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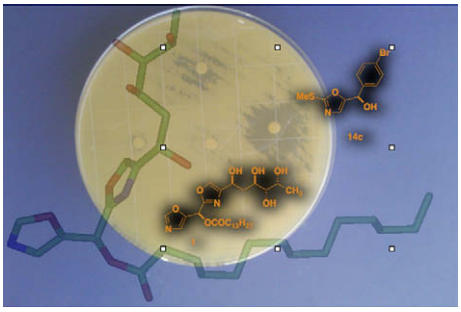
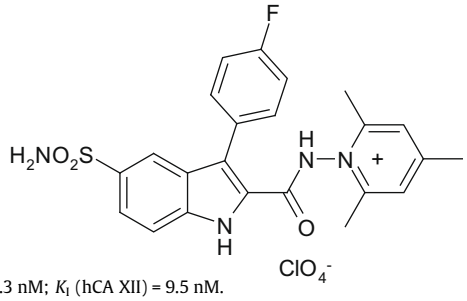
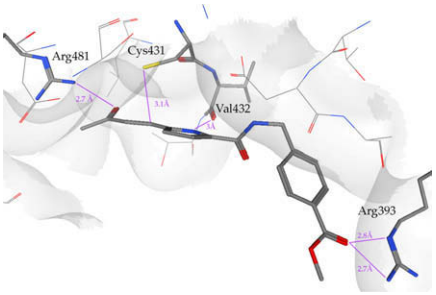
Contents

ARTICLES

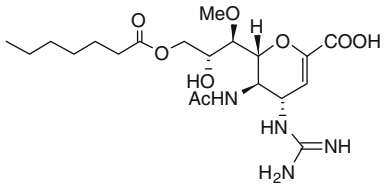




K_I (hCA I) = 7.6 nM; K_I (hCA II) = 65 nM, K_I (hCA IX) = 8.3 nM; K_I (hCA XII) = 9.5 nM.



The discovery of a novel HCV helicase inhibitor (IC_{50} = 0.26 μM) is reported.



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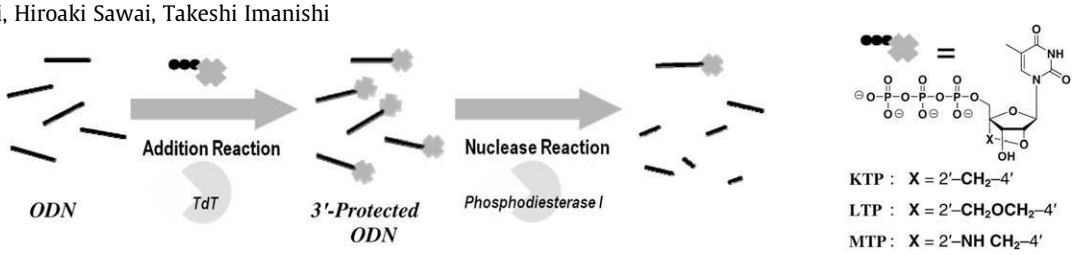
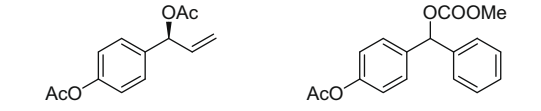
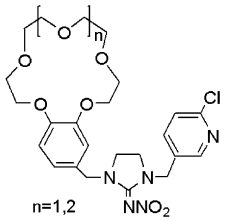
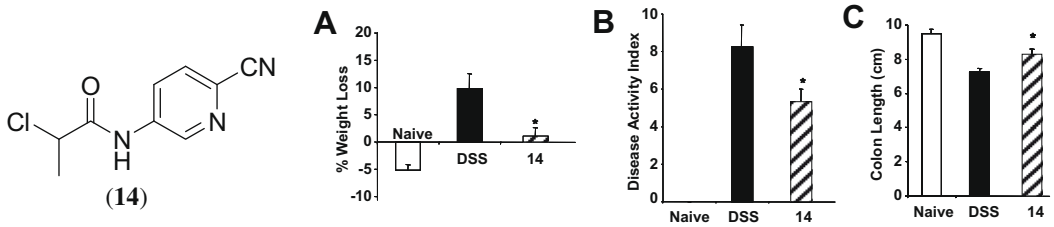


The enzymatic addition of BNA nucleotides to the 3′-end of oligodeoxyribonucleotide (ODN) was examined using terminal deoxynucleotidyl transferase (TdT); nuclease resistance was conferred on DNA, depending on the types of BNA nucleotides added.

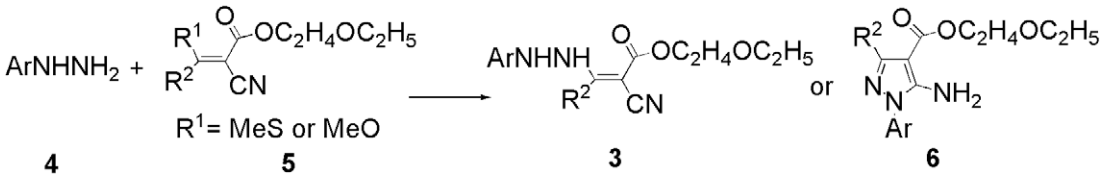


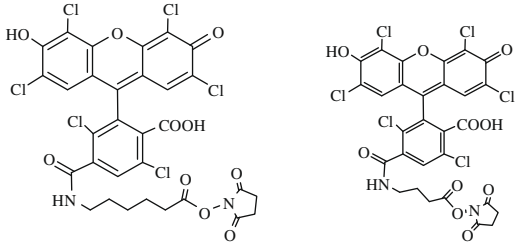


Benzocrown-capped imidacloprid displayed higher insecticidal activity than imidacloprid.

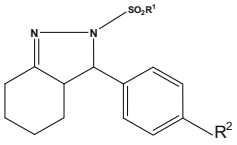


Systemic application of compound **14**, a novel mTOR inhibitor, significantly suppresses macroscopic and histologic abnormalities associated with chemically-induced murine ulcerative colitis.

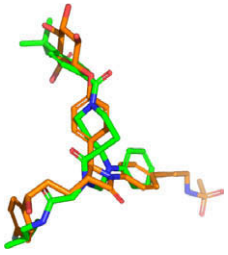




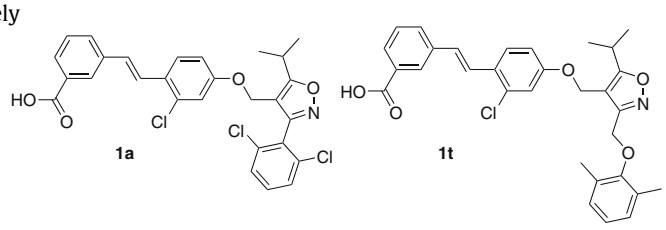
Two novel chlorinated fluoresceins 2′,4′,5′,7′-tetrachloro-6-(5-carboxypentyl)-4,7-dichlorofluorescein succinimidyl ester and 2′,4′,5′,7′-tetrachloro-6-(3-carboxypropyl)-4,7-dichloro fluorescein succinimidyl ester were synthesized as fluorescent probes for labeling proteins. The investigation in immunofluorescence histochemistry showed them had strong fluorescence, high photostability and good biocompatibility.



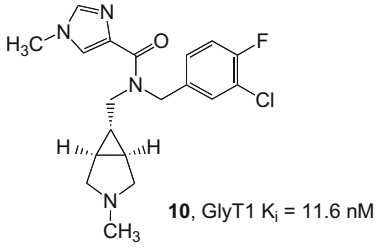
QSAR study of synthesized hexahydroindazole derivatives indicated the importance of topological parameters $^{2}\chi$ and $^{2}\chi^{v}$ in contribution to antimicrobial activity.



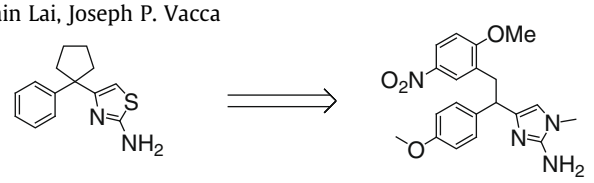
A series of spiroimidazolidinone NPC1L1 inhibitors was discovered by virtual screening of the Merck corporate sample repository using 3D-similarity-based screening.



Starting from the known FXR agonist GW 4064 **1a**, a series of alternately 3,5-substituted isoxazoles was prepared. Several of these analogs were potent full FXR agonists. A subset of this series, with a tether between the isoxazole ring and the 3-position aryl substituent, were equipotent FXR agonists to GW 4064 **1a**, with the 2,6-dimethyl phenol analog **1t** having greater FRET FXR potency than GW 4064 **1a**.

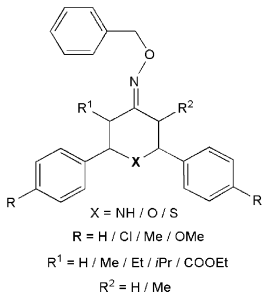


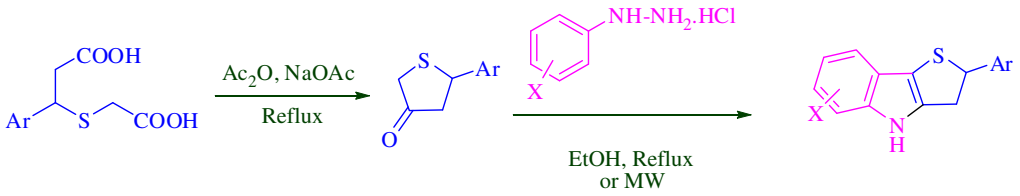
The discovery of a potent, selective inhibitor of the type 1 glycine transporter, **10**, is reported.

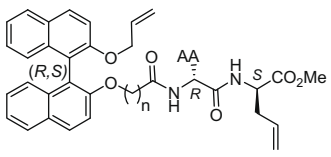


A novel series of heteroaromatic BACE-1 inhibitors is described. These inhibitors interact with the enzyme in a unique fashion that allows for potent binding in a non-traditional paradigm. In addition to the elucidation of their binding profile, a pH dependent effect on the binding affinity as a result of the intrinsic pK_a of these inhibitors and the pH of the BACE-1 enzyme binding assay is discussed.

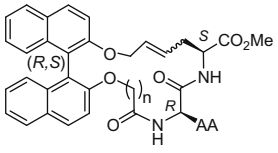
Series of N, O and S heterocyclic oxime ethers were synthesized and their stereochemistry is established. All the synthesized oxime ethers were evaluated for in vitro antibacterial and antifungal potency by serial dilution method, thus obtained MICs provide better structure–activity correlations (SAR).



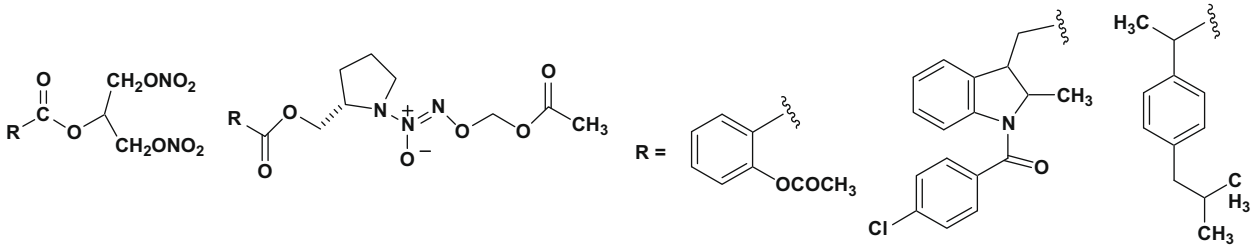


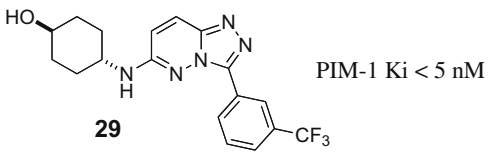


n	AA	MIC μg/mL
1	Lys	4
3	Lys	15
1	homo-Arg	8
3	homo-Arg	8



n	AA	MIC μg/mL
1	Lys	15-31
3	Lys	62
1	homo-Arg	8
3	homo-Arg	8





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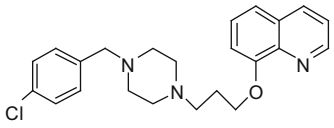
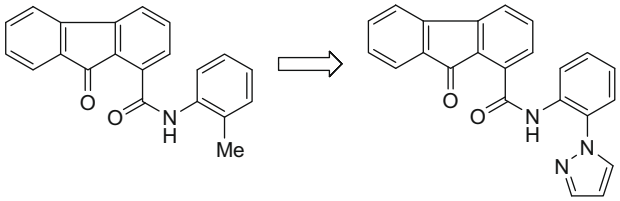
PIM-1 Ki < 5 nM



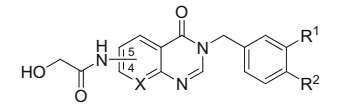
The synthesis and evaluation of a series of 1-(quinoliloxypropyl)-4-aryl piperazines for atypical antipsychotic effect is reported. Using appropriate physicochemical properties, similarity of the compounds with standard drugs has been calculated.



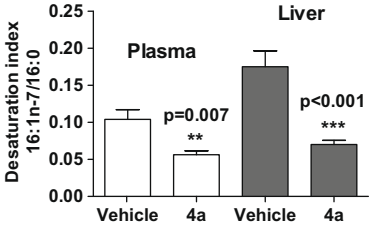
2a (hit) **6s** (lead)

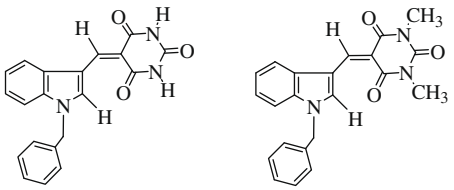
The synthesis and SAR of a group of apoptosis-inducing 9-oxo-9*H*-fluorene-1-carboxamides with modifications at the carboxamide group are reported.

We discovered a structurally novel SCD inhibitor CVT-11,563 (IC50 119 nM, HEPG2 assay), selective against Δ5 and Δ6 desaturases, with excellent PK parameters (F = 90% and dAUC 935 ng h/mL). This compound was found to have moderately selective liver distribution and low brain penetration. In a 5-day study CVT-11,563 significantly reduced SCD activity in plasma and liver.



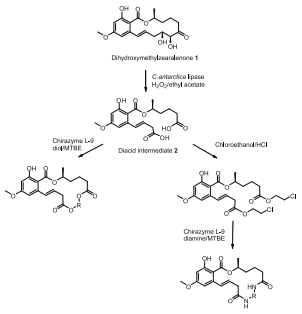
CVT-11,563 5-isomer, X = CH, $R^1 = R^2 = Cl$

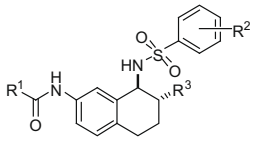




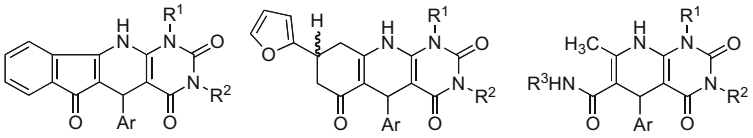
GI_{50} for:

A498 = 0.03 μM IGROV1 = 0.06 μM
MDA-MB-468 = 0.1 μM MDA-MB-468 = 0.02 μM

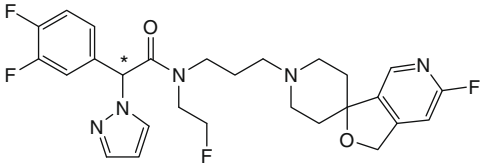




Structure–activity relationship of a new class of Kv1.5 inhibitors based on the tetraline scaffold was investigated.

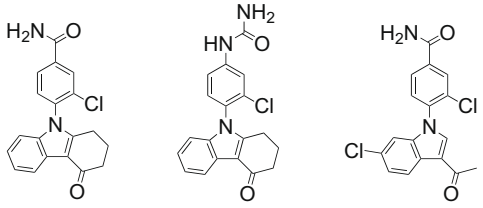


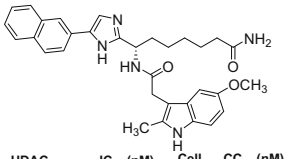
A series of pyridopyrimidine derivatives were synthesized and evaluated for their ability to inhibit cyclic nucleotide synthesis in the presence of stable toxin a of *Escherichia coli*.



3c: hMCH-1R (IC_{50}) = 0.09 nM

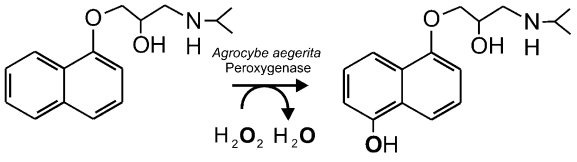
The identification of highly potent and selective MCH-1R antagonist **3c** is reported.

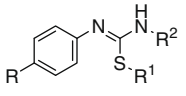




HDAC	IC_{50} (nM)	Cell	CC_{50} (nM)
1	30	HeLa	440
2	82		
3	57		
4, 5, 7 and 8	> 10,000		
6	43		

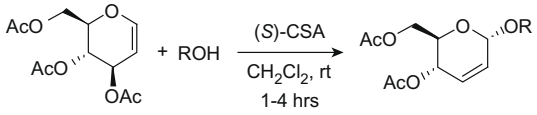
The identification of a selective class I HDAC inhibitor bearing a primary carboxamide as zinc binding group together with its efficacy in vivo is described.



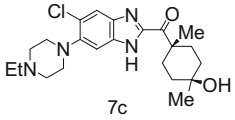


R^1 = alkyl, benzyl
R^2 = H, Et

Synthesis of series of phenylisothioureas and their inhibitory activities on the NO production in lipopolysaccharide activated macrophages are reported.

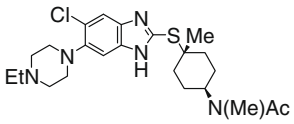


Highly stereoselective synthesis of 2,3-unsaturated glycosides has been developed by employing (*S*)-camphorsulfonic acid.



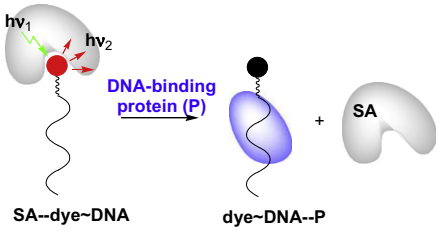
7c

We report identification of 2-cyclohexylcarbonylbenzimidazole **7c** as potent, orally available and brain-penetrable ORL1 antagonist. Compound **7c** showed satisfactory pharmacokinetic profiles and brain penetrability in laboratory animals, and good in vivo antagonism.

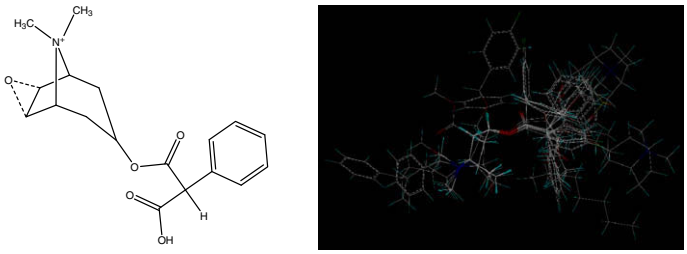


7h

Optimization of benzimidazole series as ORL1 antagonists is reported. Compound **7h** exhibited potent ORL1 activity with high selectivity over binding affinity for hERG.

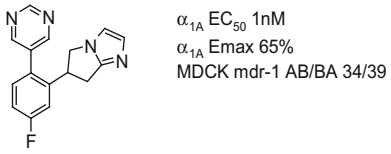


A simple, efficient and cheap method is reported for monitoring interaction between single stranded desoxyribonucleic acids and proteins by using fluorescence spectroscopy.

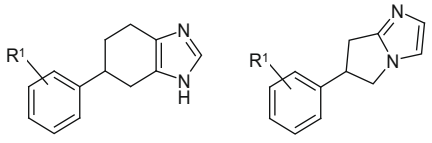


a. PMTR.Et **b**.

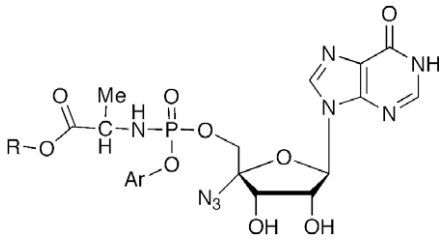
Alignment of the training set: **a** is the template structure (common fragment in red), **b** is the alignment of the training set for ligand-based model.



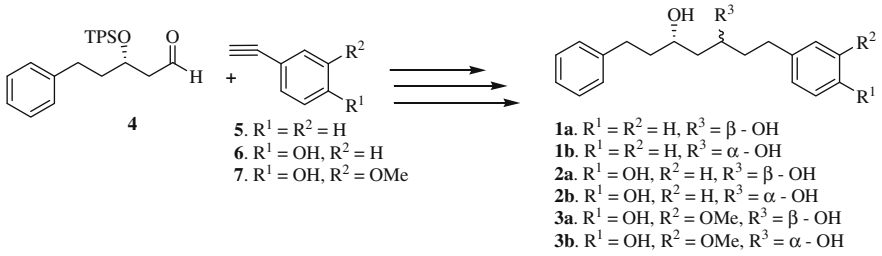
Novel pyrroloimidazoles have been identified as potent partial agonists of the α_{1A} adrenergic receptor, with good selectivity over the α_{1B}, α_{1D} and α_{2A} receptor subtypes. Pyrimidine **20** possessed attractive CNS drug-like properties with good membrane permeability and no evidence for P-gp mediated efflux.



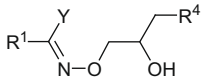
Novel imidazole frameworks have been identified as potent and selective α_{1A} partial agonists with good CNS drug-like properties.



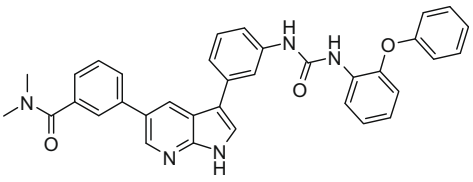
4′-Azidoinosine is inactive versus HCV, while its Pro Tides are active at μM levels.



First total stereo selective synthesis of yashabushidiol, a linear diaryl having 1,3-dio system and its analogues.



Exploration of the SAR around a series of 3,5-disubstituted-1*H*-pyrrolo[2,3-*b*]pyridines led to the discovery of novel pyrrolopyridines as nanomolar inhibitors of the IGF-1R tyrosine kinase.



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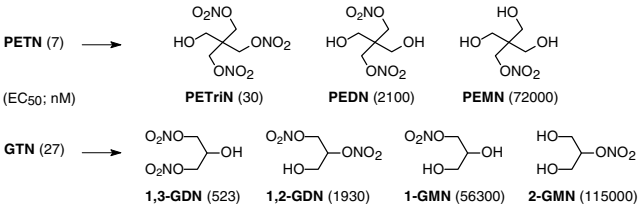
IGF-1R Ezyme IC_{50} 21 nM
Phospho IGF-1R Cellular IC_{50} 68 nM



The bioactive metabolites of GTN and PETN were synthesized and their vasorelaxant potencies measured by performing organ bath experiments with porcine pulmonary arteries.

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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