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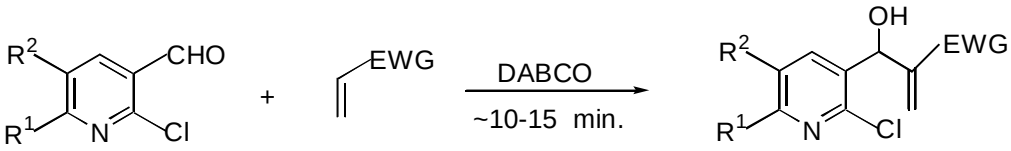
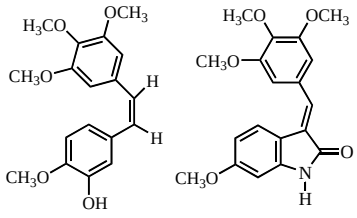
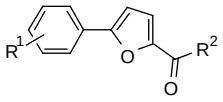
Contents

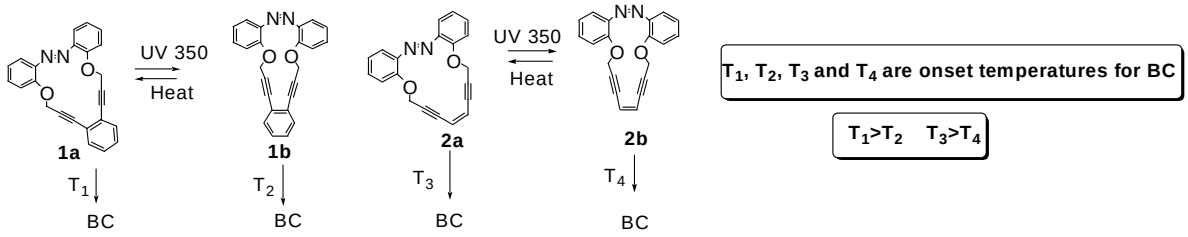
ARTICLES

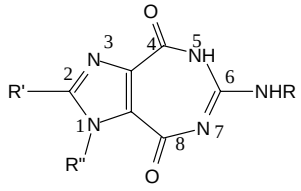






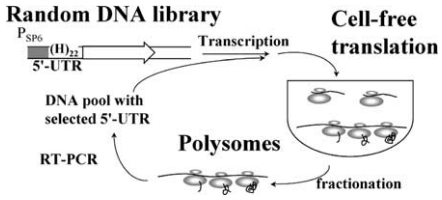
A new series of analogs of 5-phenylfuran-2-carboxylic acid was prepared and subsequently evaluated on Co(II)-, Mn(II)-, Ni(II)-, and Fe(II)-forms of *Escherichia coli* MetAP, in order to define the structural elements responsible for their potency and metalloform selectivity.



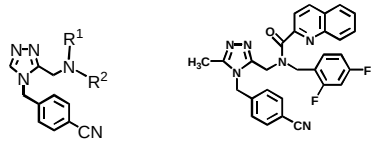


I

The synthesis and in vitro anti-HBV and anti-HCV activities of a number of ring-expanded ('fat') nucleobases containing the imidazo[4,5-*e*][1,3]diazepine-4,8-dione ring system (**I**) have been reported.



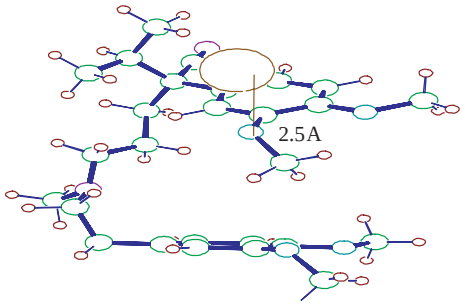
Two novel sequences that enhance translation of downstream open reading frames were obtained by random library selection through isolation of polysomes generated in vitro.

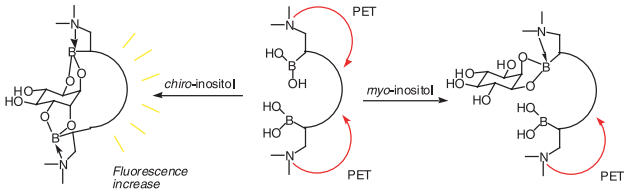


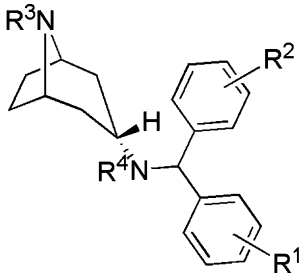
5 **19** (FTase IC50: 0.9 nM)

A novel series of potent inhibitors of Ras farnesyl transferase possessing a 1,2,4-triazole pharmacophore (**5**) is described. These inhibitors were discovered from a parallel synthesis effort and were subsequently optimized to in vitro IC_{50} value of less than 1 nM (**19**).

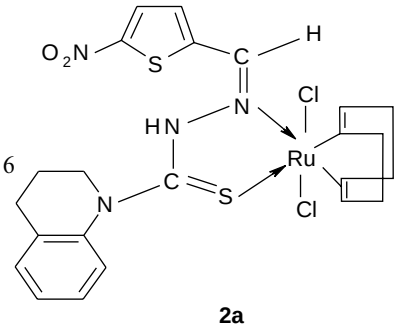
Ab initio Hartree–Fock calculations have been performed to study unprotonated and protonated forms of verapamil. The study predicts that huge conformational change as well as deprotonation is required before the drug is capable of holding Ca^{2+} ion.



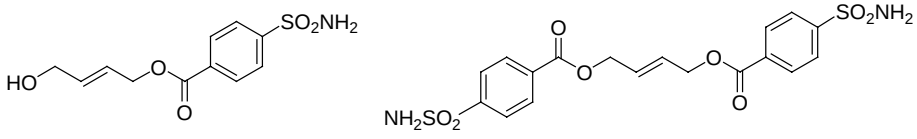




We report here the synthesis, characterization and in vitro antiamoebic activity of 5-nitrothiophene-2-carboxaldehyde thiosemicarbazones (TSC), **1**–**5**, and their complexes [Ru(η^4-C_8H_{12})(TSC)Cl_2] **1a**–**5a**. The most promising among these compounds is Ru(II) complex **2a** having 1,2,3,4-tetrahydroquinoline as N^4 substitution.

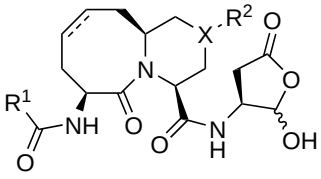


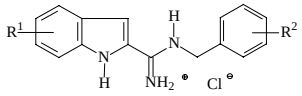
2a



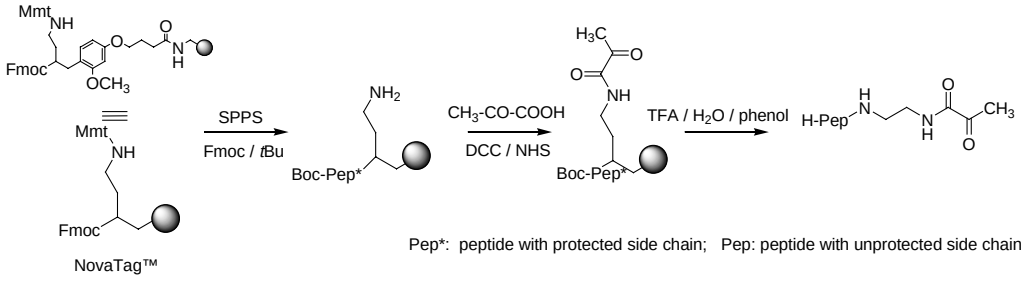
Ki = 5.3 nM Ki = 4.9 nM

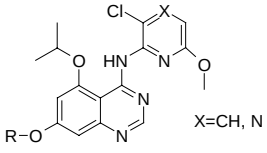
The synthesis and structure–activity relationships of a novel series of mono- and bis- benzene sulfonamides with potent binding affinity for bovine carbonic anhydrase II are reported.





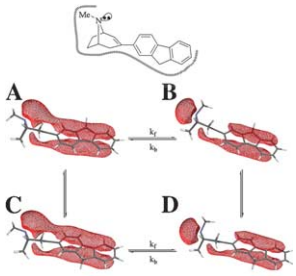
A novel series of indole-2-carboxamidines derivatives was prepared and identified as NR2B selective NMDA receptor antagonists. The influence of the substituents on the indole skeleton as well as the substitution of the benzyl moiety on the biological activity of the compounds was studied. Compound **5a** was po active in the formalin test in mouse.

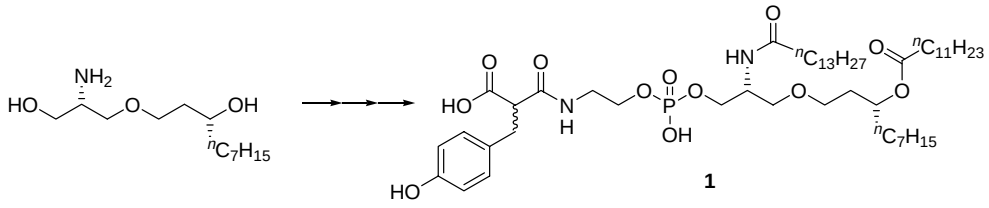




5,7-Disubstituted 4-heteroarylaminoquinazolines of the type above have been synthetised and evaluated as c-Src kinase inhibitors. Highly potent inhibition, high selectivity and physical properties suitable for oral dosing were achieved with this series.

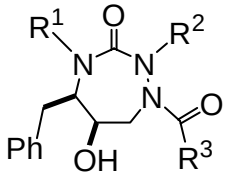
A 3-aryl-trop-2-ene ligand shown in the tentative binding pocket of a human monamine transporter. Conformational states A–D are dependent on the selection of the aromatic substituent at C3. The red colored electrostatic potential maps reveal the electron rich regions of A–D.





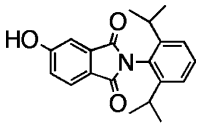
1

Phospholipid compound **1** was discovered as a novel antagonist of toll-like receptor 2 signaling. Synthesis and biological properties are described for **1** and eight related analogues.

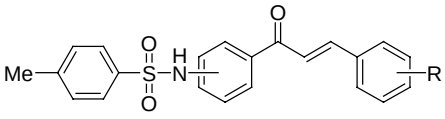


II, N-Acyl Aza-cyclic Urea

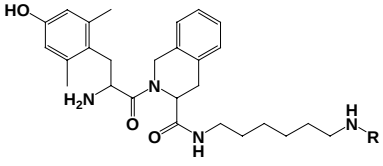
Two libraries of hMC4R agonists, **X**-**Y**-DPhe^7-Arg^8-2-Nal^9-**Z**-NH$_2$ and **X**-**Y**-DPhe^7-Arg^8-Trp^9-**Z**-NH$_2$, totaling 185 peptides were prepared using Irori radiofrequency tagging technology and Argonaut Quest 210 Synthesizer, where **X** stands for N-caps, **Y** for His^6 surrogates, and **Z** for Gly^{10} surrogates. As a result of this study, pentapeptides with Trp were found to be more hMC4R potent than the corresponding 2-Nal analogs, novel N-caps and Gly surrogates were identified, and 19 new peptides which are potent hMC4R agonists (EC_{50} 1–15 nM) and selective against hMC1R were discovered.



5HPP-33

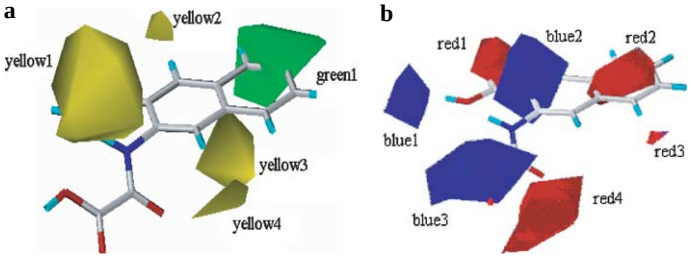


R = 4- or 3,4-OH



R = Dmt, Tic, Phe

δ-Receptor antagonism: pA_2 = 10.2–10.4.



The contour plots of CoMFA steric fields (a) and electrostatic fields (b)

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Amerliorating transthyretin amyloidogenesis by native state kinetic stabilization mediated by small molecule binding. Small molecule binding to the amyloidogenic protein transthyretin kinetically stabilizes the native tetrameric state, preventing dissociation to folded monomers that misfold and misassemble into toxic intermediates, amorphous aggregates, and amyloid fibrils. The Kelly laboratory has developed several structurally distinct inhibitor families, depicted in the background, that are undergoing pharmacological evaluation. Created by Steven M. Johnson, graduate student in Professor Jeffery W. Kelly's laboratory, Department of Chemistry, The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA.

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