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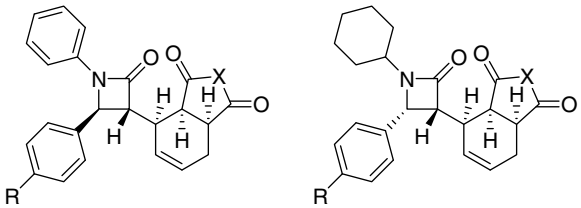
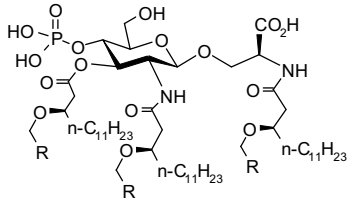
Contents

ARTICLES



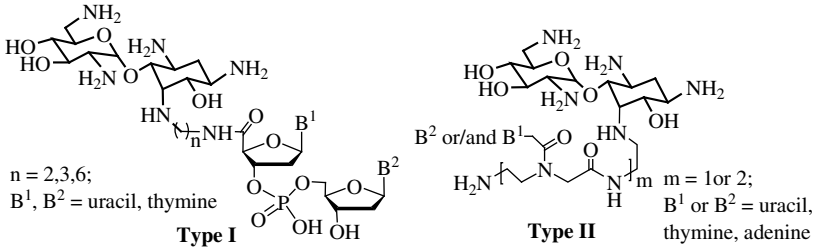
3a R=H, X=O
3b R=OCH_3, X=*N*-Ph

5a R=Cl, X= *N*-*p*-tolyl
5b R=H, X= -CH=CH-



4 R = *n*-C_9H_{19}
5 R = *n*-C_5H_{11}

The novel ether lipid AGPs **4** and **5** were synthesized by a highly convergent method and evaluated along with their ester counterparts for TLR4 activity in both in vitro and in vivo models. Unlike agonist **4**, compound **5** showed species-specific agonist/antagonist activity.



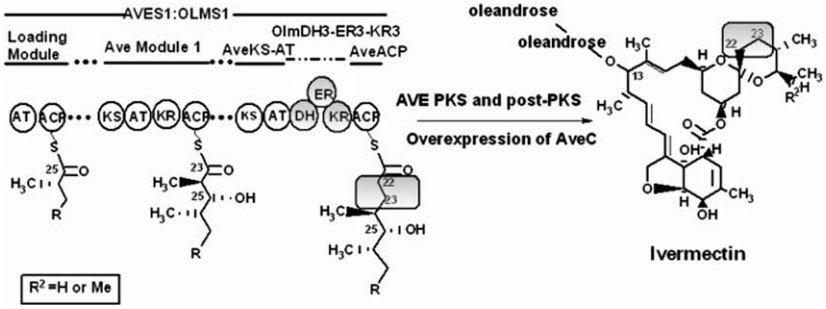
n = 2,3,6;
B^1, B^2 = uracil, thymine

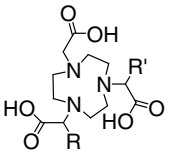
Type I

Type II

m = 1or 2;
B^1 or B^2 = uracil, thymine, adenine

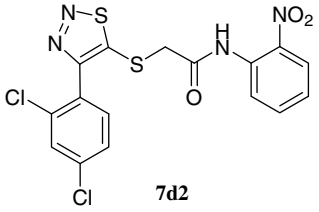
Two types of neamine derivatives were synthesized. Their binding affinities towards RNA were evaluated by SPR and the binding modes with RNA were elucidated by computer modelling.





R = 4-PhOH, 4-PhNCS
R' = H, 4-PhNCS

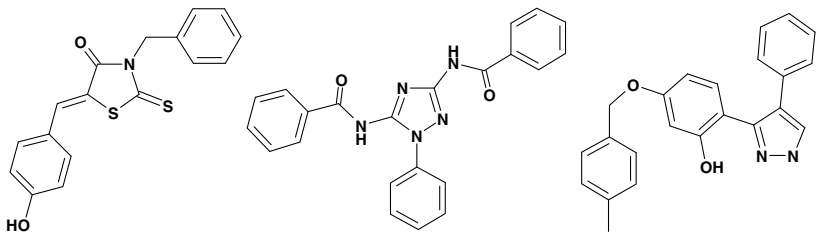
Synthesis, ^{68}Ga-radiolabelling and stability data of three powerful novel chelators for molecular imaging is reported.



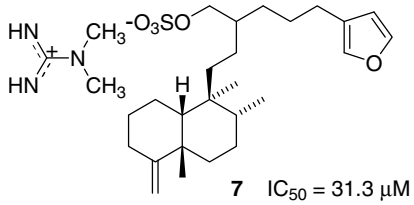
7d2

EC_{50} = 0.059 ± 0.02 μM, SI>4883

A novel series of 1,2,3-thiadiazole thioacetanilide (TTA) derivatives have been designed, synthesized and evaluated for their anti-HIV activities in MT-4 cells. Some derivatives proved to be highly effective in inhibiting HIV-1 replication at nanomolar concentrations. The structure–activity relationship (SAR) is discussed.

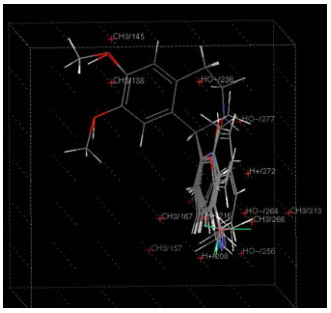


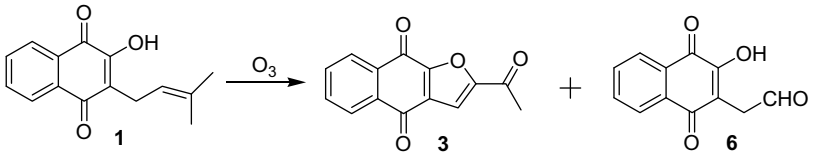
We have discovered three novel inhibitor scaffolds for extracellular signal-regulated kinase 2 (ERK2) by means of a drug design protocol involving the virtual screening with docking simulations and in vitro enzyme assay.

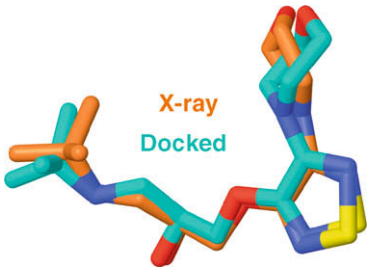


The isolation and bioactivity of seven sesterterpene sulfates are described.

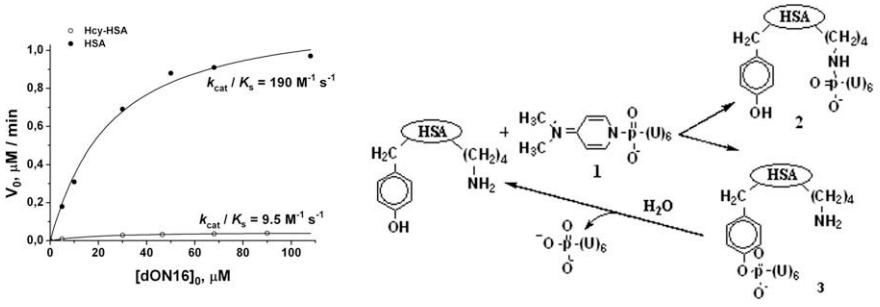
Statistically significant QSAR models have been developed for anti-HIV 1-aryl-tetrahydroisoquinoline analogs using GFA, stepwise-MLR, and MFA-G/PLS techniques. The results obtained by combining these methodologies gain insights into the structural requirements for anti-HIV activity of this class.

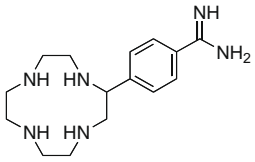






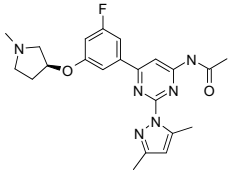
The previous use of a β_2-adrenergic receptor's X-ray in docking studies is now validated with binding data and a recently published X-ray structure with Timolol.





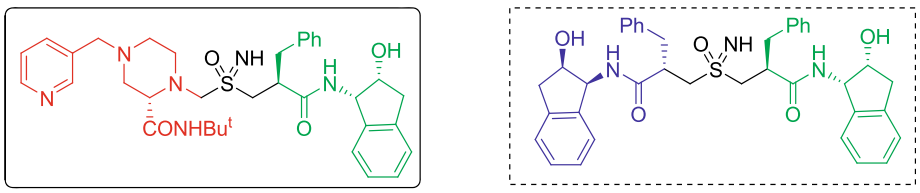
Biological testing of two novel polyazamacrocycles tagged with structural motifs recognized by the P2 aminopurine transporter show these compounds to be selectively toxic for trypanosomes.

The strategy for improving solubility and metabolic stability of a series of pyrimidine-based adenosine A_{2A} antagonists is described.

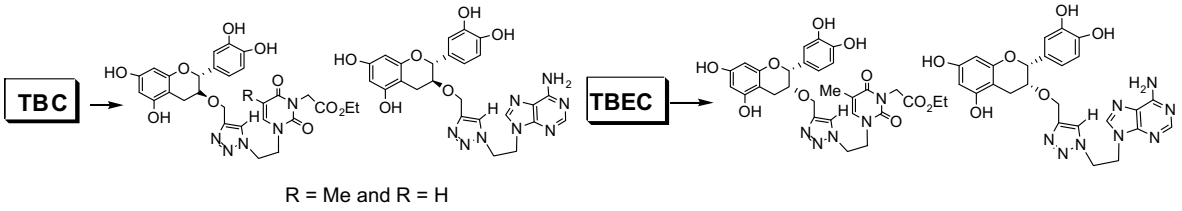


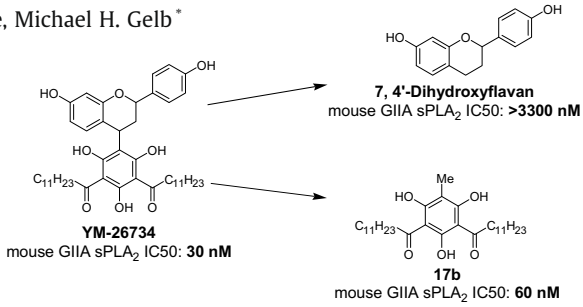
35

K_i (nM) hA_{2A}	1
hA_1/hA_{2A}	218
CL_{int} (HLM) (mL/min/kg)	3
Aqueous solubility (mg/mL)	> 4 @ pH 8.0

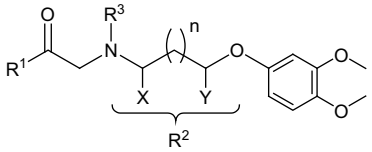


The design and synthesis of protease inhibitors featuring a sulfoximine moiety have been disclosed and the effect of sulfoximine group has been carefully studied and compared using docking models.

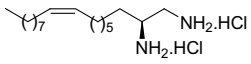




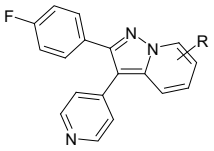
Modeling of YM-26734 in the active site of secreted phospholipase A_2 group IIA led to the design and synthesis of simplified analogs retaining nanomolar potency.



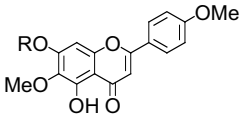
The synthesis and evaluation of (dimethoxyphenoxy)alkylamino acetamides as orexin-2 receptor antagonists are reported.



The synthesis of a selective MGL inhibitor presenting analgesic and anti-inflammatory activity is reported.

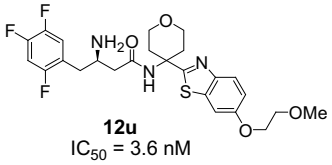


A series of pyrazolo[1,5-*a*]pyridine derivatives was designed and synthesized as novel potent p38 kinase inhibitors. Our approaches towards improving in vitro metabolism and in vivo pharmacokinetic properties of the series are described.



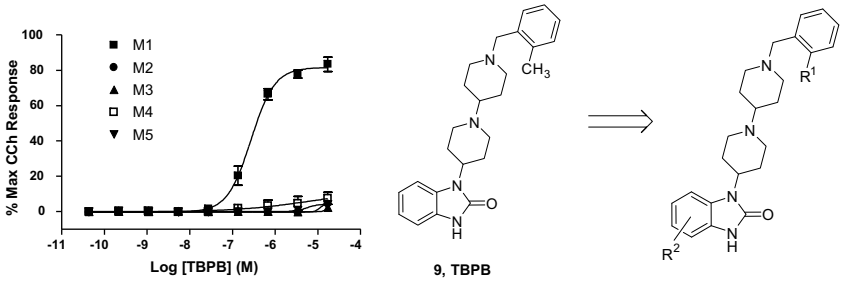
2 R = H IC_{50} 5.3 μM on Caco-2
3 R = $(CH_2)_3N(CH_3)_2$ IC_{50} 7.2 μM on COR-L23

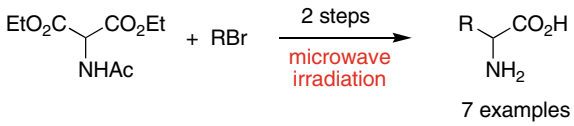
The synthesis of the 7-*O*-dialkylaminoalkyl cytotoxic pectolinarigenin derivatives is reported.

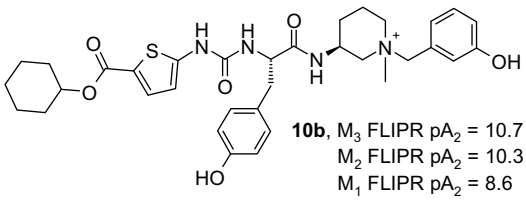


12u
IC_{50} = 3.6 nM

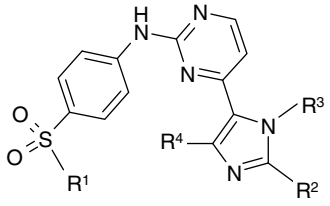
The synthesis and SAR of analogues of the M1 allosteric agonist TBPB is described. With slight structural changes, mAChR selectivity was maintained, but the degree of partial agonism varied considerably.





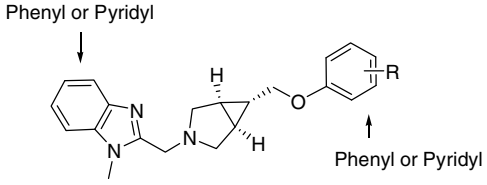


SAR exploration of multiple regions of a tyrosine urea template led to the identification of very potent muscarinic acetylcholine receptor antagonists such as **10b** with good sub-type selectivity for M_3 over M_1. The structure–activity relationships (SAR) and optimization of the tyrosine urea series are described.

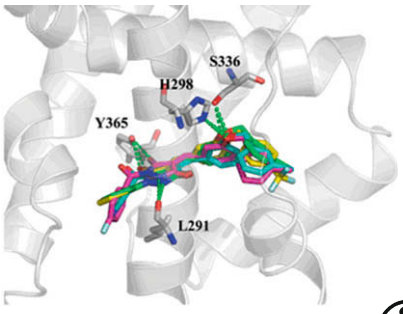


3

The SAR and development of an imidazole series (**3**) of CDK inhibitors are reported.

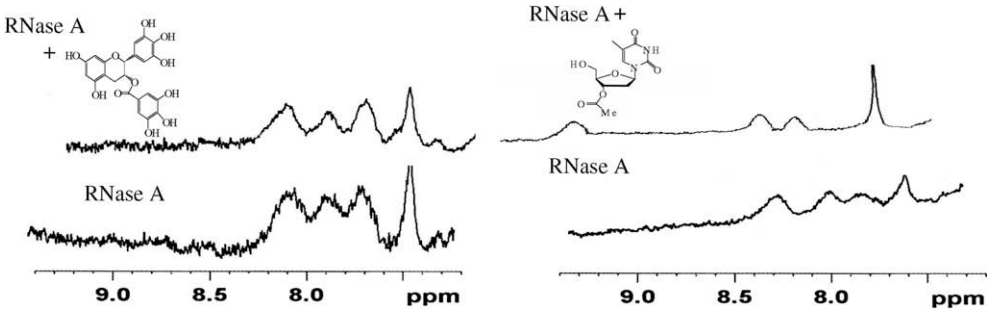


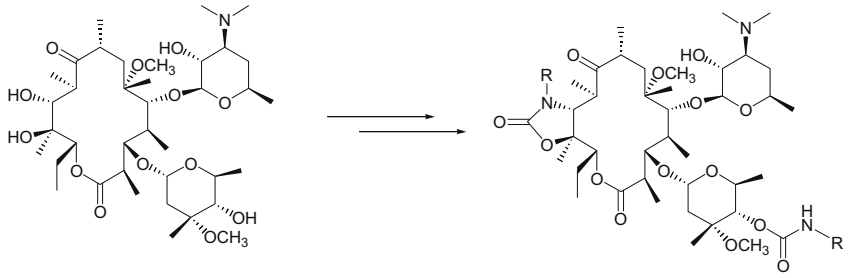
A novel series of mGluR2 positive allosteric modulators, 3-(imidazolyl methyl)-3-aza-bicyclo[3.1.0]hexan-6-yl)methyl ethers, is disclosed.



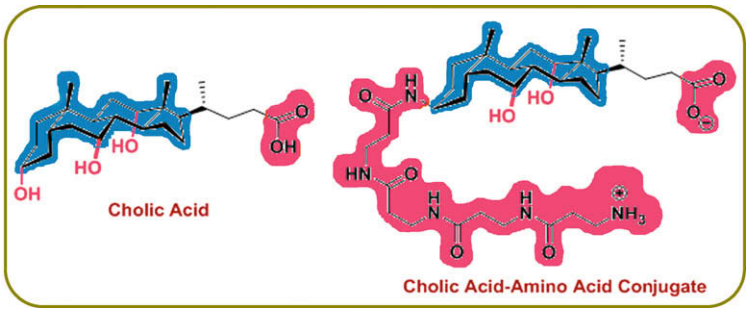
A series of novel non-steroidal compounds as FXR agonists and partial agonists was discovered by means of virtual screen and chemical synthesis.

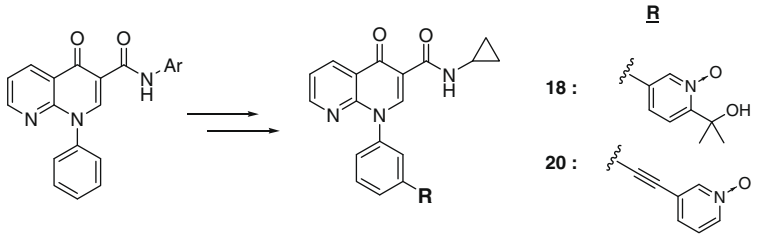
^{1}H NMR of C(2)–H of histidine residues of RNase A and its complexes with noncompetitive (left) and competitive (right) inhibitors.



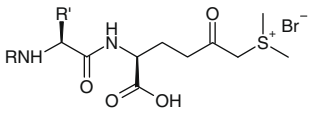


A series of novel 4″-position modified macrolide derivatives has been synthesized via a facile procedure. Their antibacterial activities were reported.

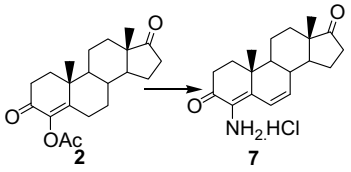




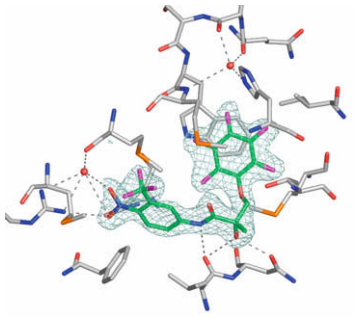
Discovery of the potent and orally active PDE4 inhibitors **18** and **20** (PDE4A IC_{50} = 6 and 7 nM; HWB IC_{50} = 0.12 and 0.18 μM) is reported.

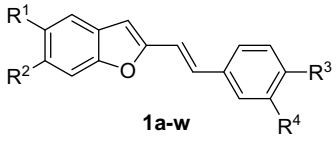


Dipeptide-based sulfonium peptidylmethylketones derived from 6-diazo-5-oxo-L-norleucine (DON) have been investigated as potential water-soluble inhibitors of extracellular transglutaminase. The lead compounds were prepared in four steps and exhibited potent activity against tissue transglutaminase.

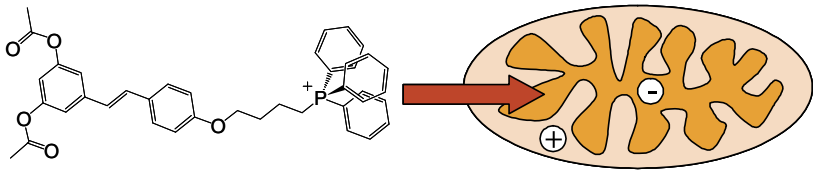


Synthesis of 4-amino-4,6-androstadiene-3,17-dione **7**, an analog of formestane used in breast cancer therapy as an aromatase inhibitor, from 4-acetoxy-4-androstene-3,17-dione **2** is described. This is the first report of a 4-amino diene (4,6) system in this series of molecules. The new and reported molecules were screened by the National Cancer Institute (NCI, Bethesda, USA) for in vitro antitumor activity against 60 human cancer cell lines. Compound **7** showed best activity against breast cancer cell line (MCF-7).

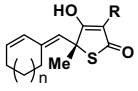




The synthesis of a novel series of aminostyrylbenzofuran derivatives **1a**–**w** and their inhibitory activities for Aβ fibril formation by thioflavin T (ThT) assay were described. Among them, compounds **1i** and **1q** exhibited excellent inhibitory activities (IC_{50} = 0.07 and 0.08 μM, respectively) than those of Curcumin (IC_{50} = 0.80 μM) and IMSB (IC_{50} = 8.00 μM) as reference compounds. Both compounds were selected as promising candidates for further biological evaluation.

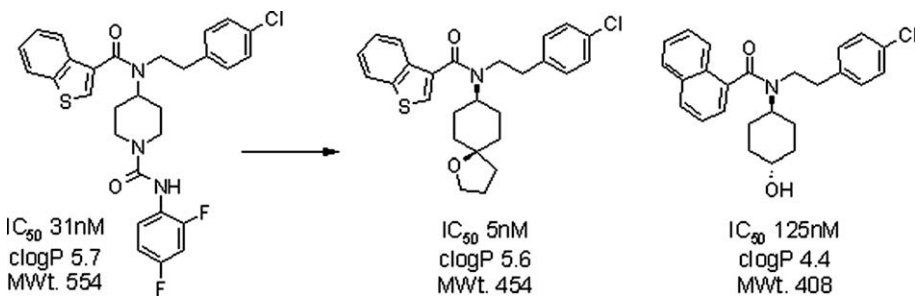


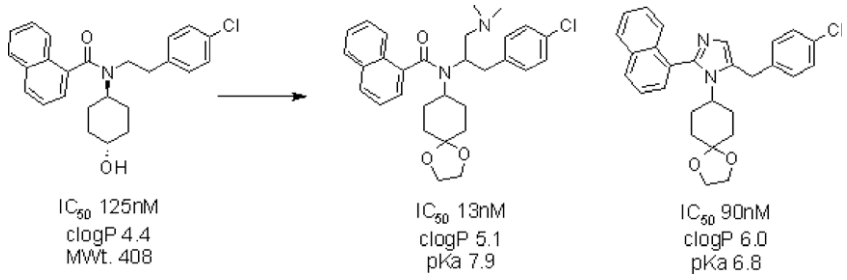
Synthesis, mitochondriotropic behavior, and cytotoxicity of resveratrol-triphenylphosphonium conjugates.

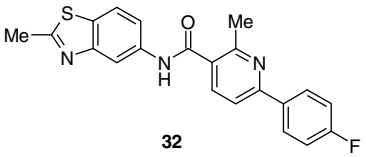


4: R = Me; **5**: R = H
a: n = 1; **b**: n = 2; **c**: n = 3.

While all the synthesized congeners lacked in vitro antibacterial activity, some of the congeners (*ent*-**4b**, **5b** and *ent*-**4c**) were found to exhibit more potent mammalian type I FAS inhibitory activity than (*S*)-3-demethylthiolactomycin (*ent*-**2**) having an unnatural configuration.

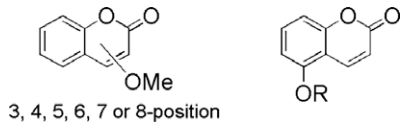




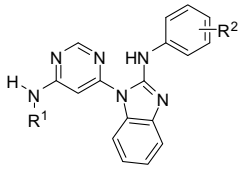


32

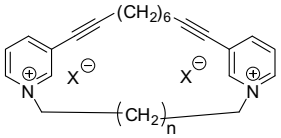
N-Quinolin-7-yl-6-phenylnicotinamide (**2**) was previously identified as a potent TRPV1 antagonist with activity in an in vivo model of inflammatory pain. Optimization of this lead through modification of both the biaryl and heteroaryl components has resulted in the discovery of 6-(4-fluorophenyl)-2-methyl-*N*-(2-methylbenzothiazol-5-yl)nicotinamide (**32**; SB-782443) which possesses an excellent overall profile and has been progressed into pre-clinical development.



All monomethoxycoumarins and several 5-alkoxycoumarins were examined nematicidal activity and environment safety using crustacean and fish. Among them 5-alkoxycoumarins produced an excellent result even though their simple skeletons.

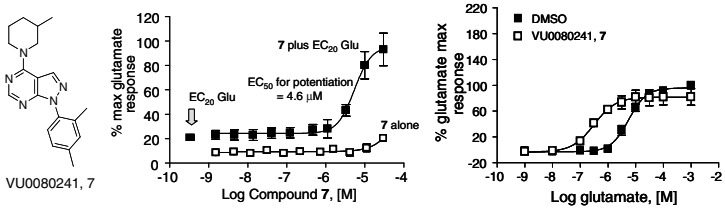


A series of 4-amino-6-benzimidazole-pyrimidines were designed and synthesized as potent Lck inhibitors.

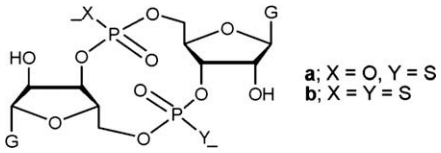


5b. n = 7, X = Br, *Ki* = 1.4 μM
5c. n = 8, X = I, *Ki* = 0.8 μM

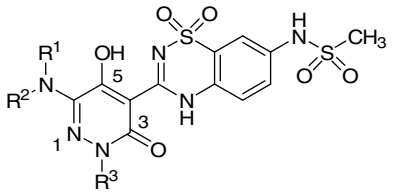
bis-Pyridinium cyclophanes (**5**) designed as conformationally restricted *bis*-quaternary ammonium compounds exhibited high affinity for the blood–brain barrier choline transporter; **5c** and **5b** (K_i = 0.8 and 1.4 μM, respectively) represent two of the most potent blood–brain barrier choline transporter ligands known.

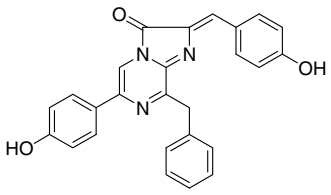


The synthesis and SAR of a novel mGluR4 positive allosteric modulator **7**, VU0080241, is described. VU0080241 displayed an EC_{50} of 4.6 μM and shifted the glutamate response curve 11.8- to 27-fold to the left.



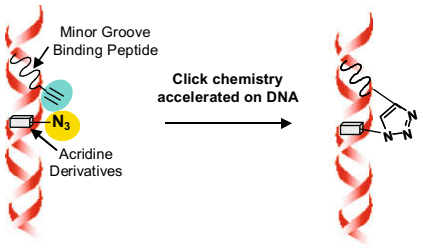
The phosphorothioate analogues of cdiGMP were synthesized and their immunostimulatory properties were compared.



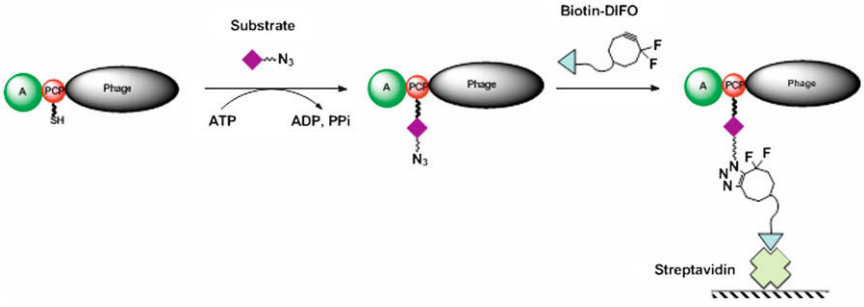


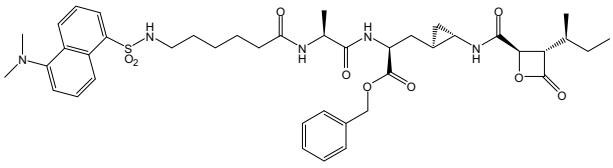
Dehydrocoelenterazine

The enhancement of pholasin luminescence by addition of dehydrocoelenterazine is reported.



We have developed a new methodology for producing new molecules that bind to dsDNA using the DNA-templated click chemistry.





OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of *R*-**22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5677.]

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