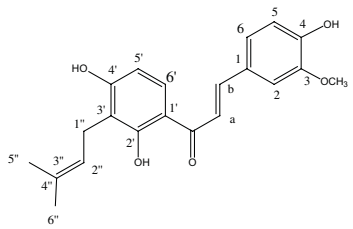
ELSEVIER

Bioorganic & Medicinal Chemistry Letters

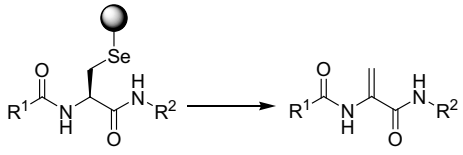
Bioorganic & Medicinal Chemistry Letters Vol. 15, No. 10, 2005

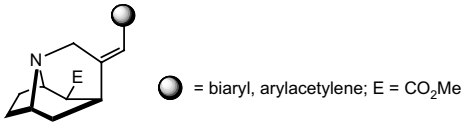
Contents

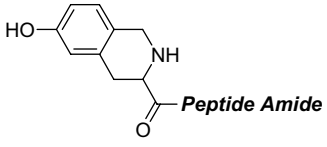
COMMUNICATIONS



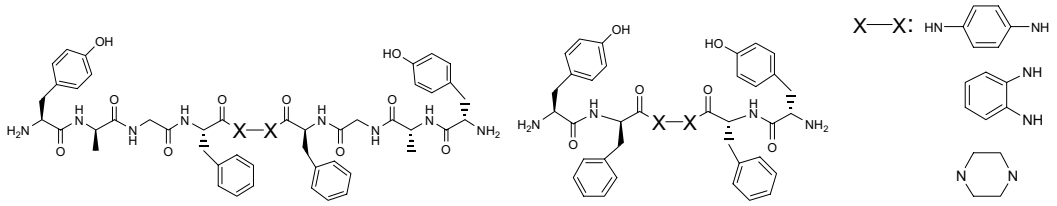
A chalcone **2**, crotaorixin, has been isolated from the aerial parts of the *Crotalaria orixensis*. Its structure has been established by extensive 1D and 2D NMR measurements. Compound **2** and few chalcones isolated from *C. medicagenia* and *C. ramosissima* have been screened for their in vitro antimalarial activity. The diprenylated chalcone **3** has shown 100% inhibition against malaria parasite *Plasmodium falciparum*'s (Strain NF-54) schizont maturation at 2 μg/ml concentration.



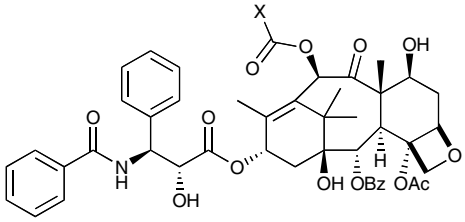




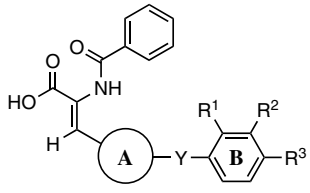
Synthesis and opioid receptor affinities of model opioid peptides with 6Htc substituting N-terminal tyrosine are reported.

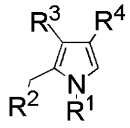


This study presents the synthesis and in vitro bioassay of new biphalin analogues with three novel non-hydrazine linkers.



A general protocol for the synthesis of paclitaxel C-10 carbamates is described. The method entails MeI-mediated activation of 2′-*O*-TBS-7-*O*-TES-10-*O*-deacetyl-paclitaxel-10-*O*-carbonylimidazole prior to reaction with amines. This method is effective for the synthesis of paclitaxel C-10 derivatives, including bifunctional molecules.

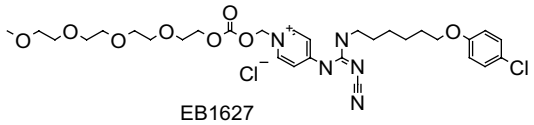




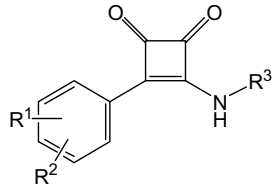
2

GI_{50} = 4–45 μM

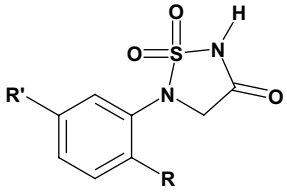
The synthesis of tetrasubstituted pyrrole derivatives **2** and their in vitro antiproliferative activity against HL60 cells is reported.



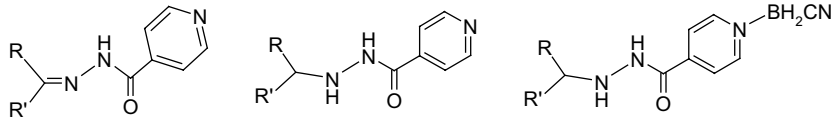
The preparation and biological activity of (EB1627), a soluble pro-drug of the potent of anticancer cyanoguanidine CHS828, is reported.



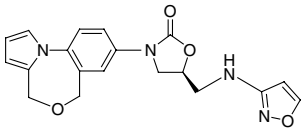
The synthesis and smooth muscle relaxant SAR of a series of novel phenyl- and benzyl-cyclobutenediones are reported.

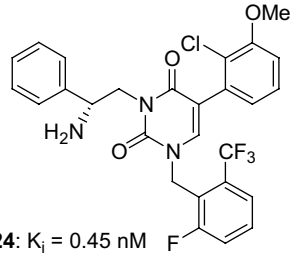


Using structure-based design, a new class of inhibitors of protein tyrosine phosphatase-1B (PTP1B) has been identified, which incorporate the 1,2,5-thiadiazolidin-3-one-1,1-dioxide template.

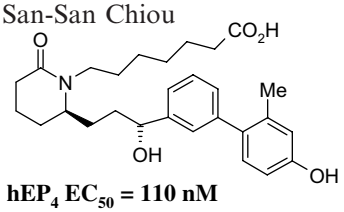


The in vitro antimycobacterial activities of some isoniazid derivatives are reported.



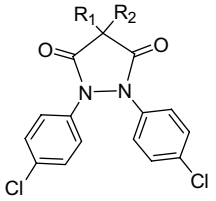


24: K_i = 0.45 nM

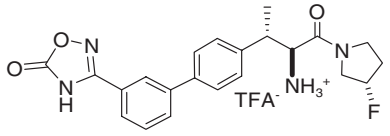


hEP_4 EC_{50} = 110 nM
>400-fold subtype selective

2-Piperidones were prepared bearing heptanoic acid or a thioether heptanoic acid at the 1-position and appropriately substituted at the 6-position to mimic the structure of prostaglandins. The stereochemical purity at the 6-position was determined to be $\geqslant$95% ee. The 2-piperidone ligands were identified as potent agonists at the EP_4 prostanoid receptor and also displayed subtype selectivity.

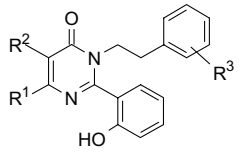


An efficient microwave-assisted synthesis of substituted pyrazolidinediones was developed. These compounds showed good activity against MurB and Gram-positive bacteria.

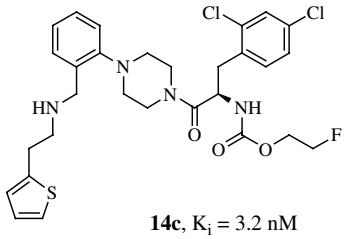


44, DPP-IV IC_{50} = 3 nM

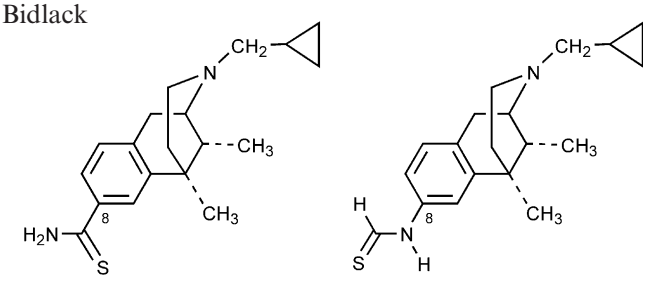
anti-Substituted β-methylphenylalanine derived amides have been shown to be potent DPP-IV inhibitors exhibiting excellent selectivity over both DPP8 and DPP9. These are among the most potent compounds reported to date lacking an electrophilic trap. The most potent compound among these is 5-oxo-1,2,4-oxadiazole **44**, which is a 3 nM DPP-IV inhibitor.



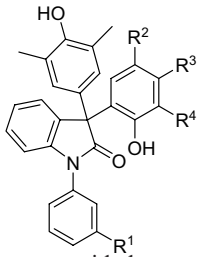
Design, new synthesis, structure–activity relationship studies and calcium receptor antagonist (calcilytic) properties of novel 3*H*-pyrimidin-4-ones are described.

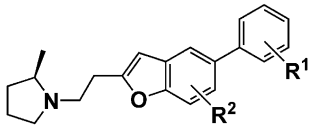


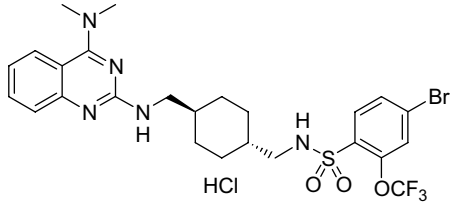
14c, K_i = 3.2 nM



8-Thiocarboxamido and 8-thioformamido analogues of cyclazocine show high binding affinity for opioid receptors.







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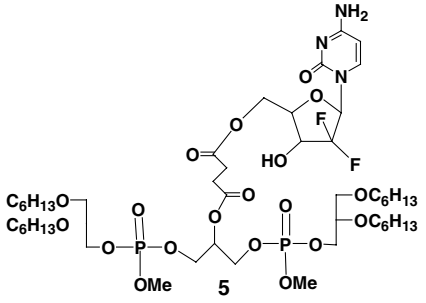
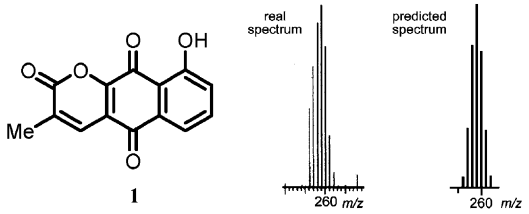
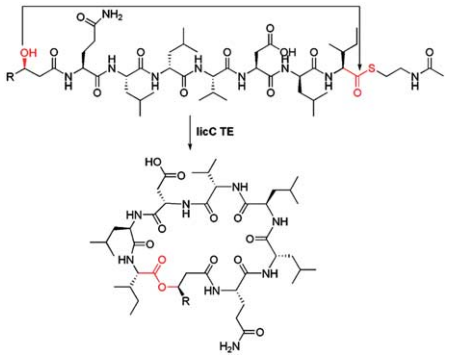
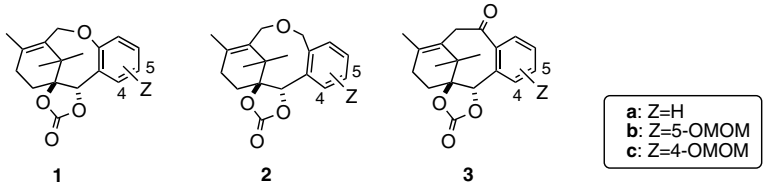


5



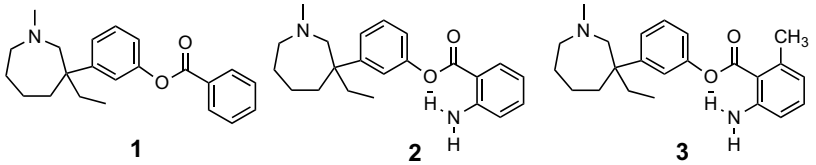
1





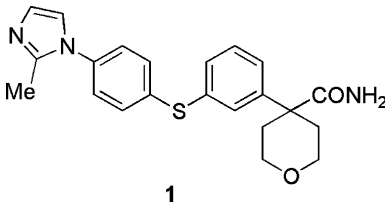
1 2 3

The synthesis of the C-aromatic taxoid analogues **1**–**3**, and their affinity for P-glycoprotein are reported. An evolution of multidrug resistant reversal activity of **2b** is also described.



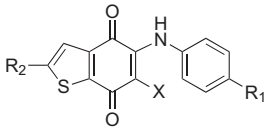
1 2 3

Three prodrugs (**1**–**3**) of meptazinol were prepared to avoid the first-pass effect of meptazinol. When evaluated in the in situ closed loop study in rats, prodrug **3** showed high absorption efficacy in rat intestine.



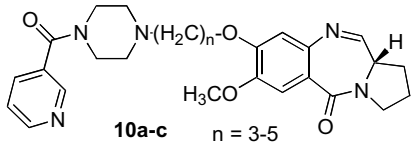
1

The improved synthesis of 5-LO inhibitor **1** was developed and enabled rapid development of structure–activity relationship.

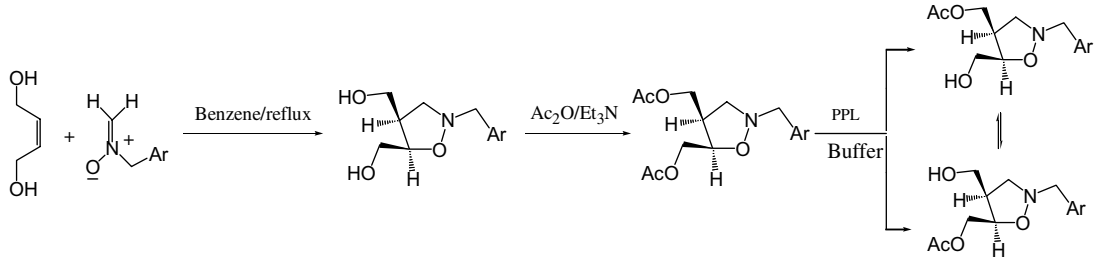


X= H or Cl ; R_1 = H, F...
R_2 = COOMe or CH_2OH

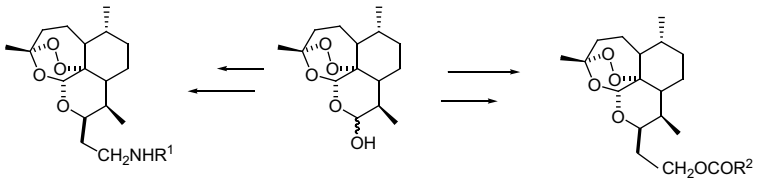
5-Arylamino-4,7-dioxobenzo[*b*]thiophenes were synthesized and tested for in vitro antifungal activity against *Candida* species and *Aspergillus niger*. Among them, 5-arylamino-6-chloro-2-(methoxycarbonyl)-4,7-dioxobenzo[*b*]thiophenes exhibited potent antifungal activity against *Candida* species.

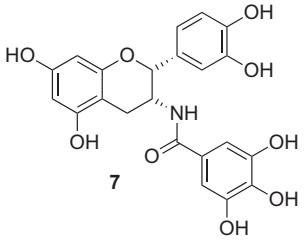


10a-c n = 3-5



(Only one enantiomer shown)

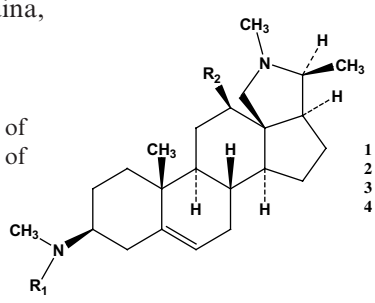




7

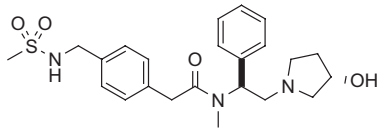
The synthesis of hydrolytically more stable analogues of (−)-epicatechin gallate (ECg) are reported with **7** reducing the resistance of methicillin resistant *Staphylococcus aureus* to oxacillin comparable to levels achieved with ECg.

Four steroidal alkaloids (**1**–**4**) were isolated from the stem bark of *Funtumia elastica*. The antiplasmodial and cytotoxic activities of these compounds are reported.



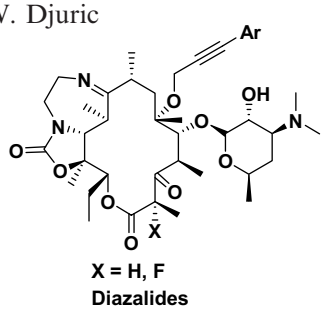
1 $R_1 = CH_3$, $R_2 = (CH_3)_2C{=}CHCH_2COO$
2 $R_1 = CH_3$, $R_2 = H$
3 $R_1 = H$, $R_2 = (CH_3)_2C{=}CHCH_2COO$
4 $R_1 = H$, $R_2 = H$

The GETAWAY approach has been applied to the study of the A_1 adenosine receptor agonist effect with excellent results. Five different approaches failed to give satisfactory models for this property.



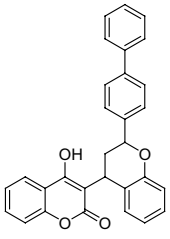
Synthetic strategies to improve the selectivity of the arylacetamide class of κ opioid agonists toward CYP2D6 is reported.

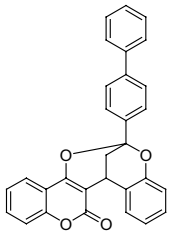
A novel series of 6-*O*-arylpropargyl diazalides was synthesized and evaluated for their antibacterial activity. Members of this series exhibited potent activity against erythromycin-resistant respiratory tract pathogens.

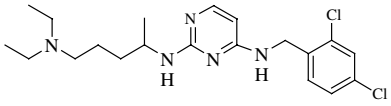


Radical scavenging activity of protein from tentacles of jellyfish *Rhopilema esculentum* by $(NH_4)_2SO_4$ fractionation and Sephadex G-100 chromatography was assayed. The protein samples showed strong scavenging activity on superoxide anion and hydroxyl radical and the radical scavenging activity was stable at high temperature.

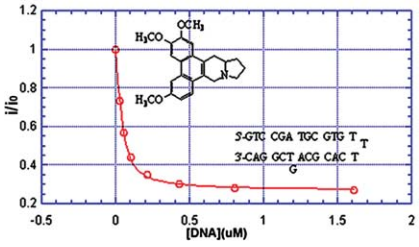
Efficient syntheses of two novel diphenacoum-derived, conformation-restricted analogues **5** and **6** are presented. Biological evaluation indicated that **5** is a potent vitamin K 2,3-epoxide reductase inhibitor and **6** is a moderate inhibitor, which may serve as a lead compound for further mode of action studies.



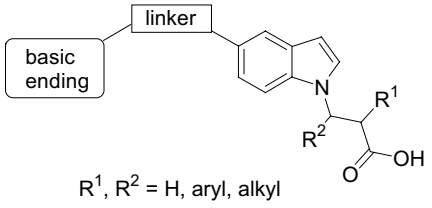


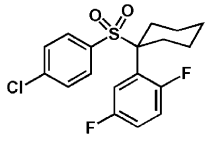


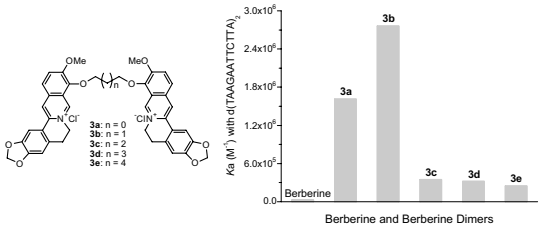
The present study reports the identification and hits to leads optimization of CCR4 antagonists. The compound shown is a high affinity, non-cytotoxic antagonist of CCR4 that blocks the functional activity mediated by the receptor.



Tylophorine B has favorable molecular interaction with bulged DNA, the oligo-deoxynucleotide, which has a tentative structure of a hairpin with a one base bulge, shows the tightest binding by tylophorine B with a dissociation constant of 18 nM.







Berberine dimers were synthesized in moderate to high yields and showed remarkably enhanced affinities toward double-stranded DNA.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

The use of synthetically modified (−)-epicatechin gallate, a constituent of green tea, to a hydrolytically more stable amide analogue, restores the antibacterial effectiveness of the β-lactam antibiotic oxacillin towards MRSA. [Anderson, J. C.; Headley, C.; Stapleton, P. D.; Taylor, P. W. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2633.]

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