ELSEVIER

Bioorganic & Medicinal Chemistry Letters

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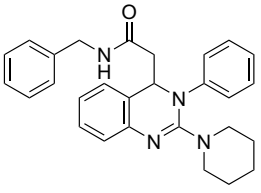
Contents

COMMUNICATIONS



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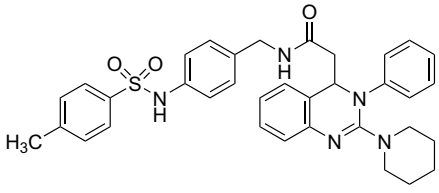

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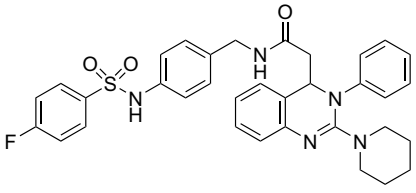
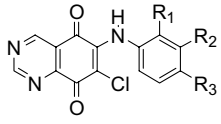
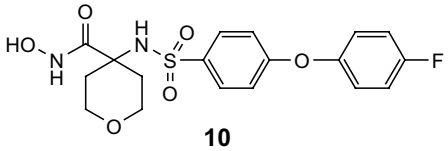


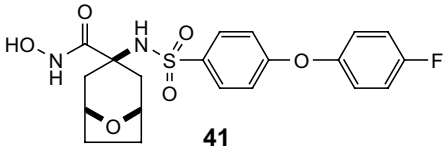
10b(KYS05042)



The cytotoxicity and DNA topoisomerase activity of a series of 6-arylamino-7-chloro-quinazoline-5,8-diones were evaluated. A new series of potential inhibitors, including 6-[(2′-bromo-4′-methyl)phenyl]amino-7-chloro-quinazoline-5,8-dione, have been identified, and thus providing novel chemical leads for the further development.



10



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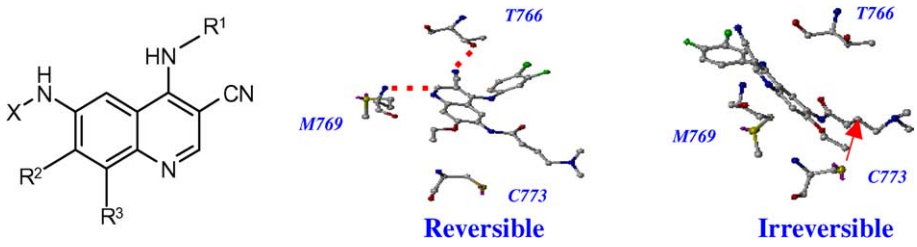
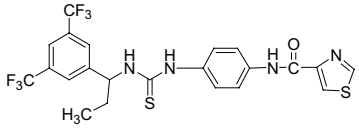
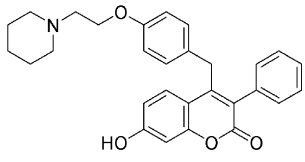


Modeling studies reveal two possible binding modes (reversible and irreversible) for 6,7 di-substituted 4-anilinoquinoline-3-carbonitriles with EGFRK.

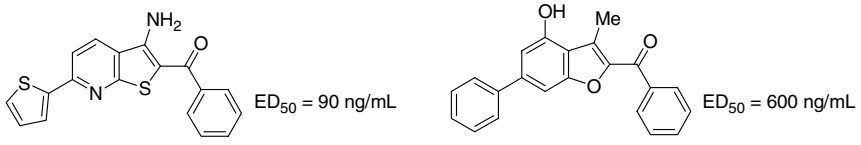


29

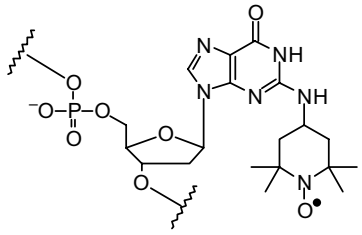
A series of highly potent thiourea inhibitors of cytomegalovirus (CMV) with improved stability properties was prepared and evaluated. Compound **29** inhibited the virus in cultured HFF cells with IC_{50} of 0.2 nM.



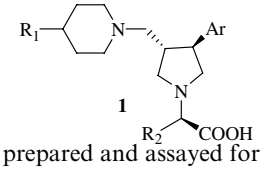
SP500263 (**13**)



A SAR study was carried out on two hit compounds of a screening to indicate their differences and optimized structures.

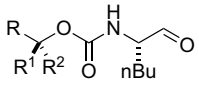


TEMPO G

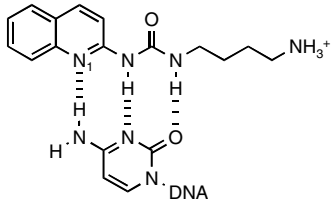


1

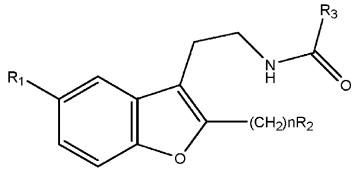
A series of pyrrolidineacetic acid derivatives (**1**) was prepared and assayed for their CCR5 receptor affinity, anti-HIV-1 activity in a HeLa cell-based assay, and oral bioavailability in the rat. These pyrrolidineacetic acid analogs (R_2) incorporated a variety of 4-heterocyclic piperidiene derivatives (R_1) to optimize these potential antiviral properties.



The synthesis and biological activity of a series of aldehyde inhibitors of cathepsin K are reported. Exploration of the properties of the S^2 and S^3 subsites with a series of carbamate derivatized norleucine aldehydes substituted at the P^2 and P^3 positions afforded analogs with cathepsin K IC_{50}s between 600 nM and 130 pM.

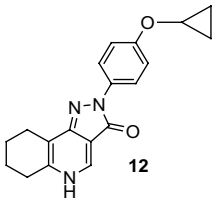


A new molecule, 2-ureidoquinoline having an alignment of hydrogen-bonding groups in the order of acceptor–donor–donor stabilizes single cytosine and thymine bulges in duplex DNAs.



1-34

Considering the importance of developing selective melatonin receptor ligands, the present paper attempts QSAR modeling of MT_1 and MT_2 binding affinity and explores selectivity requirements for MT_2 versus MT_1 binding of benzofuran derivatives using electrotopological state (E-state) index.



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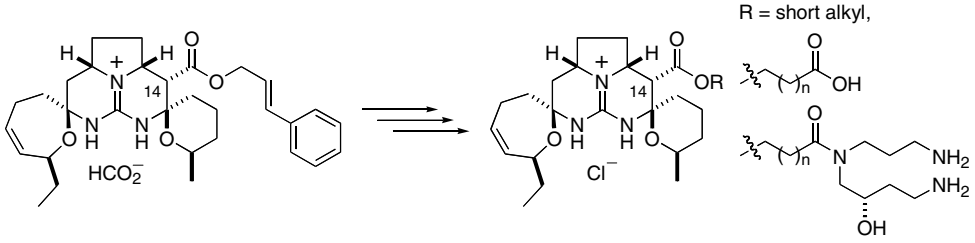
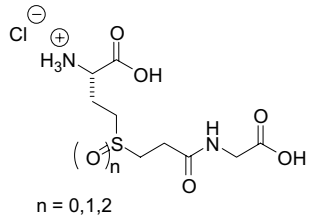
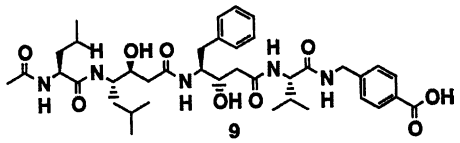


Synthesis, anticancer activity, and structure–activity relationships of crambescidin analogs that vary primarily at the C14 side chain are reported.



The synthesis of *S*-alkyl L-homocysteine glutathione analogues and their inhibition constants against rat kidney GGT are reported.

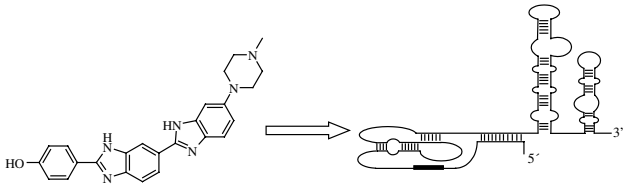


9

The multiple linear regression (MLR) analysis and back propagation neural networks (NN) were performed to examine the quantitative structure–polarization relationships (QSPR) for the formation of antibody–BTEX–EDF complex. The selected descriptors have good linear relationships and play a significant role in the formation of antibody–tracer complex. The optimum regression model is as follows

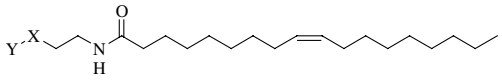
$$\underset{}{\mathrm{FP}} = \underset{(\pm 0.575)}{-2.404}[\mathrm{HA}] + \underset{(\pm 0.032)}{0.230}[\mathrm{Area}] - \underset{(\pm 1.770)}{10.027}[\mathrm{HOMO}] + \underset{(\pm 17.188)}{28.566}[C_3] + \underset{(\pm 1.520)}{4.474}[P_2] - \underset{(\pm 20.592)}{123.525}$$

$$N = 18; \quad r^2 = 0.853; \quad s = 1.679; \quad F = 13.919$$



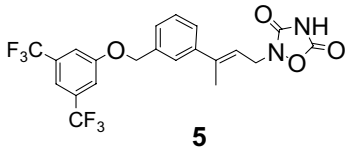
Hoechst 33258 hTR

The ability of several known nucleic acid binding ligands to inhibit recombinant human telomerase is reported. One of these, Hoechst 33258, was demonstrated to bind human telomerase RNA with high affinity, suggesting that this is the target for inhibition.

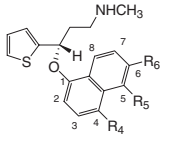


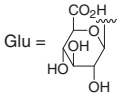
1 (NAEPA): X = O; Y = PO_3H_2; $LPA_{1/2}$ dual agonist
17: X = O; Y = PO_3H_2; EC_{50} = 40 nM (LPA_1), 108 nM (LPA_2)
19: X = S; Y = $P(S)O_2H_2$; EC_{50} = 318 nM (LPA_1), >5000 (LPA_2)

Using an *N*-oleoyl ethanolamide scaffold, a series of phosphate mimetic analogues of lysophosphatidic acid (LPA) comprised of various α-substituted phosphonates and thiophosphates was prepared and evaluated at the three LPA receptors of the endothelial differentiation gene (Edg) family.



5

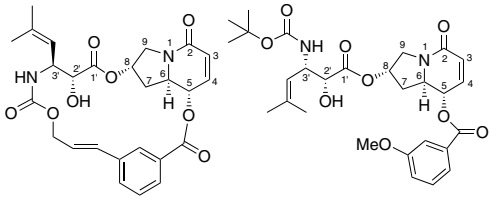




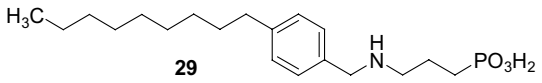
1. $R_4 = R_5 = R_6 = H$
2. $R_4 = OH$; $R_5 = R_6 = H$
3. $R_4 = R_5 = H$; $R_6 = OH$
4. $R_4 = R_6 = H$; $R_5 = OH$
5. $R_4 = H$; $R_5 = R_6 = OH$
6. $R_4 = H$; $R_5 = OH$, $R_6 = OCH_3$
7. $R_4 = H$; $R_5 = OCH_3$; $R_6 = OH$
8. C_5, C_6 dihydro analog of **5**
9. $R_4 = R_6 = OH$; $R_5 = H$

10. $R_4 = OGlu$; $R_5 = R_6 = H$
11. $R_4 = R_5 = H$; $R_6 = OGlu$
12. $R_4 = H$; $R_5 = OSO_3^-$, $R_6 = OCH_3$
13. $R_4 = H$; $R_5 = OGlu$; $R_6 = OCH_3$
14. $R_4 = H$; $R_5 = OCH_3$; $R_6 = OGlu$
15. $R_4 = H$; $R_5 = OH$; $R_6 = OGlu$ or $R_5 = OGlu$; $R_6 = OH$
16. $R_4 = OGlu$; $R_5 = H$; $R_6 = OH$ or $R_4 = OH$; $R_5 = H$; $R_6 = OGlu$

Syntheses and anti-inflammatory effects of a series of novel acanthoic acid analogs are reported. In particular, the mechanistic basis for their excellent anti-inflammatory effects is also described.

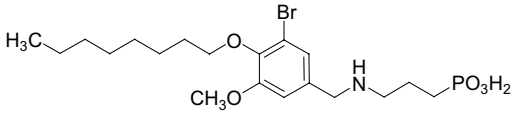


The design, synthesis, and biological activity of several novel cytotoxic alkaloids, mimicking and simplifying the taxoid skeleton are reported.



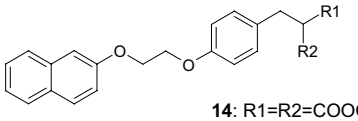
29

3-(N-Alkylamino)propylphosphinic acids exemplified by **29** are potent agonists of four of the five known sphingosine-1-phosphate (S1P) receptor subtypes.

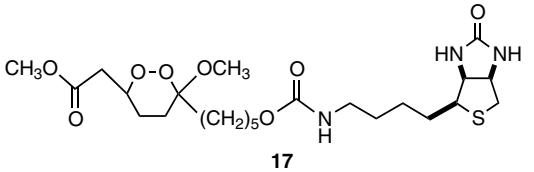


35, $S1P_1$ IC_{50} = 4.1 nM, $S1P_3$ IC_{50} = 2100 nM

3-(N-Benzylamino)propylphosphonic acid S1P receptor agonists exemplified by **35** that maintain affinity for $S1P_1$ and have decreased affinity for $S1P_3$ are efficacious, but exhibit decreased acute cardiovascular toxicity in rodents than do nonselective agonists.

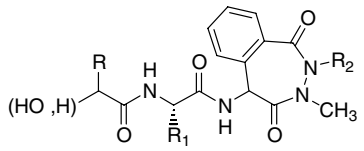


14: R1=R2=$COOCH_3$
17: R1=COOH, R2=$CONH_2$

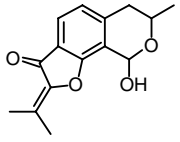


17

Two biotinylated probes to elucidate the target molecules of spongean anti-malarial peroxides were designed and synthesized. They showed potent anti-malarial activity, and one of them (**17**) was proved to form an irreversible binding with protein in a model experiment.

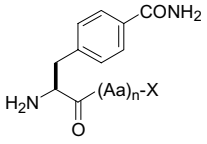


Introduced 2,3-benzodiazepin-1,4-diones as peptidomimetics at the carboxy terminus of hydroxytriamides.

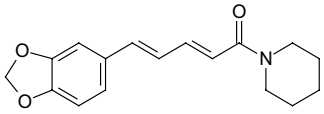


Pseudodeflectusin

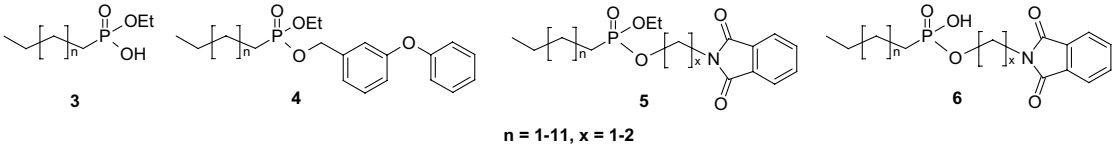
9-hydroxy-7-methyl-2-(methylethylidine) -furano[3,2-*H*]isochroman-3-one

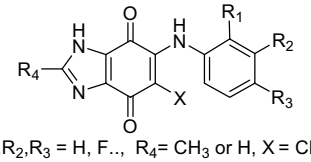


Thyromimetics having improved selectivity for TR-β1 were prepared by replacing the 3′-isopropyl group of **2** and **3** with substituents having increased steric bulk.

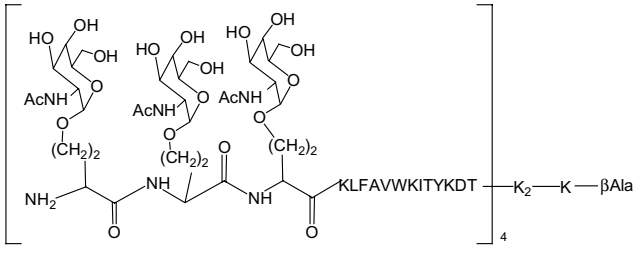


Piperine, isolated from *Piper nigrum*, and twelve synthetic derivatives were evaluated for trypanocidal activity against epimastigote and amastigote forms of the protozoan parasite *Trypanosoma cruzi*. The results obtained point to piperine as a template for the development of new drugs with trypanocidal activity.

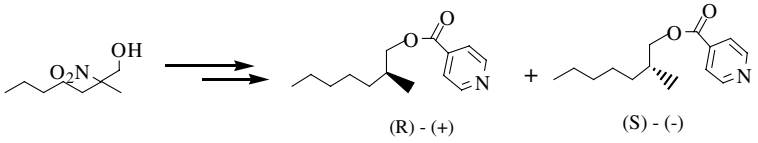


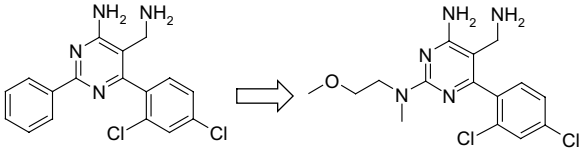


Benzimidazole-4,7-diones were synthesized and tested for their antiproliferative activity on rat aortic smooth muscle cells. Among them, 6-arylamino-5-chloro-2-methyl-benzimidazole-4,7-diones exhibited potent antiproliferative activity.

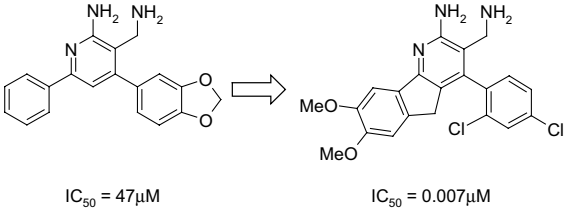


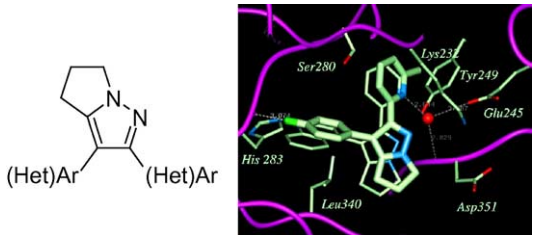
The glycopeptide vaccine MAG:Tn(hSer)3-PV induces a strong antibody immune response (IgG), which recognizes native tumor-associated antigens at the surface of human tumor cells.

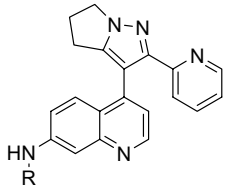


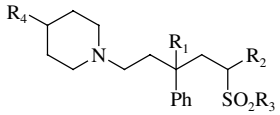


Phospholipidosis liability and CYP3A4 inhibition were addressed in a series of DPP-IV inhibitors.

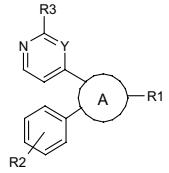




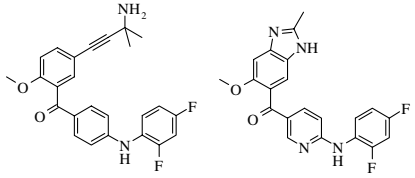




Ongoing efforts from these laboratories have resulted in the identification of 5-(piperidin-1-yl)-3-phenylpentylsulfones as a potent CCR5 antagonists. The syntheses and biological activities such as analogs are described.

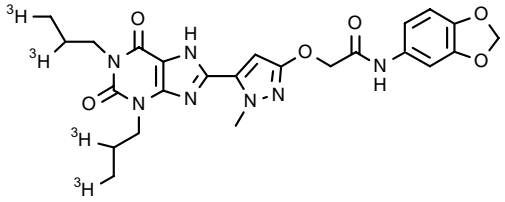


A pilot library of trisubstituted oxazoles, thiazoles, imidazoles (1,2,4- and 2,4,5-substituted) and imidazo[1,2-*b*]pyridines was prepared and evaluated in vitro and in vivo as p38α inhibitors. Four structures—**32**, **37**, **45** and **59**—were identified as potent inhibitors of p38α with high oral efficacy in three models of rheumatoid arthritis.

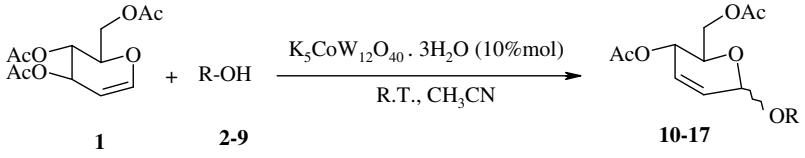


10b **17b**

10b and **17b** were identified as the most potent and selective compounds of the series, demonstrating IC_{50}s of 14 and 21 nM against p38α and efficacy in the rat CIA model with ED_{50}s of 9.5 and 8.6 mg/kg po qd. The effect of a set substituents on in vitro and in vivo potency is discussed.



The synthesis and the preliminary biological evaluation of a selective antagonist radioligand for the human A_{2B} adenosine receptors have been described.



1 **2-9** **10-17**

major (α) (84-89) %
minor (β) (11-16) %

2,3-Unsaturated glycopyranosides are produced in excellent yields with good anomeric selectivity, from treatment of tri-*O*-acetyl-D-glucal with several alcohols in the presence of catalytic amount of dodecatungstocobaltate trihydrate as a heterogeneous, cheap and reusable catalyst.

OTHER CONTENTS

*Corresponding author

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 htBl (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htBl (center) allows for functional selection against thrombin (right) [Rajagopal, S.; Meza-Romero, R.; Ghosh, I. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1389].

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