ELSEVIER

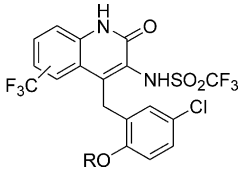
Bioorganic & Medicinal Chemistry Letters Vol. 14, No. 7, 2004

Bioorganic & Medicinal Chemistry Letters

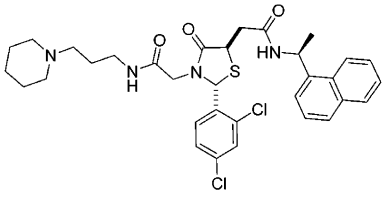
# Contents

## COMMUNICATIONS

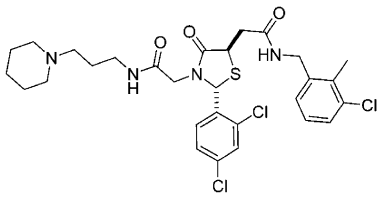







**90**




**91**

Substituted thiazolidinones were identified as CCR4 antagonists from high throughput screening. Subsequent lead optimization efforts resulted in defined structure–activity relationships and the identification of potent antagonists (compounds **90** and **91**) that inhibited the chemotaxis of Th2 T-cells in vitro.

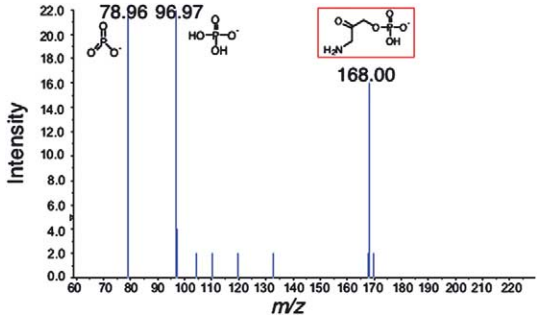



IR spectra and colorimetry data indicated that bisbenzamidines readily interact with heme in cell-free systems at pH 5.0 and 7.0.

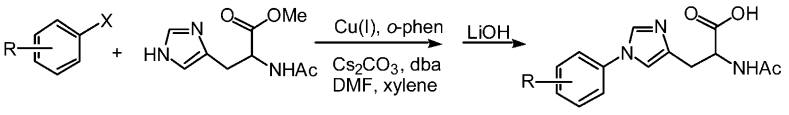

Femtosecond time resolved electron transfer dynamics of alanyl–PNA double strands where both strands contain an intercalated 9-amino-6-chloro-2-methoxy-acridine in its protonated state are investigated.



Negative ion electrospray ionization mass spectrometry (ESI-MS) and tandem mass spectrometric analysis (MS-MS) confirms that 3-amino-1-hydroxyacetone 1-phosphate (AHAP) is the product of the reaction catalyzed by 4-hydroxy-L-threonine-4-phosphate dehydrogenase (PdxA).



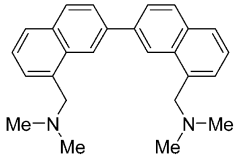


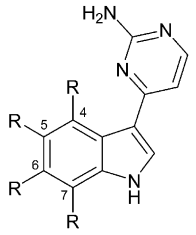

X = I
R = H, Br, Cl, OMe, Me

R = I, H, Br, Cl, OMe, Me



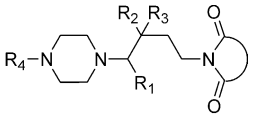



A novel type of DNA intercalator, 8,8′-bis(dimethylaminomethyl)-2,2′-binaphthalene based on 2,2′-binaphthalene skeleton, was prepared and the binding ability for calf thymus (CT) DNA was evaluated by UV–vis and fluorescence spectroscopic titrations and the melting temperature of CT DNA.



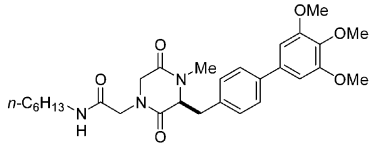
| | 4 | 5 | 6 | 7 |
|---|---|---|---|---|
| Meridianin A | OH | H | H | H |
| Meridianin B | OH | H | Br | H |
| Meridianin C | H | Br | H | H |
| Meridianin D | H | H | Br | H |
| Meridianin E | OH | H | H | Br |
| Meridianin F | H | Br | Br | H |
| Meridianin G | H | H | H | H |





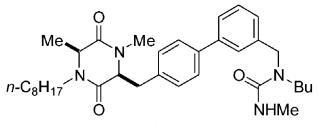
An in silico cytochrome CYP3A4 metabolism model was combined with a pharmacophore affinity model to design new metabolically protected 5-HT$_{1A}$ ligands. New molecules were prepared using parallel chemistry and screened in vitro.



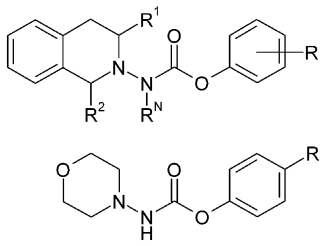


**1**
FSH $EC_{50}$ = 3.0 μM

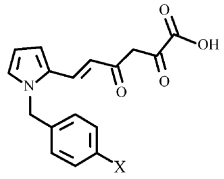




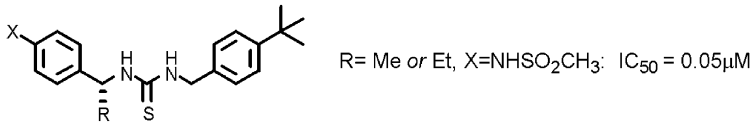
**11f**
FSH $EC_{50}$ = 1.2 nM



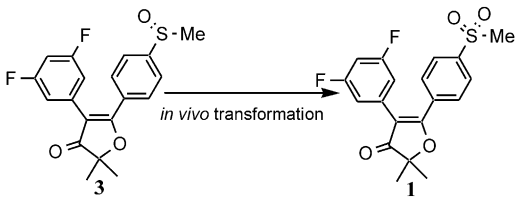


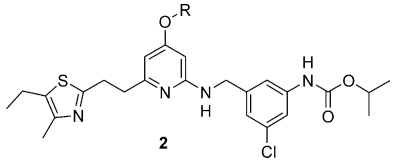










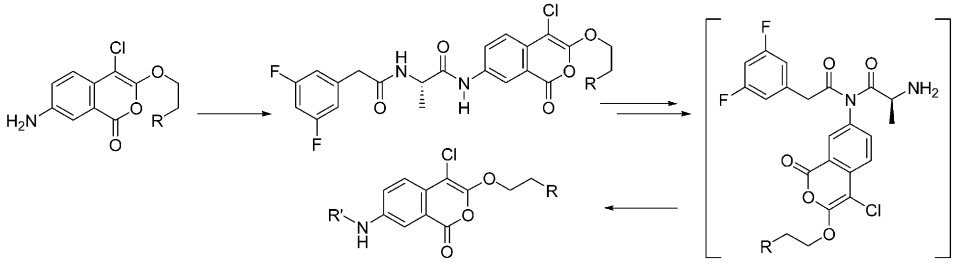

2

A series of substituted 4-alkoxy-2-aminopyridines **2** were synthesized and evaluated as neuropeptide Y Y1 receptor antagonists.



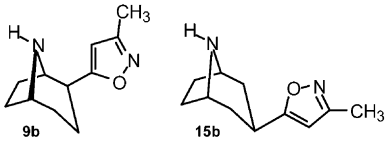
Molecular dynamics simulations of the putative HCV receptor CD81 indicate that the conformation of the two helical regions in one of the published X-ray structures is affected by crystallographic contacts and most likely does not represent the native state of the protein. The implications of this result for drug design projects aimed at the CD81/E2 interaction are discussed.






R = OMe; R' = 3,5-difluorophenylacetyl, alanyl.

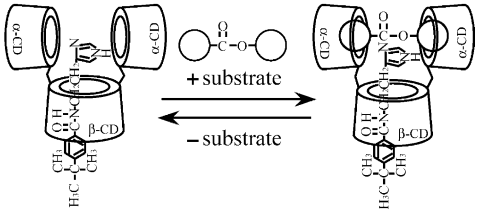




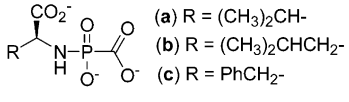

A series of epiboxidine homologues, 2- and 3-isoxazole substituted 8-azabicyclo[3.2.1]octane derivatives was synthesized and evaluated as potential ligands for neuronal nicotinic acetylcholine receptors in [$^3$H]cytisine labeled rat brain. The 2β-isoxazolyl-8-azabicyclo[3.2.1]octane **9b** ($K_i = 3$ nM) was the most potent compound of the series with a binding affinity twice that of nicotine. The 3β-isoxazolyl-8-azabicyclo[3.2.1]octane **15b** ($K_i = 148$ nM) exhibited moderate affinity while the corresponding 2α- and 3α-isomers exhibited micromolar binding affinity.

Different hydroxyl radical scavenging effect of water-soluble β-alanine $C_{60}$ adducts is closely related to the numbers of residual C=C bonds in $C_{60}$, steric effect and electron-withstanding effect of amino group especially.



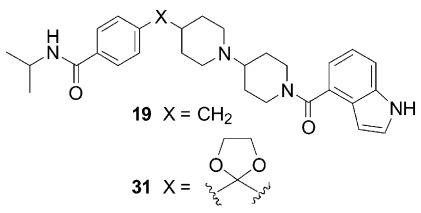


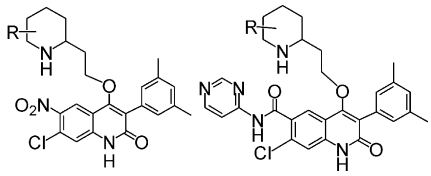



A new class of foscarnet prodrug has been prepared. The prodrugs slowly release foscarnet at physiological pH and temperature.

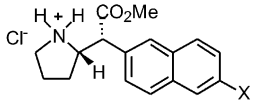




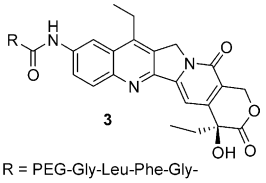


Synthesis and structure–activity relationships of piperidine-substituted quinolones as gonadotropin releasing hormone antagonists are described.







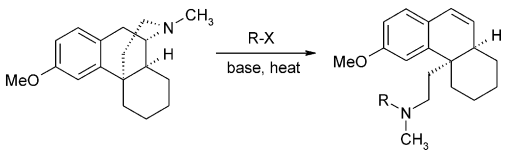


3

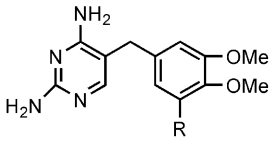
R = PEG-Gly-Leu-Phe-Gly-

Chemoselective acylation of 10-amino-7-ethyl camptothecin with poly(ethylene glycol) using phenyl dichlorophosphate is reported. Preliminary in vivo antitumor tests for **3** show high activity against P388 murine leukemia.





Treatment of dextromethorphan with various alkylating agents followed by base treatment led to Hoffman-type elimination reactions to produce tricyclic derivatives, characterized in vitro as potent sigma-1 receptor ligands.




R: -C≡C(CH$_2$)$_3$COOH, -C≡CC$_6$H$_4$(4-COOH)

## OTHER CONTENTS



*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

## COVER

*Cover figure provided by* ***Indraneel Ghosh****, Department of Chemistry, University of Arizona.* The cover depicts the **Dual Surface Selection** methodology developed by the author: the blue helix of htB1 (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htB1 (center) allows for functional selection against thrombin (right) [Rajagopal, S.; Meza-Romero, R.; Ghosh, I. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1389].



Indexed/Abstracted in: Adis LMS Drug Alerts, Beilstein, Biochemistry & Biophysics Citation Index, BIOSIS previews, CAB Abstracts, CAB Health, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/Elsevier BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

ELSEVIER

ISSN 0960-894X