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Bioorganic & Medicinal Chemistry

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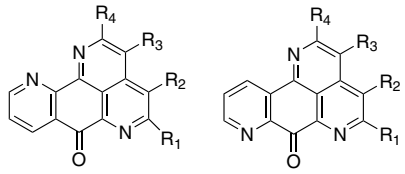
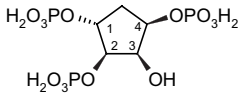
Contents

ARTICLES





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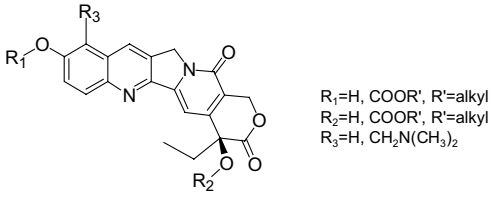
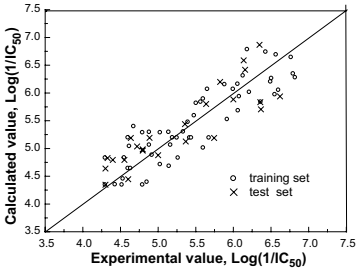
Cyclopentanic analogues of *myo*-inositol 1,4,5-tris(phosphate) were synthesised starting from cyclopentadiene, and their affinities for the Ins(1,4,5)P_3 receptors were tested.

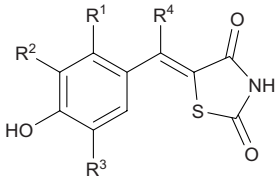


R_1=H, COOR', R'=alkyl
R_2=H, COOR', R'=alkyl
R_3=H, $CH_2N(CH_3)_2$

The bis and mono-alkyl carbonates of 10-hydroxycamptothecins were synthesized and their chemical and enzymatical stability as well as antitumor activity were studied.

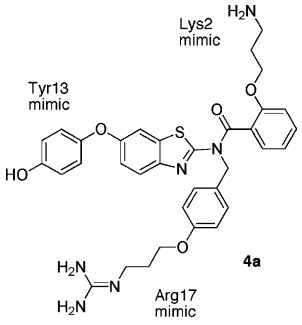


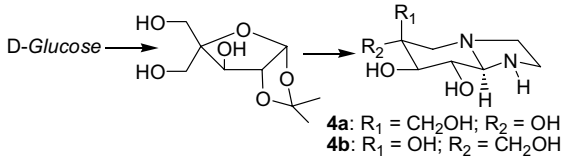
1-Phenylbenzimidazoles were reported by Palmer et al. (*J. Med. Chem.*, **1998**, 41, 5457; **1999**, *42*, 2373) as a new class of inhibitors of the platelet-derived growth factor receptor (PDGFR), which are also of interest as potential anticancer drugs. Since the existing quantitative structure–activity relationship (QSAR) models for inhibitory activities of 1-phenylbenzimidazoles are less than satisfying, we performed a QSAR study in this work and developed a QSAR model using variable connectivity indices as input parameters. The new model was developed based on the analysis of a training set of 55 active compounds, and was validated with a test set of 24 active compounds and 44 inactive compounds. The results show that the new model gives good predictions, both for active and inactive compounds, and the effects the structure of the compounds on the inhibitory activity can be represented well by the model. This work not only presents a QSAR model for inhibitory activities of 1-phenylbenzimidazoles, but also demonstrates that the variable connectivity indices, a class of not widely recognized structural descriptors, are quite useful in the QSAR studies in the fields of pharmaceutics and biochemistry, which should play a more important role in the QSAR studies in these fields.

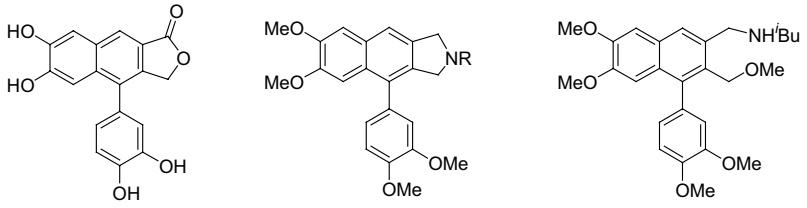


Benzylidenethiazolidine-2,4-diones **3a**–**h** were synthesized and evaluated for LDL-antioxidant activities.

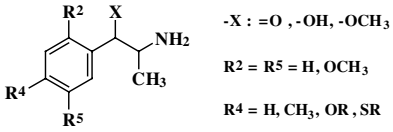
Nonpeptide mimetics possessing fragments that mimic Lys2, Tyr13 and Arg17 in ω-conotoxin GVIA have been prepared. The lead compound (**4a**) and three analogues were assayed for rat brain N- and P/Q-type VGCC binding, with **4a** exhibiting low μM binding to the N-type channel, and two compounds demonstrating promising selectivity for the N-type over the P/Q-type channel.



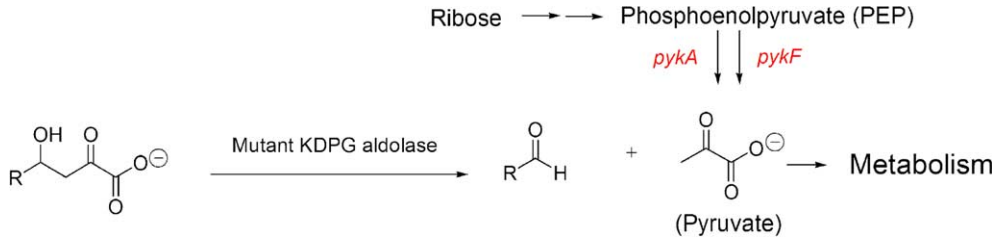




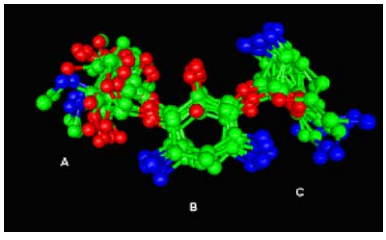
Ten lignans and nine azalignans, structurally related to two anti-HIV RT retrojusticidin B and phyllamyricin A, were prepared. Of them, compounds **5**, **22**, **23**, and **28** showed good anti-HIV activity with IC_{50} value of 0.25, 1.07, 0.01, 0.32 μg/mL, respectively.



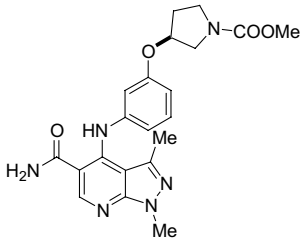
Twenty-nine arylisopropylamines with an oxo, hydroxy, or methoxy side-chain β-substituent were prepared and evaluated in vitro as MAO-A and MAO-B inhibitors.



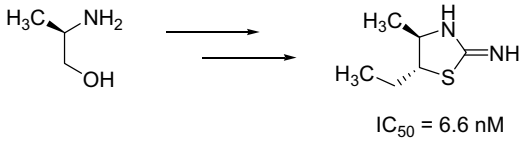
^{1}H NMR, potentiometry and molecular modeling study were applied due to characterize precisely the acid–base properties of an aminoglycoside antibiotic—sisomicin. The group protonation constants of this drug were determined, as well as the summary stability constants of six representatives of aminoglycosides.



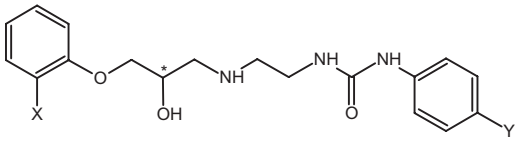
Transition-state-analogue structures and substrate variants provide two discrete paradigms for the design of reversible enzyme inhibitors; these are contrasted here and the case of substrate variants is delineated with a well-defined set of structures.



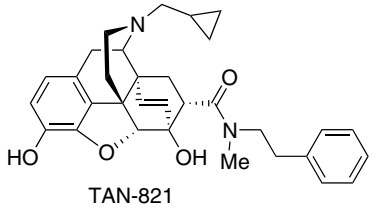
The discovery of an orally active pyrazolopyridine derivatives as a structually new PDE4 inhibitor is reported.



A series of 2-imino-1,3-thiazolidine derivatives have been synthesized and their inhibitory activity against iNOS and selectivity for iNOS both in vitro and in vivo was described.

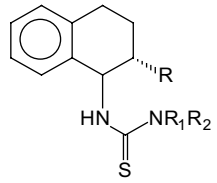


Six pairs of new compounds with the 3-aryloxy-2-propanolamine core of the selective β_1-adrenoceptor ligand, ICI 89,406 (X: CN, Y: H), were synthesized. Each pair consisted of the racemic and the (*S*)-aryloxypropanolamine derivatives. The comparison of racemic (**11a**: X: I, **11b**: X: ^{125}I, **11c**: X: ^{123}I, Y: COOH) and (*S*)- (**15a**: X: I, **15b**: X: ^{125}I, **15c**: X: ^{123}I, Y: COOH) compounds indicates that the (*S*)-enantiomer should improve the feasibility of imaging β_1-adrenoceptor density noninvasively in vivo in the human heart using the molecular imaging technique of single photon emission computed tomography (SPECT) in patients suffering from cardiac diseases like ventricular arrhythmias and heart failure.

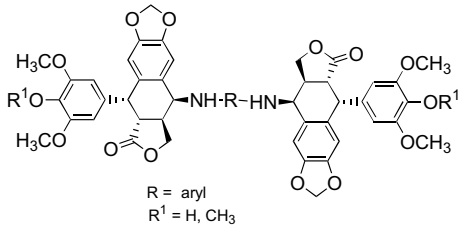


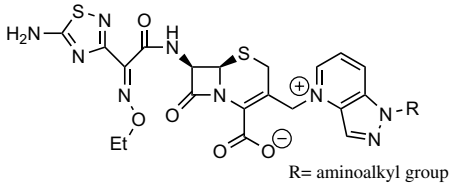
TAN-821

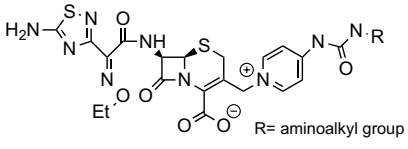
The drug design and synthesis of a series of 6,14-endoethenomorphinan-7α-carboxamide derivatives as a putative ε opioid receptor agonist are described. One of the derivatives, TAN-821, was the putative ε opioid receptor agonist.

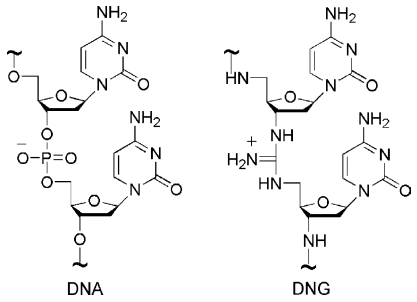


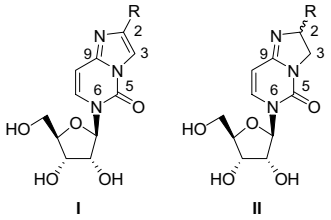
A series of thiourea derivatives of 1-aminotetrahydronaphthalene and 1-amino-2-hydroxytetrahydronaphthalene were synthesized in single pot in 48–90% yield and evaluated for their anorexigenic activity.



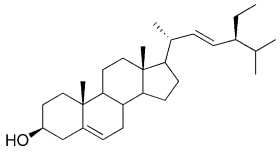




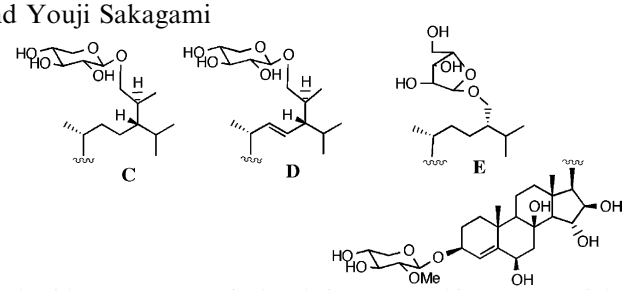




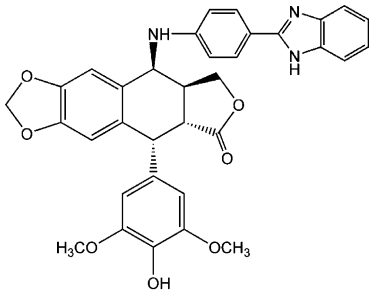
Novel 6-(β-D-ribofuranosyl)-2-alkyl/aryl-6*H*-imidazo[1,2-*c*]pyrimidin-5-one and 6-(β-D-ribofuranosyl)-5-oxo-5,6-dihydro- and 2,3,5,6-tetrahydro-imidazo[1,2-*c*]pyrimidine-2-carbonitrile nucleosides were prepared and evaluated against a wide range of viral types and strains in cell culture.



Bioassay-guided fractionation of plant extracts led to the isolation and identification of three phytosterols, stigmasterol, β-sitosterol, and β-sitosterol-β-D-glucoside, as selective DNA polymerase β lyase inhibitors.



Three new steroid glycosides, linckosides C–E, were isolated from an Okinawan starfish as mimics and synergists for the neuritogenic activity of NGF.



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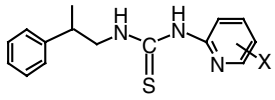
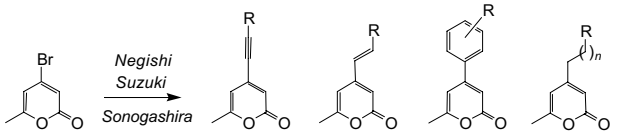


Chiral derivatives of several substituted halopyridyl and thiazolyl PETT compounds were synthesized as non-nucleoside inhibitors of the reverse transcriptase (RT) enzyme (NNRTI) of the human immunodeficiency virus (HIV-1). Molecular modeling studies indicated that because of the asymmetric geometry of the NNRTI binding pocket, the *R* stereoisomers would fit the NNRTI binding pocket of the HIV-1 RT much better than the corresponding *S* stereoisomers, as reflected by their 10^4-fold lower K_i values.



4-Bromo-6-methyl-2-pyrone is a versatile substrate for Negishi, Suzuki and Sonogashira cross-coupling reactions. The corresponding products are bioactive against a wide range of yeasts, bacteria and fungi. The alkynyl class of 2-pyrones demonstrate cytotoxic activities at the micromolar level.

OTHER CONTENTS

*Corresponding author

COVER

2004: Overlaps of the eight known aldolase alpha-beta barrels in 2-deoxyribose-5-phosphate aldolase (DERA). Ribbon model for DERA is shown in green, with key Lys residues capable of Schiff base formation highlighted in stick figure. Reactive Lys167 is shown in yellow. DeSantis, G.; Liu, J.; Clark, D. P.; Heine, A.; Wilson, I. A.; and Wong, C.-H. *Bioorganic & Medicinal Chemistry* **2003**, *11*, 43–52.

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