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Chemistry
Letters

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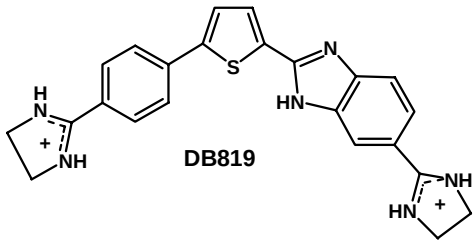
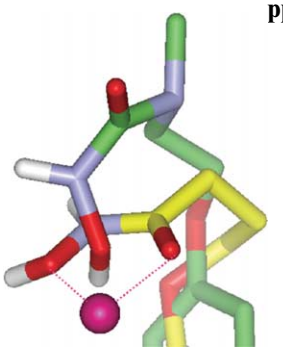
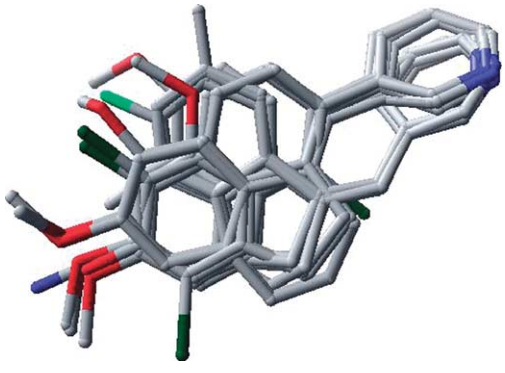
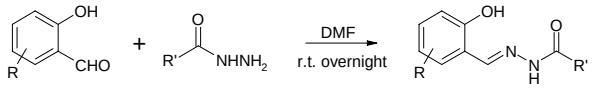
Contents

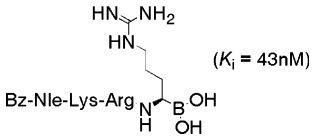
ARTICLES



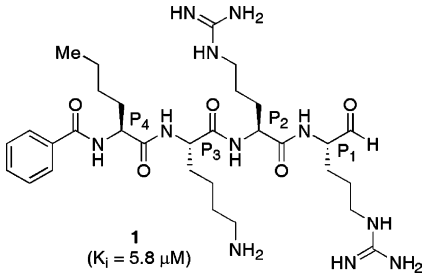




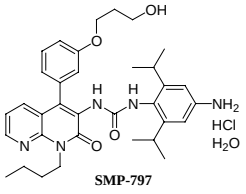




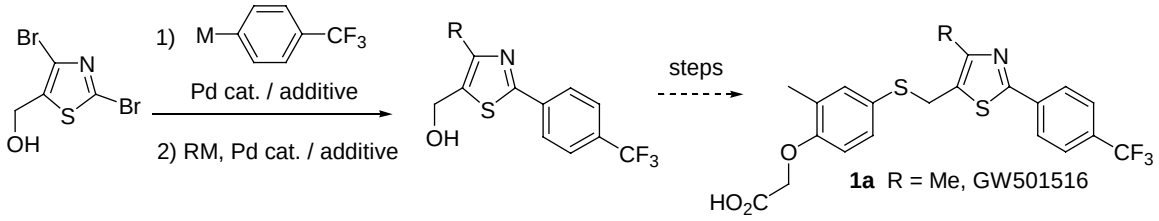
Substrate-based tetrapeptide inhibitors with various warheads were designed, synthesized, and evaluated against the Dengue virus NS3 protease. Effective inhibition was achieved by peptide inhibitors with electrophilic warheads such as aldehyde, trifluoromethyl ketone, and boronic acid. A boronic acid has the highest affinity, exhibiting a K_i of 43 nM.

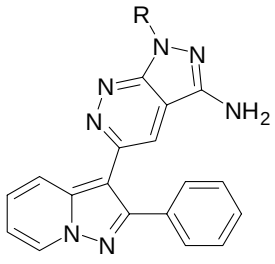


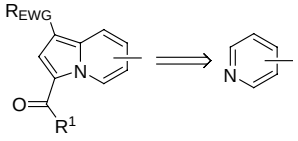
With the aim of discovering potent and selective dengue NS3 protease inhibitors, we systematically synthesized and evaluated a series of tetrapeptide aldehydes based on lead aldehyde **1** (Bz-Nle-Lys-Arg-Arg-H, K_i = 5.8 μM). In general, we observe that interactions of P_2 side chain are more important than P_1 followed by P_3 and P_4. Tripeptide and dipeptide aldehyde inhibitors also show low micromolar activity. Additionally, an effective non-basic, uncharged replacement of P_1 Arg is identified.



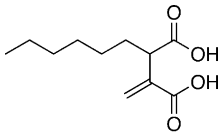
The synthesis and structure–activity relationships of 4-aryl-1,8-naphthyridin-2(1*H*)-on-3-yl urea derivatives with hydrophilic groups are described as a novel potent ACAT inhibitor.





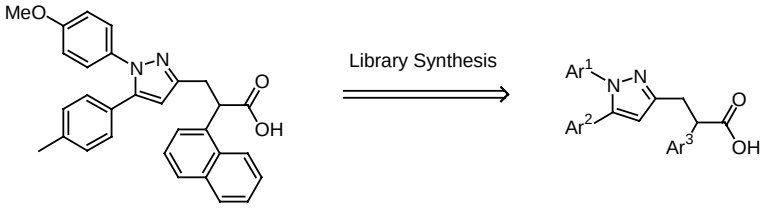


The solid-phase supported synthesis and antiphosphatase activity of a series of indolizines are reported.



Hexylitaconic acid

(−)-Hexylitaconic acid (**1**), a new inhibitor of p53–HDM2 interaction, was isolated from a culture of marine-derived fungus, *Arthrinium* sp. Compound **1** is the second inhibitor isolated from natural resources.



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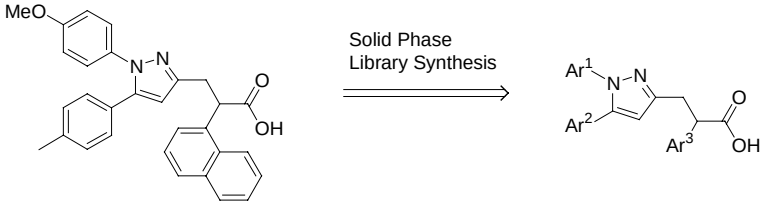

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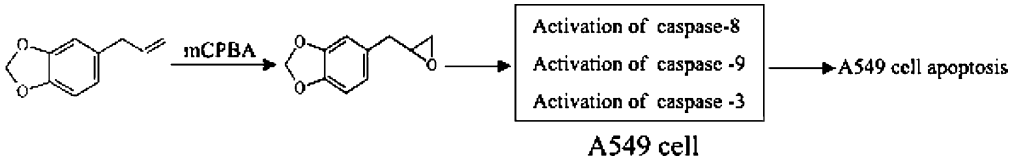
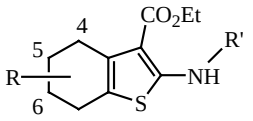
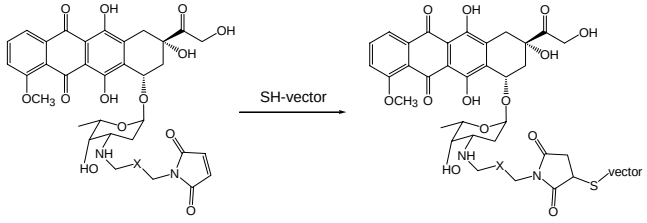


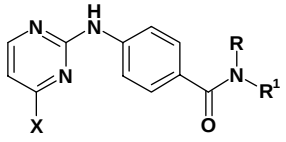
Safrole reacted with 3-chloroperoxybenzoic acid (mCPBA) in chloroform to yield 3,4-(methylenedioxy)-1-(2′,3′-epoxypropyl)-benzene (safrole oxide). Safrole oxide induced apoptosis in A549 human lung cancer cells by activating caspase-3, -8, and -9.



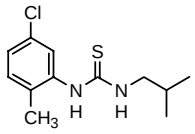
A series of tetrahydrobenzothiophenes have been prepared and identified as potent inhibitors of HCV NS5B polymerase. R = 6,6-Dimethyl, R′ = $CONHSO_2Ar$.



Two universal DOX-linkers were synthesized, which in turn allowed the parallel preparation of DOX conjugates that retain topoisomerase II activity.

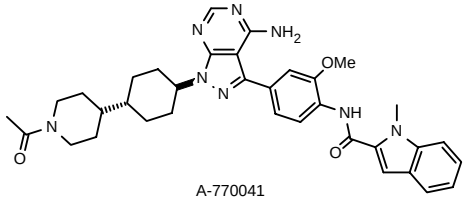


A series of 4-substituted 2-benzamido-pyrimidines has been synthesized and evaluated for their IKK2 inhibitory activities.

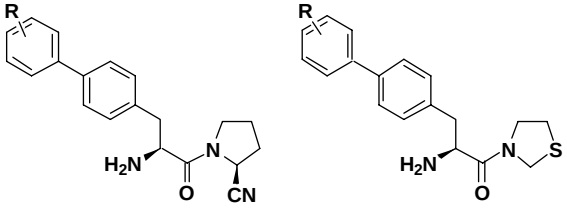


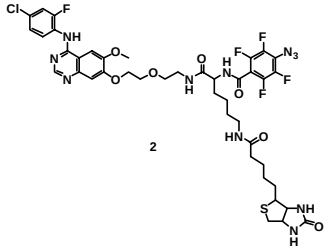
HDL376

A series of 1-alkyl-3-phenylthioureas were evaluated as HDL- and Apo A-I-elevating and triglyceride-lowering agents. Analogue **8d** (HDL376) raises HDL cholesterol in rat, hamster, dog, and monkey models.

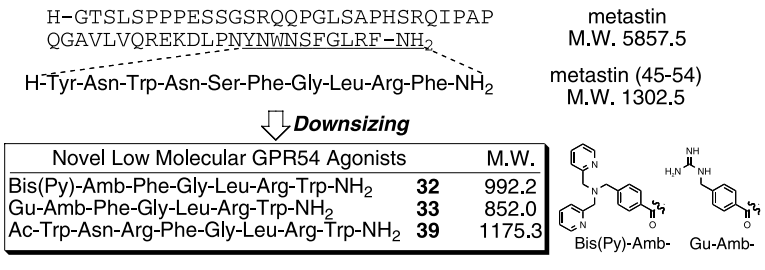


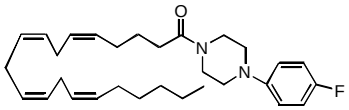
We describe the identification, SAR, and pharmacology of the src-family selective lck inhibitor A-770041 that prolongs the survival of major histocompatibility mismatched allografts in models of solid organ transplant rejection for greater than 65 days.



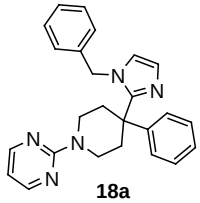


A novel biotin-tagged photoaffinity probe (**2**) was synthesized and evaluated as a vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase inhibitor.





UP70 (CB1 Ki = 0.3 μM; CB2 Ki = 5.1 μM)



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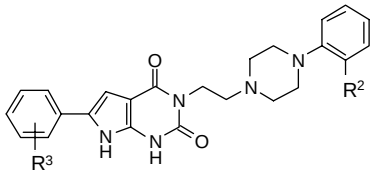
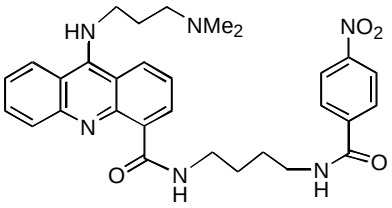
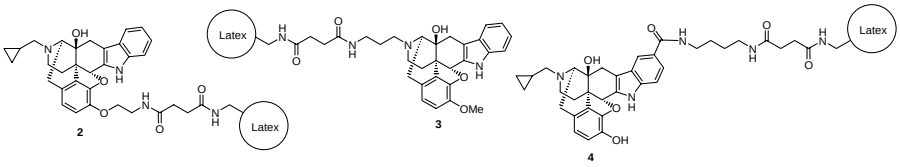
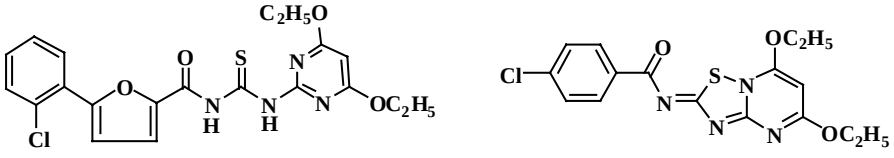




The synthesis and DNA binding of an acridine photoreactive agent are described.

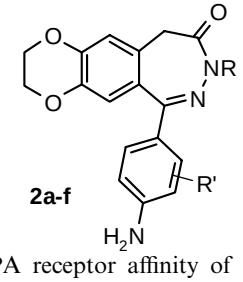


The synthesis of three types of nanoparticles carrying naltrindole derivatives and their use as probes for the affinity isolation of the δ-opioid receptor are described.

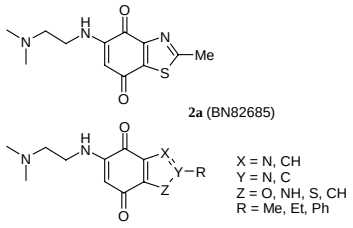


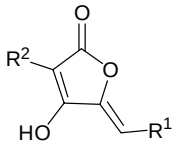
16 IC_{50} =0.08 μM **50** IC_{50} = 0.09 μM

A series of polysubstituted and fused heterocycle derivatives of acylthiourea was prepared and shown to be a novel class of highly potent and selective inhibitors of influenza virus. Derivatives **16** and **50** were further investigated as potential candidates for future development.

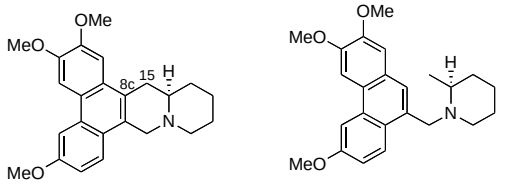


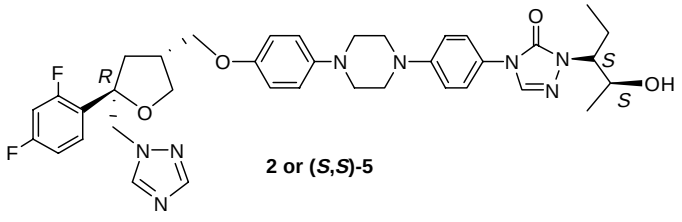
Synthesis, anticonvulsant activity and AMPA receptor affinity of 1-aryl-3,5-dihydro-7,8-ethylenedioxy-4*H*-2,3-benzodiazepin-4-ones (**2a**–**f**) are reported.

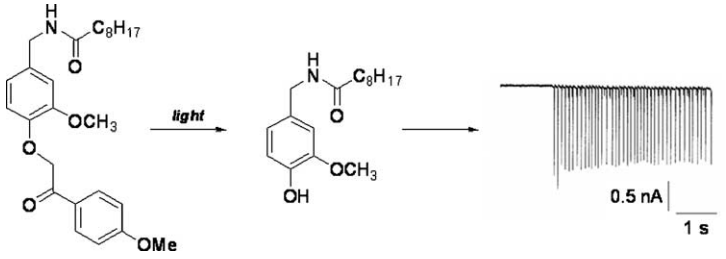




Pulvinones were synthesized (>180) in arrays and evaluated as inhibitors of early stage cell wall biosynthesis enzymes MurA–MurD. Several pulvinones inhibited Mur enzymes with IC_{50}'s in the 1–10 μg/mL range and demonstrated antibacterial activity against Gram-positive bacteria including methicillin-resistant *Staphyloccus aureus*, vancomycin-resistant *Enterococcus faecalis*, and penicillin-resistant *Streptococcus pneumoniae*.

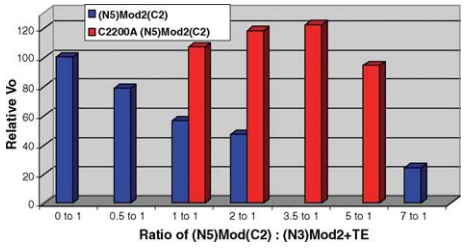


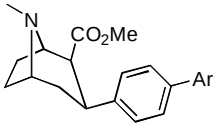




Intracellular photolysis of a novel 'caged' capsaicin analogue results in in vitro activation of the capsaicin receptor TRPV1.

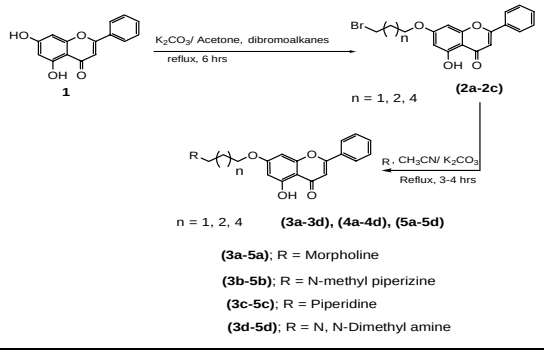
Co-incubation of two engineered variants of 6-deoxyerythronolide B synthase module 2 designed to communicate with one another results in inhibition of catalytic processing of free substrate by the downstream, acceptor module. This inhibition was relieved when a catalytically inactive form of the upstream, donor module was used.





A series of 16 new 2β-carbomethoxy-3β-[aryl or heteroaryl]phenyltropane derivatives was synthesized and evaluated for binding to monoamine transporters. Most of the compounds exhibited subnanomolar affinity for the serotonin transporter (SERT).

A series of 7-*O*-alkyl amino derivatives of chrysin were prepared and their antibacterial potential is studied.



OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

View of the crystal structure of the DB819-d(CGCGAATTCGCG)$_2$ complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 15.). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, *14*, 33.]

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