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Bioorganic & Medicinal Chemistry Letters

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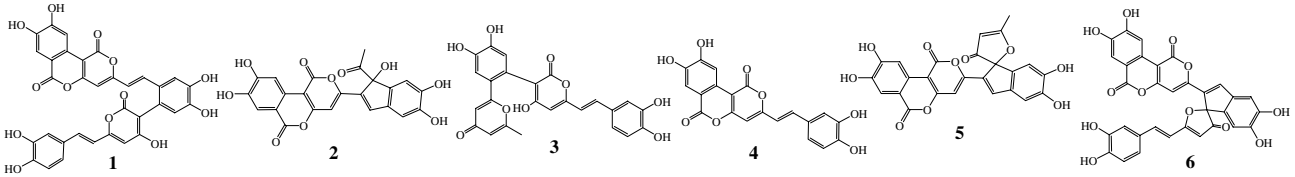
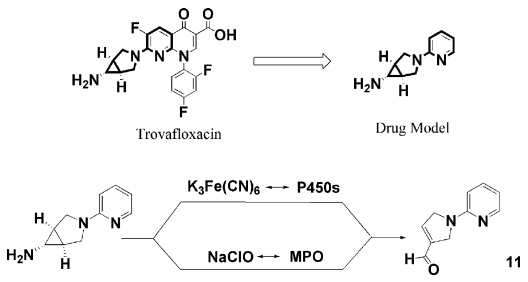
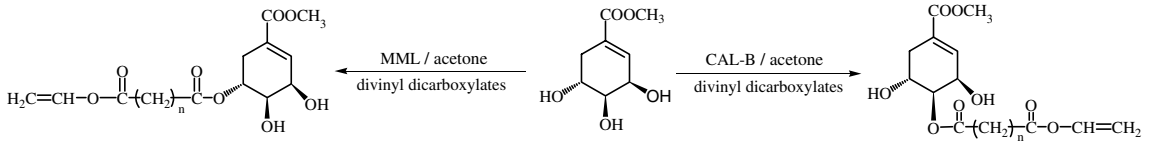
Contents

ARTICLES

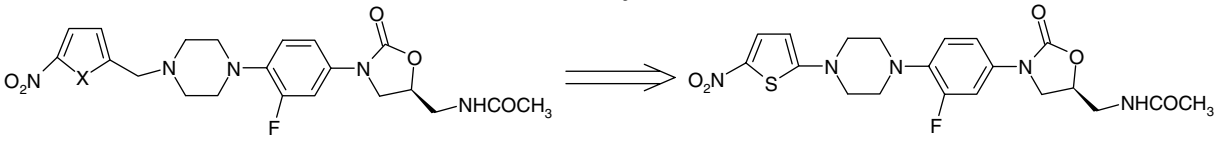


Three new free radical scavengers, inonoblins A (**1**), B (**2**), and C (**3**), were isolated from the methanolic extract of the fruiting body of the medicinal mushroom *Inonotus obliquus*, along with the known compounds phelligridins D (**4**), E (**5**), and G (**6**). Their structures were established by extensive spectroscopic analyses. These compounds exhibited significant scavenging activity against the ABTS radical cation and DPPH radicals, and showed moderate activity against the superoxide radical anion.





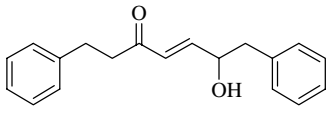
Regiocontrollable selectivity of enzymatic method for synthesis of polymerizable derivatives of methyl shikimate was described. The obtained derivatives would be useful as important monomers for potential analogues of shikimic acid.



1: X = O (HCl salt), RBx 7644 (Ranbezolid)
2: X = S

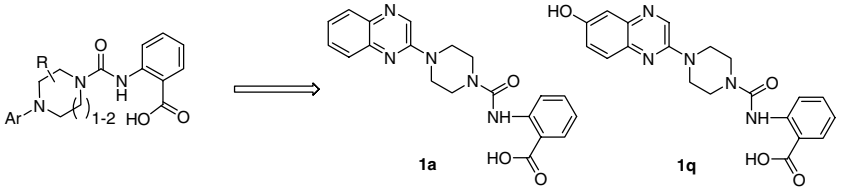
6b: RBx 8700

The potent broad spectrum oxazolidinone antibacterial agent RBx 8700 (**6b**) was obtained by systematic modification of the methylene linker of RBx 7644 (Ranbezolid, **1**) and its thienyl analogue **2**.



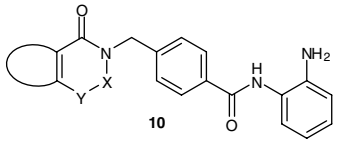
1 IC_{50} = 1.3 μM

Two new compounds 6-hydroxy-1,7-diphenyl-4-en-3-heptanone (**1**) and 6-(2-hydroxy-phenyl)-4-methoxy-2-pyrone (**4**) along with three known compounds were isolated from the extracts of *Alpinia officinarum* under bioassay-guided purification. The isolated diarylheptanoids exhibited potent PAF receptor binding inhibitory activities.



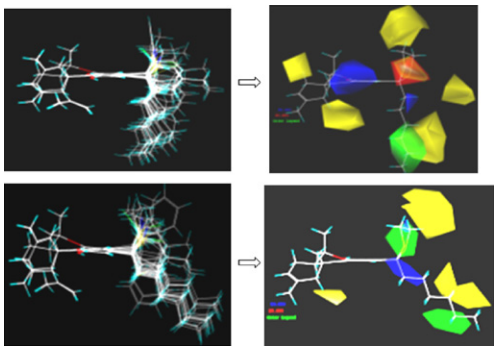
1a **1q**

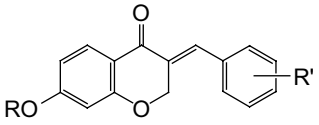
A urea class of high affinity niacin receptor agonists was discovered. Compound **1a** displayed good PK, better in vivo efficacy in reducing FFA in mouse than niacin, and no vasodilation in a mouse model. Compound **1q** also demonstrated equal affinity to GPR109A as niacin.



10

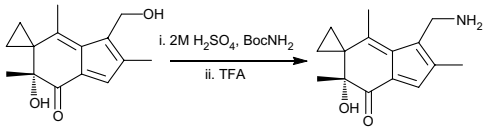
A variety of *N*-(2-amino-phenyl)-4-(heteroarylmethyl)-benzamides of general structure **10** were designed, synthesized, and evaluated as histone deacetylase (HDAC) inhibitors.

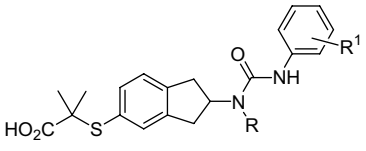




R= Me; Et; *n*-Pr; *n*-Bu
R'= 4-OH; 3,4-$(OH)_2$; 2-MeO;
3-MeO; 4-MeO; 4-OH-3,5-$(OMe)_2$

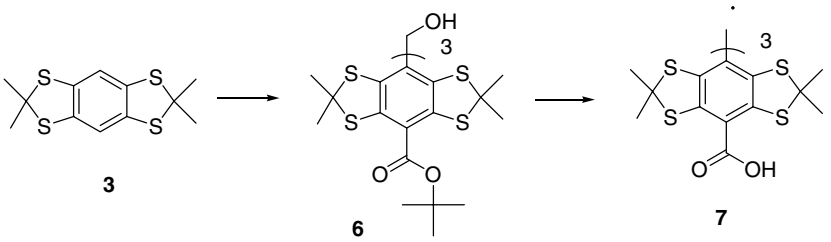
A series of substituted 3-benzylidene-7-alkoxychroman-4-ones were synthesized and evaluated for their antioxidant activities. 3-benzylidene-7-alkoxychroman-4-one derivatives bearing catecholic group on benzylidene moiety exhibited excellent antioxidant activity.



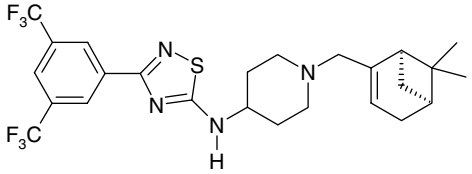


1

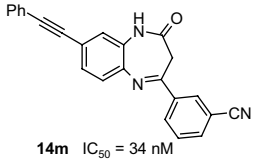
The synthesis and SAR of novel, highly potent PPARα agonists based on an indane scaffold are reported.



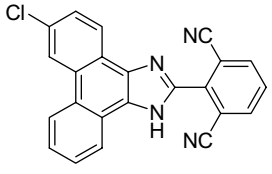
Tetrathiatriarylmethyl radicals are ideal spin probes for biological electron paramagnetic resonance spectroscopy and imaging. We report the large-scale synthesis of the radical **7** using an improved procedure and its characterization.



Development of a lead series of piperidinylurea CXCR3 antagonists has led to the identification of molecules with alternative linkages, which retain good potency. A piperidinyl thiadiazole derivative was found to have satisfactory in vitro metabolic stability and to be orally bioavailable in mice, giving high plasma concentrations and a half life of 5.4 h.

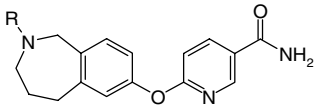


A series of 1,3-dihydro-benzo[*b*][1,4]diazepin-2-one derivatives was evaluated as non-competitive mGluR2/3 antagonists. Attachment of an 8-(2-aryl)-ethynyl-moiety produced compounds inhibiting the binding of [^{3}H]-LY354740 to rat mGluR2 with low nanomolar affinity and consistent functional effect at both mGluR2 and mGluR3.

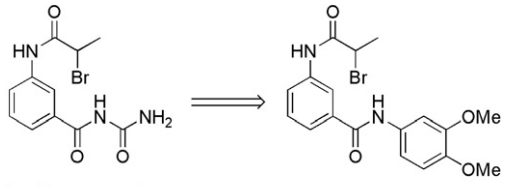


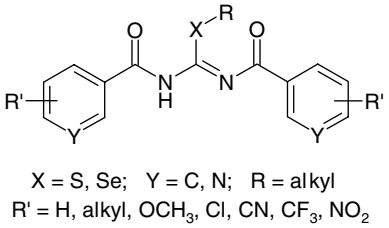
3 (MF63)

Phenanthrene imidazole **3** has been identified as a novel potent, selective, and orally active mPGES-1 inhibitor.



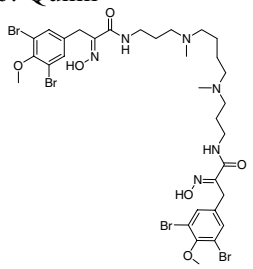
A series of 6-bicycloaryloxynicotinamides were identified as opioid receptor antagonists at mu, kappa and delta receptors. Compounds in the 6-(2,3,4,5-tetrahydro-1*H*-benzo[*c*]azepin-7-yloxy)nicotinamide scaffold exhibited potent in vitro functional antagonism at all three receptors.

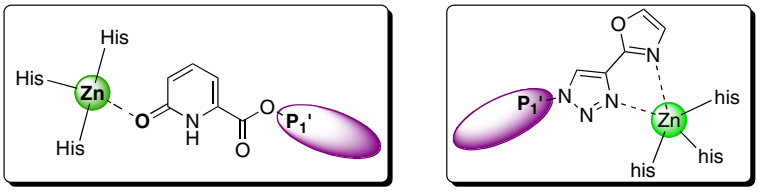




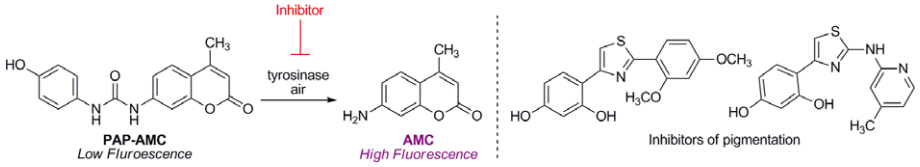
Significant in vitro antiproliferative activity against human prostate cancer cell (PC-3) of novel symmetrical imidoselenocarbamates is showed.

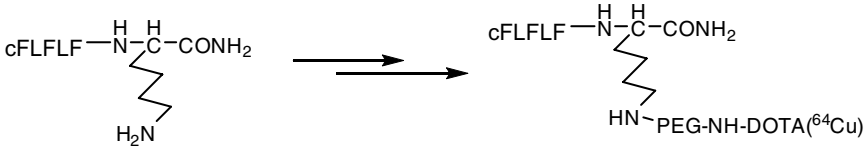
The Australian marine sponge, *Pseudoceratina* sp. yielded spermatinamine, a novel alkaloid with a bromotyrosyl-spermine-bromotyrosyl sequence, as the bioactive constituent. Spermatinamine is the first natural product inhibitor of Icmt.

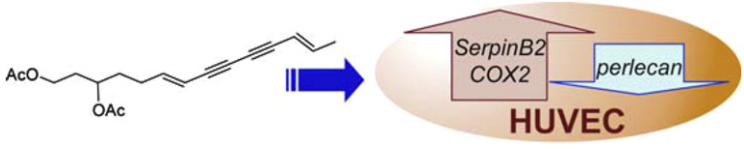

Spermatinamine



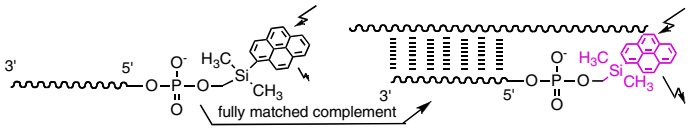
A variety of novel heterocyclic compounds were synthesized and evaluated for MMP inhibition. Broad spectrum inhibition of MMPs 1, 2, 9, and 12 was found with pyridinone-based compounds while *N*-heterocyclic triazoles and tetrazoles were largely ineffective. A highly selective tetrazole inhibitor for MMP-2 was discovered.



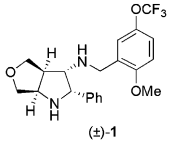


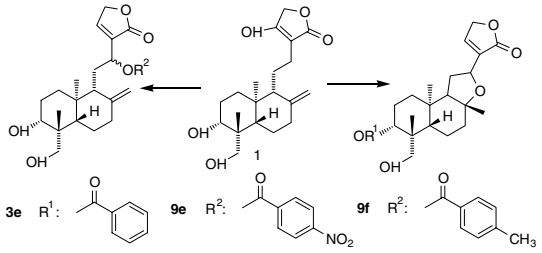


New activities were found from old medicine through a screening based on DNA microarray and real-time PCR.



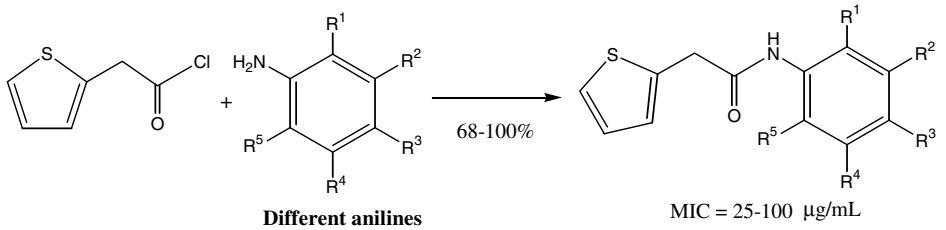
Novel fluorescent oligoDNA exhibited marked fluorescent signal upon binding to the fully matched complementary DNA strand.





Andrographolide and its derivatives were evaluated in the ELISA for the inhibitory potency in the secretion of TNF-α and IL-6 of LPS-stimulated mouse macrophages. The derivatives **3e**, **9e**, **9f** have better inhibitory effect than andrographolide.

The present article describes a series of 21 *N*-(aryl)-2-thiophen-2-ylacetamides, which were synthesized and evaluated for their in vitro antibacterial activity against *Mycobacterium tuberculosis*.



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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