Bioorganic & Medicinal Chemistry Letters 19 (2009) 6819–6829

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

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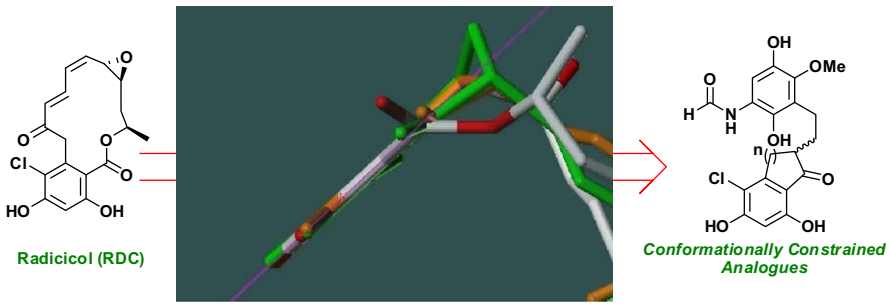
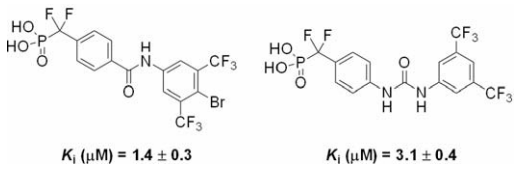
Bioorganic & Medicinal Chemistry Letters Volume 19, Issue 24, 2009

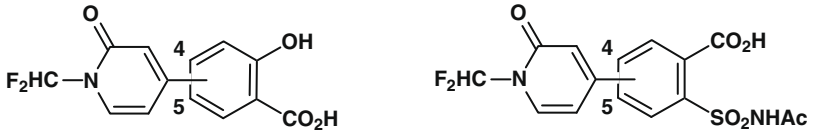
Contents

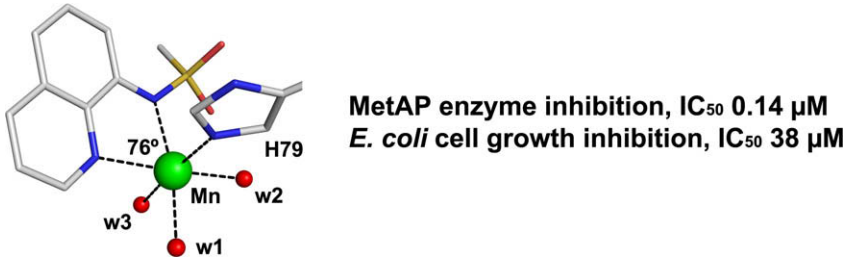
ARTICLES

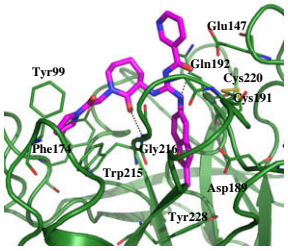


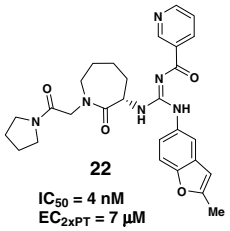


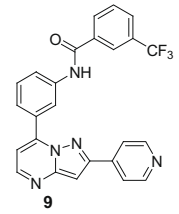
The development of low μM inhibitors of the *Mycobacterium tuberculosis* phosphatase PtpA is reported.



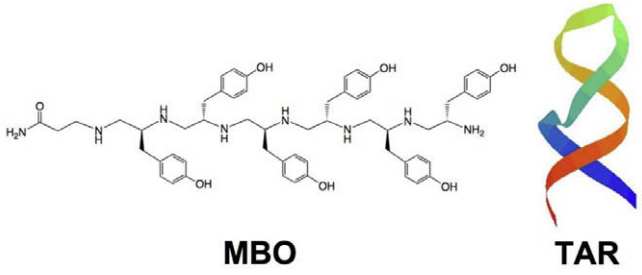


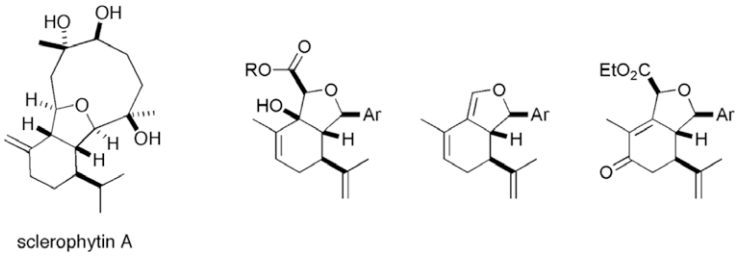




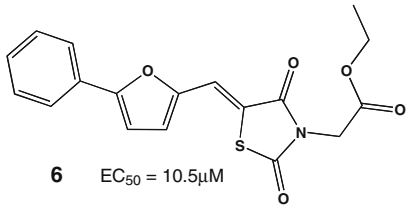


Structure guided design was utilized to optimize the pyrazolo[1,5-*a*]pyrimidine scaffold by introducing kinase hinge region interacting groups in the 2-position. This strategy led to the identification of lead compound **9** with enhanced enzyme and cellular potency, while maintaining good selectivity over a number of kinases.

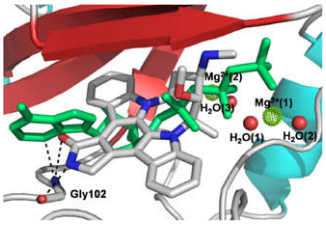




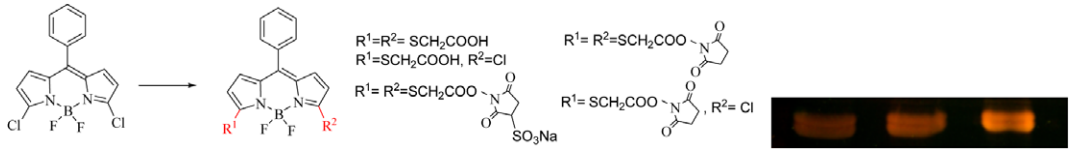
Seco analogs of sclerophytin A prepared in three or four steps exhibit sub-micromolar growth inhibitory activity against the RPMI-8226 leukemia and HOP-92 non-small cell lung cancer cell lines.

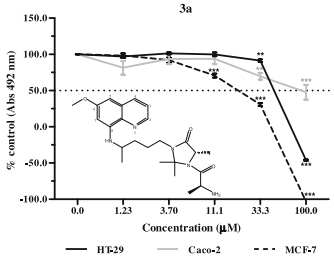


Novel allosteric agonists of integrin CD11b/CD18 were identified. Initial SAR exploration and structural model of binding site are presented.

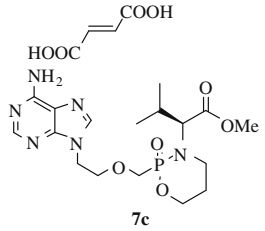


This work describes the structural basis of the IKKβ inhibition by staurosporine and quercetin in ATP binding site.



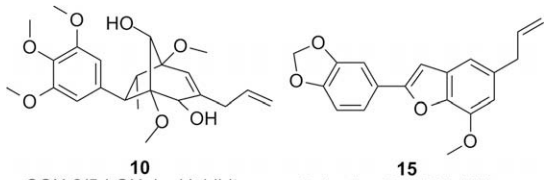


The anti-proliferative activity of primaquine, and related quinolinic antimalarials, against three human tumoral cell lines is reported.



7c

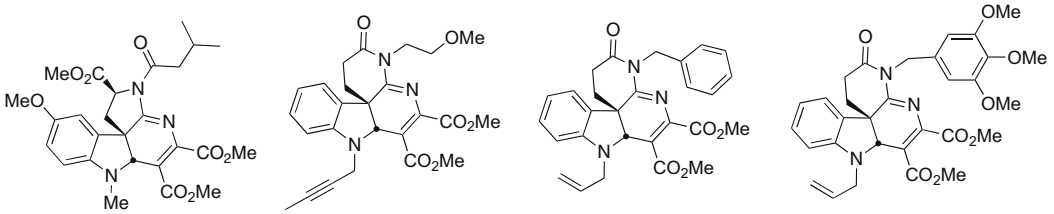
A series of novel oxazaphosphorine prodrugs of PMEA is disclosed. L-valine methyl ester (**7c**) demonstrated highly potent anti-HBV activity, excellent stability in human plasma and release of the parent compound PMEA in human microsomes.



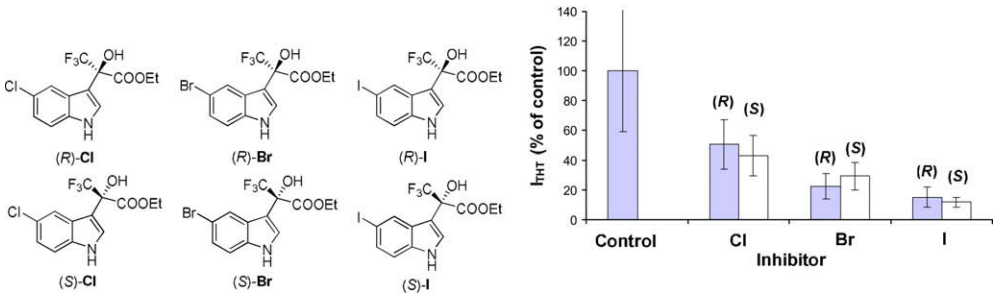
10 COX-2/5-LOX dual inhibitor

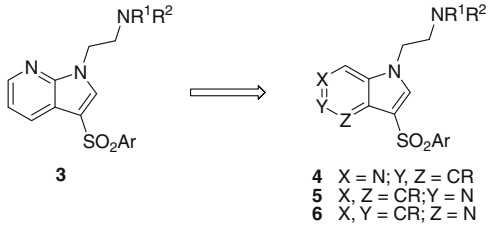
15 Selective COX-2 inhibitor

Inhibition of COX-1, COX-2, 5-LOX and agonist-induced platelet aggregation for 26 neolignans is reported.

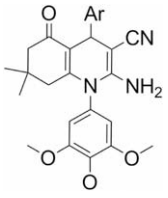


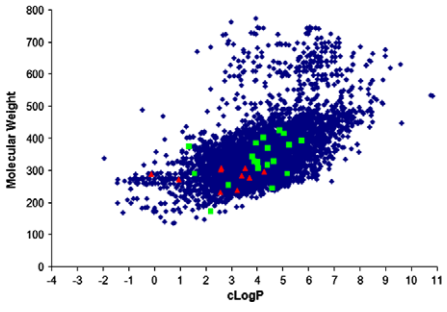
IC_{50} 5.7 μM IC_{50} 2.0 μM IC_{50} 1.4 μM IC_{50} 2.0 μM

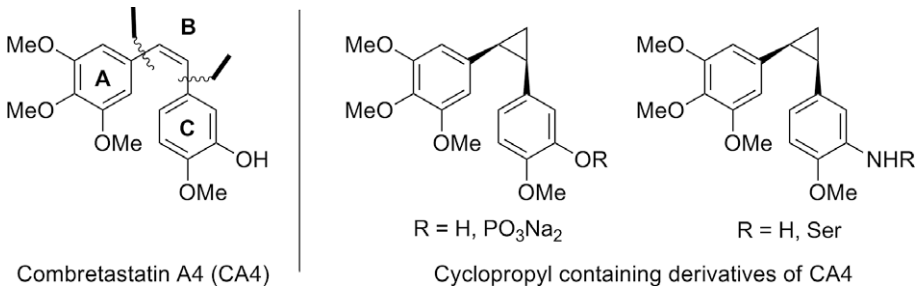


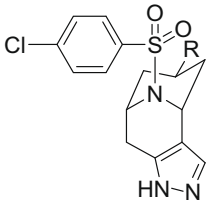


Pyrrolopyridines **4**, **5**, and **6** have been prepared and tested as 5-HT$_6$ ligands.



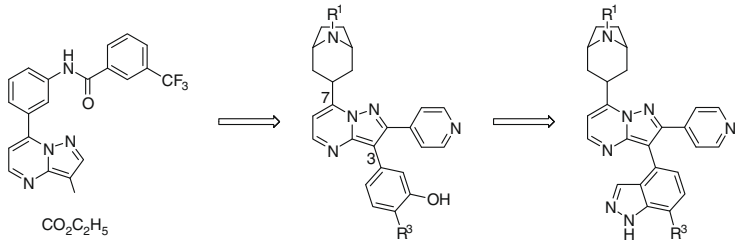


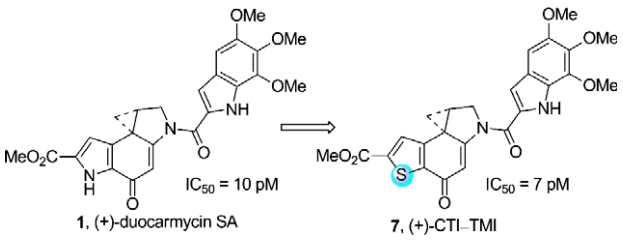


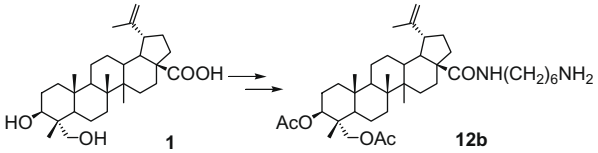


The structural modification of a series of [3.3.1] bicyclic sulfonamide based γ-secretase inhibitors is described. Appropriate substitution on the bicyclic scaffold provides a significant increase in the metabolic stability of the compounds resulting in an improved in vivo metabolic profile.

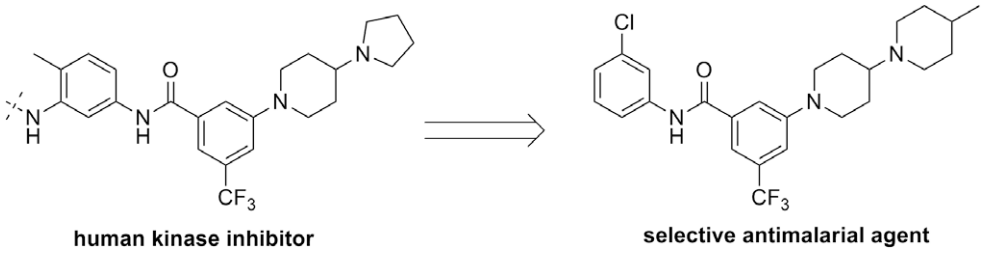
A novel series of pyrazolo[1,5-*a*]pyrimidines bearing a 3-hydroxyphenyl group at C(3) and substituted tropanes at C(7) have been identified as potent B-Raf inhibitors. Exploration of alternative functional groups as a replacement for the C(3) phenol demonstrated indazole to be an effective isostere. Several compounds possessing substituted indazole residues, such as **4e**, **4p**, and **4r**, potently inhibited cell proliferation at submicromolar concentrations in the A375 and WM266 cell lines, and the latter two compounds also exhibited good therapeutic indices in cells.

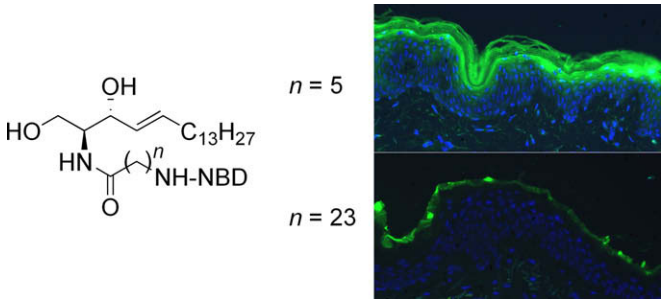


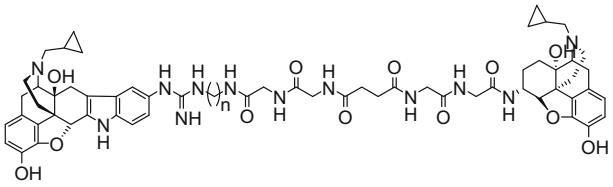




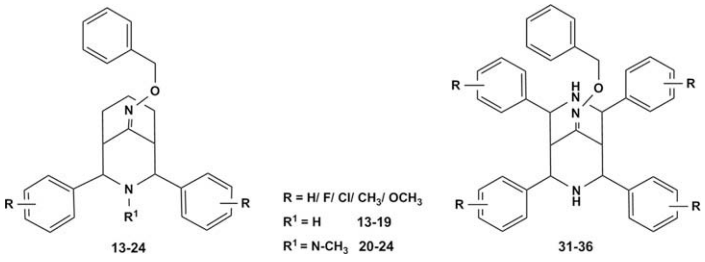
A series of 23-hydroxybetulinic acid derivatives were prepared and evaluated as a new class of inhibitors of glycogen phosphorylase (GP), among which **12b** was the most potent GPa inhibitor (IC_{50} = 3.5 μM).



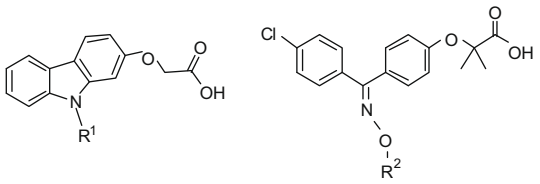




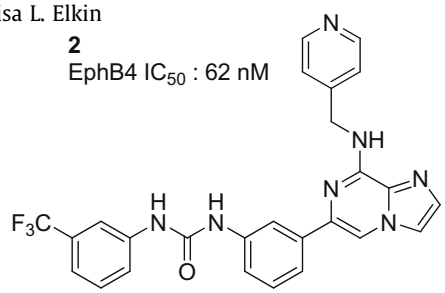
A series of bivalent ligands containing κ- and μ-antagonist pharmacophores were designed and reported as chemical tools for studying κ–μ heterodimers.



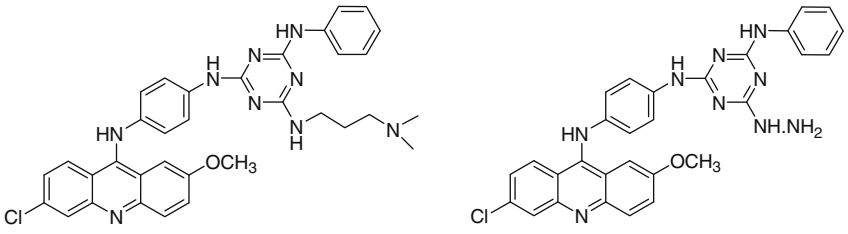
Two series of heterobicyclic oxime ethers viz, 3-ABN-9-one and 3,7-DABN-9-one *O*-benzyloximes were synthesized and stereochemistry was established by their spectral and crystal studies. All the synthesized oxime ethers were screened against a set of pathogenic bacteria and fungi. From the results, structure–activity relationship was discussed.



The synthesis and activity data of N-substituted carbazole- and O-substituted fenofibrate-derived γ-secretase modulators are presented. Out of 19 screened compounds, seven exhibited promising activity against $A\beta_{42}$ secretion at a low micromolar level. We suggest that the γ-secretase modulators interact with lys624 at the membrane interface and that the lipophilic substituent anchors the compound in the membrane.

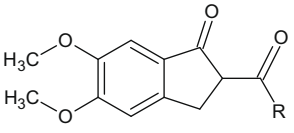


The identification of imidazo[1,2-*a*]pyrazine diarylureas as potent inhibitors of the receptor tyrosine kinaseEphB4 is reported.



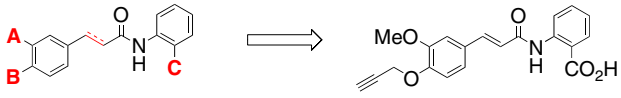
13, IC_{50} = 4.21nM **22**, IC_{50} = 4.27nM

A series of new class of hybrid 9-anilinoacridine triazines were synthesized and screened in vitro for their antimalarial activity against CQ-sensitive 3D7 strain of *Plasmodium falciparum*. The compounds **13** and **29** displayed >96.59% and 98.73% suppression, respectively, orally against N-67 strain of *Plasmodium yoelii* in swiss mice at dose 100 mg/kg for four days.

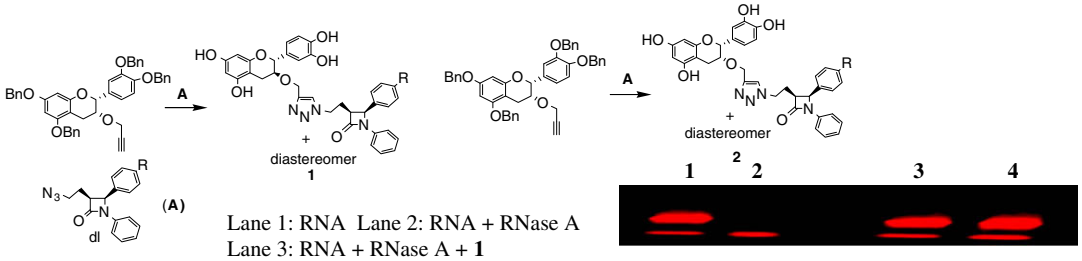


5_a-5_n

In present investigation, a series of substituted phenyl-5,6-dimethoxy-1-oxo-2,5-dihydro-1*H*-2-indenylmethanone analogues were synthesized and were evaluated for antimycobacterial activity against *Mycobacterium tuberculosis* H_{57}Rv and INH resistant *M. tuberculosis*. All the newly synthesized compounds were showing moderate to high inhibitory activities, with compound 5,6-dimethoxy-1-oxo-2,5-dihydro-1*H*-2-indenyl-4-fluorophenylmethanone (**5g**) produced was found to be the most promising compounds active against *M. tuberculosis* H_{57}Rv and isoniazid (INH) resistant *M. tuberculosis* with Minimum inhibitory concentration 0.10 and 0.10 μM.



A panel of cinnamoyl anthranilates were investigated for their antifibrotic activity through their ability to reduce collagen formation stimulated by the cytokine transforming growth factor-β. The most active compound was shown to reduce albuminuria in a hypertensive rat model of progressive type II diabetes.



Lane 1: RNA Lane 2: RNA + RNase A
Lane 3: RNA + RNase A + **1**
Lane 4: RNA + RNase A + **2**

*Corresponding author
Supplementary data available via ScienceDirect

COVER

MW versus cLogP for drugs (red), clinical candidates (green) and bioactive compounds (blue) for Cannabinoid receptor CNR1. [Tyrchan, C.; Blomberg, N.; Engkvist, O.; Kogej, T.; Muresan, S. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 6943.]

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ISSN 0960-894X