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Letters

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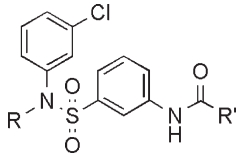
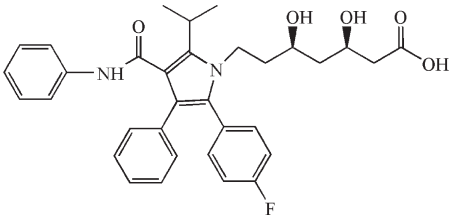
Contents

ARTICLES

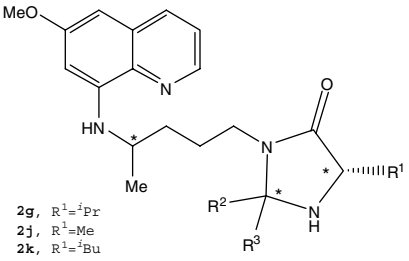


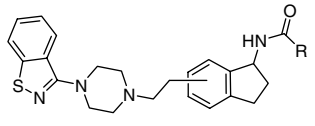
T-type calcium channel antagonists were designed using a protocol involving the program SPROUT constrained by a ComFA-based pharmacophore model. From this exercise, a novel series of potent and selective T-type channel antagonists containing a biaryl sulfonamide core were discovered.



Atorvastatin was determined to be a competitive inhibitor of DPP-IV with $K_i = 57.8 \pm 2.3$ μM.

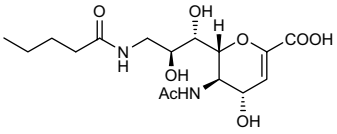
The anti-*Pneumocystis carinii* and antiplasmodial activities of compounds **2** were evaluated and found to be correlated. Cycloheptanone-derived imidazolidin-4-ones **2g**, **2j**–**k** (R^2 and $R^3 = -(CH_2)_6-$) were the most active.





R= alkyls, substituted aryls

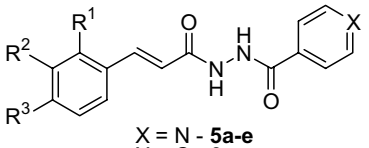
As part of an on-going effort to investigate the chemical space requirements for D_2/5-HT_{2A} receptor antagonists as atypical antipsychotics, new 1-aminoindanes were synthesized. The replacement of the heterocycle (oxindole) in ziprasidone with a carbocycle (indane) was well tolerated and found to retain binding affinities for dopamine D_2, serotonin 5-HT_{2A}, and serotonin 5-HT_{1A} receptors. Such compounds hold promise as a new chemical motif with atypical antipsychotic properties for the treatment of schizophrenia and related disorders.



10h

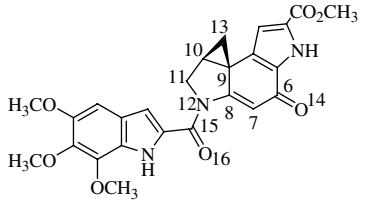
Human Sialidase	$IC_{50}(\mu M)$
NEU1	10
NEU2	>1000
NEU3	>1000
NEU4	>1000

The synthesis and human sialidase inhibitory activities of some amide-linked C9 modified DANA analogues **10a–j** are described.

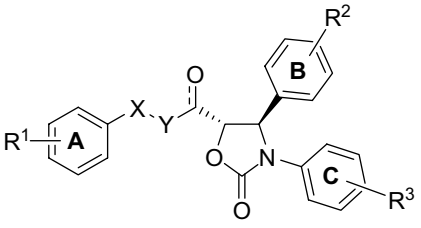


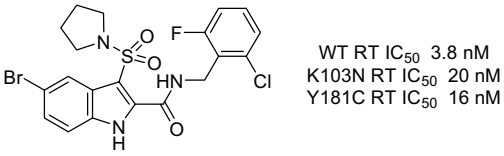
X = N - **5a-e**
X = C - **6a-e**

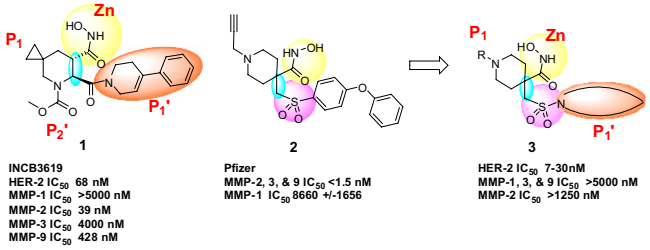
The present article describes a series of ten new *trans*-cinnamic acid hydrazide derivatives, which were synthesized and evaluated for their in vitro antibacterial activity against *Mycobacterium tuberculosis*.

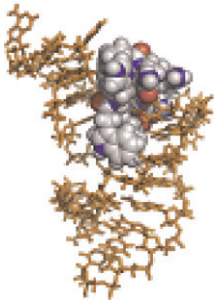


(+)-Duocarmycin (DSA)

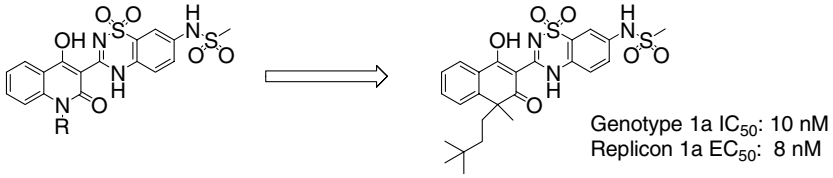




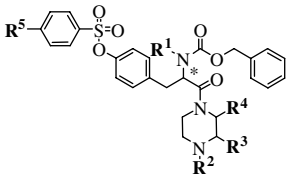


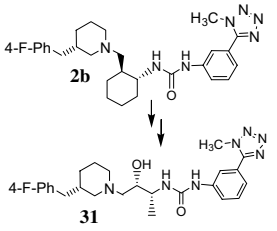


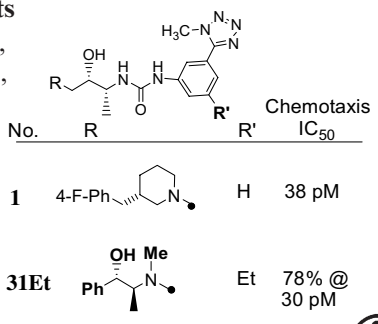
Non poly-cationic cyclic peptides that target RNA are presented.

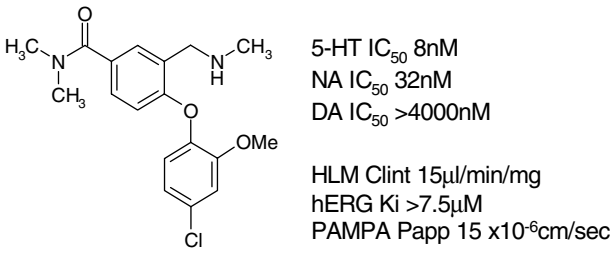


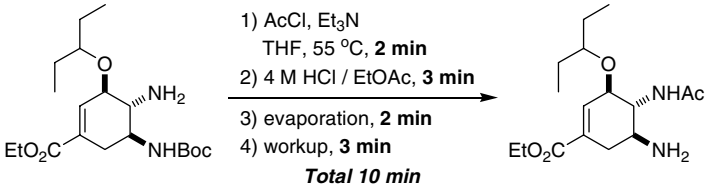
The synthesis and SAR of a series of novel 1,1-dialkyl-2(1*H*)-naphthalenones as potent HCV polymerase inhibitors is reported.

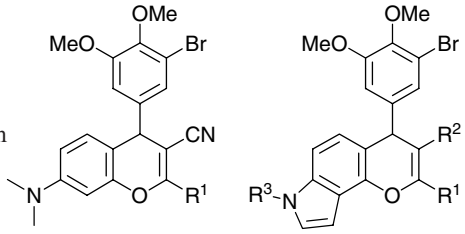


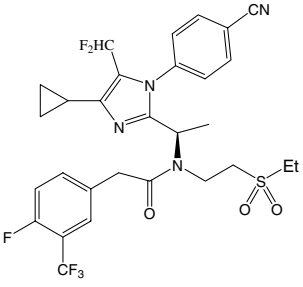


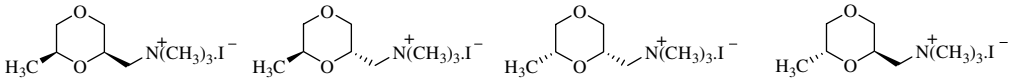


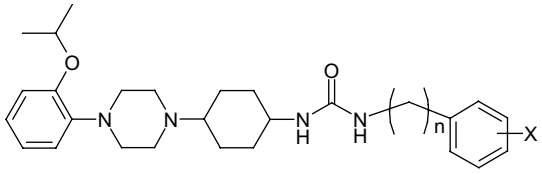




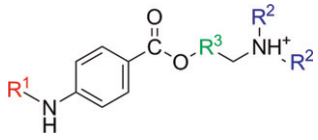


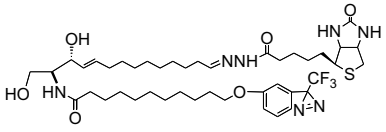


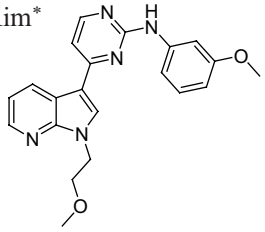




A series of (phenylpiperazinyl)cyclohexylureas that show selectivity to human $\alpha_{1a/1d}$ adrenergic receptors were developed. These compounds have potential for the treatment of BPH/LUTS.

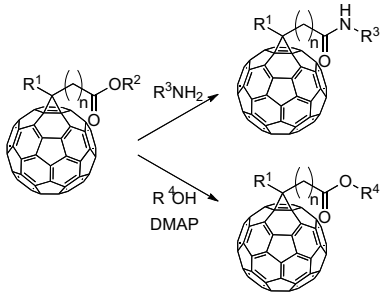


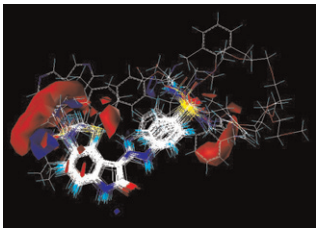


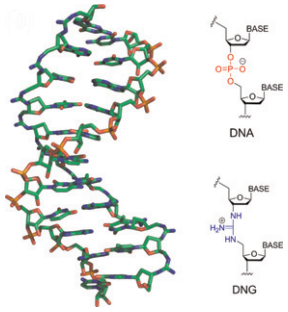


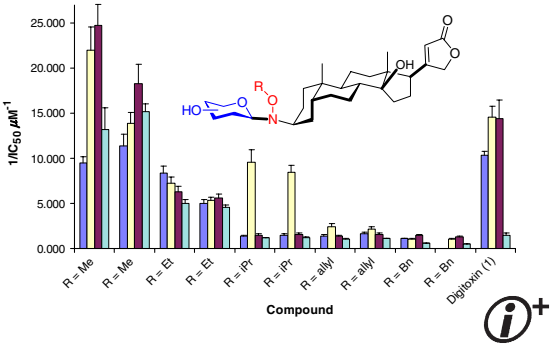
22, NF-kB, IC_{50} = 1.4 μM

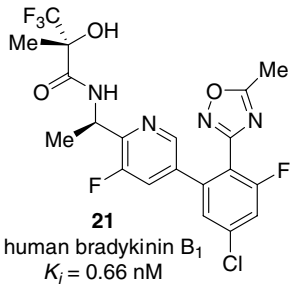
Novel heterocyclic ring-substituted pyridines have been designed as inhibitors of glycogen synthase kinase-3β and compound **22** exhibited good GSK-3β and NF-κB inhibition as well as desirable cellular activity.





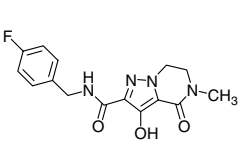




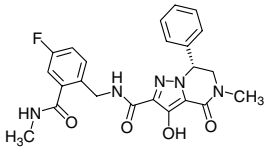


21
human bradykinin B_1
K_i = 0.66 nM

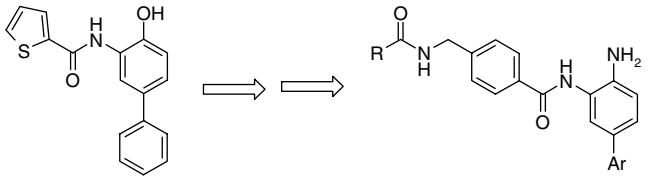
A series of 4-oxo-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-2-carboxamides was synthesized and tested for their inhibition of HIV-1 integrase catalytic activity and HIV-1 replication in cells. Structure–activity studies around lead compound **5** indicated that a coplanar relationship of metal-binding heteroatoms provides optimal binding to the integrase active site. Identification of potency-enhancing substituents and adjustments in lipophilicity provided **17b** which inhibits integrase-catalyzed strand transfer with an IC_{50} value of 74 nM and inhibits HIV-1 replication in cell culture in the presence of 50% normal human serum with an IC_{95} value of 63 nM.



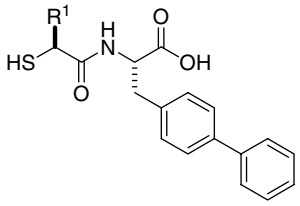
5



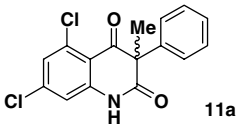
17b



A class of biaryl benzamides was identified and optimized as selective HDAC1&2 inhibitors (SHI-1:2). SAR development based on an initial lead led to a series of potent and selective inhibitors with reduced off-target activity and tumor growth inhibition activity in a HCT-116 xenograft model.

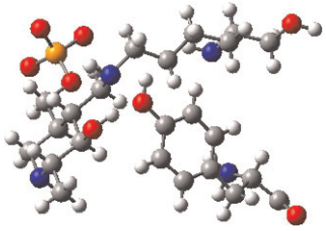


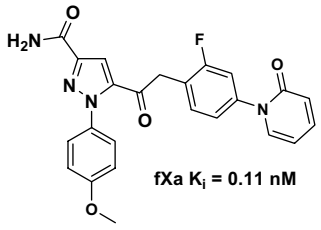
Screening of a metalloprotease library led to the identification of a thiol-based dual ACE/NEP inhibitor as a potent ACE2 inhibitor. Modifications of the P^1 benzyl moiety led to improvements in ACE2 potency as well as to increased selectivity versus ACE and NEP.

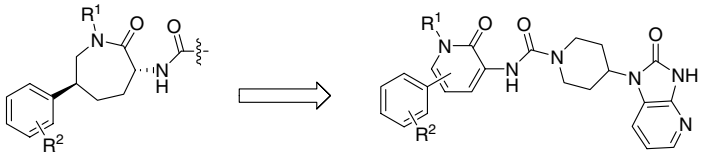


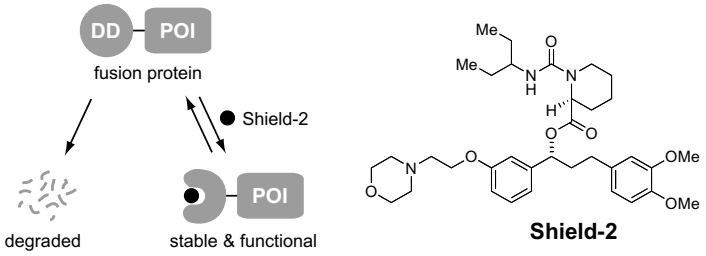
11a

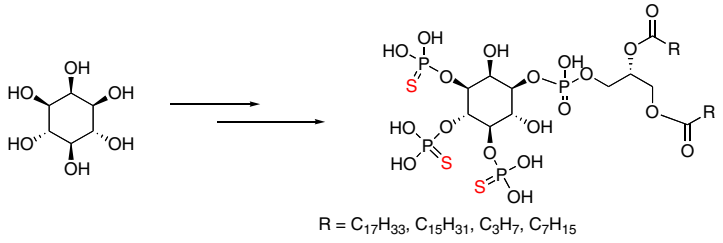
A series of 3-methyl-3-phenyl-1*H*-quinoline-2,4-diones was prepared and evaluated for 5-HT$_6$ receptor antagonistic activity.

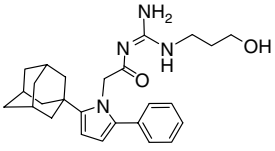


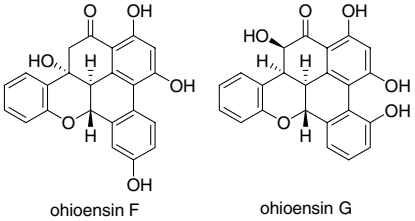


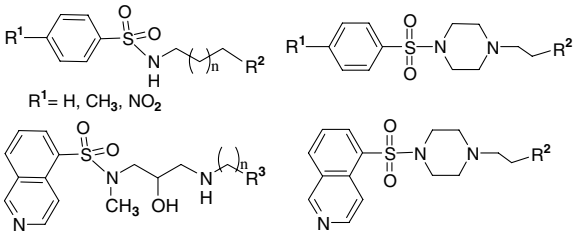


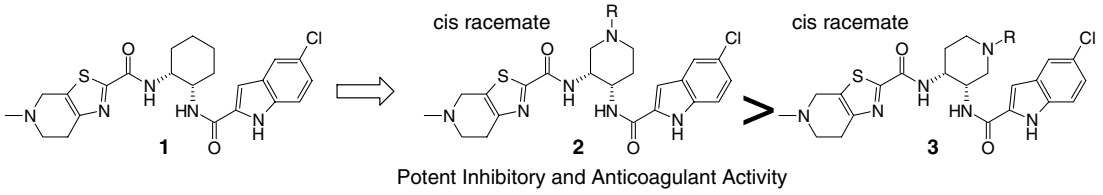




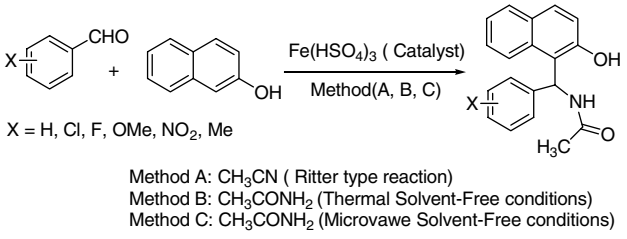


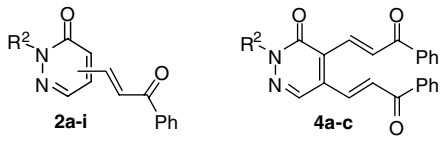


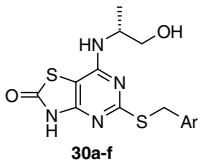




An efficient and direct protocol for the preparation of amidoalkyl naphthols employing a multi-component, one-pot condensation reaction of β-naphthol, aromatic aldehydes and acetamide in the presence of ferric hydrogensulfate under solvent, solvent-free and microwave conditions is described. The thermal solvent-free and microwave green procedures offer advantages such as shorter reaction times, simple work-up, excellent yield and recovery and reusability of catalyst. It is noteworthy that 1-amidomethyl-2-naphthols can be converted into important biological 'drug like' active 1-aminomethyl-2-naphthol derivatives by amide hydrolysis.

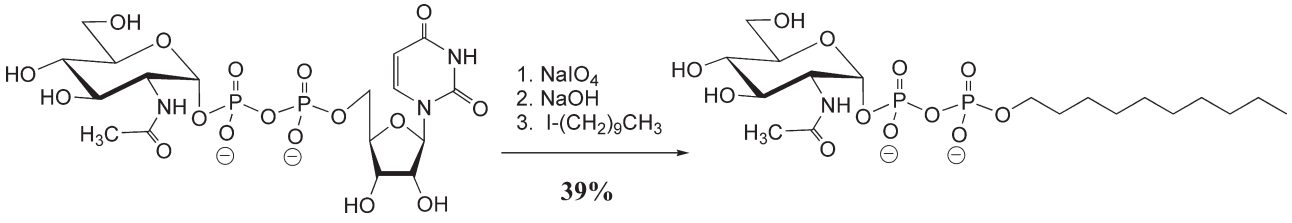


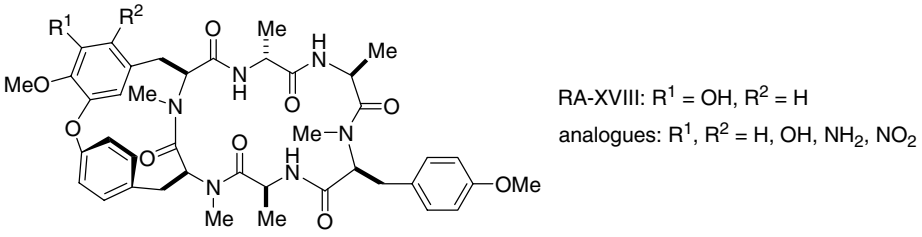


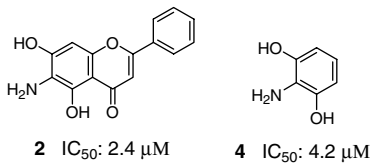


30a-f

The SAR of a series of pyrimidine-based fused bicyclic heterocycles at the CXCR2 receptor was investigated, leading to the discovery of a series of potent, bioavailable thiazolo[4,5-*d*]pyrimidine-2(3*H*)-one antagonists **30a**–**f** with additional CCR2 activity.

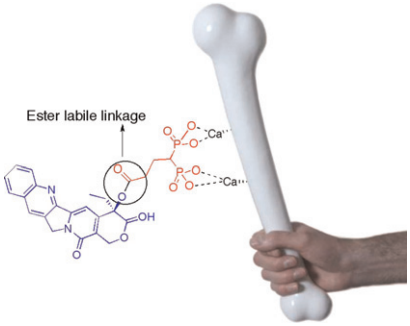




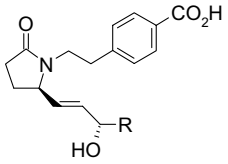


2 IC_{50}: 2.4 μM **4** IC_{50}: 4.2 μM

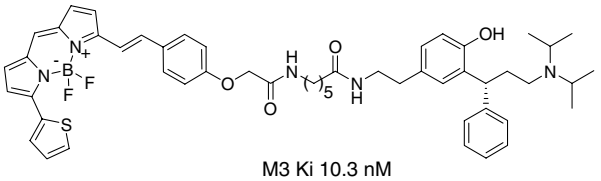
The 2-aminoresorcinol moiety of 6-amino-5,7-dihydroxyflavone (**2**) is important to exert the α-glucosidase inhibitory activity and 2-aminoresorcinol (**4**), itself, is a potent α-glucosidase inhibitor.



γ-Lactam analogs (**2**) of EP_4 receptor agonists were identified by substitution of the pyrazolidinone ring (**1**) with a pyrrolidinone ring. Several compounds (such as **2a**, **2h**) with high potency, selectivity, and acceptable PK profiles were discovered. These were assessed in animal models of ovulation induction and bronchoconstriction.



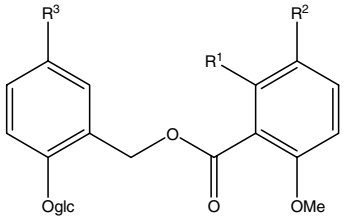
2



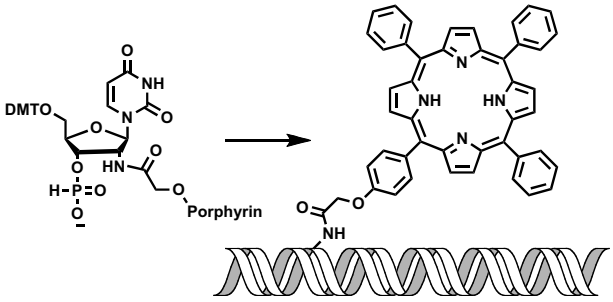
M3 Ki 10.3 nM

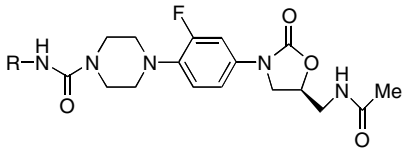
The design and concise synthesis of a potent and fluorescent BODIPY-tolterodine conjugate antimuscarinic probe is reported.

Four novel polyphenols could be efficient fibril inhibitors in Alzheimer's disease: malvidin and its glucoside and curculigosides B and D. Moreover, molecules with the particular C_6-linkers-C_6 structure could be potent inhibitors.



	R^1	R^2	R^3	
12	OMe	H	OH	**curculigoside A**
13	OH	H	OH	**curculigoside B**
14	OMe	OH	H	**curculigoside D**





The syntheses of a series of novel oxazolidinone analogues possessing an urea functionality are reported. The SAR around the urea functional group resulted in interesting antibacterial compounds.

OTHER CONTENTS

*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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