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Bioorganic & Medicinal Chemistry Letters

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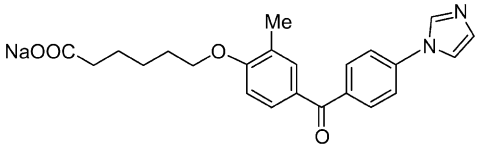
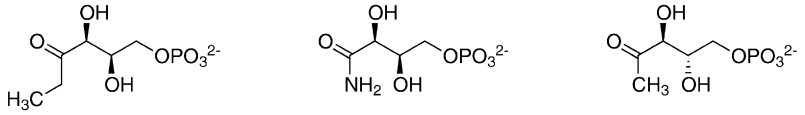
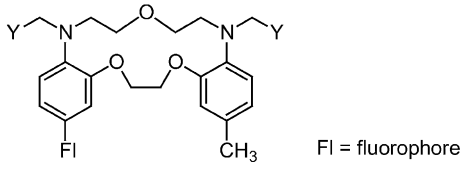
Contents

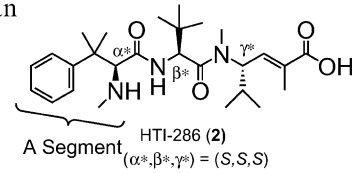
COMMUNICATIONS



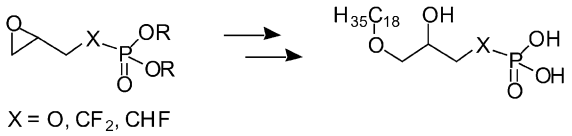
7c : IC_{50} 7.9nM

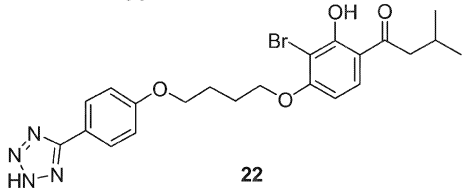




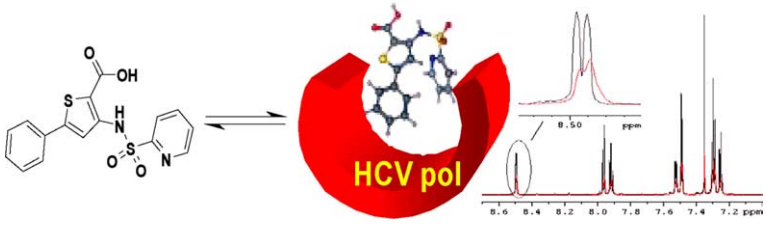


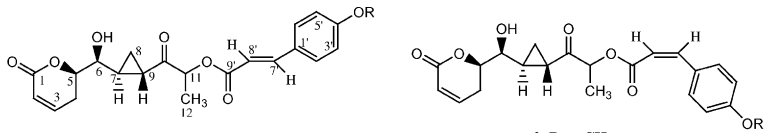
Analogs of HTI-286 (**1**), containing various aromatic rings in the A segment, were synthesized as potential inhibitors of tubulin polymerization, and the structure–activity relationships related to stereo- and regio-chemical effects of substituents on the aromatic ring in the A segment were studied.



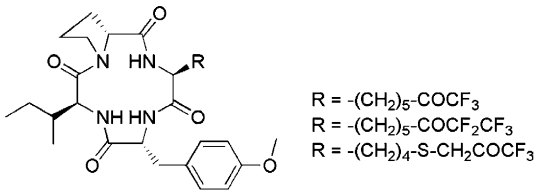


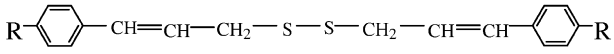
We have identified and synthesized a series of aryl-tetrazoyl acetophenones as positive allosteric potentiators of the metabotropic glutamate receptor 2. Structure activity relationship studies directed toward improving the potency and level of potentiation led to the discovery of **22** (EC_{50} = 93 nM, 128% potentiation).



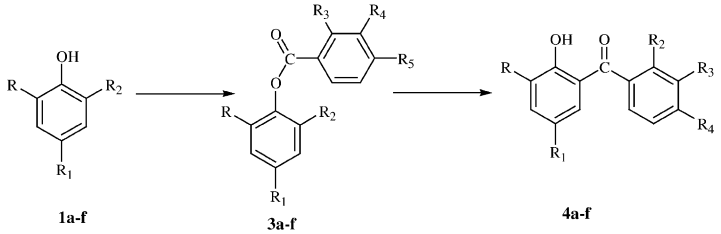


The 70% aqueous methanol extract of the Peruvian plant *Lippia alva* (Verbenaceae) was found to contain three novel compounds, **1**, **2**, and **3**, which were identified as inhibitors of the chemokine receptor CCR5. The structures of **1**–**3** were established based on extensive NMR studies. Compounds **1**–**3** inhibited CCR5 receptor signaling as measured by a calcium mobilization assay with IC_{50} values of 5.5, 6.0, and 7.2 μg/mL, respectively.

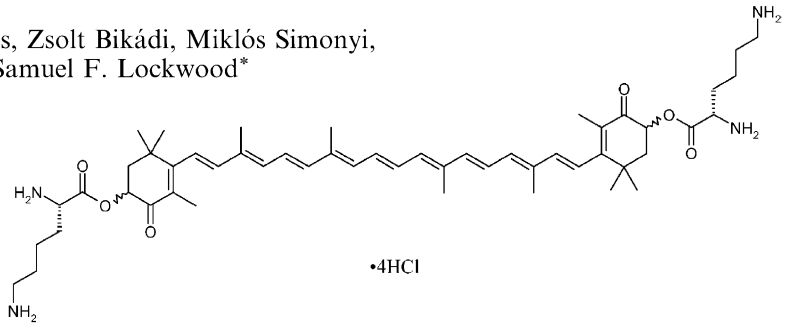




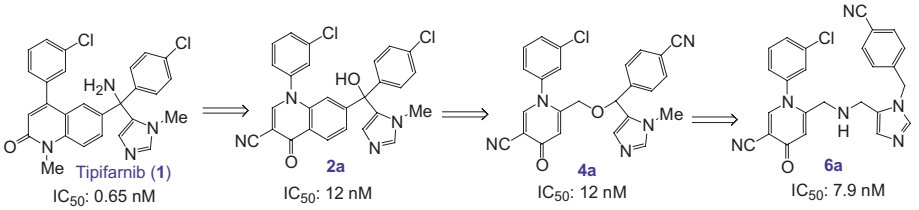
Novel derivatives of diallylsulfide, an active principle found in garlic, have been synthesized. The synthetic scheme, involving the Wittig reaction has been outlined. Among these derivatives, bis[3-(4′-nitrophenyl)prop-2-ene]disulfide has been found to be effective in lowering lipid levels and in inhibiting the activity of the enzyme HMG-CoA reductase, in Wistar rats.

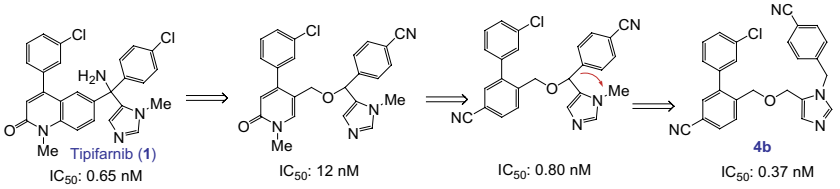


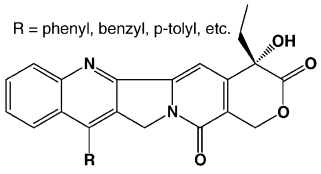
The newly synthesized compounds dibenzoyl phenols **4a**–**f** using microwave irradiation were screened for their anti-inflammatory activity and compared with standard drugs.

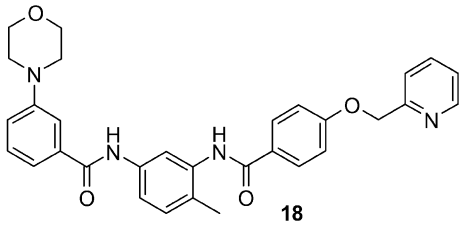


Distinct monomeric and chirally-complexed binding of astaxanthin dilysinate tetrahydrochloride to human serum albumin.

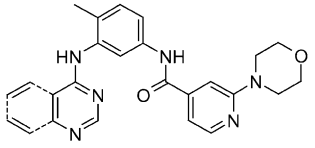




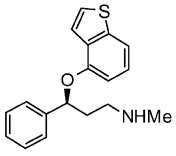




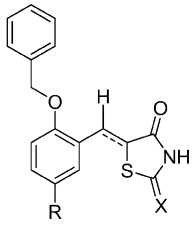
The discovery, rational analogue design, synthesis and SAR of a novel bisamide class of p38 MAP kinase inhibitor are reported. The activity in vitro is described for the series. The activity in vivo and pharmacokinetic properties are exemplified for the more potent analogues, such as **18**.



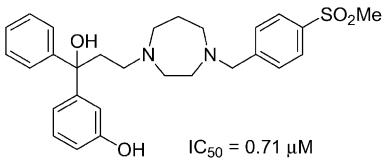
SAR studies led to the identification of 4-(3-benzoylamino-6-methyl-anilino)quinazolines as potent and selective inhibitors of p38 MAP kinase. Further optimisation led to the identification of a series of 4-(3-benzoylamino-6-methyl-anilino)pyrimidines as potent inhibitors of the p38 MAP kinase signalling pathway in vitro and in vivo.



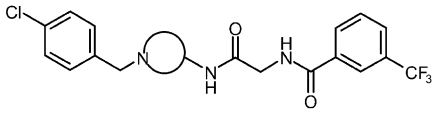
A series of benzothienyloxy phenylpropylamines have been prepared and are demonstrated to be inhibitors of both serotonin and norepinephrine reuptake.



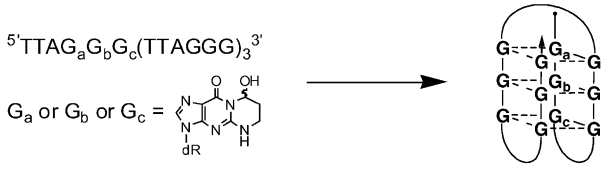
A series of 2′-benzyloxy-5′-substituted-5-benzylidene-thiazolidine-2,4-thione and -dione derivatives was synthesized and evaluated as inhibitors of translation initiation.



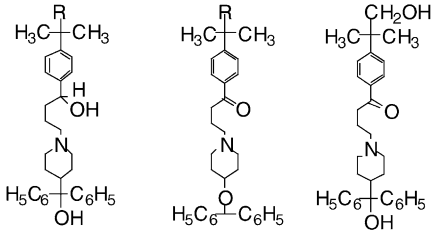
The discovery, the lead optimization, and the structure–activity relationship of *N*,*N*′-disubstituted homopiperazines are reported.

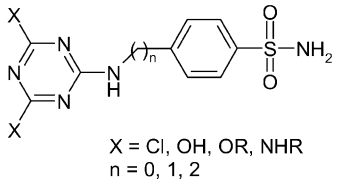


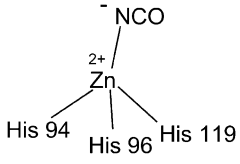
A lead evolution process is described that utilized the SAR of a homopiperazine series for the discovery of alternative cyclic diamine derivatives as nanomolar inhibitors of the interaction between MCP-1 and the CCR2b receptor.

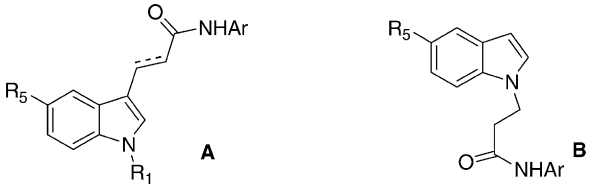


Fexofenadine **5** and carebastine **6** were obtained in good yield by optimization of culture conditions of microorganisms. Oxidation of **1** into **9** was observed as described in mammalian metabolism.

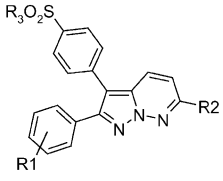








R_1 = H, Bn, 4Cl-Bn, morpholinoethyl; R_5 = H, Cl
Ar = 4-aminopyridine, 3-pycolylamine or 2-amino-4,6-dimethylpyridine



OTHER CONTENTS

*Corresponding author

COVER

Carbonic anhydrase (CA) isozyme XIII (CA XIII), a cytosolic isoform recently described, is able to catalyze carbon dioxide hydration to bicarbonate in the presence of high concentrations of bicarbonate/chloride, unlike CA I or CA II (other cytosolic isoforms) from which it mainly differs by the amino acid in position 200 (His in CA I, Thr in CA II and Val in CA XIII). The CA XIII resistance to inhibition by these physiological anions (bicarbonate and chloride) suggests an evolutionary adaptation of this isozyme to the presence of high concentrations of such anions, for example in the reproductive tract of both female and male, and its participation in metabolons with proteins involved in the anion exchange and transport, such as the anion exchangers (AE1-3) or the sodium bicarbonate cotransporter (NBC1 and NBC3) proteins [Innocenti, A.; Lehtonen, J. M.; Parkkila, S.; Scozzafava, A.; Supuran, C. T. *Bioorg. Med. Chem. Lett*. **2004**, *14*, 5435–5439].
Part of this cover graphic has been taken from the following paper: Lehtonen, J.; Shen, B.; Vihinen, M.; Casini, A.; Scozzafava, A.; Supuran, C. T.; Parkkila, A.-K.; Saarnio, J.; Kivelä, A. J.; Waheed, A.; Sly, W. S.; Parkkila, S. *J. Biol. Chem*. **2004**, *279*, 2719–2727.

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