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Special Section

David W. Robertson Memorial Issue

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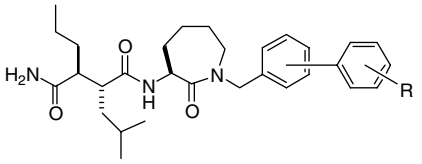
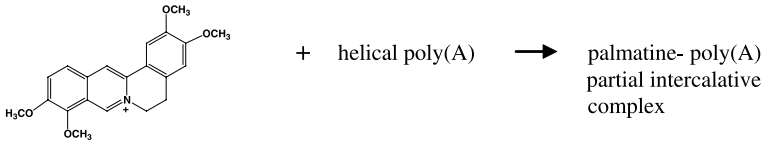
Contents

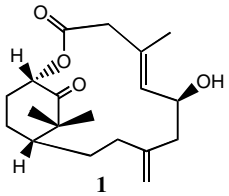


The synthesis, evaluation, and structure–activity relationships of a series of succinoyl lactam inhibitors of the Alzheimer's disease γ-secretase are described.

REGULAR COMMUNICATIONS



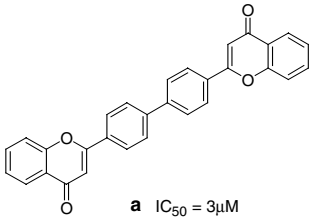
Palmatine, the plant alkaloid, binds strongly to single stranded (ss) poly(A) by mechanism of partial intercalation, leading to its usefulness in inhibition of gene expression in eukaryotic cells.

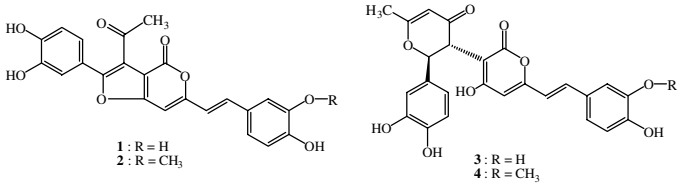


1

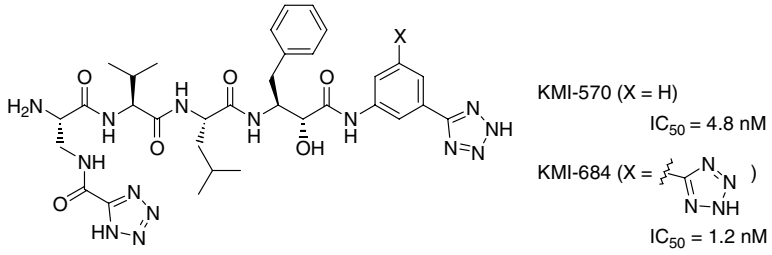
Two new diterpenoids, designated cespitulactones A (**1**) and B, were isolated from *Cespitularia taeniata* collected in Taiwan.

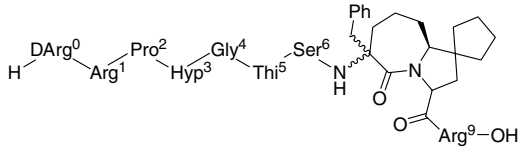
A series of C–C biflavones was designed to investigate the relationship between structural array of a different flavone–flavone subunit linkage and the inhibitory activity against phospholipase A_2 (PLA2). Among six classes of C–C biflavones designed, four classes of C–C biflavones, which have flavone–flavone subunit linkages at A ring–A ring, A ring–B ring, B ring–B ring, and B ring–C ring, were synthesized. The synthetic biflavones exhibited somewhat different inhibitory activities against $sPLA_2$-IIA. Among them, the biflavone **a** having a C–C 4′–4′ linkage showed comparable inhibitory activity with that of the natural biflavonoid, ochnaflavone, and 7-fold stronger activity than that of amentoflavone. Further chemical modification is being carried out in order to obtain the chemically optimized biflavonoids.



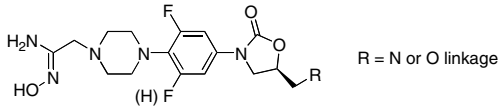


Three new free radical scavengers (**1**, **2**, and **4**) were isolated from the methanolic extract of the fruiting bodies of *Inonotus xeranticus* (Hymenochaetaceae), along with the known compound davallialactone (**3**). Their structures were established as hispidin analogs by extensive NMR spectral data. Compounds **3** and **4** displayed significant scavenging activity against the superoxide radical anion, ABTS radical cation, and DPPH radical, while **1** and **2** exhibited potent antioxidant effect only against ABTS radical cation.

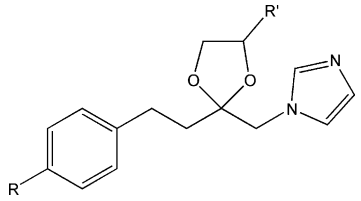




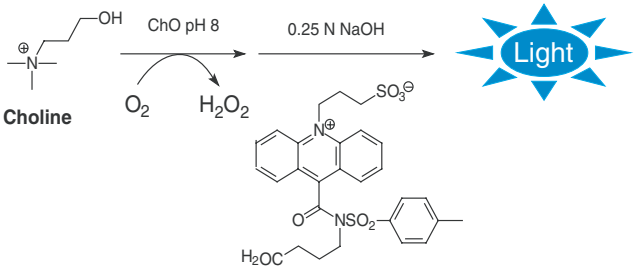
A structure–activity relationship study of Icatibant analogues modified with dipeptide mimetic β-turn inducers is reported.



The synthesis of oxazolidinones possessing *N*-hydroxyacetamidine group on piperazine scaffold and their in vitro antibacterial activity profile are disclosed herein.



A series of imidazole–dioxolane compounds were assayed for inhibitory activity in *Plasmodium falciparum* cultures.



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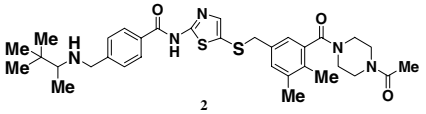
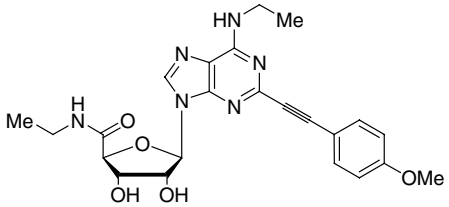


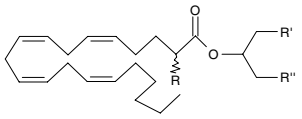
2
Itk IC_{50} = 96 nM
Jurkat IL-2 I_{50} = 700 nM

A series of structurally novel aminothiazole based small molecule inhibitors of Itk were prepared to elucidate their structure–activity relationships (SARs), selectivity, and cell activity in inhibiting IL-2 secretion in a Jurkat T-cell assay. Compound **2** is identified as a potent and selective Itk inhibitor which inhibits anti-TCR antibody induced IL-2 production in mice in vivo.

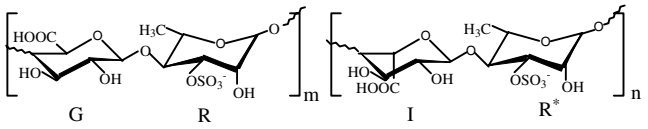


ZR1121

A new adenosine analogue ZR1121 is reported. Compared with currently widely used hA_3 agonists IB MECA and Cl-IB MECA, this compound has similar activity and about 100 times higher hA_3/hA_1 selectivity.



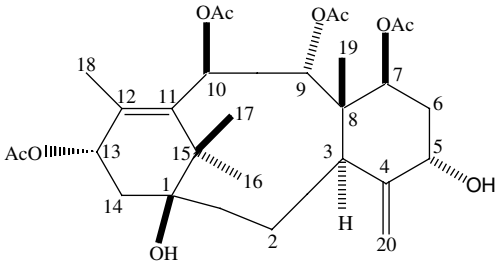
1a R=(R)-methyl, R'=R''=OH
1b R=(S)-methyl, R'=R''=OH
2a R=(R)-methyl, R'=OH, R''=F
2b R=(S)-methyl, R'=OH, R''=F
3a R=(R)-methyl, R'=R''=F
3b R=(S)-methyl, R'=R''=F



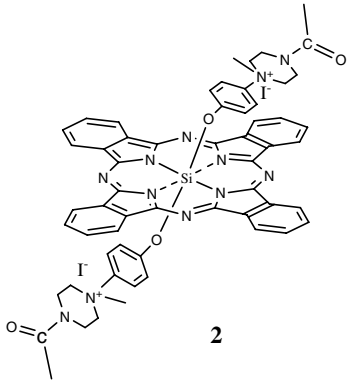
G R I R*

Acetylated and benzoylated ulvans were prepared and their in vitro antioxidant activities were determined.

From the needles of *Taxus wallichiana*, a taxoid was isolated, characterized and its cytotoxic and immunomodulatory activities were evaluated.



The new silicon (IV) phthalocyanine **2** was found to be essentially non-aggregated and strongly fluorescent in water. The compound and its non-covalent bovine serum albumin conjugate (**2**-BSA) exhibited extremely high photodynamic activities toward B16 melanoma cancer cell line with IC_{50} values down to 33 and 38 nM, respectively.



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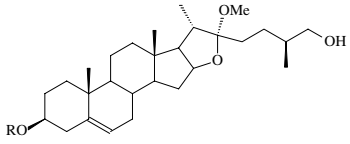
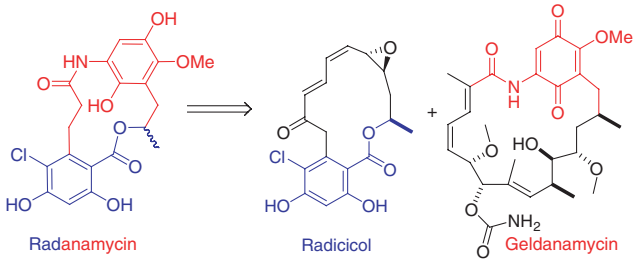
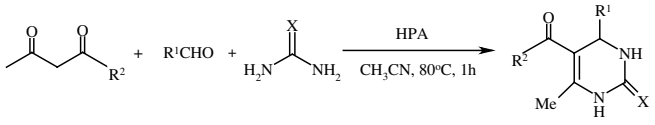


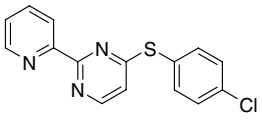
Icogenin: R = α-L-rhamnopyranosyl-(1 → 2)-[β-D-glucopyranosyl(1 → 3)]-β-D-glucopyranosyl (**1**). The designed analogue of icogenin: R = α-L-rhamnopyranosyl-(1 → 2)-[β-D-glucopyranosyl(1 → 3)]-α-D-glucopyranosyl (**2**).



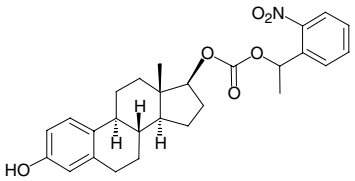
A chimera of radicicol and geldanamycin has been prepared and evaluated against MCF-7 breast cancer cells.

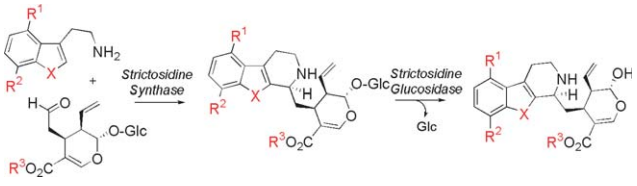


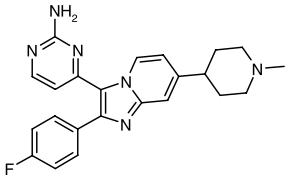
One-pot synthesis of dihydropyrimidones catalyzed by heteropoly acids as efficient, inexpensive, easily available and environmentally friendly catalysts. High to excellent yields, short reaction times and compatibility with various functional groups are features of this new procedure.



Structure–activity relationship investigation of thiopyrimidines as mGluR5 antagonists.







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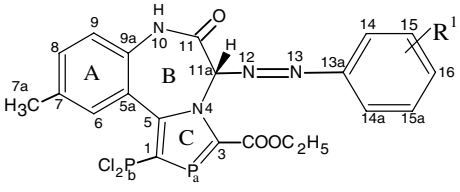
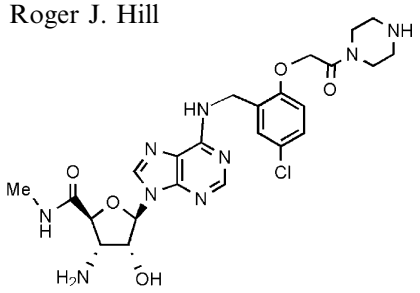
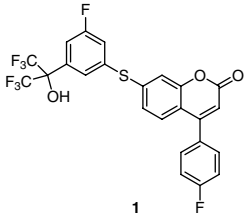
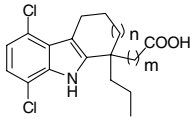
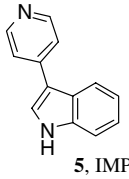




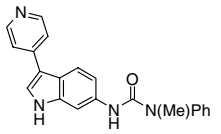


1





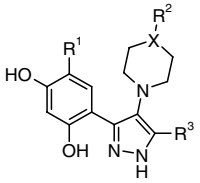
5, IMPDHII IC_{50} 1.15 μM

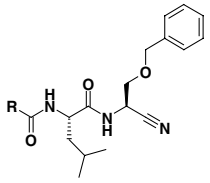


22, IMPDHII IC_{50} 84 nM

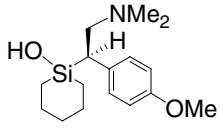
The elaboration of previously reported indole fragments as inhibitors of inosine monophosphate dehydrogenase (IMPDH) is described. The synthesis, in vitro inhibitory values for IMPDH II, PBMC proliferation and physicochemical properties are discussed.

Novel piperazinyl, morpholino and piperidyl derivatives of the pyrazole-based Hsp90 inhibitor CCT018159 have been prepared and the observed SAR explained by X-ray co-crystallography with Human Hsp90. The most potent of the new compounds has an IC_{50} of less than 600 nM against the enzyme and demonstrates low micromolar inhibition of tumour cell proliferation.





A series of dipeptidyl nitriles as inhibitors of cathepsin K have been explored starting from lead structure **1** (Cbz–Leu–NH–CH_2–CN, IC_{50} = 39 nM). Attachment of non-natural amino acid side chains in P1 and modification of the P3 subunit led to inhibitors with higher potency and improved pharmacokinetic properties.



(R)-2

The in vitro profile and in vivo anti-emetic activity of the selective noradrenaline reuptake inhibitor (*R*)-**2** are reported.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Reagents and Conditions (Fm = 9-fluorenylmethyl): (a) HATU, DIEA, DMF, rt; (b) 25% piperidine in DMF, repeat; (c) caprolactam, PyBOP, DIEA, DMF, rt, repeat; (d) Boronic acid, $Pd(PPh_3)_4$, THF, 2 M Na_2CO_3, 60 °C, 16 h; (e) 50% TFA/DCM, rt. [Thompson, L. A.; Liauw, A. Y.; Ramanjulu, M. M.; Kasireddy-Polam, P.; Mercer, S. E.; Maduskuie, T. P.; Glicksman, M.; Roach, A. H.; Meredith, J. E.; Liu, R-Q.; Combs, R. C.; Higaki, J. N.; Cordell, B.; Seiffert, D.; Zaczek, R. C.; Robertson, D. W. Olson, R. E. *Bioorg. Med. Chem. Lett.* **2006,** *16,* 2357.]

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