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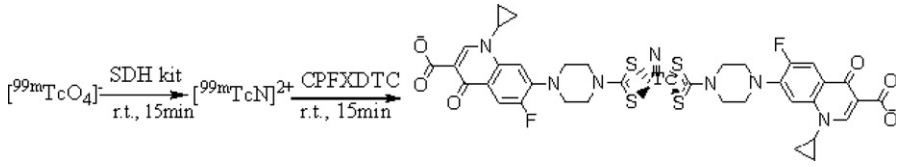
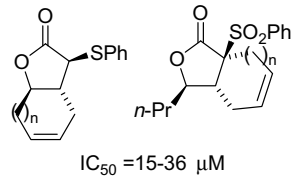
Contents

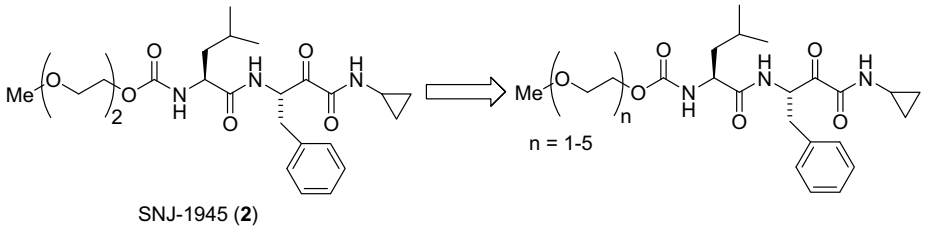
ARTICLES

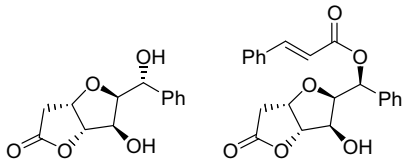


The ciprofloxacin dithiocarbamate (CPFXDTC) was synthesized and radiolabeled with $[^{99m}TcN]^{2+}$ to form ^{99m}TcN-CPFXDTC in high yield. The biodistribution results suggested ^{99m}TcN-CPFXDTC would be a novel potential infection imaging agent.



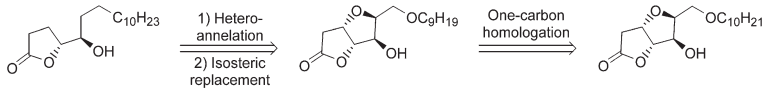
The synthesis and antiproliferative activity of γ-lactones α,β-fused and β,γ-fused to carbocycles are reported.





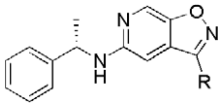
ent-**1** *ent*-**2**

The unnatural styryl lactones (−)-7-*epi*-goniofufurone (*ent*-**1**) and (−)-crassalactone C (*ent*-**2**) have been synthesized and evaluated for their in vitro antitumour activities against a number of human neoplastic cell lines.

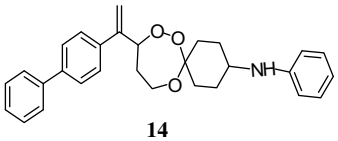


1 (IC_{50} 25.85 μM) **3** (IC_{50} 1.53 μM) **4** (IC_{50} 0.14 μM)

(−)-Muricatacin (**1**) and the related mimics **3** and **4** have been synthesized and evaluated for their in vitro antitumour activity.

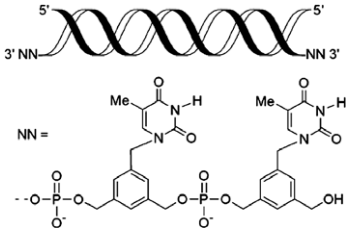


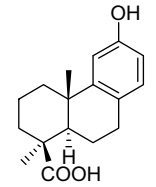
A series of 2-amino-isoxazolopyridine analogs was identified as inhibitors of Polo-like kinase (Plk). Co-crystal structures of inhibitors with Plk demonstrate key binding motifs. Differential selectivity among the three Plk isoforms is observed.



14

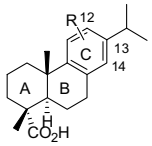
A series of new amino functionalized 1,2,4-trioxepanes **8–16** and ester functionalized 1,2,4-trioxepanes **17–19** have been synthesized and evaluated against multi-drug resistant *Plasmodium yoelii* in Swiss mice. Amino functionalized trioxepanes **14**, the most active compound of the series, showed 100% clearance of parasitaemia by oral route on day 4 and 75% protection to the treated mice beyond day 28.



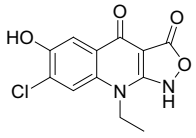


Podocarpic acid

We found that the podocarpic acid structure provides a new scaffold for chemical modulators of large-conductance calcium-activated K^+ channels (BK channels).

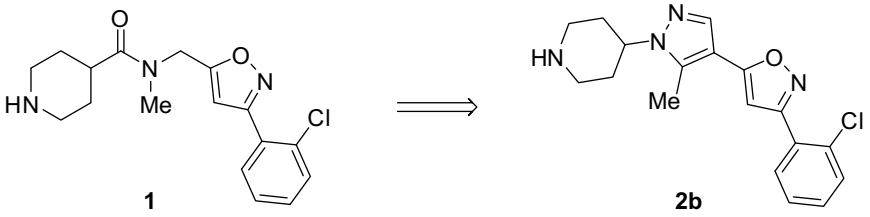


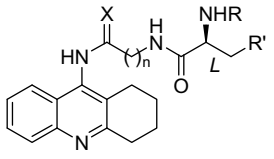
A series of dehydroabietic acid derivatives was synthesized and evaluated as BK channel openers in an assay system of CHO-K1 cells expressing hBKα channels.



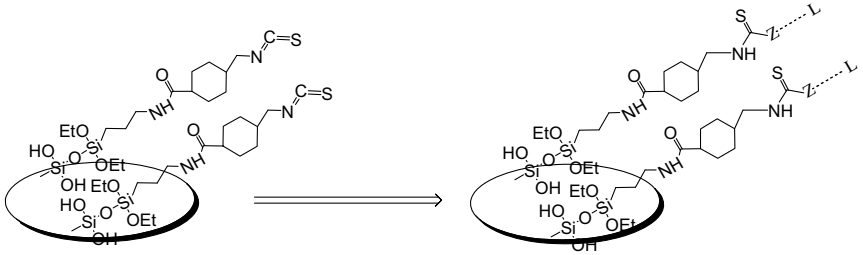
19

SAR studies guided by molecular modeling led to a potent inhibitor, **19**, against Pim-1 (K_i = 2.5 nM) and Pim-2 (K_i = 43.5 nM). The hydroxyl group is crucial for an H-bond interaction to the hinge region of the kinase active domain.

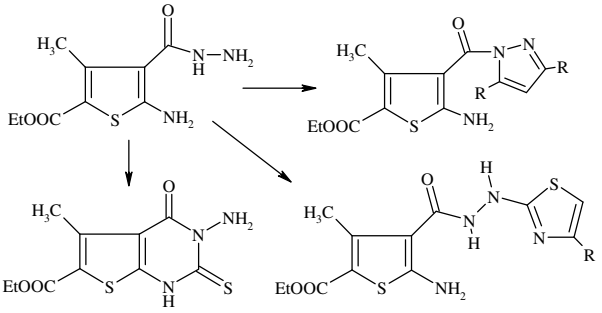




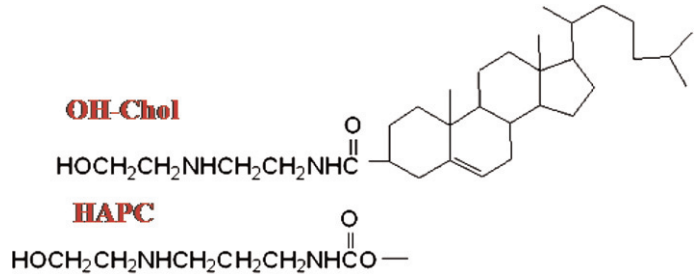
Synthesis and biological evaluation of tacrine based *h*ChEIs containing specific peptidic tethers is described.



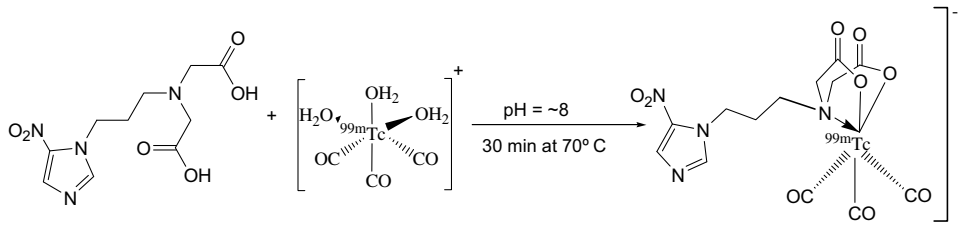
L = Ligands, peptides, oligonucleotides; Z = S, N.

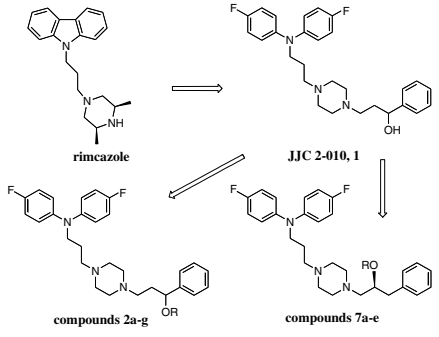


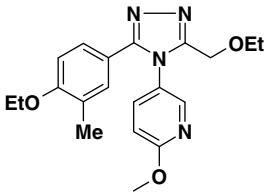
Two series of 5-ethyl-2-amino-3-pyrazolyl-4-methylthiophenecarboxylate and 2-thioxo-N^3-aminothieno[2,3-*d*]pyrimidines were prepared from 3,5-diethyl-2-amino-4-methylthio-phenecaboxylate and evaluated as anti-inflammatory, analgesic and ulcerogenic activities. Among the compounds studied, compounds which containing the substituted hydrazide at C-3 position **7**, **16**, and **17a** showed more potent anti-inflammatory and analgesic activities than the standard drug (Indomethacin and Aspirin), along without ulcerogenity. While compounds **2**, **5**, **9**, **10**, and **11c** showed moderate activities. Some of the newly synthesized compounds have good to excellent antimicrobial activity.



The structure of cationic derivatives of cholesterol.

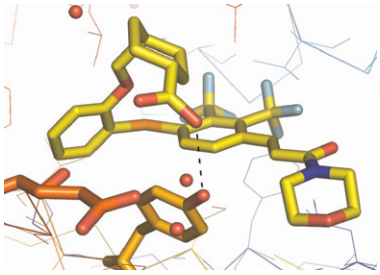






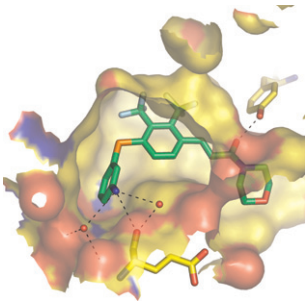
11

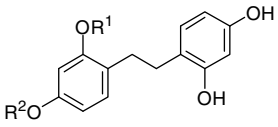
Several potent aryl ether/triazole oxytocin antagonists are described. The lead compound in this series, **11**, had significantly improved aqueous solubility over related systems containing a biaryl substituent.



X-ray co-crystal data assisted the design of LFA-1 ICAM inhibitors based on *ortho*- and *meta*-phenol templates, leading to a compound which exploited a new hydrogen bond to the I-domain and which exhibited subnanomolar potency in the LFA-1/ICAM1-Ig assay.

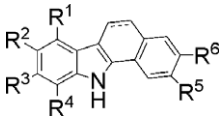
A series of *meta*-substituted anilines were designed and synthesized to inhibit the interaction of LFA-1 with ICAM for the treatment of autoimmune disease. Design of these molecules was performed by utilizing a co-crystal structure for structure-based drug design. The resulting molecules were found to be potent and to possess favorable pharmaceutical properties.



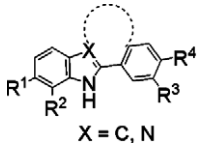


1: R^1 = Xyl, R^2 = H
2: R^1 = H, R^2 = Xyl
3: R^1 = R^2 = Xyl

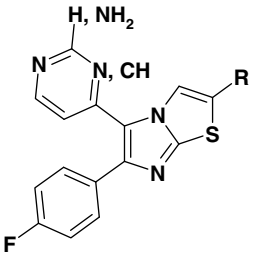
In order to develop water soluble tyrosinase inhibitors, bibenzyl xyloside **1** isolated from *Chlorophytum arundinaceum* (liliaceae), and its derivatives **2** and **3** were synthesized by using Wittig reaction and trichloroimidate glycosylation procedure as key steps. Xylosides **1**–**3** showed potent tyrosinase inhibitory activity with IC_{50}s of 1.6, 0.43, and 0.73 μM, respectively, although each NMR data of synthetic bibenzyls was not identical to that of naturally occurring xyloside **1**.



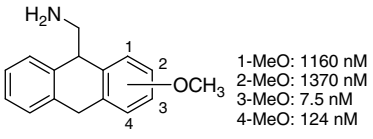
A novel series of benzo[*a*]carbazole-based small molecule agonists of the thrombopoietin (Tpo) receptor is reported. Members of this series have been identified which are full agonists with functional potency <50 nM and oral bioavailability in mice.



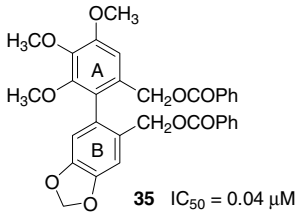
The lead optimization of a novel series of benzo[*a*]carbazole-based small molecule agonists of the thrombopoietin (Tpo) receptor is reported. Analog **21** demonstrates equivalent efficacy in the human megakaryocyte differentiation (CFU-mega) assay compared to Eltrombopag™.

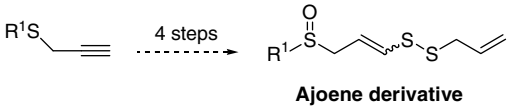


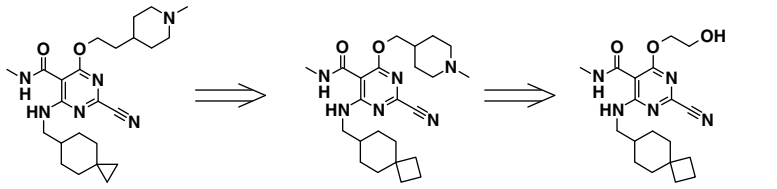
In this study, we present the synthesis and biological activity of 5,6-diarylimidazo[2,1-*b*][1,3]thiazoles, whose antiparasitic activity against *Eimeria* is due to inhibition of a parasite-specific cGMP-dependent protein kinase (PKG). From this series, several compounds showed subnanomolar in vitro activity and commercial levels of in vivo activity.

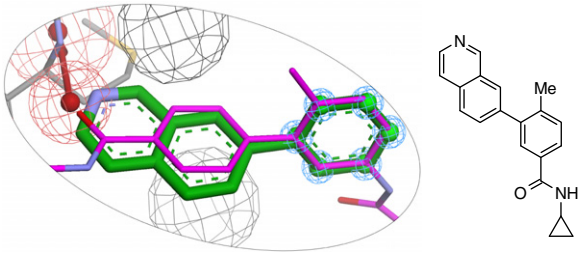


The synthesis and 5-HT_{2A} receptor affinities of a series of methoxy-substituted 9-aminomethyl-9,10-dihydroanthracene (AMDA) derivatives are reported. Molecular modeling techniques are used to elucidate probable binding modes for the compounds.



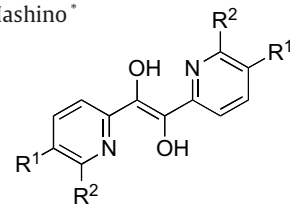




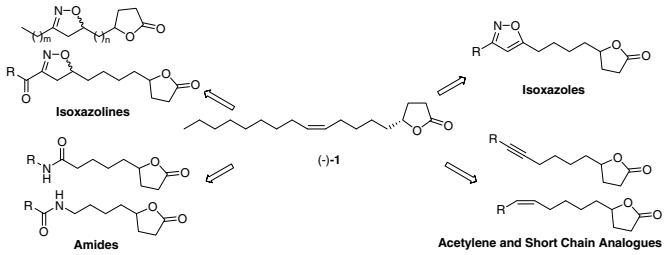


Most kinase-directed array strategies aim to add functionality to a fragment that binds in the purine subpocket of the ATP-site. Here, an alternative pharmacophore-guided array approach is described which set out to discover novel purine subpocket-binding groups. Results are shown for p38α and cFMS kinase, for which multiple different series with nanomolar potency were discovered.

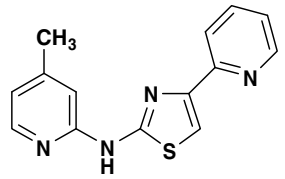
The protective effects of 2,2′-pyridoin derivatives against oxidative stress in the HL-60 cell were evaluated. The derivatives **1**–**3** and **5**–**6** inhibited H_2O_2-induced cell death and intracellular oxidative stress more than ascorbic acid.



1: $R^1 = H$, $R^2 = H$
2: $R^1 = H$, $R^2 = CH_3$
3: $R^1 = H$, $R^2 = OCH_3$
5: $R^1 = CH_3$, $R^2 = H$
6: $R^1 = OCH_3$, $R^2 = H$



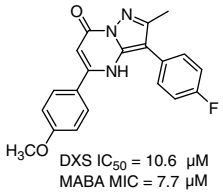
This paper describes a series of modifications of the side chain of micromolide, an anti-tuberculosis natural product. Most of the synthesized compounds showed significantly decreased activities, which suggests that the long aliphatic side chain of micromolide and its double bond are essential to its activity.



(13)

Compds	$K_{Ca}2.2$ Thallium Flux IC_{50} (μM)	$K_{Ca}2.3$ [^{125}I}-Apamin Displacement IC_{50}(μM)
13	0.059 (± 0.017)	0.004 (± 0.002)

An initial SAR study on a series of apamin-displacing 2-aminothiazole $K_{Ca}2$ channel blockers is described. Potent inhibitors such as *N*-(4-methylpyridin-2-yl)-4-(pyridin-2-yl)thiazol-2-amine (**13**) are disclosed.



2-Methyl-3-(4-fluorophenyl)-5-(4-methoxy-phenyl)-4H-pyrazolo[1,5-*a*]pyrimidin-7-one is identified to inhibit *Mycobacterium tuberculosis* DXS with an IC_{50} of 10.6 μM.

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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