ELSEVIER

Bioorganic & Medicinal Chemistry Letters

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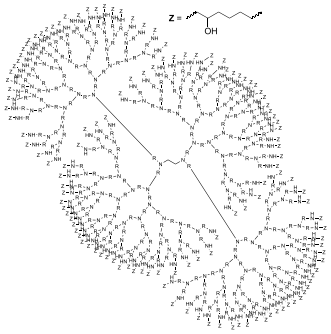
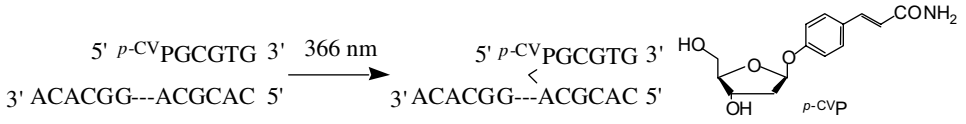
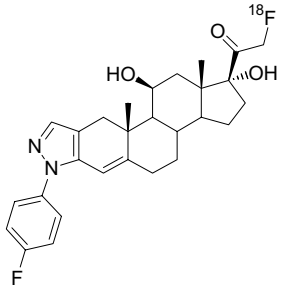
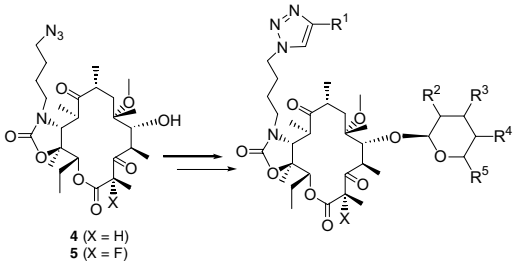
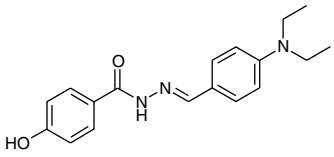
Contents



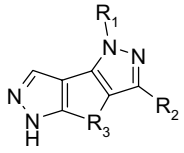






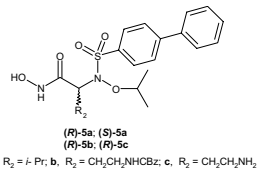


The synthesis of a selective ligand for the estrogen-related receptors ERRβ/γ is reported.

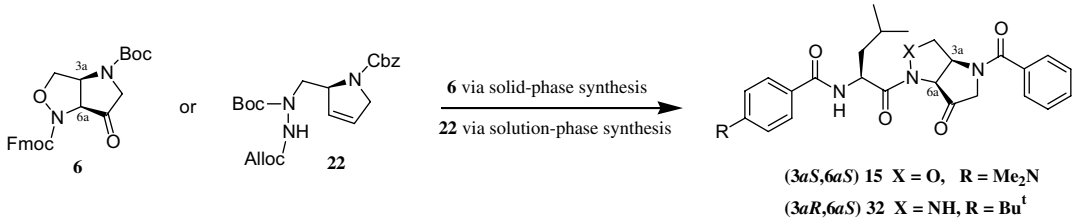


The synthesis and the preliminary structure–activity relationship results of this class are reported.

Structural manipulation of the pharmacophoric model of type **A** selective MMP inhibitors (MMPi), obtained by the insertion of some alkyl substituents R_2 possessing an appropriate geometry, steric bulkiness and lipophilicity, is able to improve potency, in the subnanomolar range on MMP-2, and to give a good MMP inhibition on MMP-14 (MT1-MMP) in the designed MMPi of type **C**, while maintaining a good MMP-1/MMP-2 selectivity profile. The simultaneous inhibition of these two enzymes yields type **C** compounds, which are potent antiangiogenic agents, able to block a chemoinvasion model on HUVEC cells under the micromolar range.

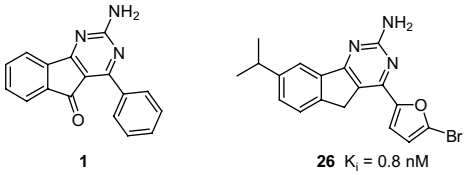


(*R*)-5a; **(*S*)-5a**
(*R*)-5b; **(*R*)-5c**
a, R_2 = *i*- Pr; **b**, R_2 = CH_2CH_2NHCBz; **c**, R_2 = $CH_2CH_2NH_2$

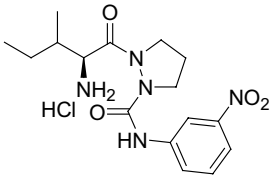


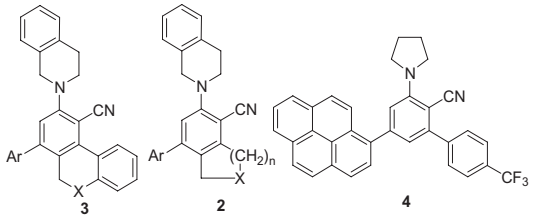
6 via solid-phase synthesis
22 via solution-phase synthesis

(3*aS*,6*aS*) 15 X = O, R = Me_2N
(3*aR*,6*aS*) 32 X = NH, R = Bu^t

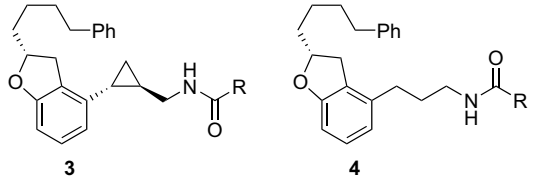


The structure–activity relationship investigation using **1** as a template led to the identification of a novel class of compounds as potent and selective antagonists of the A_{2A} receptor. Compound **26** was identified to be the most potent A_{2A} antagonist ($K_i = 0.8$ nM) with 100-fold selectivity over the A_1 receptor.

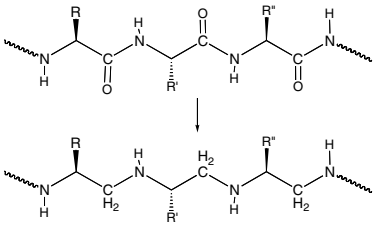


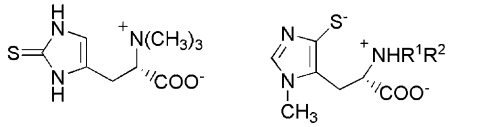


Synthesis and antihyperglycemic activity of biaryls are reported.

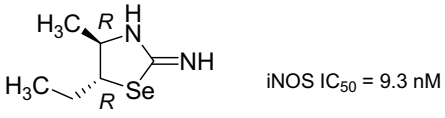


(*R*)-2-(4-Phenylbutyl)dihydrobenzofuran derivatives (e.g., **3** and **4)** were synthesized as novel melatoninergic ligands with significantly lower vasoconstrictive activity in vitro in the rat tail artery. Binding affinity assays were performed on cloned human MT_1 and MT_2 receptors stably expressed in NIH3T3 cells.





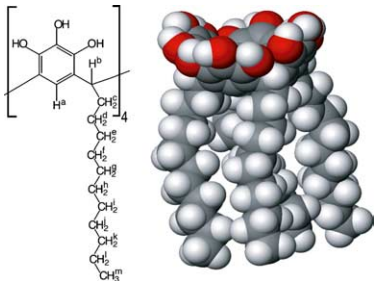
A detailed ab initio electronic structure analysis of ergothioneine and ovothiol is reported, which evaluates the thermodynamics of these thiols with alkyl thiols, hydroxide radicals, hydrogen peroxide and ascorbate.

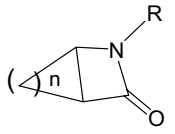


Compound **4**
(ES-2133)

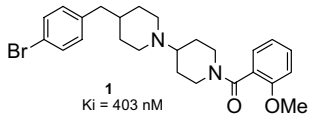
The synthesis and evaluation of compound **4** (ES-2133) and its related optically active compounds as iNOS inhibitor is reported. In addition, an alternative synthetic method to the selected compound **4** and its pharmacokinetic profile is also reported.

Molecular recognition of neurotransmitters with an amphiphilic resorcinarene receptor in an aqueous micelle system is studied by ^{1}H NMR measurements and theoretical chemical shift calculation.



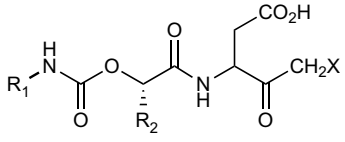


n= 3, 4, 5, 6
R= H, $C_6H_5CH_2$

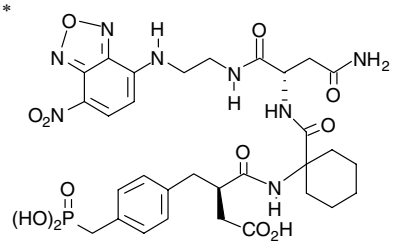


1
Ki = 403 nM

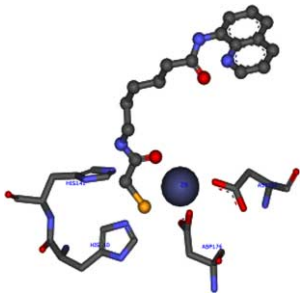
The structure–activity relationship of bipiperidine **1** as a CCR3 antagonist has been evaluated.

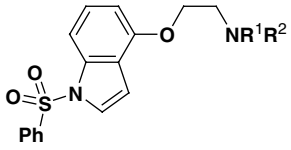


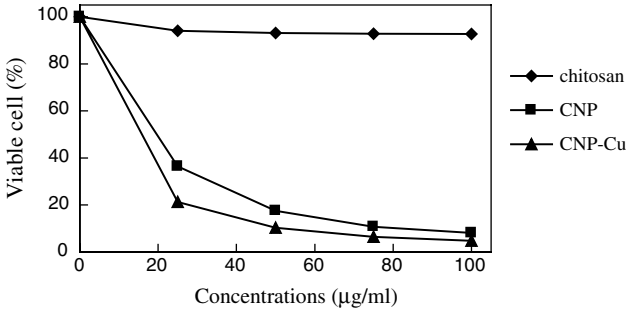
The synthesis and biological evaluation of a group of peptidomimetic α-carbamoyl-alkylcarbonyl-aspartyl fluoromethethylketones as capase inhibitors is reported.

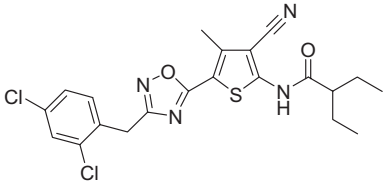


Grb2 SH2 Domain K_D = 119 ± 0.6 nM

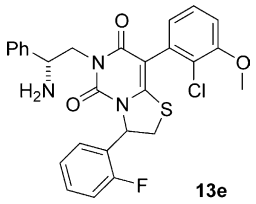








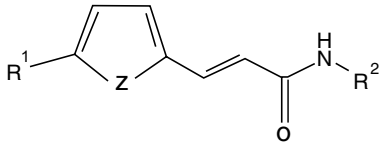
13 cAMP IC_{50} = 34 nM



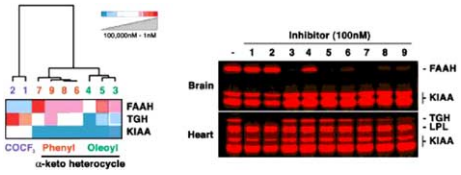
13e

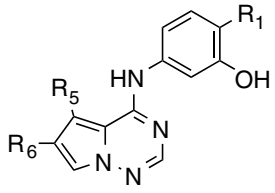
Treatment of various 2-methyl oxazolines or thiazolines with chlorocarbonyl isocyanate gives the corresponding bicyclic oxazolino- or thiazolino[3,2-c]pyrimidin-5,7-dione derivatives in very good yield. This reaction has been applied to the rapid syntheses of human gonadotropin-releasing hormone (*h*GnRH) receptor antagonists for SAR study, resulting in **13e** with binding affinity in the low nanomolar range (4.5 nM).

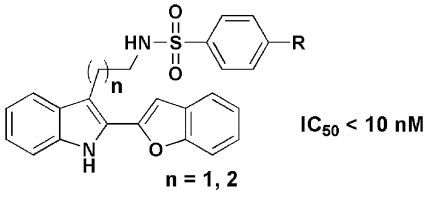
Procedures for synthesizing α-amino acids on a chip for coordination with transitional metal ions and a His-Tagged protein have been successfully developed as a stable protein microarray. Using the recombinant His-Tagged 3CL-protease ($3CL^{pro}$) as a model for attachment to chips containing D-/L-Glu, Asp, Orn, Ser via different transitional metal ions, it was found that the Orn chip was the best of affinity binding and stability by which Zn^{2+} was the best metal ion for affinity while Co^{2+} was the best metal ion for stability. Thus, this protein microarray can be alternatively used as a high throughput screening method for rapid detection against SARS CoV $3CL^{pro}$ and/or efficient purification of other Tagged proteins.

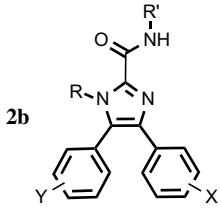


Eight novel Nifurtimox analogues were synthesized and tested in vitro against *Trypanosoma cruzi* epimastigotes.

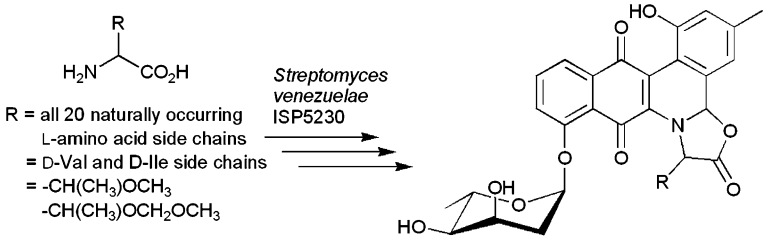


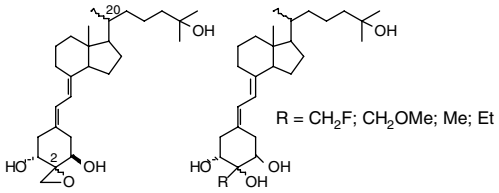




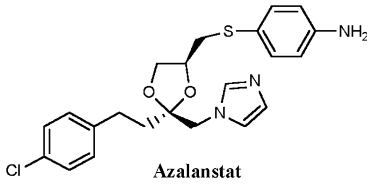


The synthesis and structure–activity relationships for a series of substituted 4,5-diphenylimidazole-2-carboxamide derivatives **2b** as selective, orally active human CB1 inverse agonists are described.





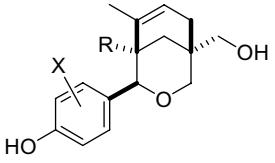
Novel 2,2-disubstituted 19-norvitamin D_3 analogs were synthesized and their binding affinity to the vitamin D receptor and transcriptional activity were evaluated.



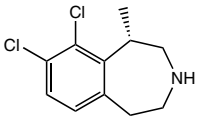
Azalanstat

IC_{50} = 6 μM (rat spleen, HO-1)
IC_{50} = 28 μM (rat brain, HO-2)

The synthesis and biological activity of novel heme oxygenase (HO) inhibitors based on the lead structure of azalanstat is presented. Potency and selectivity in the inhibition of HO-1 and HO-2 isozymes were found to be dependent on the configurational and structural features of these compounds.

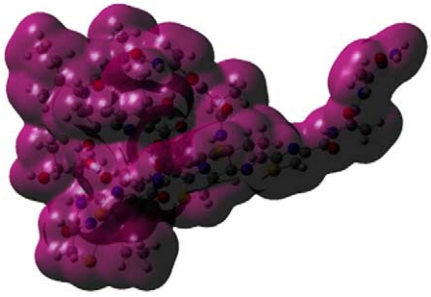


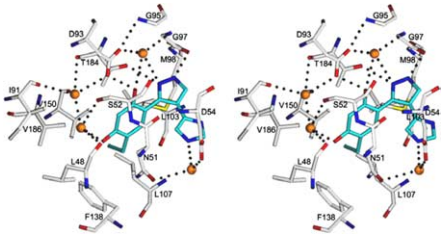
The synthesis and estrogen receptor α/β agonist activity of compounds from this novel scaffold are reported.

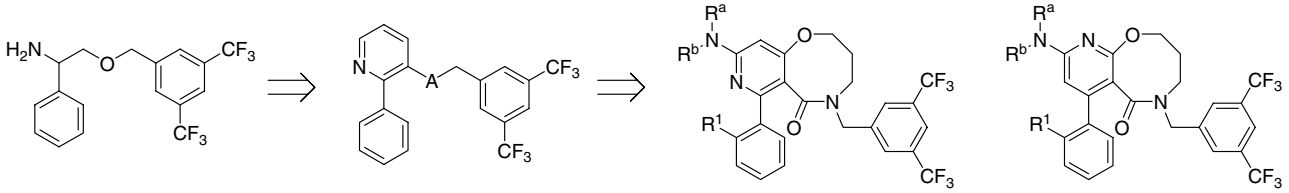


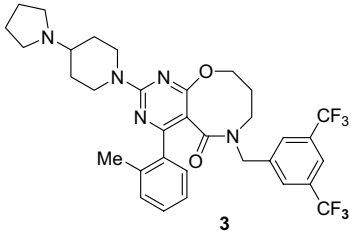
(S)-18c EC_{50} = 3 nM

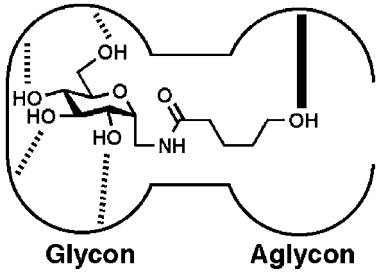
The synthesis and SAR of a 3-benzazepine series of selective 5-HT_{2C} agonists is described.

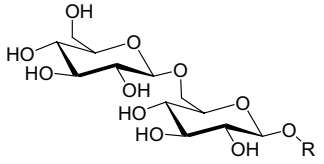




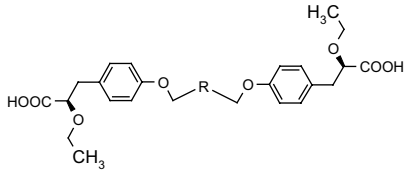




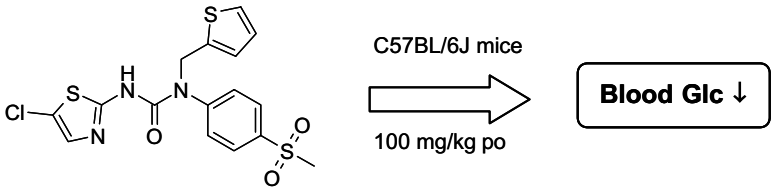




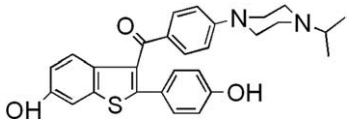
The synthesis of amygdalin analogs as peptidomimetics of peptide T is reported.



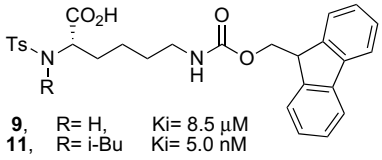
The SAR of dimeric PPAR agonists is reported.



Ureas that lower blood glucose levels in vivo by activating glucokinase are described.

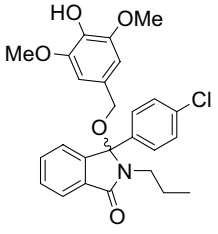


Benzothiophenes bearing piperazine side chains were synthesized and identified to be high-affinity ligands with high selectivity for ER α subtype, and they were potent agonists in bone tissue.

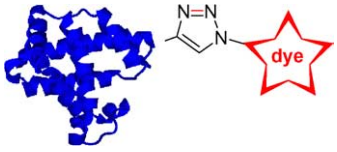


A screening assay program carried out on commercially available N-protected amino acids showed that *N*α-sulfonamide-*N*ε-Fmoc-L-lysine **9** displayed an 8.5 μM inhibition constant. Addition of an isobutyl group at the Nα-position allowed the discovery of the lead candidate **11** exhibiting a 5.0 nM K_i. The discovery, synthesis and SAR studies are described.

The design, synthesis and evaluation of 24 isoindolinones as potential inhibitors of the MDM2–p53 interaction is described. The most potent inhibitor NU8231 (ELISA: $IC_{50} = 5.3 \pm 0.9$ μM) displays cellular activity in human SJSA cells.



NU8231



A bioconjugation using a genetically encoded alkyne in *Escherichia coli* is reported.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Proteome screening for FAAH selectivity. (Left) Comparison of the potencies and relative selectivities of FAAH inhibitors. IC_{50} values are clustered into three classes: highly potent and highly selective α-ketoheterocycle inhibitors with phenyl side chain (red), moderately potent α-ketoheterocycle inhibitors with oleoyl side chain (green) and trifluoromethyl ketone inhibitors selective for TGH (purple). (Right) Competitive profiling of FAAH inhibitors (100 nM) with RFP (100 nM) in brain and heart membrane proteome [Leung, D.; Du, W.; Hardouin, C.; Cheng, H.; Hwang, I.; Cravatt, B. J.; Boger, D. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1423].

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