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Bioorganic & Medicinal Chemistry Letters

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Contents

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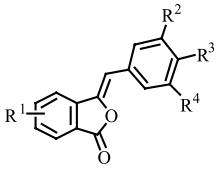

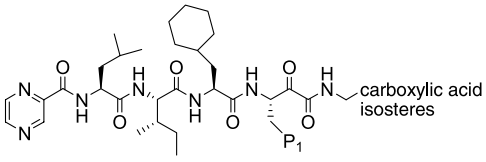

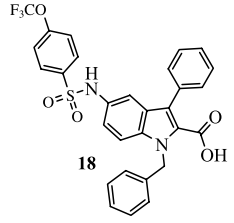

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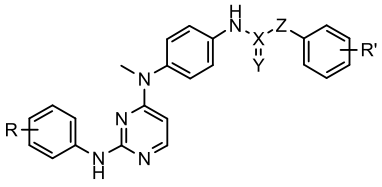
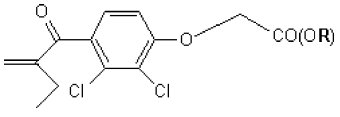
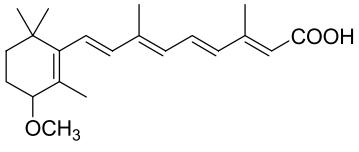


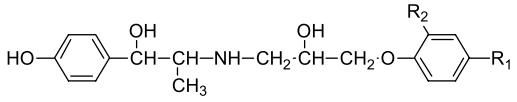
A series of dianilinopyrimidineureas show potency as VEGFR2 kinase inhibitors.



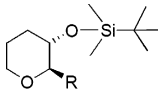
The purpose of this study was to synthesize a novel prodrug of ethacrynic acid (ECA) with short chain polyethylene glycols and codrugs of ECA with the β-adrenergic blocking agent atenolol or timolol to overcome the adverse effects of ECA and to enhance its physicochemical properties.



Impurity found in commercial tretinoin samples.

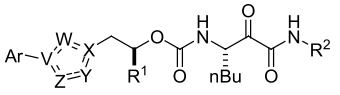


The design, synthesis and evaluation of racemic 1-(4-hydroxyphenyl)-2-[3-(substituted phenoxy)-2-hydroxy-1-propyl]amino-1-propanol hydrochlorides as novel uterine relaxants is reported.

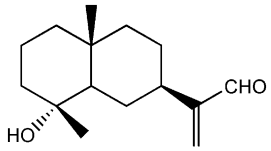


GI_{50} = 6–86 μM

The synthesis of enantiomerically pure (2*R*,3*S*)-disubstituted tetrahydropyranes and their in vitro activity against HL60 promyelocytic leukemia cells and MCF7 breast cancer cells are reported. A structure–activity relationship is discussed.

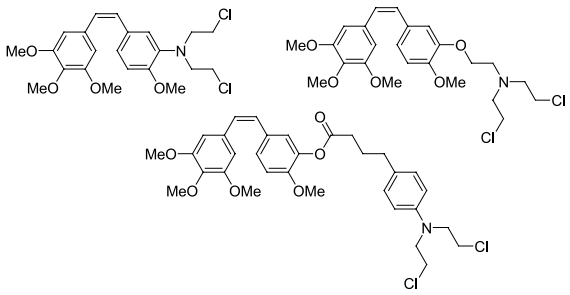


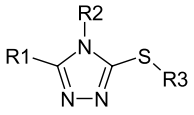
An orally bioavailable series of ketoamide-based cathepsin K inhibitors with good pharmacokinetic properties has been identified. Starting from a potent inhibitor endowed with poor drug properties, conformational constraint of the P^2–P^3 linker and modifications to $P^{1'}$ elements led to an enhancement in potency, solubility, clearance, and bioavailability. These optimized inhibitors attenuated bone resorption in a rat TPTX hypocalcemic bone resorption model.



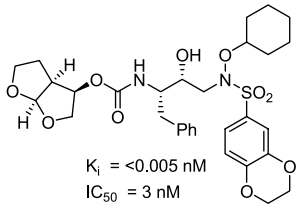
UI: 0.20 ± 0.12
DI: 96%

A series of sesquiterpene compounds possessing both eudesmane and eremophilane skeletons were tested as gastric cytoprotective agents on rats.



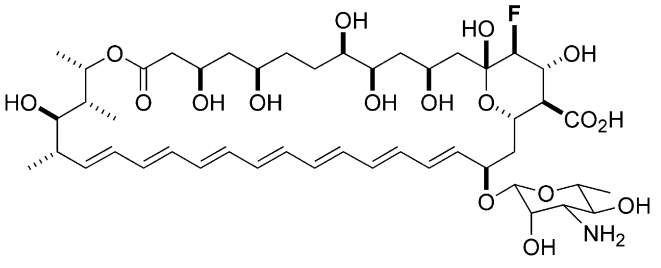


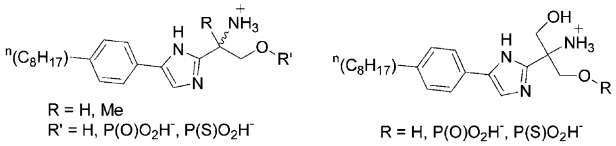
Novel 3-thio-1,2,4-triazoles have been obtained via a solution-phase parallel synthesis strategy, affording potent non-peptidic human somatostatin receptor subtypes 2 and 5 agonists.



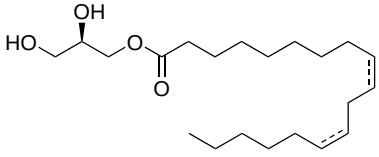
A series of novel *N*-alkoxy-arylsulfonamide HIV protease inhibitors with low picomolar enzyme activity and single digit nanomolar antiviral activity is disclosed.

The first stably fluorinated analogue of the antifungal polyene macrolide amphotericin B has been prepared taking into account biological and ion-channel activities similar to those of the original compound.



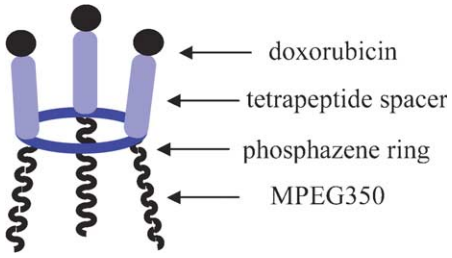


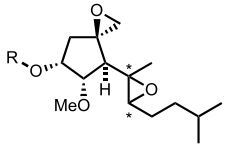
We report the syntheses, potencies and efficacies of several selective S1P receptor agonists.

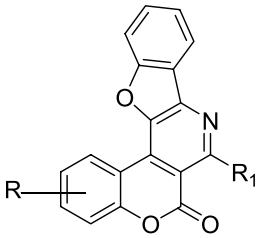


(*R*)-Glycerol-monolinoleate **4** and (*R*)-glycerol-monostearate **5** were isolated from the ethyl acetate extracts of *Saururus chinensis* roots and (*R*)- or (*S*)-fatty acid glycerols **4** and **5** were synthesized for evaluating their inhibitory activities against Lp-PLA_2.

A new biodegradable water-soluble phosphazene trimer–doxorubicin conjugate was synthesized and exhibited lower than free doxorubicin (IC_{50} = 0.10 μM) but reasonably high in vitro cytotoxicity (IC_{50} = 1.1 μM) against the leukemia L1210 cell line.

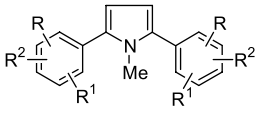






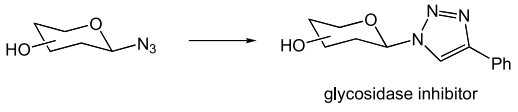
Novel angularly fused pentacyclic heterocycles with coumarin and benzofuran fused to the pyridine ring were synthesized and show promising anti-inflammatory activities.

We examined the neuroprotective effects of naturally occurring biflavonoids on oxidative stress-induced and amyloid β peptide-induced cell death in neuronal cells. Among the nine biflavonoids tested, amentoflavone, ginkgetin, and isoginkgetin exhibited strong neuroprotection against cytotoxic insults induced by oxidative stress and amyloid β, suggesting their therapeutic potential against neurodegenerative diseases, including ischemic stroke and Alzheimer's disease.

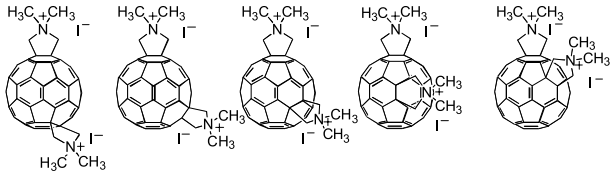


R = H, OMe, Me, Cl, CF_3, F
R^1 = H, F
R^2 = NHC(=NH)NH_2

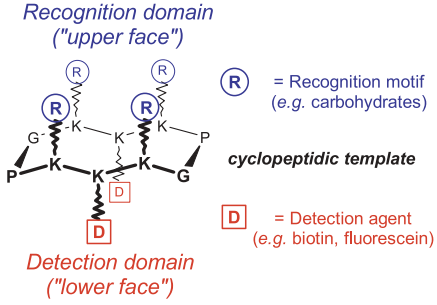
The design, synthesis, and antifungal activity profile of a series of novel 2,5-bis(guanidino-aryl)-1-methyl-1*H*-pyrroles are discussed.



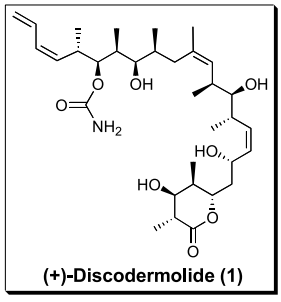
Glycosyl triazoles have been prepared by a 'click' reaction between glycosyl azides and alkynes. These triazoles are inhibitors of β-galactosidases from *Escherichia coli* and bovine liver.

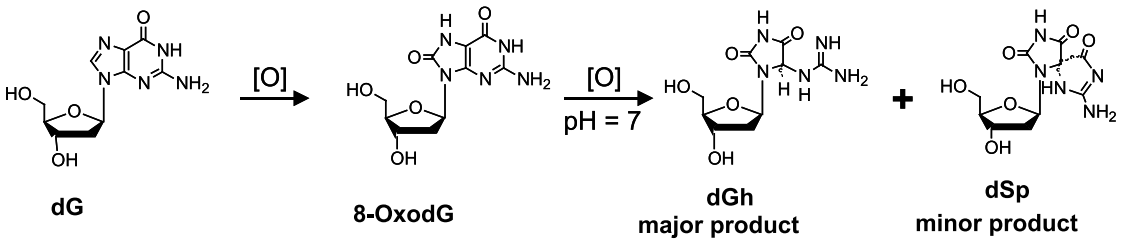


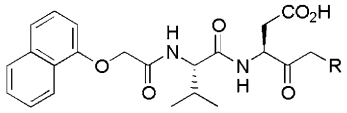
A series of regioisomeric bis-fulleropyrrolidines bearing two ammonium groups have been synthesized and their activities against HIV-1 and HIV-2 have been evaluated. Two trans isomers have been endowed with interesting antiviral properties, confirming the importance of relative positions of the substituent on a C_{60} cage. In addition, reduced amphiphilicity of the molecules to other compounds previously reported decreases their cytotoxicity in CEM cell cultures. None of the compounds showed any inhibitory activity against a variety of DNA and RNA viruses other than HIV.



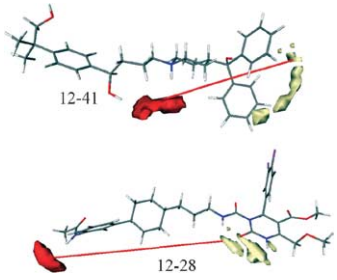
The synthesis of cyclodecapeptidic template displaying clustered carbohydrates for recognition and probes for detection is reported as a tool for glycomic research.







Various heterocyclic hetero-methyl ketones of the 1-naphthyloxyacetyl-Val-Asp backbone have been prepared. A study of their structure–activity relationship (SAR) related to caspase-1, -3, -6, and -8 is reported. Their efficacy in a cellular model of cell death is also discussed. Potent broad-spectrum caspase inhibitors have been identified.



Computational QSAR models constructed from pharmacophore-based GRIND descriptors were found to be predictive for hERG channel blockers.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Active site of the X-ray co-crystal structure of compound **6o** complexed with cathepsin K. The cathepsin K carbons are colored magenta with inhibitor **6o** carbons colored cyan. The semi-transparent white surface represents the molecular surface, while hydrogen bonds are depicted as yellow dashed lines. The coordinates have been deposited in the Brookhaven Protein Data Bank, Accession No. 1YT7. This figure was generated using PYMOL version 0.97 (Delano Scientific, www.pymol.org). [Barrett, D. G.; Boncek, V. M.; Catalano, J. G.; Deaton, D. N.; Hassell, A. M.; Jurgensen, C. H.; Long, S. T.; McFadyen, R. B.; Miller, A. B.; Miller, L. R.; Payne, J. A.; Ray, J. A.; Samano, V.; Shewchuk, L. M.; Tavares, F. X.; Wells-Knecht, K. J.; Willard, D. H. Jr.; Wright, L. L.; Zhou, H.-Q. Q. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2540.]

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