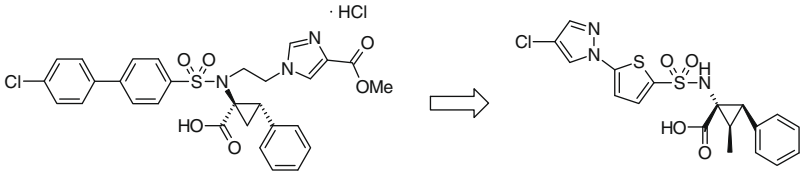
1: f152A1 = LL,Z-1640-2 **15**: ER-803064

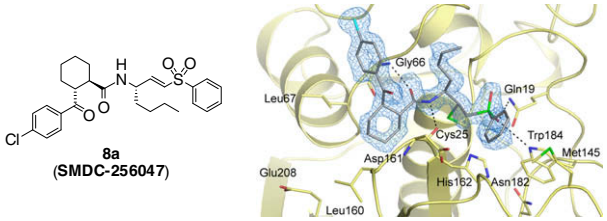




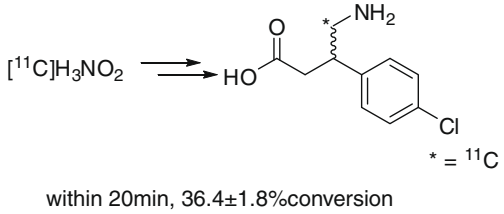
Unique bicyclic α,ω-dicarboxylic acid derivatives were isolated from a marine colonial tunicate and their biological evaluations were performed.

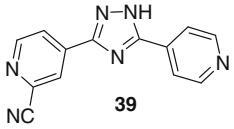






We describe here the identification of non-peptidic vinylsulfones that inhibit parasite cysteine proteases in vitro and inhibit the growth of *Trypanosoma brucei brucei* parasites in culture. A high resolution (1.75 Å) co-crystal structure of **8a** bound to cruzain reveals how the non-peptidic P2/P3 moiety in such analogs bind the S2 and S3 subsites of the protease, effectively recapitulating important binding interactions present in more traditional peptide-based protease inhibitors and natural substrates.





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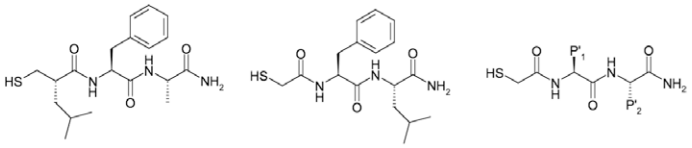
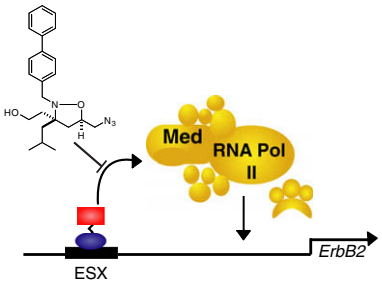
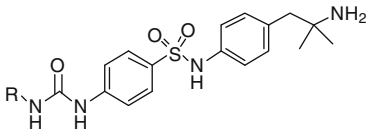


Burns et al., 1990 — K_i = 0.3 μM

Kessler et al., 1982 — K_i = 0.2 μM

Present Study





*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of *R*-**22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5677.]

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