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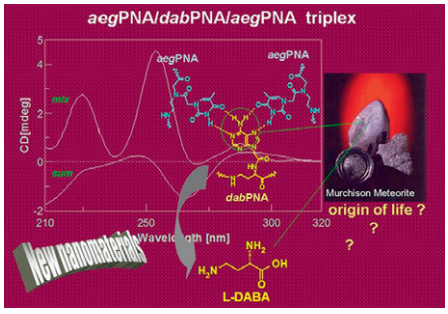
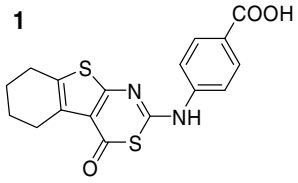
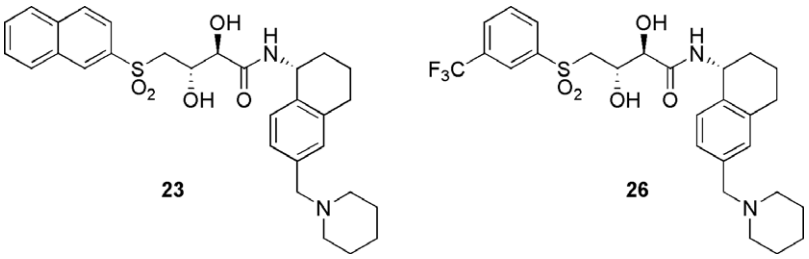
Contents

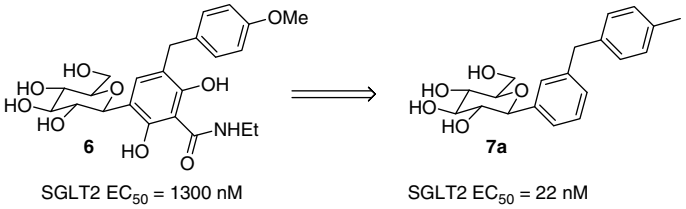
ARTICLES



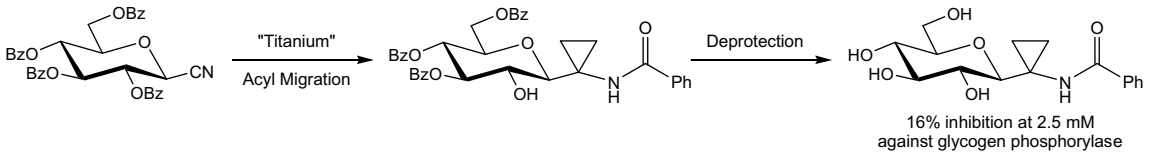


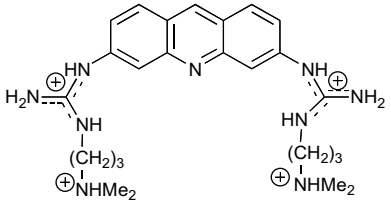
Structure of compound **1** a novel lead for selective inhibitors of multidrug resistance-associated proteins (MRPs).



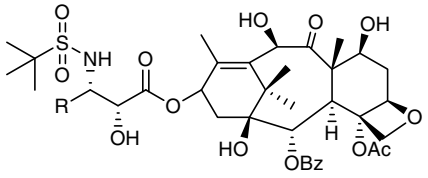


The evolution of potent and selective *C*-arylglucoside SGLT2 inhibitors from lead **6** to **7a** is described.



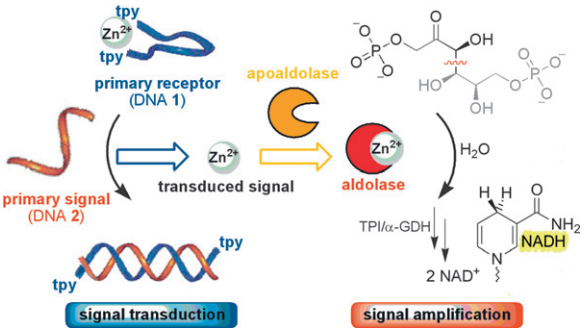


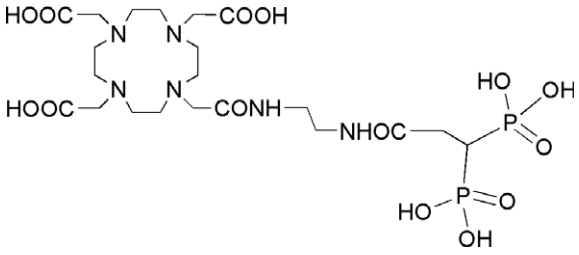
The synthesis and spectroscopic analysis of guanidinoacridines are reported.

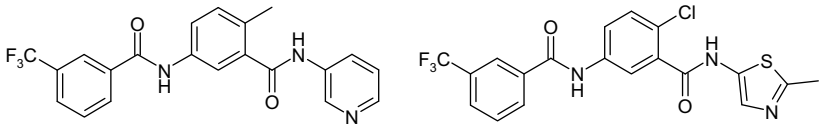


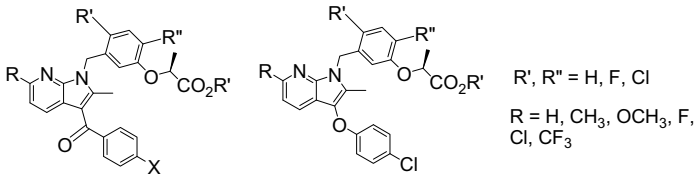
10a R=Ph
10b R=2-Py N-oxide
10c R=3-Py N-oxide

The synthesis of three novel 3′-*N*-*tert*-butylsulfonyl analogues of docetaxel **10a–c** with potent cytotoxicity against several human tumor cell lines is reported.

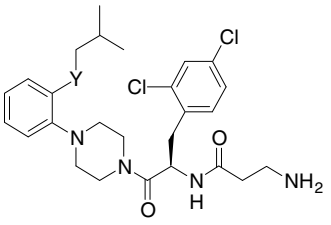




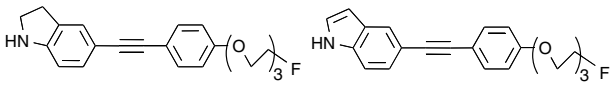




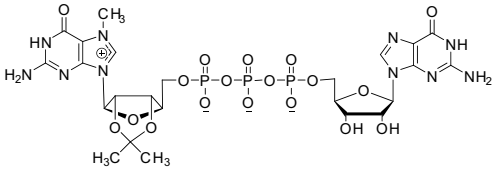
A series of highly functionalized 3-aroyl and 3-phenoxy-2-methyl-7-azaindoles have been identified, which are potent selective PPARγ modulators (SPPARγMs). The SAR around substitution at the 6-position of the azaindole as well as substitution of the *N*-benzyl moiety is reported. 7-Azaindoles have significantly improved off-target profiles compared to the parent indole series.



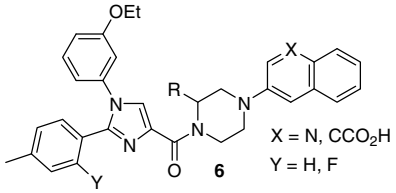
11a: Y = CO, K_i = 24 nM
14a: Y = CHOH, K_i = 8.1 nM
15a: Y = $CHNH_2$, K_i = 3.2 nM



8, *K*i = 4.0 ± 0.8 nM, logP = 2.95 **14**, *K*i = 1.5 ± 0.3 nM, logP = 2.56

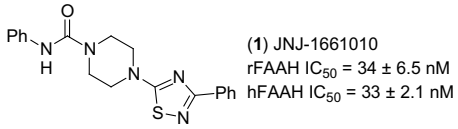


The synthesis and biological evaluation of C2′ and C3′ disubstituted at m^7Guo cap analog, that is, $m^{7,2',3'\text{-isopropylidene}}G[5']ppp[5']G$ is reported.

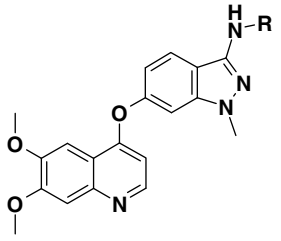


X = N, CCO_2H
Y = H, F
6

The synthesis and biological profile of imidazole carboxamides of general structure 6 as potent and selective cholecystokinin 1 receptor (CCK1R) agonists are described.

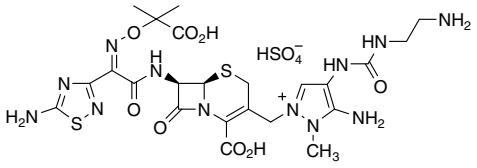


A series of thiadiazolopiperazinyl aryl urea fatty acid amide hydrolase (FAAH) inhibitors is described. The molecules were found to inhibit the enzyme by acting as mechanism-based substrates, forming a covalent bond with Ser241. SAR and PK properties are presented.



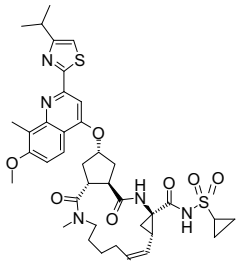
1

A novel class of potent and selective inhibitors of KDR incorporating an indazole moiety **1** is reported. The discovery, synthesis, and structure–activity relationships of this series of inhibitors have been investigated. The most promising compounds were also profiled to determine their pharmacokinetic properties and evaluated in a VEGF-induced vascular permeability assay.



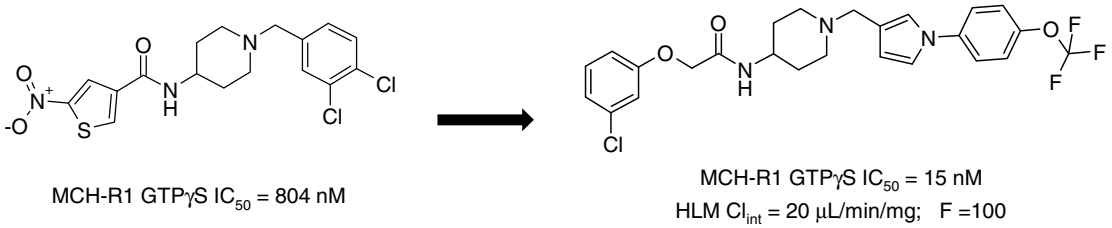
FR264205

Synthesis and biological evaluation of novel cephalosporins with excellent anti-pseudomonal activity are reported.

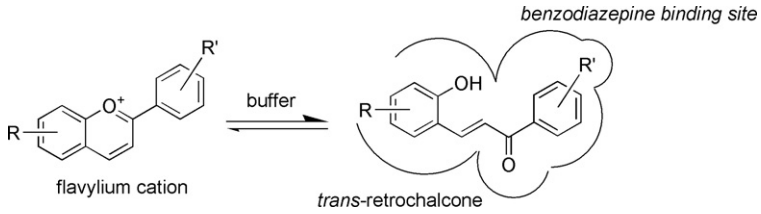


32c
(TMC00435350)

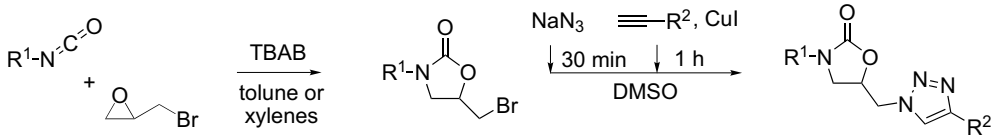
Lead optimization performed on cyclopentane-containing macrocyclic hepatitis C virus NS3/4A protease inhibitors led to the identification of TMC435350, **32c**, as a clinical candidate.



The optimization of an HTS-derived hit compound into a potent and metabolically stable MCH-R1 antagonist is described.

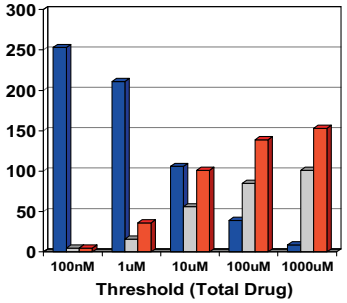


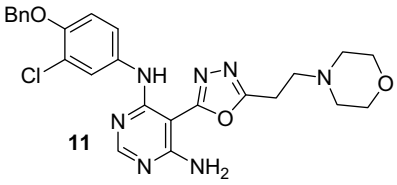
The synthesis of a series of derivatized flavylium cations was undertaken and the affinity to the benzodiazepine binding site on the GABA-A receptor evaluated. The observed high affinity for some derivatives (sub-μM range) was explained by an in vitro transformation of the flavylium cation into the corresponding *trans*-retrochalcone, component which is proposed to be the active species in this series.



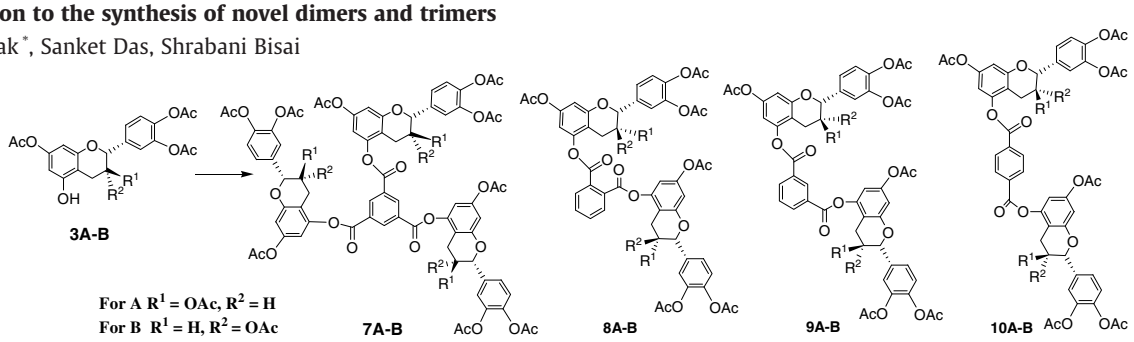
Triazole-oxazolidinones were synthesized using a three-component reaction and screened for antimicrobial activity.

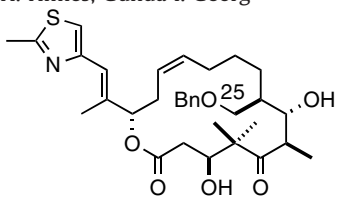
Relationships between physicochemical drug properties and toxicity were inferred from a data set consisting of animal in vivo toleration (IVT) studies on 245 preclinical Pfizer compounds; an increased likelihood of toxic events was found for less polar, more lipophilic compounds. This trend held across a wide range of types of toxicity and across a broad swath of chemical space.





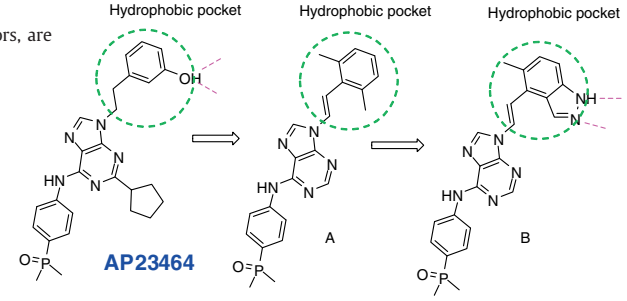
A novel 5-[1,3,4-oxadiazol-2-yl]-*N*-aryl-4,6-pyrimidine diamine **11** was synthesized and found to have potent dual EGFR/HER2 kinase inhibitory activity. The design, synthesis, and proposed binding conformation of **11** in EGFR kinase is described.





The total synthesis of C25-benzyloxy epothilone C is described. A sequential Suzuki–Aldol–Yamaguchi macrolactonization strategy was utilized employing a novel derivatized C8–C12 fragment. The C25-benzyloxy analog exhibited significantly reduced biological activity in microtubule assembly and cytotoxicity assays. Molecular modeling simulations indicated that excessive steric demand in the C25 position may reduce activity by disrupting key hydrogen bonds that are crucial for epothilone binding to β-tubulin.

Novel N^9-arenethenyl purines, optimized potent dual Src/Abl tyrosine kinase inhibitors, are described.



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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