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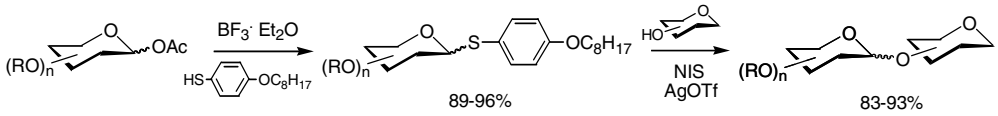
Medicinal
Chemistry
Letters

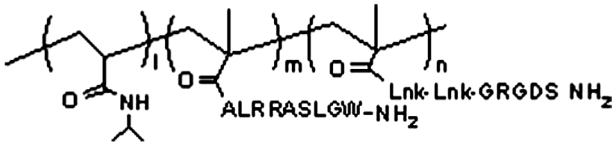
Bioorganic & Medicinal Chemistry Letters Vol. 16, No. 22, 2006

Contents

ARTICLES

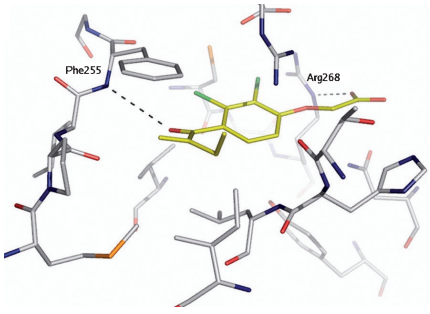


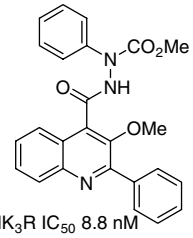
Under Odorless Conditions



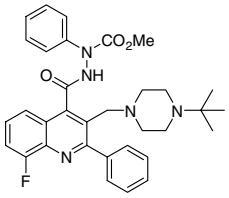
Development and evaluation of RGD peptide modified signal-responsive gene carrier are reported.

Novel inhibitors of *Trypanosoma brucei* and human UDP-Glc 4′-epimerase with micromolar potency were identified by screening marine natural products and drug-like molecules.

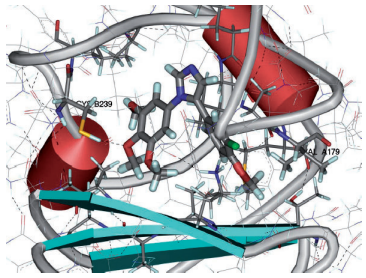


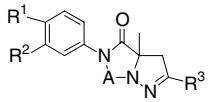


2g hNK_3R IC_{50} 8.8 nM



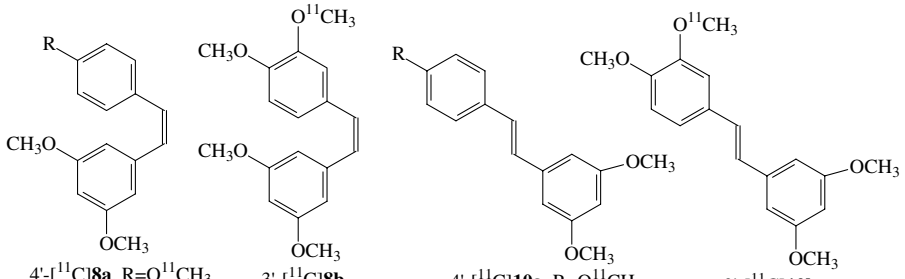
8m hNK_3R IC_{50} 4.0 nM



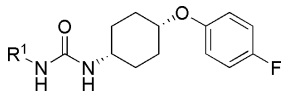


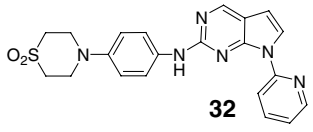
novel hydantoins

A novel series of hydantoin derivatives were identified by in vivo studies as tissue selective androgen receptor modulators. SAR around this series revealed that the function of the ligand could be altered by minor structural modification.



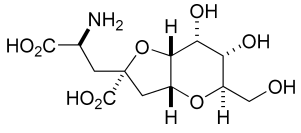
4'-[^{11}C]**8a**, R=O^{11}CH$_3$ 3'-[^{11}C]**8b**
4'-[^{18}F]**12a**, R=^{18}F
4'-[^{11}C]**10a**, R=O^{11}CH$_3$ 3'-[^{11}C]**10b**
4'-[^{18}F]**13a**, R=^{18}F



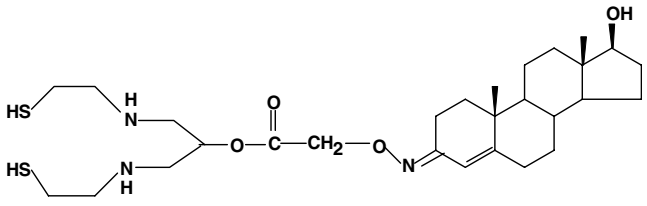


32

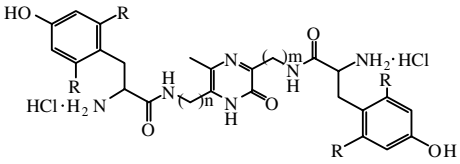
The synthesis of a potent Aurora-A inhibitor **32** (IC_{50} = 0.8 nm) is reported.

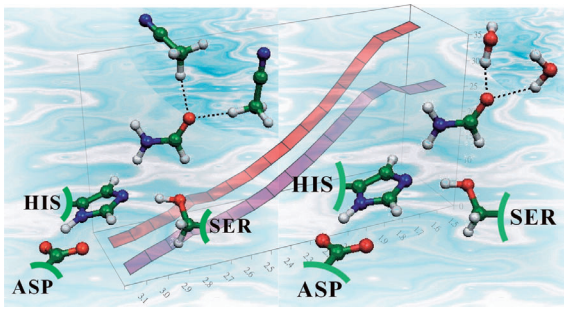


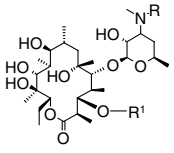
The total synthesis and biological evaluation of neodysiherbaine A analogue are described.



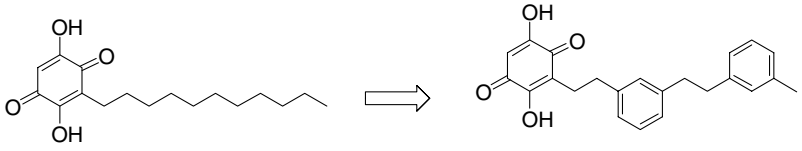
A novel testosterone–BFCA conjugate is prepared and radiolabeled with ^{99m}Tc, an ideal diagnostic radioisotope, in an attempt to prepare an agent for targeting androgen receptors. The bio-efficacy studies of the radiolabeled agent toward suitable cell line expressing androgen receptors showed retention of biological activity.







The synthesis of a new class of 9-(*S*)-dihydroerythromycin derivatives and their anti-inflammatory activity are reported.

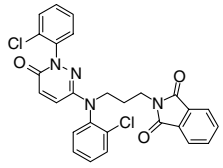


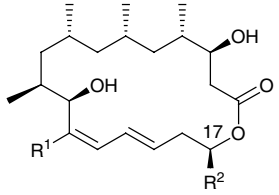
1, Embelin (initial lead)

K_i = 0.40 ± 0.13 μM to XIAP BIR3

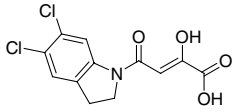
6g

K_i = 0.18 ± 0.09 μM to XIAP BIR3

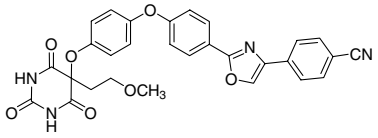


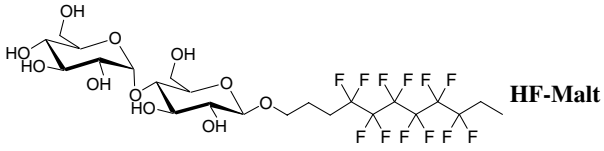


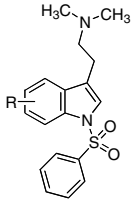
An SAR analysis of borrelidin analogues is presented.



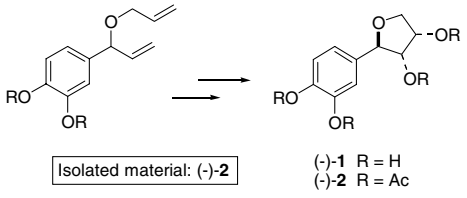
The synthesis of aniline and indoline amide ketoacids as inhibitors of HIV integrase.



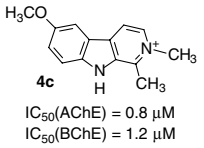




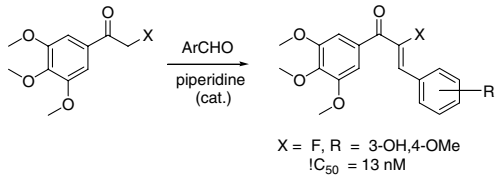
Comparative analysis indicates that N_1-unsubstituted- and N_1-benzenesulfonyltryptamines bind differently at 5-HT$_6$ receptors. Additionally, evaluation of conformationally constrained analogs suggests that a non-coplanar benzenesulfonyl moiety may be optimal for binding.

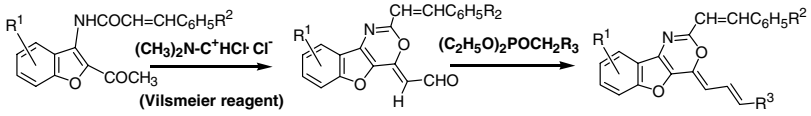


Stereoselective synthesis of a novel metabolite from a strain of the phytopathogenic fungus *Colletotrichum gloeosporioides* was carried out. The tetraol (−)-**1** showed free radical scavenging activity comparable to that of protocatechuic acid.

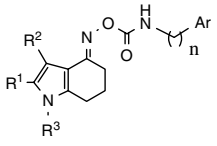


A series of β-carbolines and β-carbolinium salts were synthesized and their inhibitory activities towards AChE and BChE measured. Micromolar inhibitors with some selectivity toward AChE were identified.

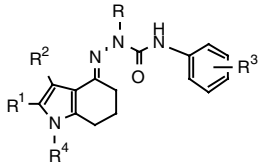




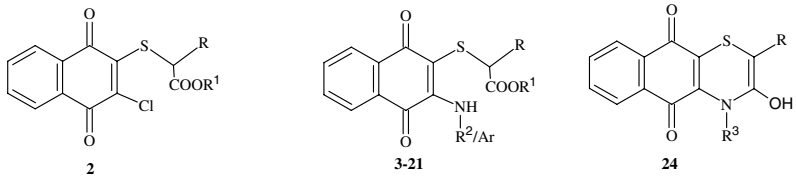
A novel ring closure reaction using the Vilsmeier reagent afforded (*Z*)-((*E*)-2-styrylbenzo[*b*]furo[3,2-*d*][1,3]oxazin-4-ylideno)acetaldehydes which gave butadiene compounds having potent anti-osteoclastic bone resorption activity.



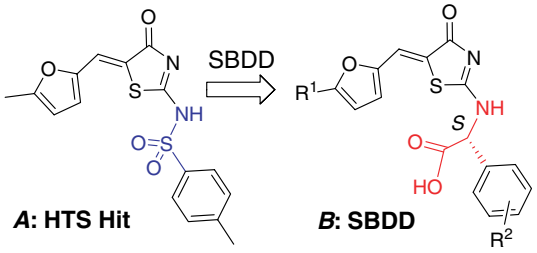
A novel class of tetrahydroindolone-derived carbamates has been discovered whose members are potent Kv1.5 blockers. The in vitro data show that compounds **6** and **29** are quite potent. They are also very selective over hERG (>450-fold) and L-type calcium channels (>450-fold).

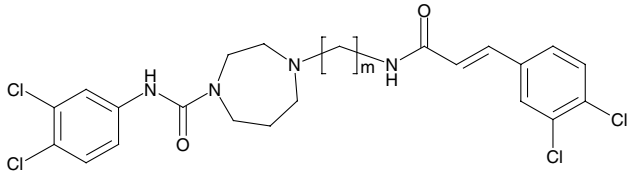


A novel class of tetrahydroindolone-derived semicarbazones has been discovered as potent Kv1.5 blockers. In in vitro studies, several compounds exhibited very good potency for blockade of Kv1.5. Compound **8i** showed good selectivity for blockade of Kv1.5 vs hERG and L-type calcium channels. In an anesthetized pig model, compounds **8i** and **10c** increased atrial ERP by 17–26% in the right atrium without affecting ventricular ERP.

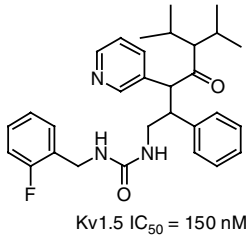


The synthesis, antibacterial and antifungal activities of **2**–**24** are described.

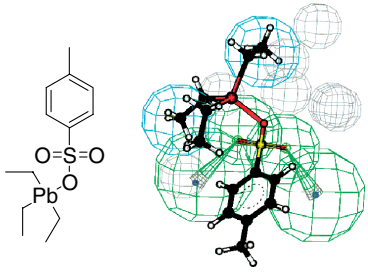




11g (m=4): IC_{50} (hLGPa)= 170 nM

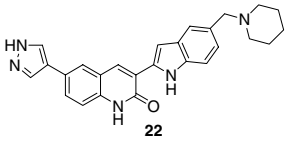


Kv1.5 IC_{50} = 150 nM

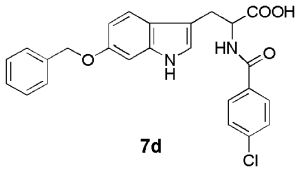


In silico-based discovery of new potent pseudomonal quorum sensing inhibitors is reported.

6-Substituted 3-(indol-2-yl)quinolinones are reported as potent Chek1 inhibitors.

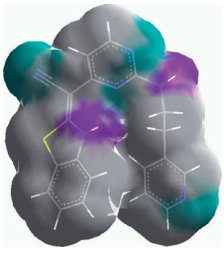


Chek1 IC_{50} = 0.65 nM
Cell EC_{50} = 97 nM



A series of 3-(6-benzyloxy-1*H*-indol-3-yl)-2-acylaminopropionic acid derivatives were designed, synthesized, and tested for the PPARγ protein binding activities. Compounds **7d** possessed potent binding activity ($K_D = 6.86 \times 10^{-6}$ mol/L) close to marketed drug rosiglitazone ($K_D = 4.98 \times 10^{-6}$ mol/L) in vitro.

We have developed a 3D-QSAR model and performed a series of structural studies on a series of benzothiazole-2yl acetonitrile derivatives with high inhibition activity towards c-Jun N-terminal kinase-3. The results were compared with experimental structure-based studies using JNK3 crystal structure to gain insight into the structural requirements for inhibitory activity of this class.



OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

View of the crystal structure of the DB819-d(CGCGAATTCGCG)$_2$ complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 15). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, *14*, 33.]

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