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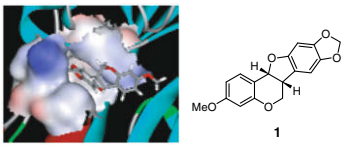
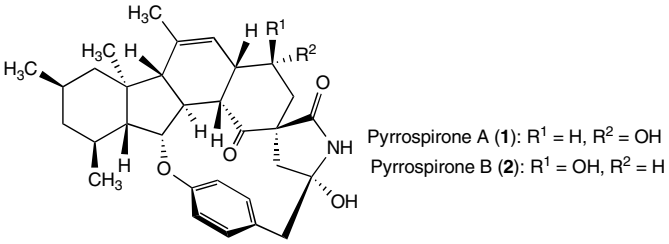
Contents

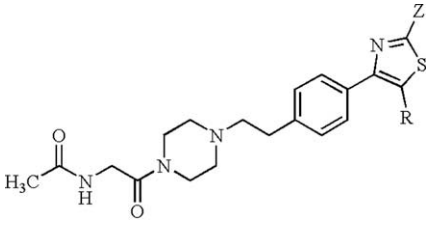
ARTICLES

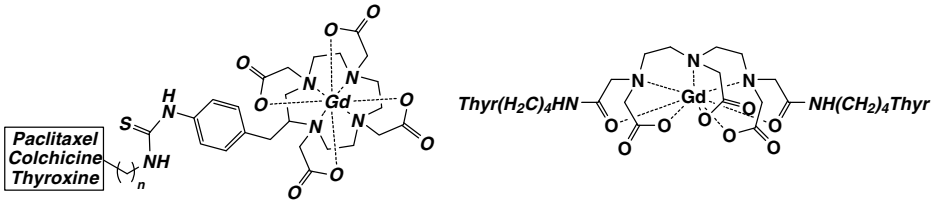


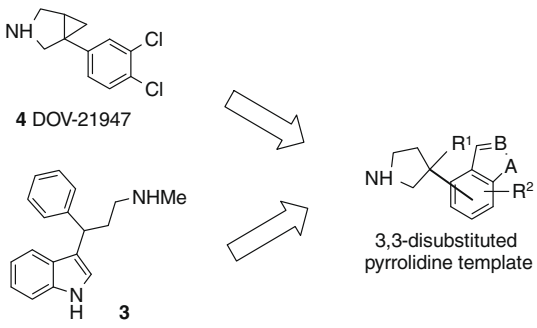
Neuraminidase inhibitory capacity of pterocarpans and flavanones from *Sophora flavescens* was studied. Especially, pterocarpan skeleton was found as a lead structure for neuraminidase inhibitor.

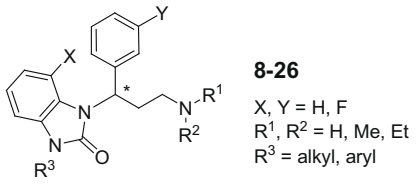


Pyrrospirones A and B have been isolated from the endophytic fungus *Neonectria ramulariae* Wollenw KS-246. The compounds exhibited cytotoxicity and induced apoptosis in human promyelocytic leukemia HL-60 cells.

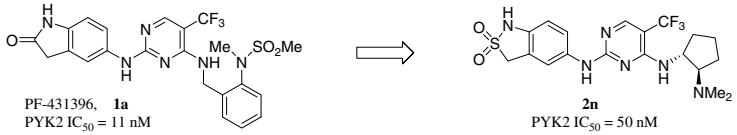




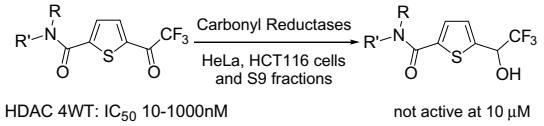




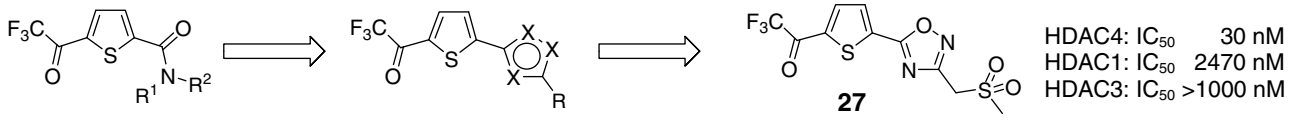
Several compounds from a novel class of 3-(3-amino-1-phenyl propyl)-1,3-dihydro-2*H*-benzimidazol-2-ones demonstrated potent norepinephrine reuptake inhibition (IC_{50} 6–25 nM) and excellent selectivity (>100-fold) against serotonin and dopamine uptake transporters.



Synthesis and structure–activity relationships for a series of diaminopyrimidines as proline-rich tyrosine kinase (PYK2) inhibitors are described. Strategies for the elimination of reactive metabolite formation within this chemical series are also described.

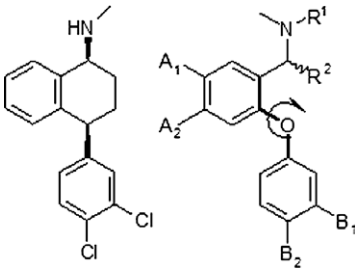


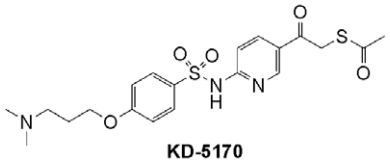
The cause for the lack of cellular activity of the 5-(trifluoroacetyl)-thiophene-2-carboxamides was investigated. A rapid screening assay identified analogs as potent, selective, and metabolically stable class II HDAC inhibitors.

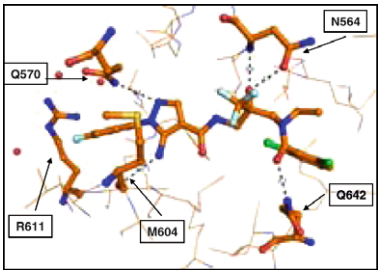


Replacement of the carboxamide moiety of trifluoroacetylthiophene HDAC4 inhibitors with bioisosteric pentatomic heteroaromatics led to the discovery of a novel series of potent and highly selective low nanomolar class II HDAC inhibitors.

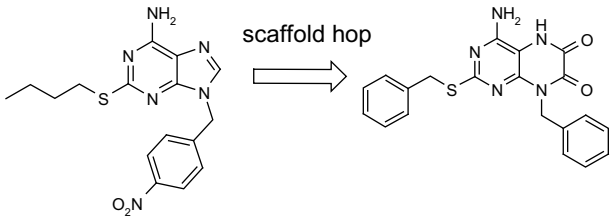
QSAR models have been used to evaluate activities for compounds in the phenoxyphenyl-methanamine (PPMA) class of compounds. These models utilize Hammett-type donating–withdrawing substituent values as well as simple parameters to describe substituent size and elucidate the SAR of the 'A' and 'B' rings. Using this methodology, intuitive QSAR relationships were found for the three biological activities with R^2 values of 0.73, 0.45, and 0.58 for 5HT$_{2A}$, SerT, and hERG activities.



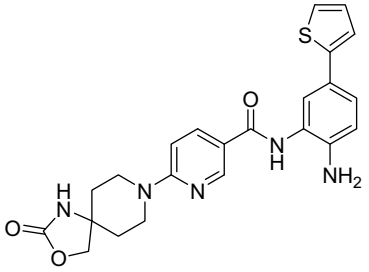


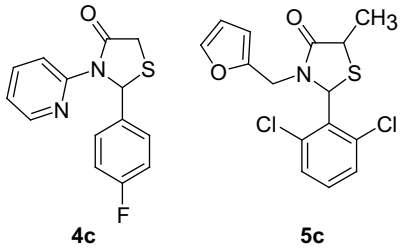


The X-ray crystal structure of **1** in the GR ligand-binding domain is reported.



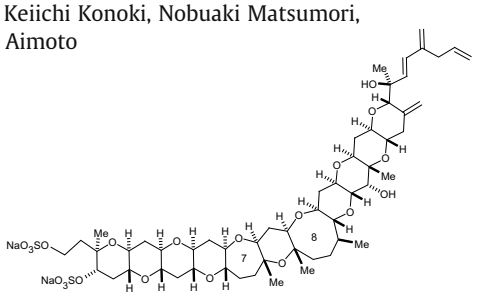
A successful scaffold-hopping approach gave a novel series of inhibitors of bacterial glutamate racemase (MurI). Early SAR studies of the 8-benzyl pteridine-6,7-diones led to compounds with micromolar enzyme potency and antibacterial activity.



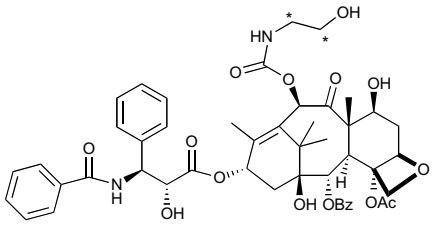


4c **5c**

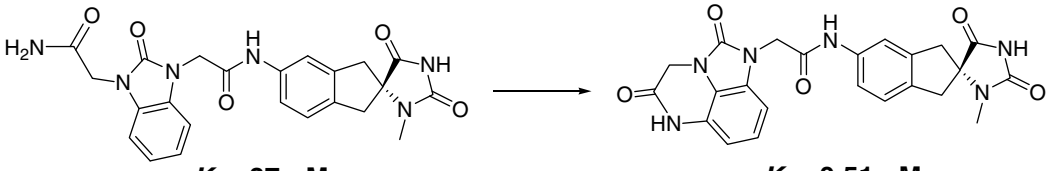
A library of 4-thiazolidinones was evaluated for their ability to inhibit HCV NS5B. The two most active compounds **4c** and **5c** exhibited an IC_{50} of 31.9 μM and 32.2 μM, respectively, against HCV NS5B.



Saturation transfer difference NMR spectra revealed that yessotoxin interacts with glycophorin A with a polyene side chain and angular methyl groups.

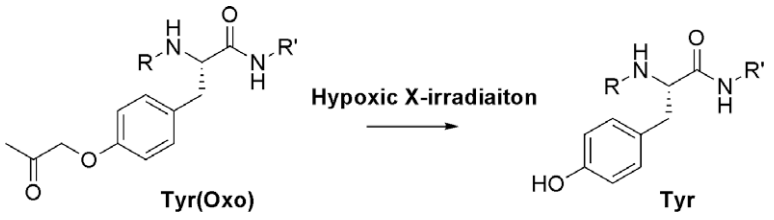


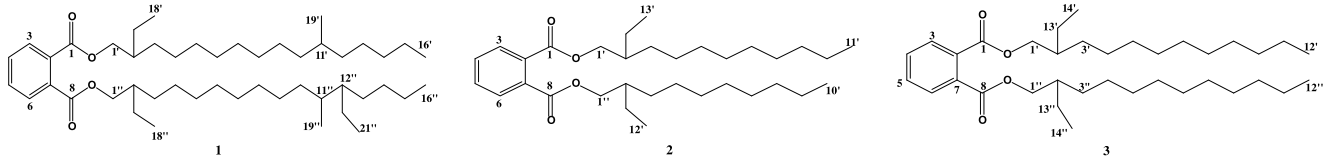
[^{14}C]-CNDR-29



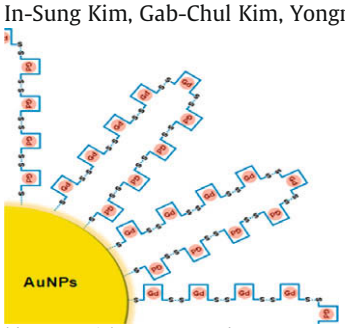
K_i = 37 nM K_i = 0.51 nM

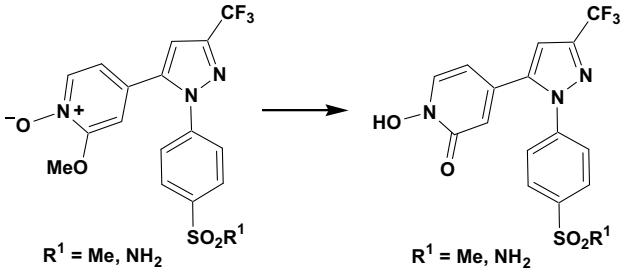
Elaboration of the benzimidazolone core of spirohydantoin CGRP receptor antagonists is described.

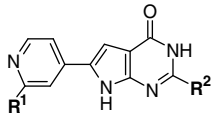




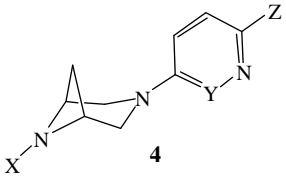
Three new phthalate acid derivatives, 2,12-diethyl-11-methylhexadecyl 2-ethyl-11-methylhexadecyl phthalate (**1**), 2-ethyldecyl 2-ethylundecyl phthalate (**2**), and bis(2-ethyldodecyl) phthalate (**3**), were isolated from seahorse, *Hippocampus Kuda* Bleeler, together with a known natural analog bis(2-ethylheptyl) phthalate (**4**). The four phthalate derivatives showed dose-dependent cathepsin B inhibitions activities with IC_{50} values of 0.13 mM (**1**), 0.21 mM (**2**), 0.18 mM (**3**), and 0.29 mM (**4**), respectively.





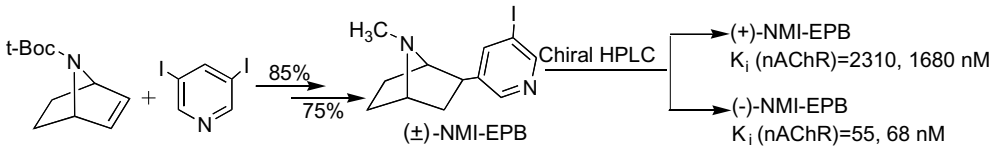


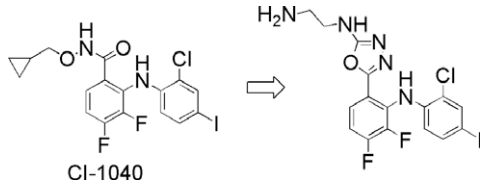
1

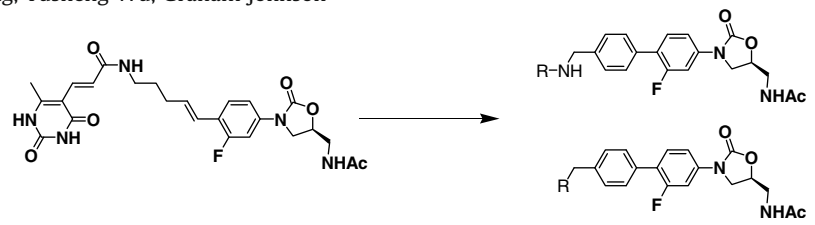


4

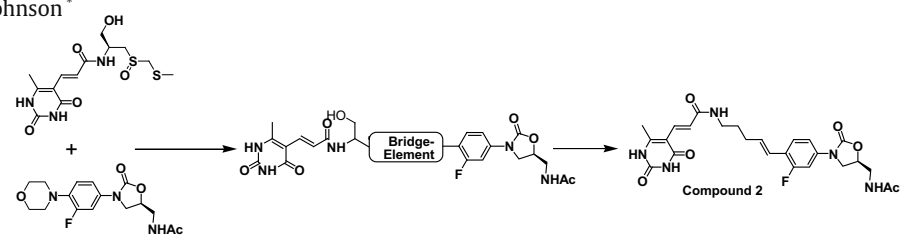
X = H, Y = CH, Z = Cl (**a**)
X = H, Y = CH, Z = H (**b**)
X = H, Y = CH, Z = Br (**c**)
X = H, Y = CH, Z = NO_2 (**d**)
X = H, Y = N, Z = Cl (**e**)
X = CH_3, Y = CH, Z = Cl (**f**)



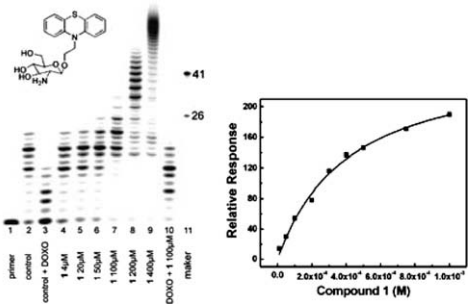




We have developed a first generation of hybrid sparsomycin–linezolid compounds into a new family of orally bioavailable biaryloxazolidinones that have activity against both linezolid-susceptible and -resistant Gram-positive bacteria as well as the fastidious Gram-negative bacteria *Haemophilus influenzae* and *Moraxella catarrahalis*. The convergent synthesis of these new compounds is detailed.

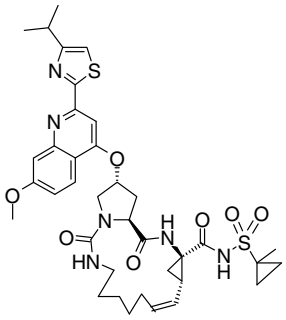


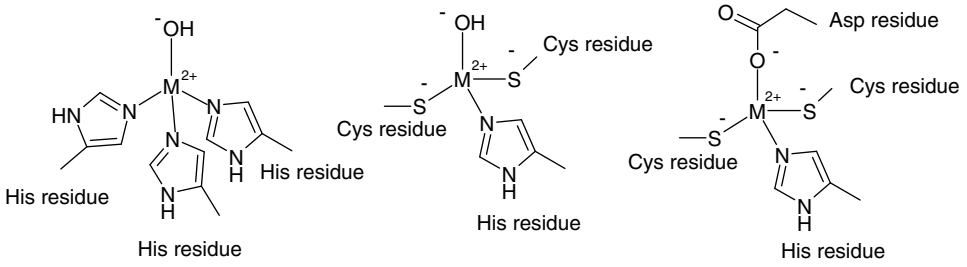
From the X-ray crystal structures of linezolid and the non-selective antibiotic sparsomycin, we have derived a new family of hybrid oxazolidinones. From this initial compound set we have developed a new biaryloxazolidinone scaffold that shows both potent antimicrobial activity as well as selective inhibition of ribosomal translation. The synthesis of these compounds is outlined.



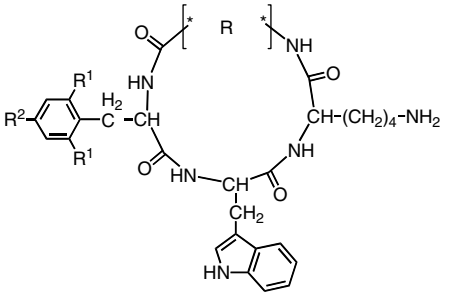
A novel wedge-shaped bulge binder phenothiazine aminosugar was designed and synthesized, which could stimulate DNA slippage synthesis in vitro. The compound–DNA interactions were quantitated by surface plasmon resonance.

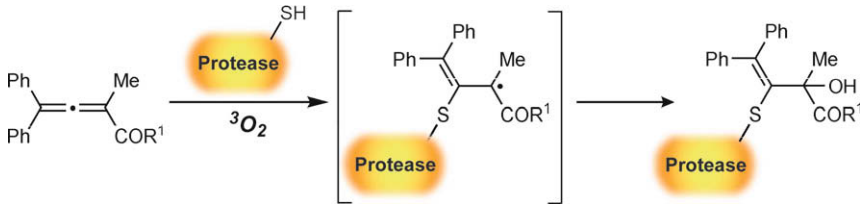
Lead optimization performed on a series of proline-urea based macrocycles led to the identification of very potent and drug like HCV NS3/4A protease inhibitors.

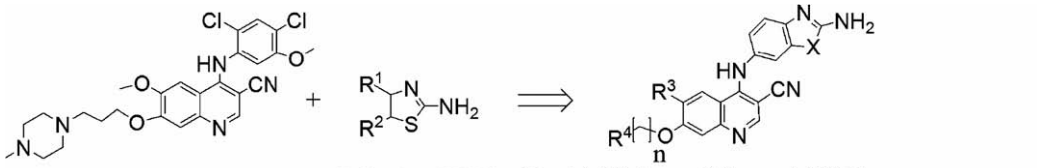


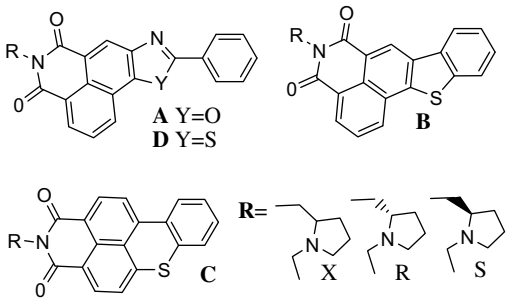


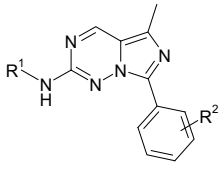
The cyclic somatostatin analogues containing pyrazinone ring and Tyr-D-Trp-Lys that is essential for antiproliferative activity, moderately inhibited the growth of tumor cells. We report herein the SAR study of Tyr residue substituted with more hydrophobic aromatic residues.



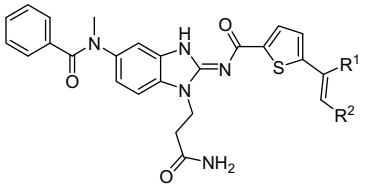




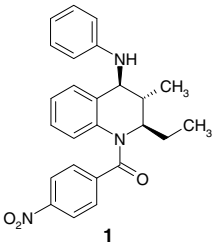




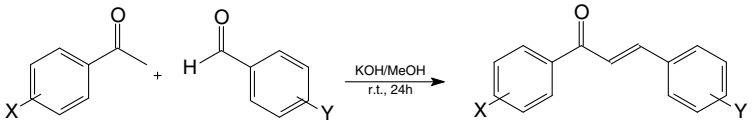
The synthesis and biological activities of imidazo[5,1-*f*][1,2,4]triazin-2-amines (imidazotriazines) as novel polo-like kinase 1 inhibitors are reported.

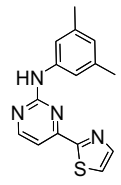


R^1= H or CH_3
R^2= H, CN, COOMe, aromatics and heterocycles

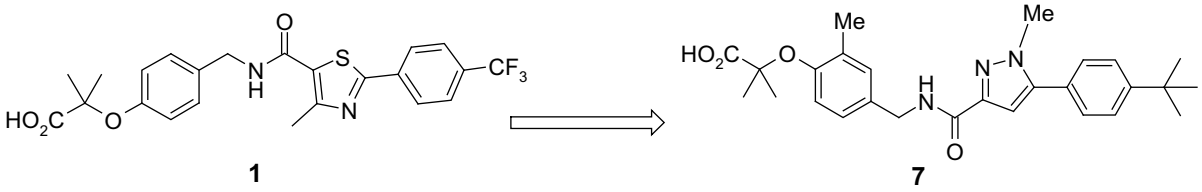


1
FLIPR IC_{50} = 1.6 μM
Binding K_i = 0.5 μM

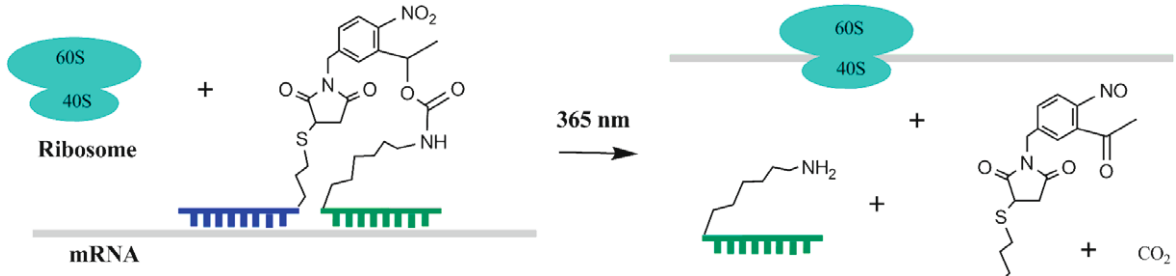




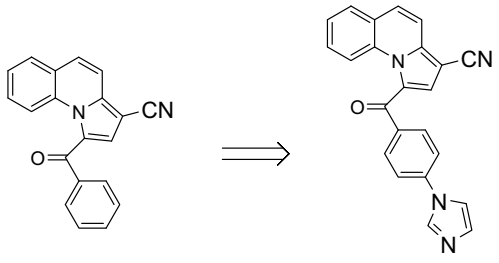
17 K_i = 8 nM



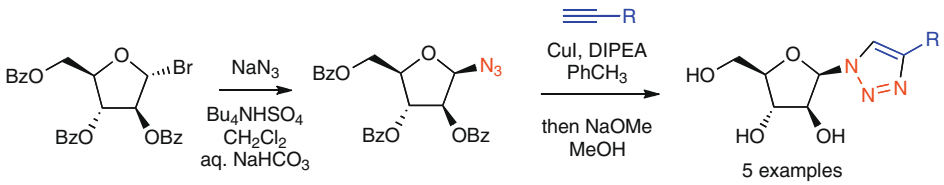
We report the design and synthesis of equipotent PPARα/γ dual agonists starting from the selective PPARα agonist **1**. In vivo data for **7** in the Zucker fa/fa rat are presented.

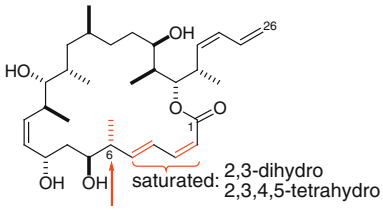


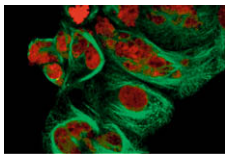
The discovery and SAR studies of a series of apoptosis inducing 1-benzoyl-3-cyanopyrrolo [1,2-*a*]quinolines with modifications at the 1- and 3-positions is reported.



2a (initial hit) **2k** (lead)



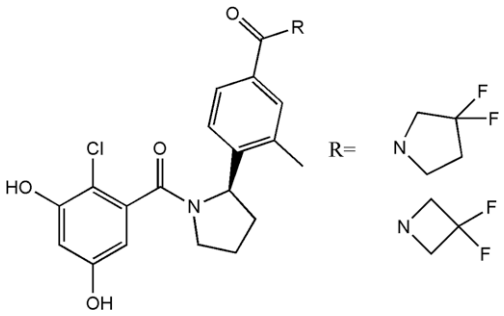


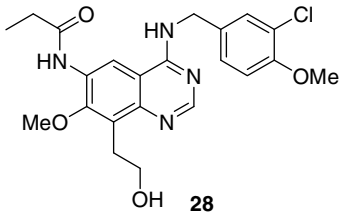


PANC-1 after 100 nM incubation with 6-desmethyldictyostatin

6-Desmethyldictyostatin and 2,3-dihydrodictyostatin displayed low nanomolar antiproliferative activity in Taxol-sensitive and resistant cell lines, intermediate between dictyostatin and discodermolide, while 2,3,4,5-tetrahydrodictyostatin showed activity comparable to discodermolide.

A series of dihydroxylphenyl amides as Hsp90 inhibitor was discovered from a HTS hit using structure based design and library synthesis techniques.





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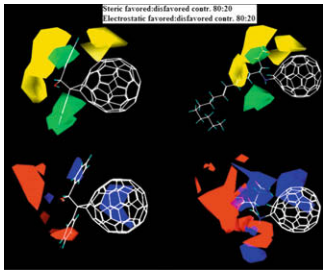
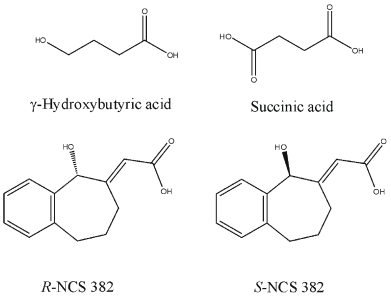
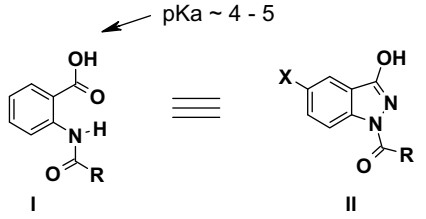


For the first time, a set of experimentally reported [60] fullerene derivatives were subjected 3D-QSAR studies by employing the CoMFA and CoMSIA methodologies. The aim of this study is to propose a series of novel [60] fullerene-based inhibitors with optimal binding affinity for the HIV-1 PR enzyme.





This paper describes the discovery of 1-acylindazol-3-ols as a novel bioisostere of an anthranilic acid. The synthesis and structure–activity relationships of the indazol bioisosteres are described herein.

*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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