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Chemistry
Letters

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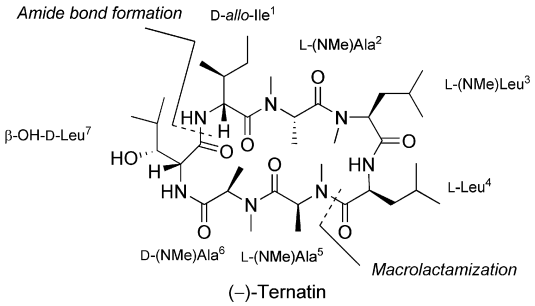
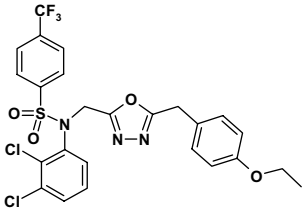
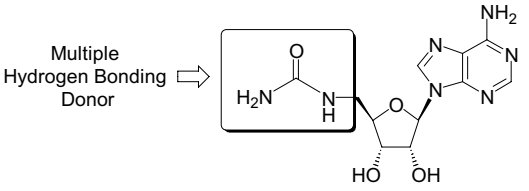
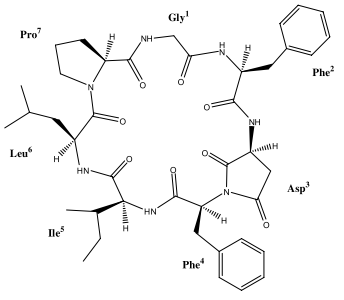
Contents

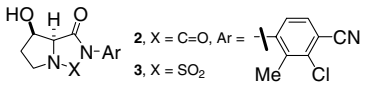
ARTICLES



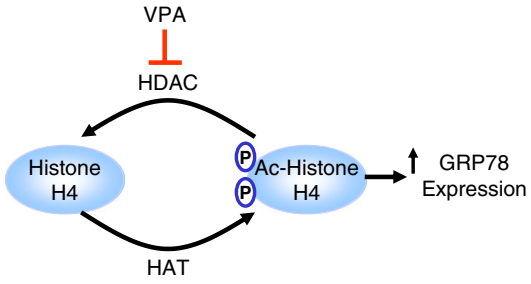




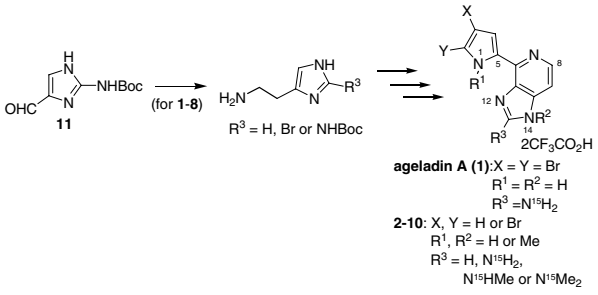


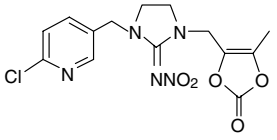


Herein, we report the effects of replacing the 3-oxo group of **2** with a sulfonyl group (e.g., **3**). These tetrahydropyrrolo[1,2-*b*][1,2,5]thiadiazol-2(3*H*)-one 1,1-dioxide analogues were found to be potent SARMs. Synthesis, binding and functional assay SAR, as well as in vivo characterization of a selected analogue in a standard rodent model are presented.

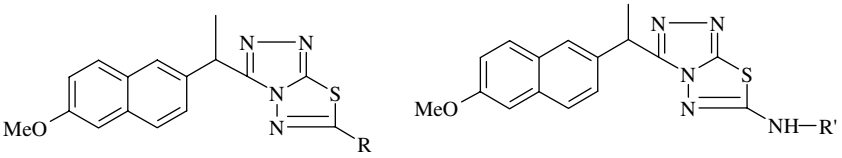


MMP-12 inhibitory activity assay clearly disclosed that the two bromine atoms and the three NH groups (1-NH, 14-NH and 15-NH_2) were indispensable for **1** to exhibit excellent activity.



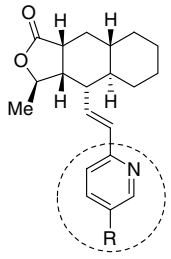


Preparation and biological behavior of prodrugs of imidacloprid is reported.

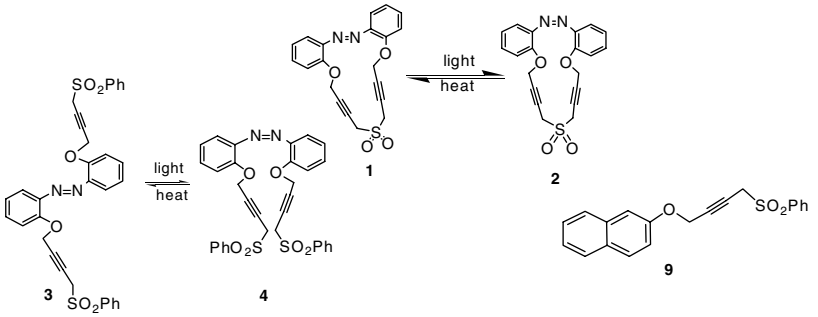


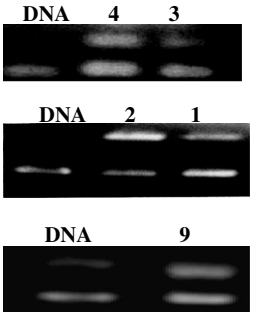
Some 6-substituted-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazole derivatives (**4a**–**f** and **5a**–**d**) have been synthesized by cyclisation of 4-amino-5-[1-(6-methoxy-2-naphthyl)ethyl]-3-mercapto-(4*H*)-1,2,4-triazole (**3**) with various substituted aromatic acids and aryl/alkyl isothiocyanates, through a single step reaction. The target compounds were pharmacologically evaluated for their anti-inflammatory and analgesic potentials by known experimental models.

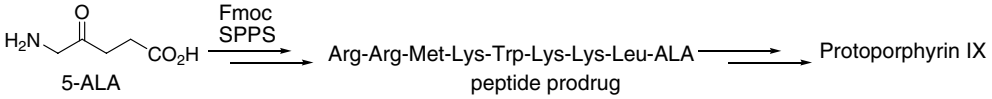
The SAR of the pyridine ring of himbacine derived thrombin receptor (PAR-1) antagonists is described.

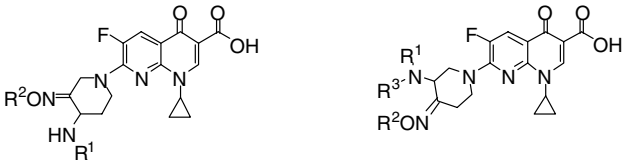


Pyridine-Ring SAR:
PAR-1 IC_{50}: 11 to >1000 nM



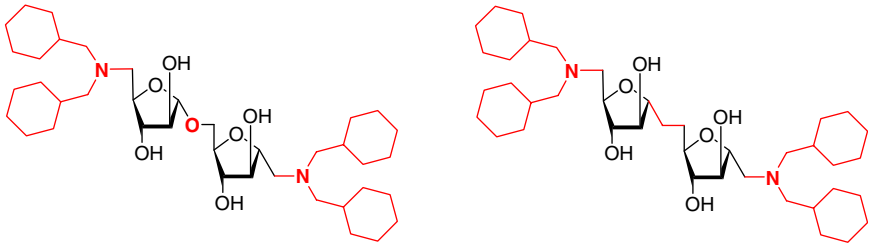


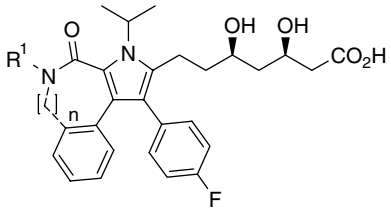




The design, synthesis, and antibacterial activity of new fluoroquinolones possessing substituted piperidine rings at the C-7 position are described.

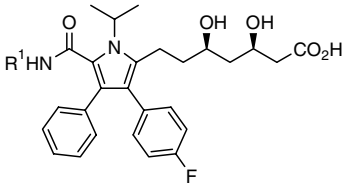
Syntheses of symmetrical C-linked and pseudo-symmetrical O-linked disaccharides structurally related to Ara*f* motifs present in the cell wall of MTB and their arabinosyltransferase activity and in vitro inhibitory activity versus MTB $H_{37}Ra$ and *Mycobacterium avium* are reported.

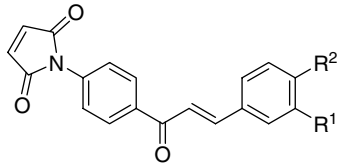




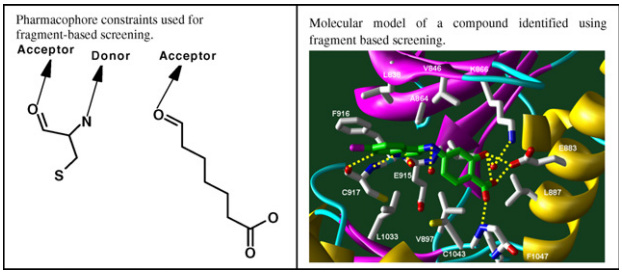
Using structure-based design, a novel series of conformationally restricted, pyrrole-based inhibitors of HMG-CoA reductase inhibitors were discovered.

This manuscript describes the design and synthesis of a series of *N-iso*-propyl pyrrole-based inhibitors of HMG-CoA reductase for the treatment of hypercholesterolemia.

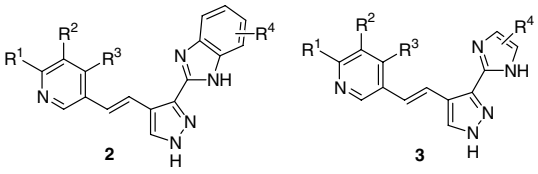


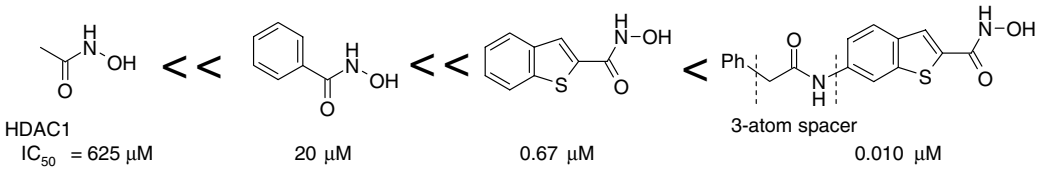


A series of 4′-aminochalcone-based maleimides were identified as novel cytostatic agents against three representative cancer cell lines. Representative compounds were well tolerated by mice in in vivo survival and toxicity studies.

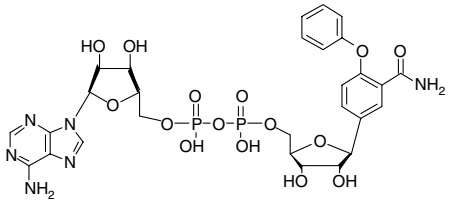


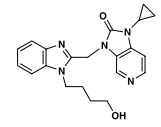
Two series of 3,4-disubstituted pyrazole analogues, 3-(imidazol-2-yl)-4-[2-(pyridin-3-yl)-vinyl]-pyrazoles (**2**) and 3-(benzimidazol-2-yl)-4-[2-(pyridin-3-yl)-vinyl]-pyrazoles (**3**), were synthesized as novel cyclin-dependent kinase (CDK) inhibitors. Representative compounds showed potent and selective CDK inhibitory activities and inhibited in vitro cellular proliferation in various human tumor cells. The design, synthesis, and preliminary biological evaluation of these pyrazole compounds are reported.





Benzo[*b*]thienyl hydroxamic acids were identified via a targeted screen of small molecule hydroxamic acids. Various substitutions were explored in the benzo[*b*]thiophene C5- and C6-positions which lead to a consistent finding that a three-atom spacer in the C6-position yielded optimal HDAC1 inhibition and anti-proliferative activity.





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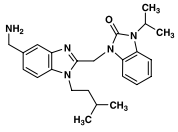

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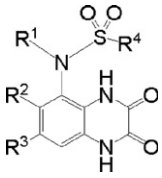
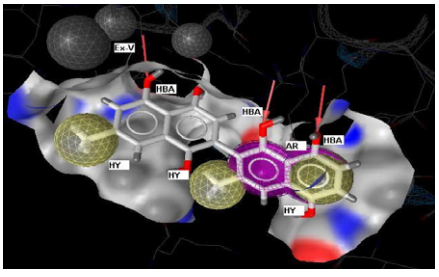
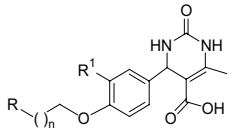
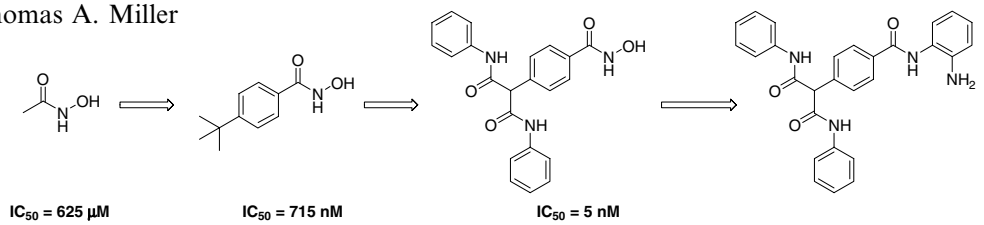
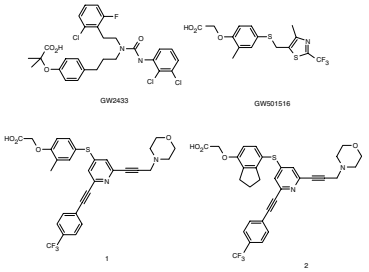




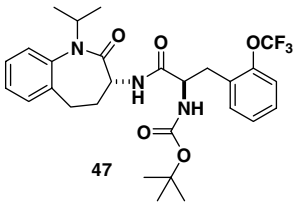


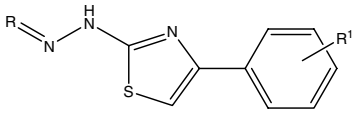


2-(4-{[(2-Aminophenyl)amino]carbonyl}phenyl)-*N*,*N*′-diphenylmalonamide containing excellent HDAC and cellular proliferation inhibitory activities was identified as a novel benzamide-derived HDAC inhibitor through iterative design starting from acetohydroxamic acid.

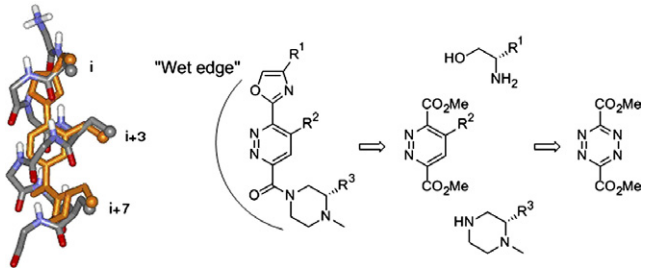


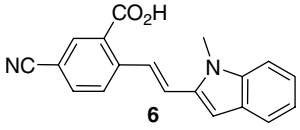
A series of benzodiazepines and benzazepinones were synthesized and evaluated as potential sodium channel blockers in a functional, membrane potential-based assay. One member of the benzazepinone series, compound **47**, displayed potent, state-dependent block of $hNa_v1.7$, and was orally efficacious in a rat model of neuropathic pain.





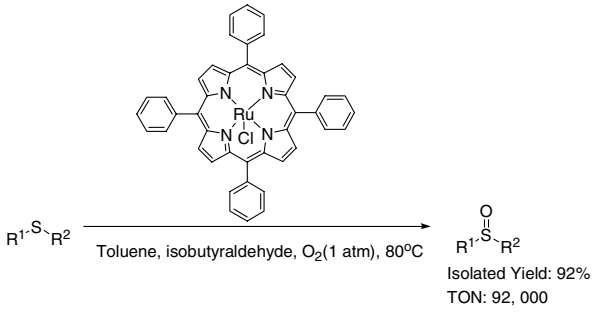
A novel series of 2-thiazolylhydrazone derivatives were prepared and evaluated for their in vitro activities against 22 clinical isolates of *Candida* spp., representing six different species, compared to clotrimazole as a reference compound.

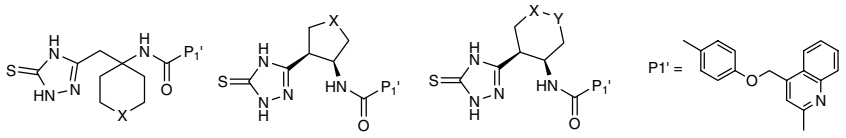




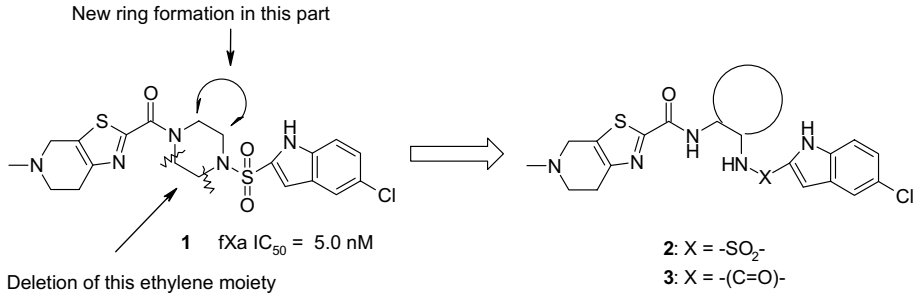
6

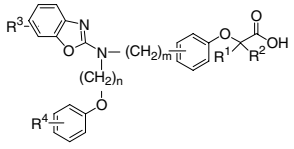
This paper describes the discovery of a novel fluorescent probe **6** and its utility in measuring compounds, affinity for human serum albumin (HSA).



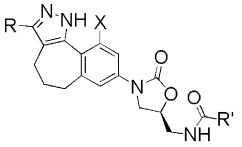


A novel series of TNF-α converting enzyme (TACE) inhibitors which are non-hydroxamate have been discovered. These compounds use a triazolethione moiety as the zinc binding ligand and exhibit IC_{50} values from 1.5 to 100 nM in a porcine TACE assay. They also have excellent selectivities over other MMPs.

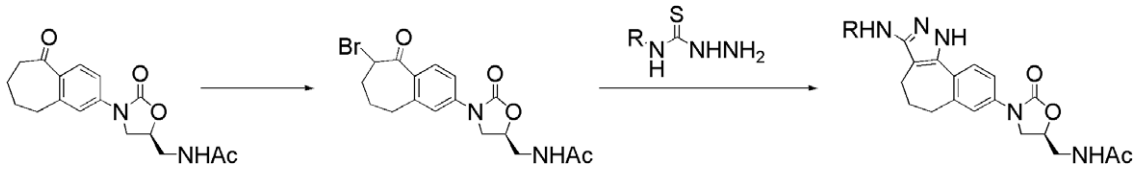


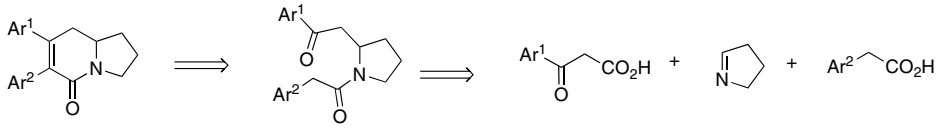


A combination of benzoxazole, phenoxyalkyl side chain and phenoxybutyric acids was identified as highly potent and selective h-PPARα agonists. The synthesis, SAR studies and in vivo activities of the representative compounds are described.

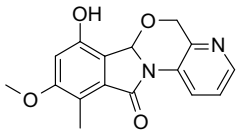


A novel series of conformationally-restricted oxazolidinones were synthesized which possess a fused pyrazole ring substituted with various alkyl, aryl and heteroaryl substituents





A 6,7-diaryl-2,3,8,8*a*-tetrahydroindolizin-5(1*H*)-one library was constructed and assayed for cytotoxicity toward the HCT-116 colon cancer cell line. Micromolar and sub-micromolar potencies were observed. One of the compounds displayed promising activity in the NCI's mouse hollow fiber assay.



22f

Starting from 2-(anilinomethyl)-phenols **3** we report herein the design and synthesis of a series of novel 2,3-dihydroisoindol-1-ones structurally related to cyclothialidine **2** with DNA gyrase inhibitory activity. In this series, some compounds exhibited promising antibacterial activity.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Typical snapshot of **7b** bound to HIV-RT from an MC simulation. Carbon atoms of **7b** are gold; from the left, Tyr181, Tyr188, Phe227, Leu100, Lys101; Trp229 at the top, Val106 at the bottom. H-bond with Lys101 O on right. Some residues in front including Glu138 have been removed for clarity. The water on N5 is also H-bonded to a carboxylate O of Glu138. [Thakur, V. T.; Kim, J. T.; Hamilton, A. D.; Bailey, C. M.; Domaoal, R. A.; Wang, L.; Anderson, K. S.; Jorgensen, W. L. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5664.]

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