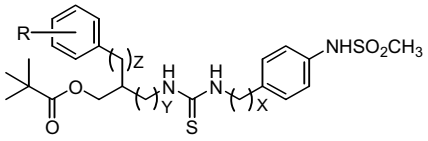
ELSEVIER

Bioorganic &
Medicinal
Chemistry

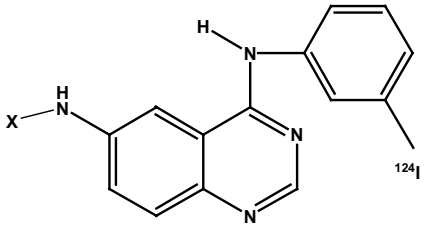
Bioorganic & Medicinal Chemistry Vol. 12, No. 13, 2004

Contents

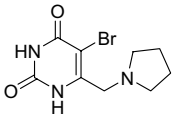
ARTICLES



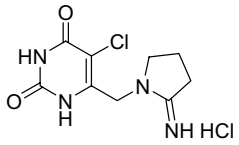
Analysis of structure–activity relationship with the *N*-(3-acyloxy-2-benzylopropyl)-*N′*-[4-(methylsulfonylamino)benzyl]thiourea template for vanilloid receptor antagonism.



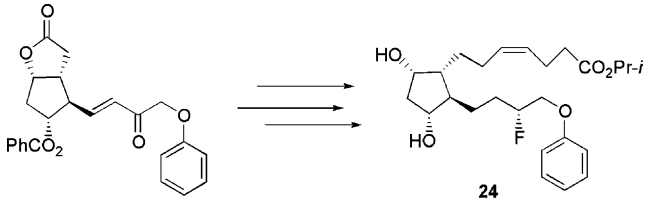
X = $MeOCH_2CO$-, $ClCH_2CO$-, $Me_2NCH_2CHCHCO$-



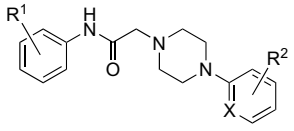
Discovery, synthesis, and evaluation of novel orally active human thymidine phosphorylase inhibitors are reported.

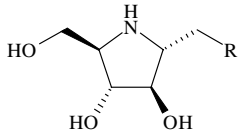


A series of novel 6-methylene-bridged uracil derivatives, as the inhibitors of human thymidine phosphorylase have been optimized for clinical use.

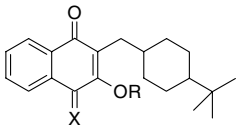


3 microgram dose, 39% drop in monkey intraocular pressure



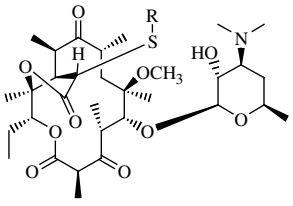


Syntheses and evaluation as competitive β-glucosidase inhibitors of a collection of C-1 derivatives of the potent, naturally occurring glycosidase inhibitor DMDP are reported.

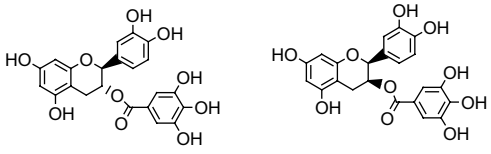


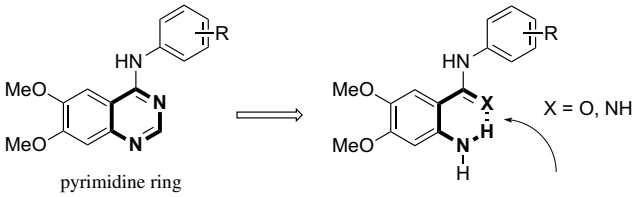
1: X = -O, R = -H (Buparvaquone)
2: X = -NOH, R = -H
3: X = -$NOCH_3$, R = -H
4: X = -O, R = -CH_3
5: X = -NOH, R = -CH_3

A new series of ketolides A with a fused five-membered lactone ring was synthesized on the basis of commercially available clarithromycin as a starting material. The chemical approach as well as chemical and biological properties of lactone ketolides A are described.



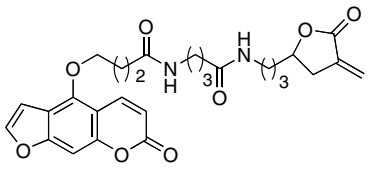
A: R = aryl, alkyl, arylalkyl





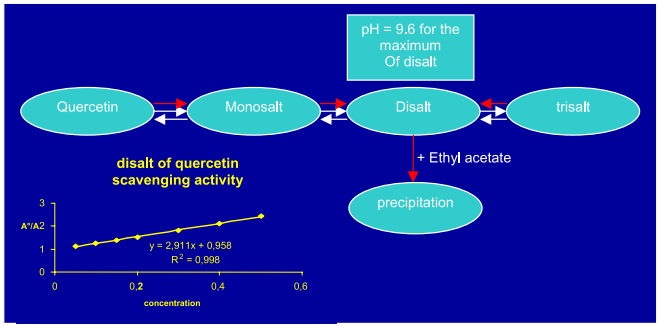
pyrimidine ring

pseudocycle formation through an intramolecular hydrogen bonding

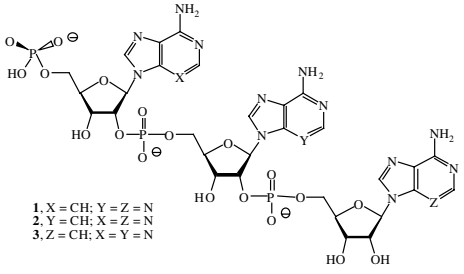


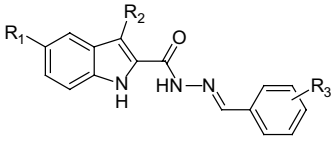
New α-methylene-γ-butyrolactone-psoralen heterodimers were synthesized and their photoantiproliferative activity assessed on three human cancer cell lines. These compounds were found to be nonphototoxic on mice skin according to the MEST.

Hydroxyl radical scavenging constant of di-salt of quercetin isolated ($K_s = 1.3 \times 10^{10}\ M^{-1}\ s^{-1}$).

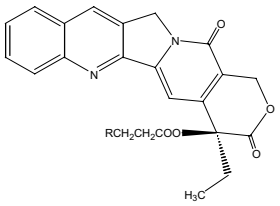


Sequence-specific 3-deazaadenosine (c^3A)-substituted analogues of trimeric 2′,5′-oligoadenylate, p5′A2′p5′A2′p5′A, were synthesized and evaluated for their ability to activate human RNase L (EC 3.1.2.6) aiming at the elucidation of the nitrogen-3 role in this biochemical process.

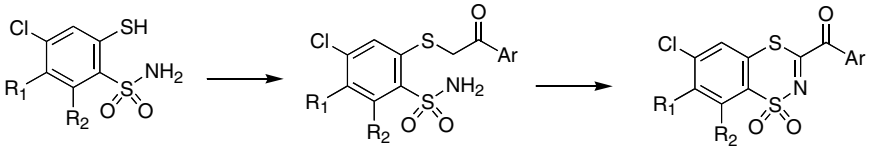


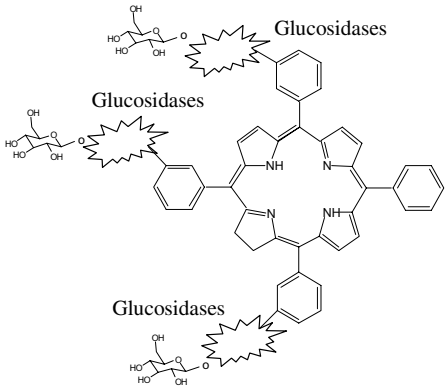


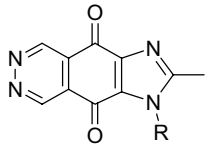
The discovery of indole-2-carboxylic acid benzylidene-hydrazides as a new series of potent inducers of apoptosis using a cell- and caspase-based HTS assay, as well as SAR studies and characterization of these compounds as inducers of apoptosis and tubulin inhibitors are reported.



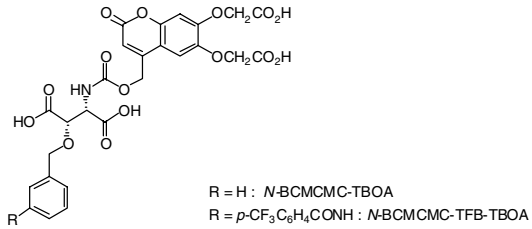
A series of nitrogen-based 20*S*-hydroxyl camptothecin derivatives were prepared. 3-Aminopropionate of camptothecin was found more cytotoxic in vitro on several human tumor cell lines than 3-amidopropionate of camptothecin. Ester **16** showed best antitumor activity in vivo and in vitro in all esters prepared.



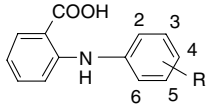


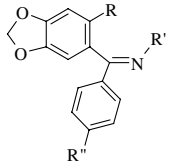


R: a=Me, b=Et, c=Pr, d=^{i}Pr, e=^{n}Bu, f=Ph, g=Tolyl

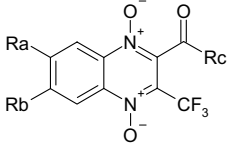


Carbamate-type caged blockers for glutamate transporters, *N*-BCMCMC-TBOA and *N*-BCMCMC-TFB-TBOA, were synthesized and revealed to be stable in aqueous solution. Photolysis of *N*-BCMCMC-TBOAs immediately released L-TBOAs to inhibit glutamate uptake.

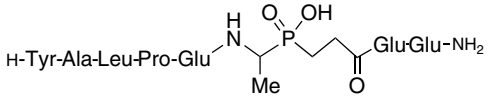




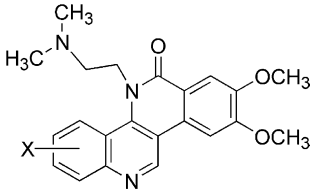
A series of 1-substituted 2-[(4-aryl)-methyl]-4,5-methylenedioxybenzene derivatives were synthesized and sound-induced seizure test was used to evaluate their anticonvulsant activity.



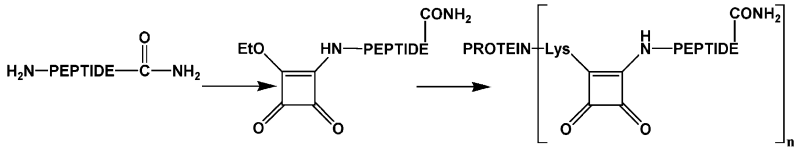
New series of 2-alkylcarbonyl and 2-benzoyl-3-trifluoromethylquinoxaline 1,4-di-*N*-oxide derivatives have been synthesized and evaluated for in vitro antitumor activity against a 3-cell line panel, consisting of MCF7 (breast), NCI-H460 (lung), and SF-268 (CNS). These active compounds were then evaluated in the full panel of 60 human tumor cell lines derived from nine cancer cell types. The results have shown that, in general, anticancer activity depends on the substituents in the carbonyl group (Rc), improving in the order: ethyl < isopropyl < *tert*-butyl < phenyl-ones. Among these, the compounds **4c**, **6e**, their difluorinated analogs (**4g** and **6g**), and **5c** were the most active, with mean GI_{50} values of 1.02, 0.42, 0.52, 0.15, and 0.49 μM, respectively. All of them were also found to inhibit the growth of the all of the Leukemia cell lines studied (with 75% of the GI_{50} values less than 0.15 μM) and therefore, were selected for further evaluation for the in vivo hollow fiber assay.



The *Staphylococcus aureus* sortase transpeptidase, SrtA, is competitively inhibited by the phosphinate containing peptidomimetic, NH_2-YALPE-AlaΨ{PO_2H–CH_2}Gly-EE-NH_2.



Where X = H, NO_2, NH_2



OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

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.

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

ELSEVIER

ISSN 0968-0896