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Chemistry

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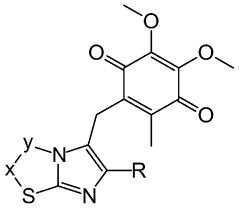
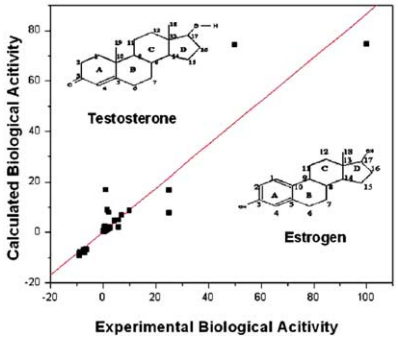
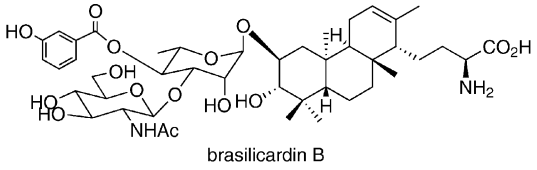
Contents

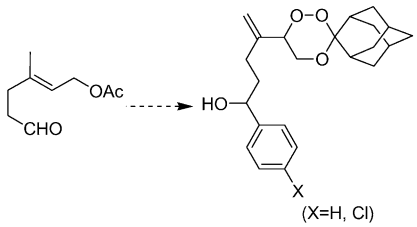
ARTICLES

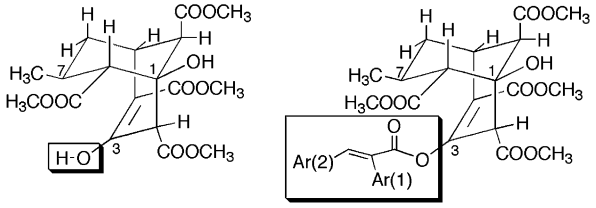


Development of generalized QSAR model is a mammoth task and in general a large number of descriptors are to be used to get a satisfactory correlation. In order to obtain a generalized model for QSAR, the structure–activity relationship has been developed for testosterone and estrogen derivatives with the help of a conceptually simpler single descriptor; namely the electrophilicity index. Results reinforce that electrophilicity index is suitable to effectively describe the biological activities.

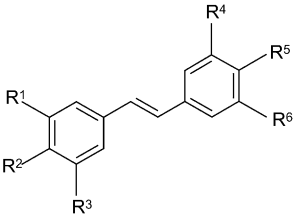






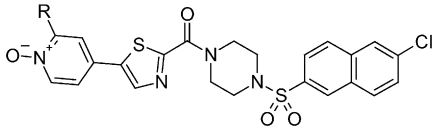


A series of hydroxylated and methoxylated *trans*-stilbenes were synthesized and evaluated for their ability to inhibit COX-1 and COX-2. Some of the hydroxylated derivatives are highly selective COX-2 inhibitor with potency comparable or better than clinically established drugs.

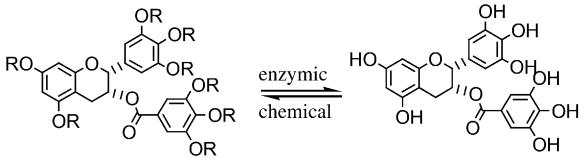


R^1, R^2, R^3, R^4, R^5, R^6 = H, OH, OCH_3

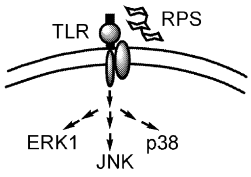
To optimize the S4 binding element of a factor Xa inhibitor, a series of thiazol-5-ylpyridine *N*-oxides **3a**–**d** were synthesized. Among these compounds, 4-(thiazol-5-yl)pyridine *N*-oxides **3a** and **3d** had potent anti-fXa activities that excelled over the tetrahydrothiazolopyridine derivative **1b** in potency. 2-Methylpyridine *N*-oxide **3d** exhibited moderate selectivity over thrombin.



3a: R = H, **3d**: R = Me

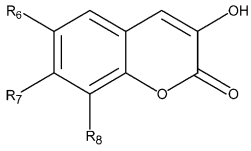


1 (R=Ac), as prodrug **(-)-EGCG**

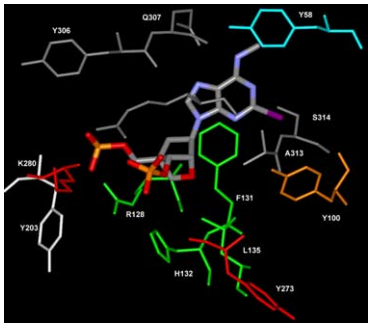


Isolation of Reishi polysaccharides for the study of their effect on cytokine expression in mouse splenocytes.

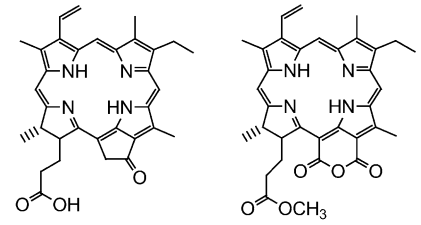
Human umbilical cord blood MNCs were treated with polysaccharides of *Ganoderma lucidum* F3 and cultured for 7 days. Analysis of various subsets of UCB mononuclear cells revealed relative increments of macrophage, dendritic cells, and natural killer cells detected by flow cytometry after the culture period.



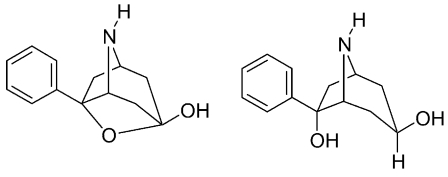
A series of hydroxylated 3-hydroxycoumarins was synthesised and evaluated for their antioxidant properties. The compounds substituted on the C-7 position were almost as antioxidant as quercetin or vitamin C. The antioxidant properties were related by an EPR study to their abilities to give stable semiquinonic or polyhydroxylated radicals.

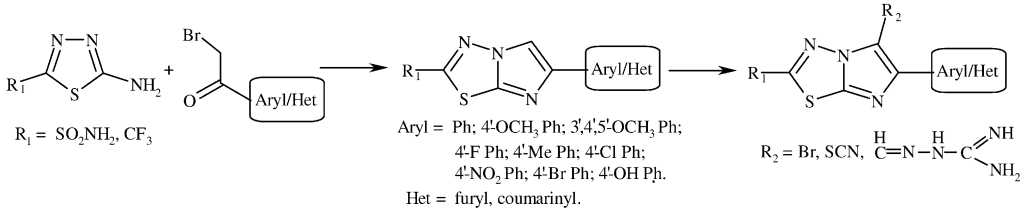


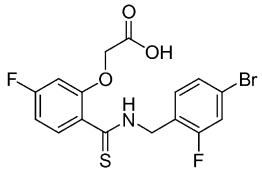
We have synthesized nucleotide analogues substituted with two novel ring systems and examined them as P2Y receptor ligands: (1) a (N) locked-carbocyclic (*c*LNA) derivative containing the oxabicyclo[2.2.1]heptane ring system and (2) L-α-threofuranosyl derivatives. We have also compared potencies and preferred conformations of these nucleotides with the known anhydrohexitol-containing $P2Y_1$ receptor antagonist MRS2283.

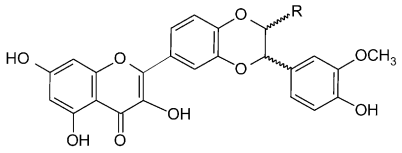


Compound	c-Raf-1 kinase IC_{50} (μg/mL)
pyropheophorbide *a*	<0.31
purpurin 18 methyl ester	2.8
chlorophyll *a*	>10.0



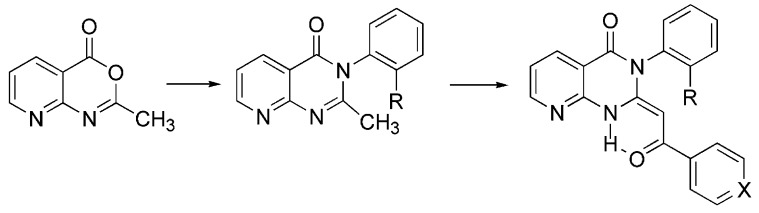


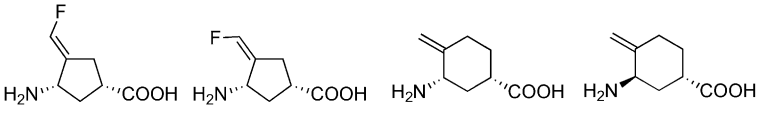




12 (3*aS*, 6*aR*) **13** (3*aS*, 7*aR*)

Fmoc protected 5,5 and 6,5-bicyclic ketones **12** and **13** were prepared through the corresponding diazomethylketone intermediates via a lithium chloride/acetic acid promoted carbene insertion reaction. Building blocks **12** and **13** were used in the solid phase synthesis of peptidomimetic inhibitors of a range of CAC1 cysteinyl proteinases. Compound **10**, a potent and selective inhibitor of cathepsin K exhibited promising activity in an in vitro cell-based human osteoclast assay of bone resorption.





OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

The front cover illustrates an example of a new *cis*-5,5-bicyclic scaffold for the design of potent inhibitors of CAC1 cysteinyl proteinases. Shown is a predicted binding conformation for *si* stereofacial thiolate addition to (3*aS*,6*aR*)-4-*tert*-butyl-*N*-[3-methyl-1-(3-oxo-hexahydrofuro[3,2-*b*]pyrrole-4-carbonyl)butyl]benzamide modelled in an active site slice of the cathepsin K crystal structure 1mem. [Quibell, M.; Benn, A.; Flinn, N.; Monk, T.; Ramjee, M.; Wang, Y.; Watts, J. *Bioorg. Med. Chem.* **2004**, *12*, 5689–5710].

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