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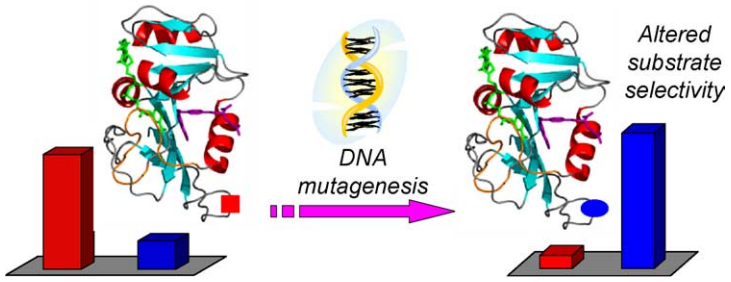
Bioorganic &
Medicinal
Chemistry

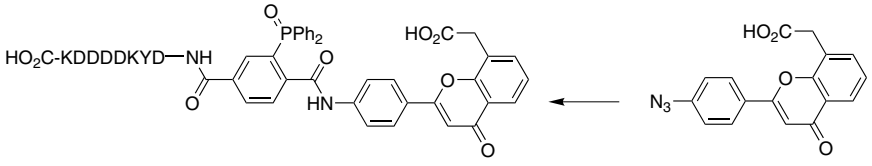
Bioorganic & Medicinal Chemistry Vol. 13, No. 8, 2005

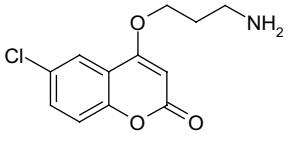
Contents

REVIEW

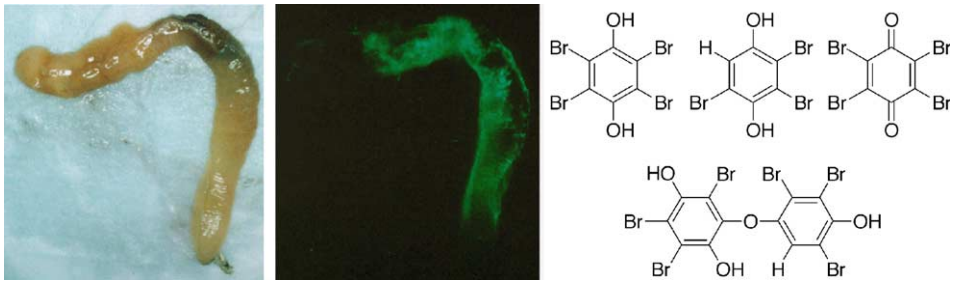


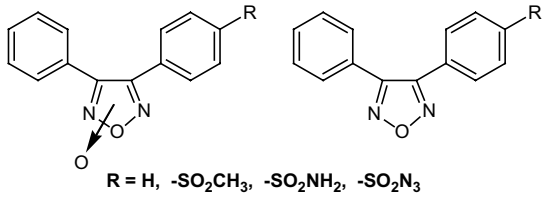
ARTICLES

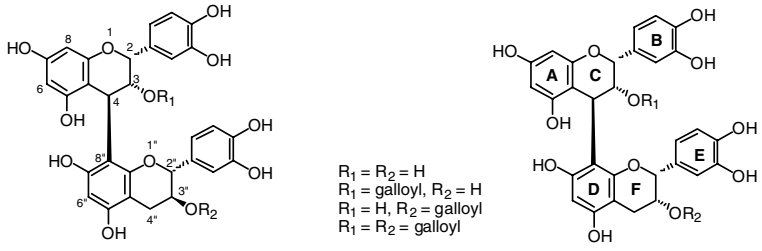


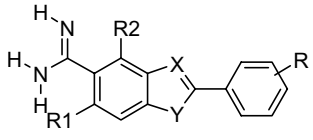


Coumarin 30



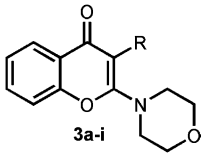


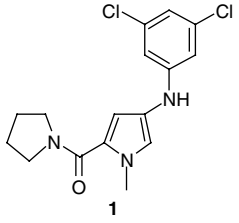




3D-QSAR/CoMFA models have been generated for a series of indole/benzoimidazole-5-carboxamidines as trypsin-like serine protease inhibitors viz. tPA, factor Xa, thrombin, plasmin, and trypsin, which can be employed in designing novel selective serine protease inhibitors of therapeutic interest.

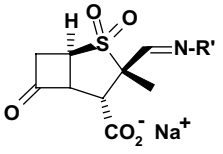
Hck	V	T338	E	Y	M
p110γ	M	I879	E	I	V
p110α	L	I	E	V	V
PI3KC2α	M	V	E	L	V
VPS34	A	I	E	F	I
MEC1	I	L	E	M	V





1

Novel pyrrole-2-carboxamide derivatives were designed and synthesized as androgen antagonists. Compound **1** is more active androgen antagonist than flutamide.

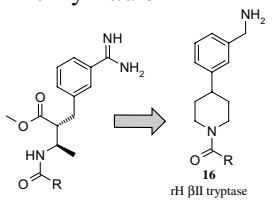


17a-n: R' = OMe, OEt, O-allyl, OCH_2CH_2OH, O-tert-butyl, O-cyclopropylmethyl, O-methoxymethyl, O-pyridin-2-ylmethyl, O-piperidin-2-ylmethyl, etc.

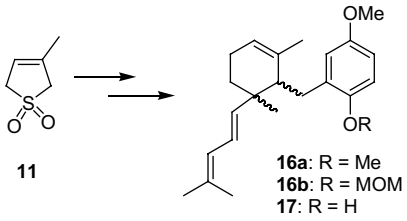
18a-f: R' = $NHCOCH_3$, NHCOPh, $NHCSNH_2$, $NHCONH_2$, $NHCOOCH_2Ph$, 2-oxo-1-imidazolidinyl

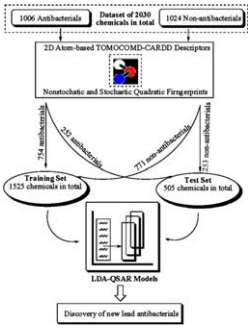
Synthesis of 2β-substituted-oxyimino and -hydrazone penam sulfones and their β-lactamase inhibitory activities against class A and C β-lactamases are presented.

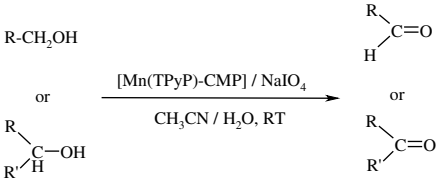
Tryptase is a serine protease implicated in the etiology of asthma. Screening of in-house inhibitors of factor Xa (a closely related serine protease) identified β-amidoester benzamidines as potent inhibitors of recombinant human βII tryptase. X-ray structure driven template modification and exchange of the benzamidine to optimize potency and pharmacokinetic properties gave selective, potent and orally bioavailable 4-(3-aminomethyl phenyl)piperidinyl-1-amides **16**.

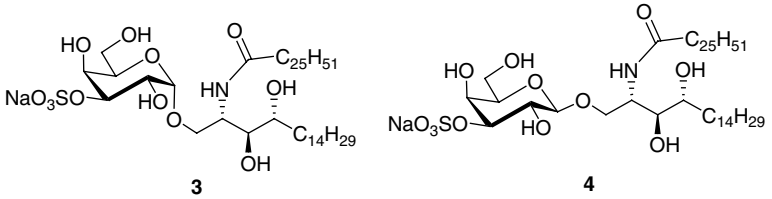


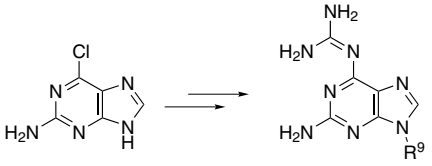
16
rH βII tryptase
K_i = 15nM to >30μM



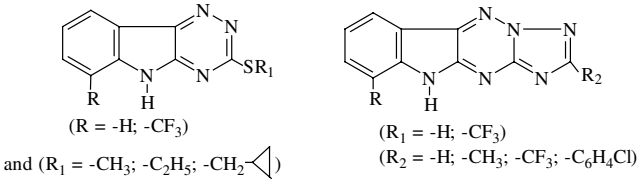


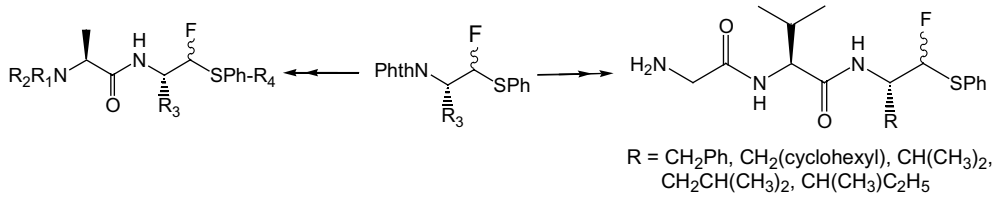


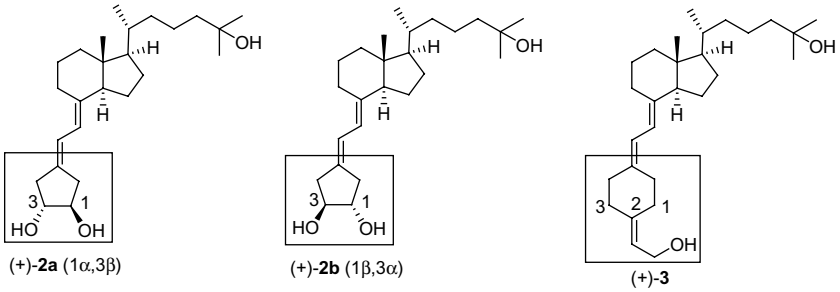




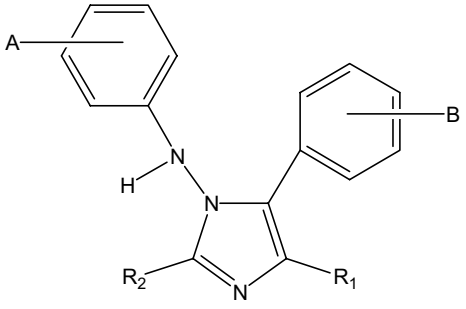
The total syntheses of (*R*)-goniothalamin (**1**) via catalytic asymmetric allylation of α-benzyloxyacetaldehyde (**2**), followed by ring-closing metathesis and Wittig olefination and via catalytic asymmetric allylation of *trans*-cinnamaldehyde followed by ring-closing metathesis are reported. The antiproliferative activities of (*R*)-**1** and its *Z*-isomer **10** as well as of the synthetic dihydropyranone intermediates **7** and **8** against eight different cancer cell lines are also described.

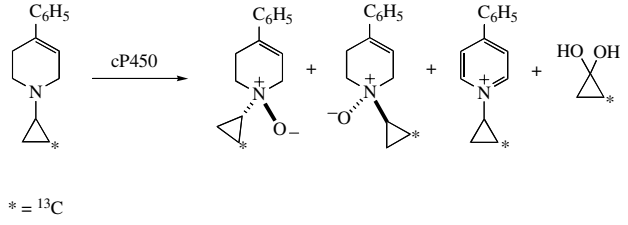


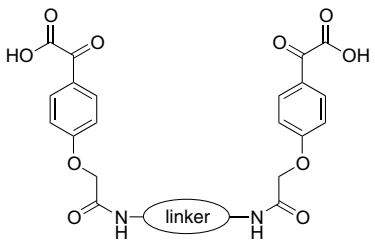


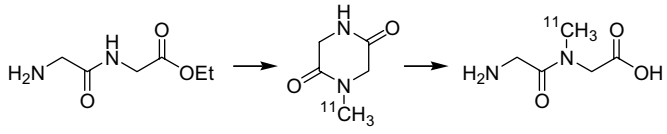


Cytotoxicity data of anti-HIV (human immunodeficiency virus) 5-phenyl-1-phenylamino-1*H*-imidazole derivatives have been subjected to quantitative structure–activity relationship (QSAR) study by linear free energy related (LFER) model of Hansch using principal component factor analysis and genetic function approximation.



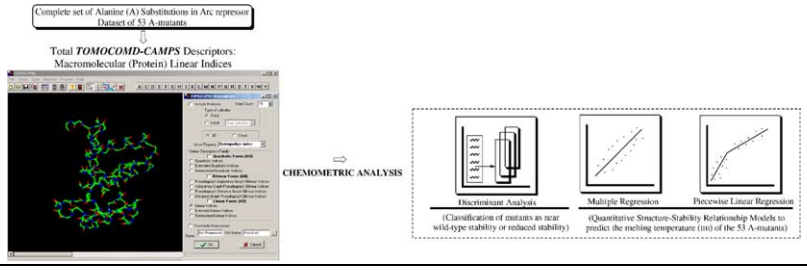




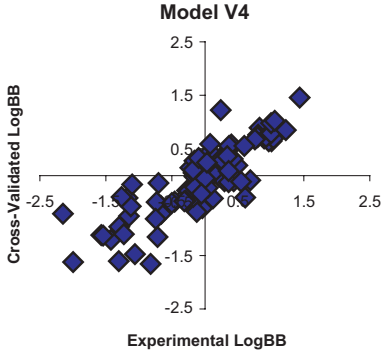


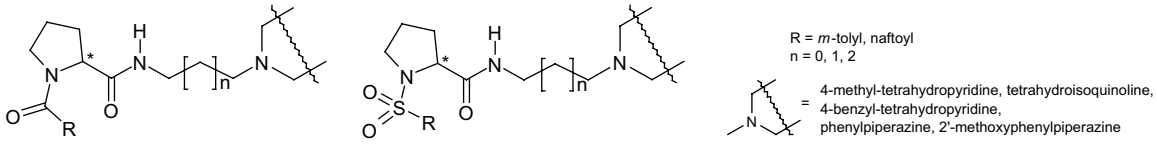
3* 4*

C-11 labeled (Gly-Sar) **4*** and [^{11}C]*cyclo*(Gly-Sar) [1-methylpiperazine-2,5-dione] **3*** were synthesized as potential radiotracers to investigate the localization and in vivo function of the peptide transporter PepT2 in mouse kidney.



Predictive models for blood–brain barrier permeation were derived using 116 diverse compounds, 324 molecular descriptors, VSMP, a systematic variable selection method and multiple linear regression. Validation tests demonstrate that the models possess excellent predictive power and can be applied to virtual screening studies.





The parallel solid-phase synthesis of a series of sulfonamide and carboxamide proline derivatives and their in vitro binding affinities for serotonin 5-HT$_7$, 5-HT$_{1A}$ and dopamine D$_2$ receptors are presented.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Protocols that are commonly employed for altering the substrate specificity and selectivity profiles of proteins include rational and random DNA mutagenesis methods as well as techniques that entail selection and screening. This figure was designed using the programs pyMOL, Microsoft Powerpoint, and Microsoft Excel [Antikainen, N. M.; Martin, S. F. *Bioorg. Med. Chem.* **2005**, *13*, 2701–2716].

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ISSN 0968-0896