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Bioorganic & Medicinal Chemistry Letters

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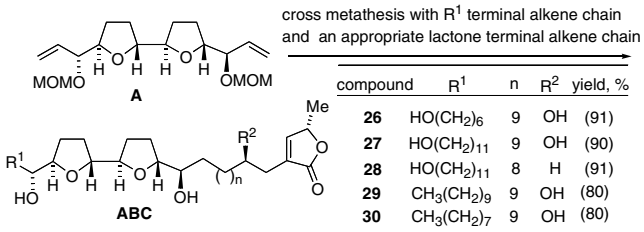
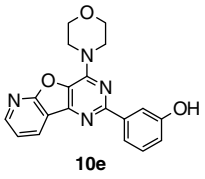
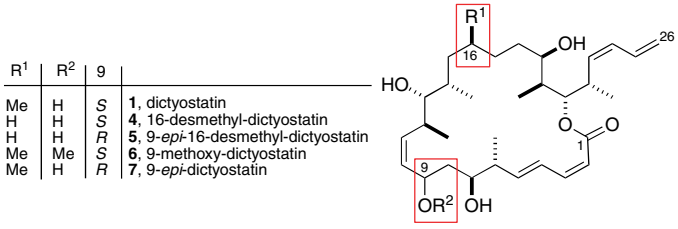
Contents

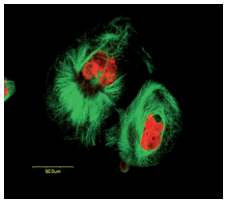
ARTICLES



Side-chain analogs of Annonaceous acetogenins with a *threo*, *trans*, *threo*, *trans*, *threo*-bis-tetrahydrofuran core unit have been prepared and tested for cytotoxicity against HCT-116 human colon cancer cells.

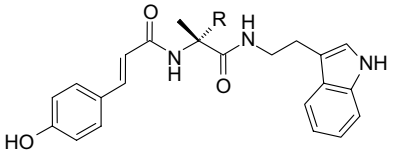


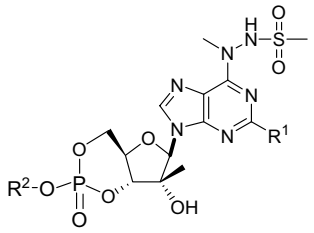


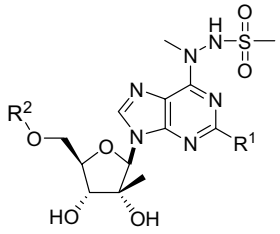


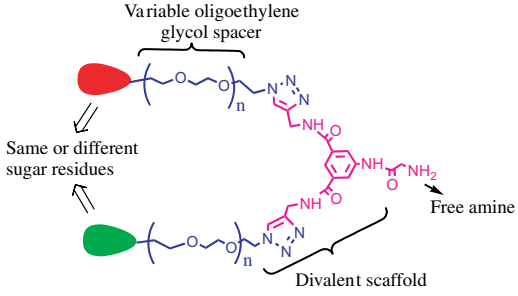
PANC-1 after 100 nM incubation with **6**.

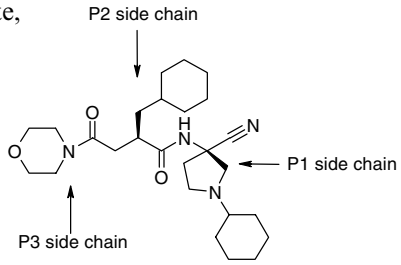
Novel analogues of the microtubule-stabilising agent dictyostatin were designed, synthesised and evaluated in vitro for growth inhibition against a range of human cancer cell lines.

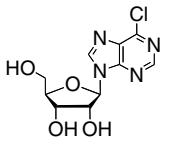




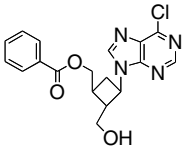




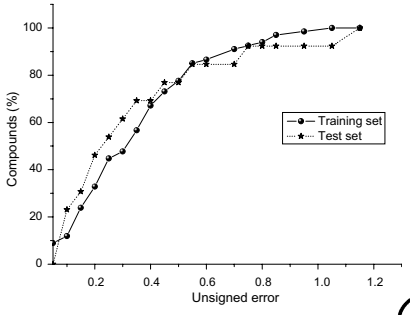


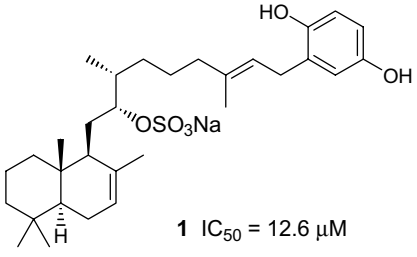


1: IC_{50} = 48.7 μM

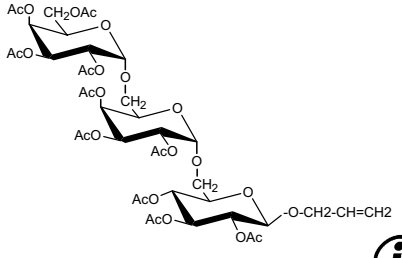


11: IC_{50} = 14.5 μM

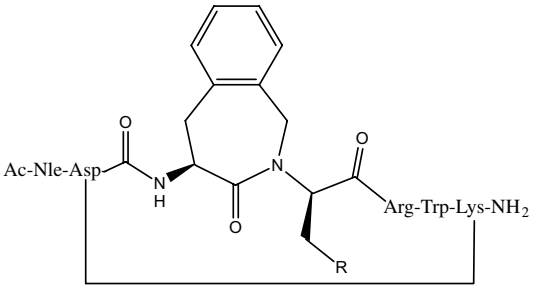




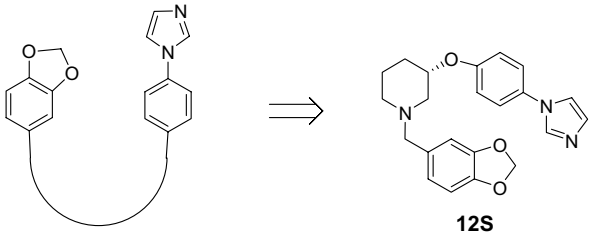
1 IC_{50} = 12.6 μM



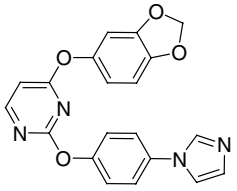
12 MIC = 3~25 μg/ml



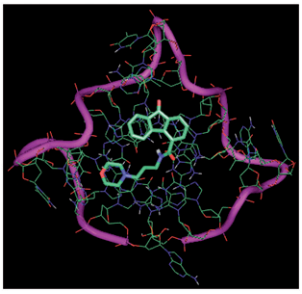
A new series of 1-(1,3-benzodioxol-5-ylmethyl)-3-[4-(1*H*-Imidazol-1-yl)phenoxy]- piperidine analogs were discovered as potent and selective inhibitors of NO formation. Compound **12S** showed high potency and high iNOS selectivity versus nNOS and eNOS.

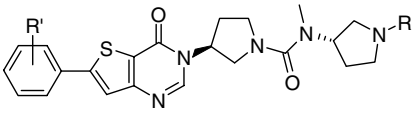


12S

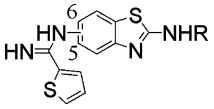


A novel class of compounds that block nitric oxide formation from cells overexpressing iNOS is described.

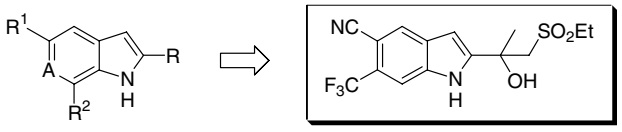


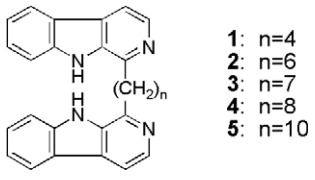


A series of thienopyrimidinone bis-aminopyrrolidine ureas were designed, synthesized, and evaluated for their ability to bind melanin-concentrating hormone receptor-1. These compounds exhibit potent binding affinity ($K_i = 3$ nM) and good in vitro metabolic stability.

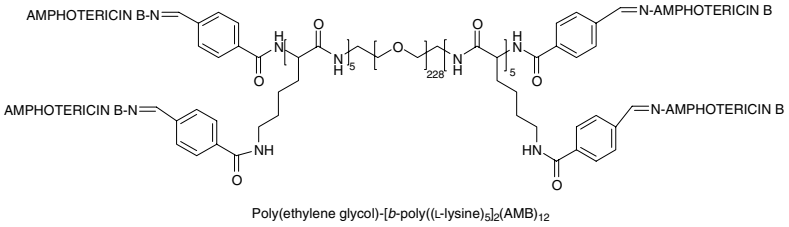


A novel series of 2-aminobenzothiazoles were synthesized and shown to be selective inhibitors of neuronal nitric oxide synthase (nNOS).

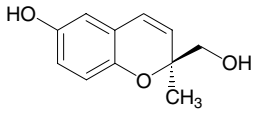




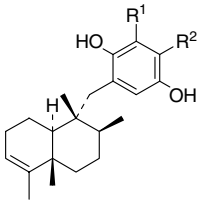
The non-covalent complexes of five bis-β-carbolines **1-5** with three different 12-mer double-stranded oligodeoxynucleotides were investigated by ESI-FT-ICR MS. The structure–activity relationships and sequence selectivities were discussed.



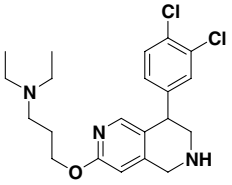
A new intravenous of pH-sensitive conjugate of amphotericin B (AMB) has been synthesized and characterised: poly(ethylene glycol)-[*b*-poly(L-lysine)$_5$]$_2$-(AMB)$_{12}$ (M_w = 26,700).



Quercinol (**1**)

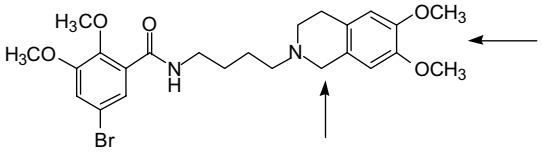


Semisynthesis of 13 new thio avarol derivatives (**4**–**16**) and in vitro evaluation on the photodamage response induced by UVB irradiation are described. Their ability to inhibit NF-κB activation and TNF-α generation in HaCaT cells as well as their antioxidant capacity in human neutrophils has been also reported.

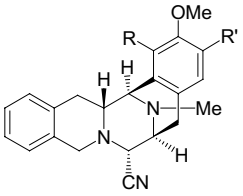


12f, hH_3 K_i=7 nM, hSERT K_i=26 nM

The synthesis and in vitro activity of novel histamine H_3 antagonists with serotonin reuptake activity are reported.

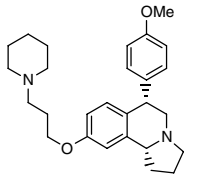


Synthetic modification at two sites on the tetrahydroisoquinolinyl benzamide resulted in significant changes to σ receptor affinity and selectivity.



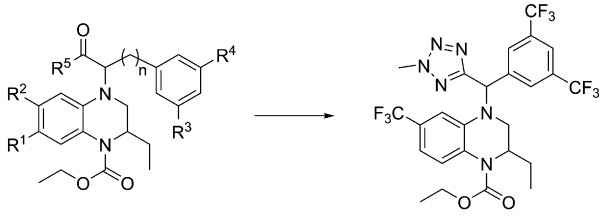
The synthesis and biological evaluation of (1,3′)-bis-tetrahydroisoquinolines and pentacyclic piperazine core alkaloids is reported.

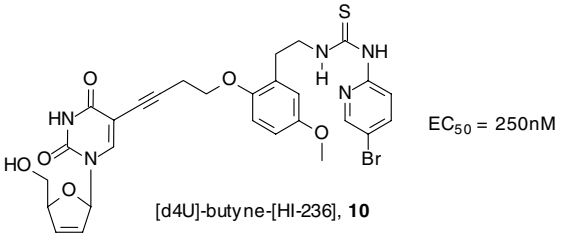
A series of novel and potent pyrrolidino-tetrahydroisoquinolines with dual histamine H_3 antagonist/serotonin transporter inhibitor activity is described. A highly regio- and diastereoselective synthesis of the pyrrolidino-tetrahydroisoquinoline core involving acid mediated ring-closure of an acetophenone intermediate followed by reduction with $NaCNBH_3$ was developed. In vitro and in vivo data are discussed.

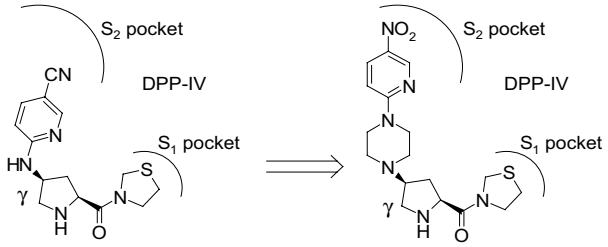


7o hH_3 K_i = 0.7 nM
hSERT K_i = 3.3 nM

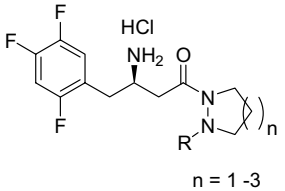
The SAR and synthesis of a series of substituted tetrahydroquinoxaline CETP inhibitors is described from early lead to advanced analogs.

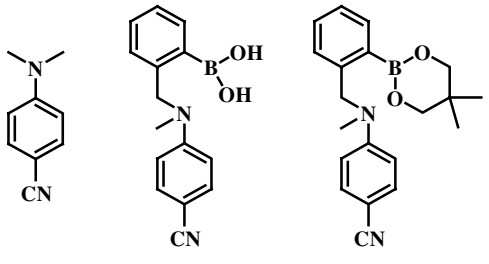




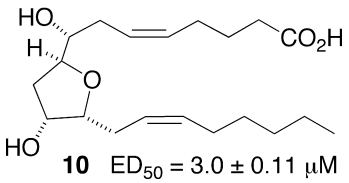


6, IC_{50} = 25 nmol/L **21e**, IC_{50} = 0.92 nmol/L



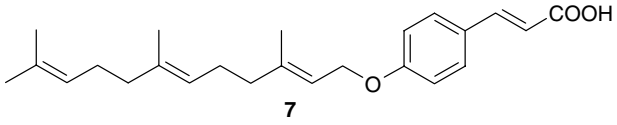


DMABN **1** **2**



10 $ED_{50} = 3.0 \pm 0.11\ \mu M$

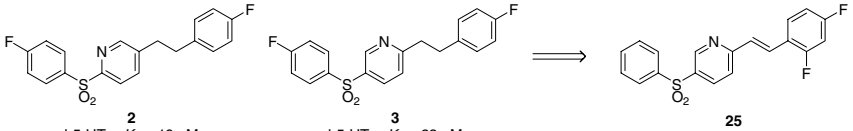
Eight tetrahydrofuran-diols (THFDs), originating from epoxyeicosatrienoic acids (EETs), were prepared from D-(+)-glucose. THFD **10** was eqivalent to 14, 15-EET as a vasodilator of pre-contracted bovine arteries.



7

$IC_{50} = 28\mu M$

The synthesis of some natural and semisynthetic prenyloxyphenylpropanoids and their selective inhibitory activity on geranylgeranyl transferase I are reported.

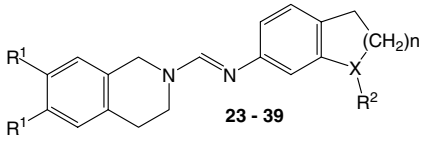


2
h5-HT_{2A} K_i = 19 nM
h5-HT_{2C} K_i > 4000 nM

3
h5-HT_{2A} K_i = 23 nM
h5-HT_{2C} K_i = 2670 nM

25
h5-HT_{2A} K_i = 0.86 nM
h5-HT_{2C} K_i > 4000 nM

This report describes the effect of replacing the central basic amine present in many known 5-HT_{2A} ligands with an aromatic residue. We targeted the isomeric phenethylpyridines **2** and **3** and these compounds proved to be excellent leads, possessing good 5-HT_{2A} receptor binding affinity and selectivity over the 5-HT_{2C} subtype. Optimization of one isomer led to the identification of **25**, a compound with sub-nanomolar 5-HT_{2A} affinity and selectivity over 5-HT_{2C} of greater than 4600-fold.



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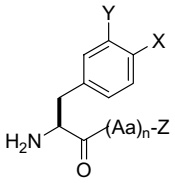
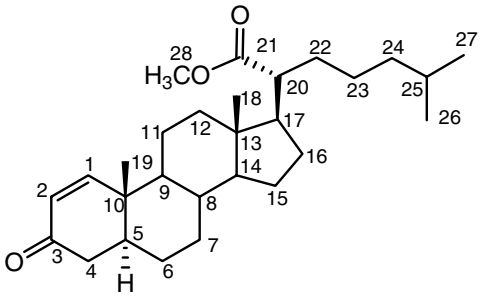
Based upon the activity of natural products, new compounds with activity in an *in vivo* model of schizophrenia have been designed and synthesised.



A new steroid with an uncommon 21-oic acid methyl ester moiety designated methyl spongoate (**1**) which exhibited potent cytotoxicity against BEL-7402 tumor cells in vitro with IC_{50} value of 0.14 μM has been isolated from the Sanya soft coral *Spongodes* sp.. Its structure was determined by detailed interpretation of spectroscopic data.



Methyl spongoate (1)

OTHER CONTENTS

*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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