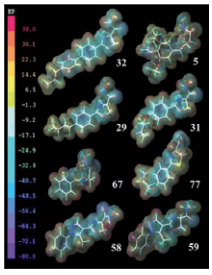
ELSEVIER

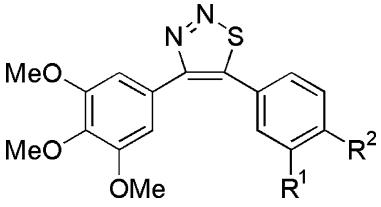
Bioorganic &
Medicinal
Chemistry
Letters

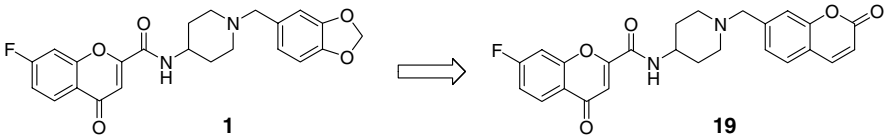
Bioorganic & Medicinal Chemistry Letters Vol. 17, No. 4, 2007

Contents

ARTICLES

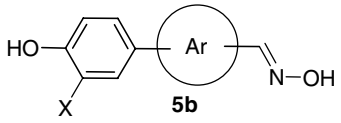




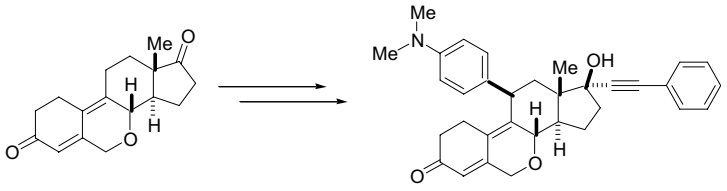


1
MCHr1 IC_{50} = 0.003 μM
Ca^{2+} IC_{50} = 0.029 μM
hERG IC_{50} = 15.1 μM

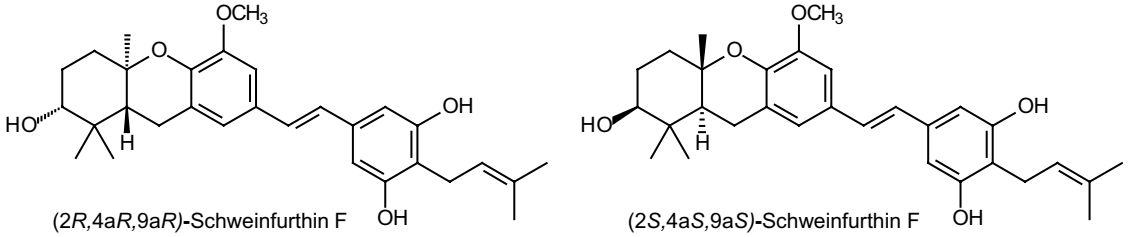
19
MCHr1 IC_{50} = 0.001μM
Ca^{2+} IC_{50} = 0.046 μM
hERG IC_{50} = 51.1 μM



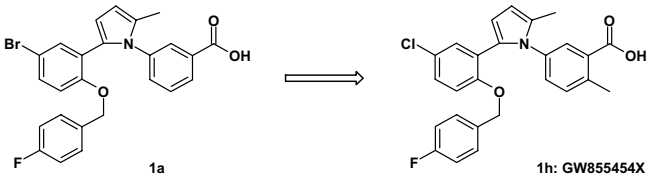
A series of 4′-hydroxyphenyl-aryl-carbaldehyde oximes (**5b**) was prepared and found to have high-affinity (4 nM) and modest selectivity (39-fold) for estrogen receptor-β.

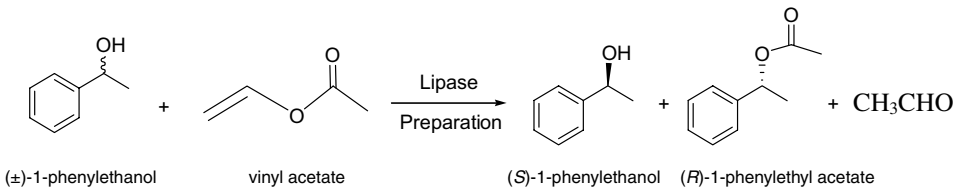


Novel 7-oxa-steroids were synthesized and indentified as new potent and selective progesterone receptor antagonists.

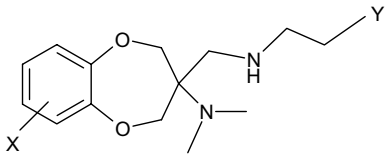


Substitution of the benzoic acid moiety of compounds such as **1a** led to the identification of **1h**, which was active in the established FCA model of inflammatory pain and showed good pharmacokinetics in the rat.

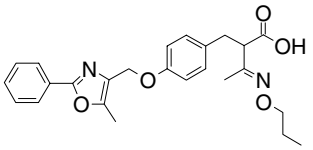




It is shown that high activity preparations of the lipases are far superior to the lyophilized powders in kinetic resolution of (±)-1-phenylethanol in [Bmim][PF_6].

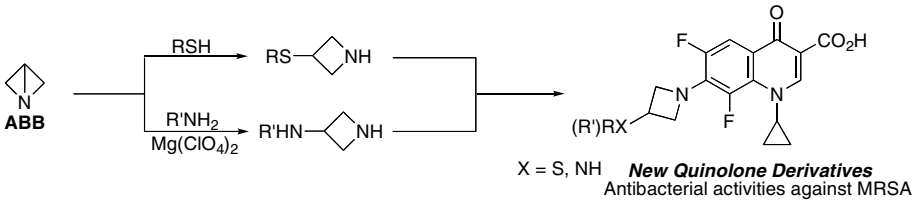


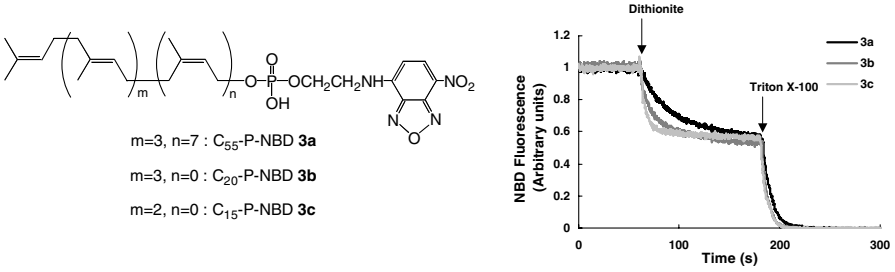
The structure–activity relationships of novel 1,5-benzodioxepin derivatives as muscarinic M_1–M_3 receptor antagonists are reported.



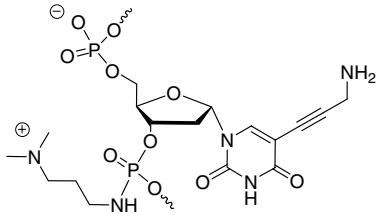
11l

Compound **11l** exhibited potent in vitro activities in PPARα and γ (EC_{50} = 19, 13 nM). It showed better glucose lowering effect than rosiglitazone as well.

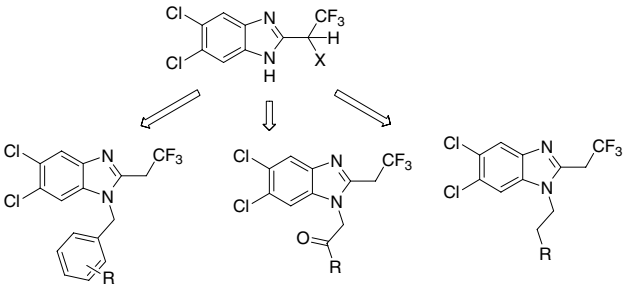


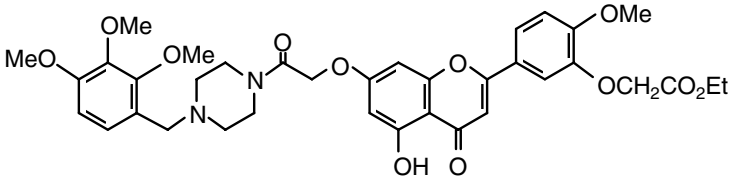


Novel NBD-labeled fluorescent polyprenyl phosphate analogues were synthesized for transmembrane movement study of polyprenyl phosphates, which may promise a methodology for the direct observation of the lipids flip-flop.



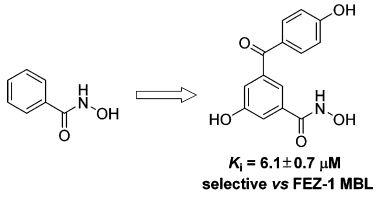
Incorporation of 5-propynylamino and 5-propynyl α-2′-deoxyuridine into α-oligonucleotides (α-ON) allows high-affinity targeting of complementary DNA for anionic and neutral but not for cationic α-ON.



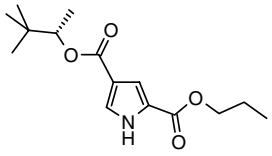


1

Most of 27 synthesized piperazinyl flavones displayed micromolar in vitro inhibition of *Plasmodium falciparum*, including **1** also active when given orally to *Plasmodium yoelii nigeriensis* infected mice.

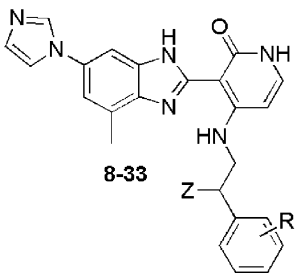


The development of a FEZ-1 metallo-β-lactamase inhibitor.

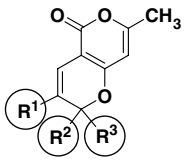


Investigation on the metabolic fate of the pyrrole mGluR1 antagonist class is presented.

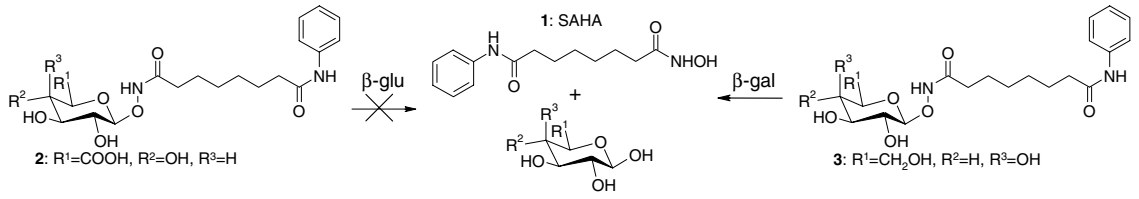
A novel class of benzimidazole–pyridone inhibitors of insulin-like growth factor I (IGF-1R) kinase is described.

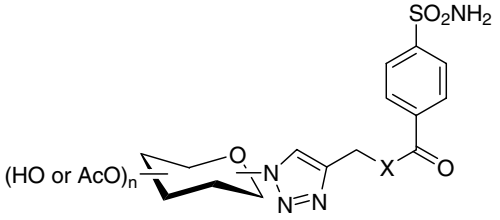


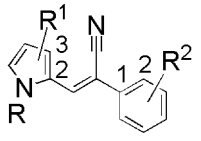
8-33



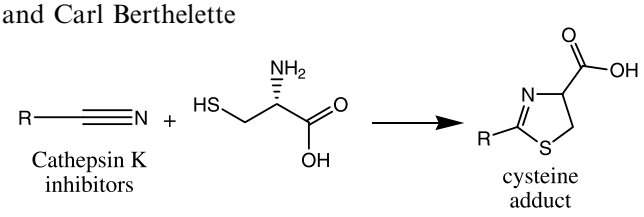
The title compounds were synthesized efficiently. Their in vitro antiproliferative/cytotoxic activity was evaluated with human SH-SY5Y neuroblastoma cells. IC_{50} values are ranging from 6.7 to >200 μM.



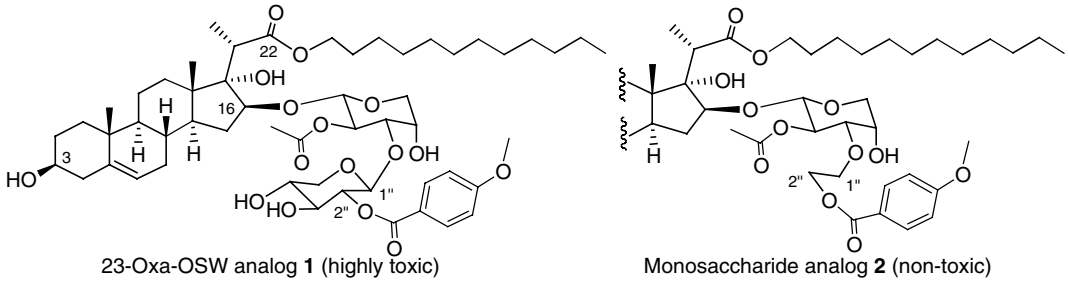


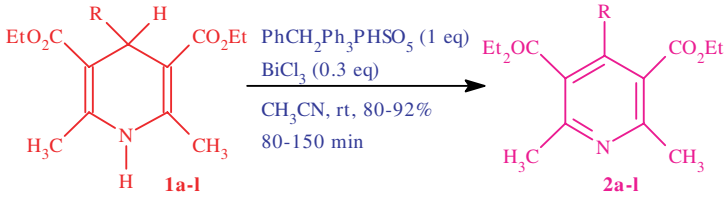


We describe the synthesis of a set of (*Z*)-2-phenyl-3-(1*H*-pyrrol-2-yl)acrylonitrile derivatives and the in vitro screening of these compounds against the animal parasites *Haemonchus contortus* and *Ctenocephalides felis*.

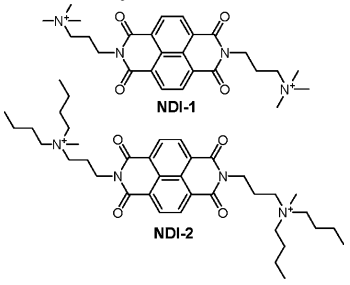


A simple theoretical calculation (reactivity of nitriles with methanethiol) was used to predict the electrophilicity of diverse nitrile warheads. These calculated electrophilicities were found to correlate with the extent of thiazoline adduct formed upon incubation of the nitriles with cysteine.

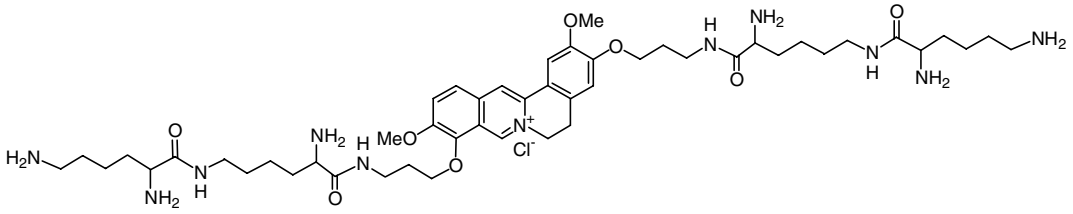


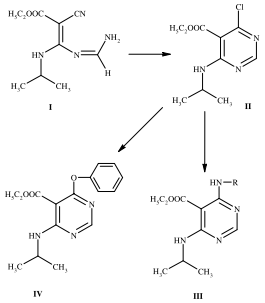


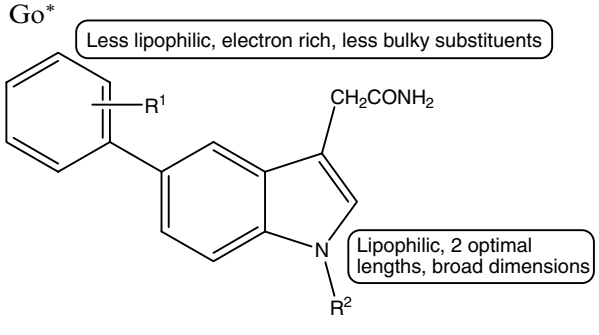
Aromatization of 1,4-dihydropyridines **1a–l** to the corresponding pyridine derivatives **2a–l** has been studied using benzyltriphenylphosphonium peroxymonosulfate **BTPPMS** in the presence of $BiCl_3$ at ambient temperature.

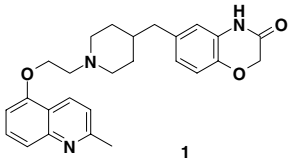


Topoisomerase I unwinding assay is used to determine the relative DNA-binding affinities of homologous naphthalene diimides as well as the binding mode adopted by several known DNA-binding agents.

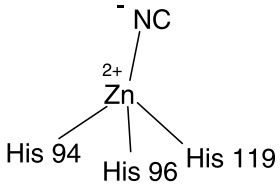


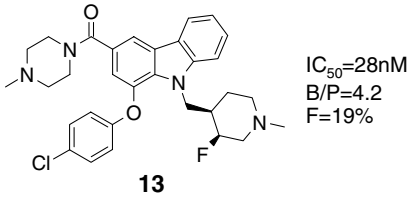






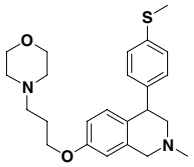
1



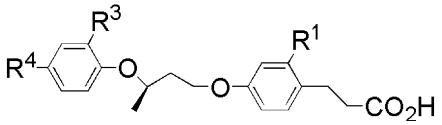


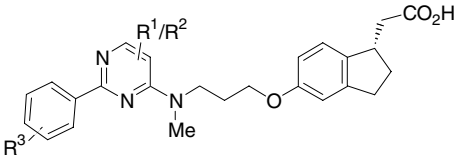
13

A series of carbazoles showing antagonist activity at the NPY Y1 receptor were prepared and characterised. Compound **13** combines potent activity with good brain penetration and modest bioavailability.



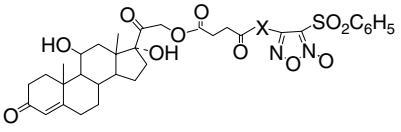
(+)-12x, hH_3 K_i=11 nM, hSERT K_i=3.8 nM





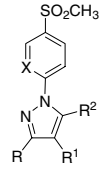
The indanylacetic acid structural motif has proven useful in the generation of potent and tunable PPAR ligands. Modification of the substituents on the linker and the heterocycle tail group modulated the selectivity at the different receptor subtypes.

A series of furoxan-based nitric oxide-releasing glucocorticoid derivatives was synthesized and evaluated for their anti-inflammatory activity and safety.

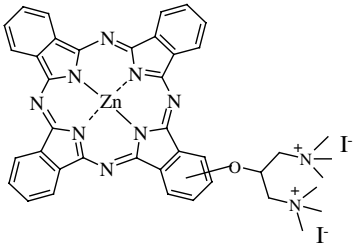


X= $O(CH_2)_2O$, $HNCH_2CH_2O$, $O(CH_2)_3O$, $OCH_3(CH_2)_2O$ $O(CH_2)_2O(CH_2)_2O$, $OCH_2C_6H_5O$, or $O(CH_2)_2C_6H_5O$

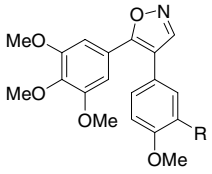
The SAR of the 5-heteroatom and aryl substituted pyrazoles with 4-nitrile substitution shows substantial improvement in activity against the COX enzymes. Molecular modelling studies were done to understand the reasons for such difference in activity. The potential interactions of the nitrile and pyridyl nitrogen within the active site that could explain this difference are highlighted.



R = CF_3, CF_2H; R^1 = H vs CN; R^2 = Ar, NR^3R^4, OR^5
X=N, CH



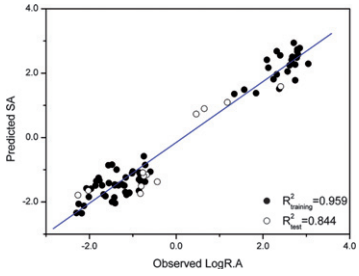
A novel series of mono-substituted zinc(II) phthalocyanines have been prepared which exhibit a high photodynamic activity against HT29 human colorectal carcinoma cells with IC_{50} values down to 0.08 μM.



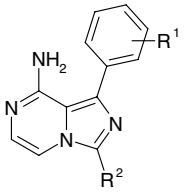
6d, R = OH
6e, R = NH_2

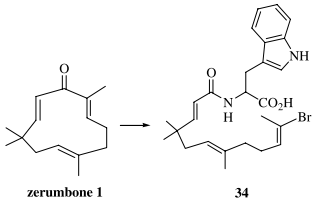
A series of 4,5-diarylisoxazoles related to combretastatin A-4 (**CA-4**) were synthesized, and compounds **6d** and **6e** showed strong cytotoxicity against three human cancer cell lines.

A diverse approach to the QSAR of tacrine derivatives against acetylcholinesterase (AChE) activity was studied using variable selections of stepwise multiple linear regression (MLR).



A series of novel 8-amino-1,3-disubstituted-imidazo[1,5-*a*]pyrazines was designed and synthesized as IGF-IR inhibitors.





zerumbone 1 **34**

YycG inhibition: IC_{50} (μM)	43.9
MRSA: MIC (μg/mL)	100
VRE: MIC (μg/mL)	50

The synthesis of the novel YycG inhibitor **34** (IC_{50} = 43.9 μM) showing growth inhibition against MRSA and VRE is reported.

*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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ISSN 0960-894X