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Bioorganic & Medicinal Chemistry Letters

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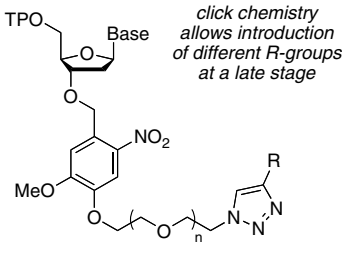
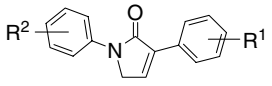
Contents

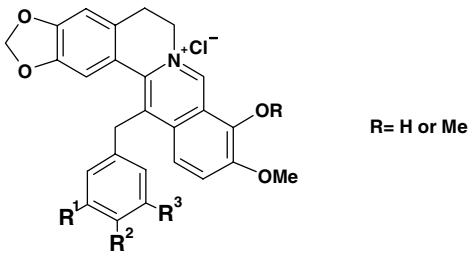
ARTICLES





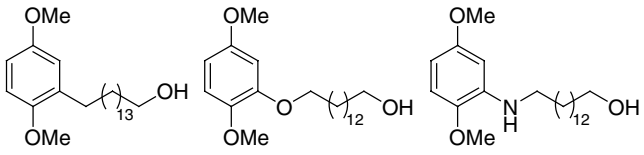
7

The synthesis of a new class of potent and selective 5-HT_{2C} antagonists (**7**) is reported.

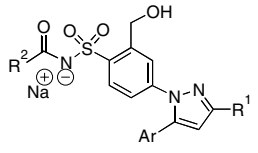


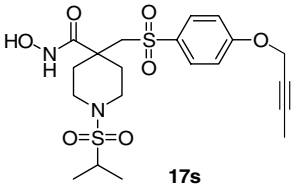
We report the synthesis and antifungal activities of 13-(substituted benzyl) berberine and berberrubine derivatives.

Following the promising activity of Q_2FA15 on axonal growth, two new series of N/O-substituted QFAs were synthesized, based on a S_N2-type reaction. O-alkylated QFA bearing 14 carbon atoms on the side chain ($n = 14$) shows a very potent activity on axonal growth though lowered when compared to Q_2FA15. While O-alkylation allows good retention of the biological activity, N-alkylation abolishes it nonetheless. A solid-phase-supported synthesis of Q_2FA15 allowing the conception of new hybrid compounds is also described.

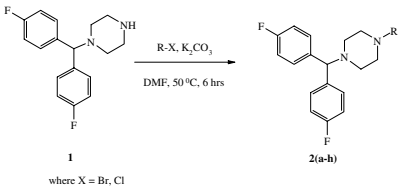


Q_2FA15 **O-QFA14** **N-QFA14**

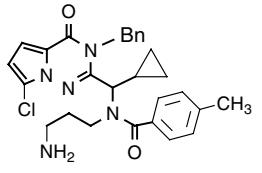


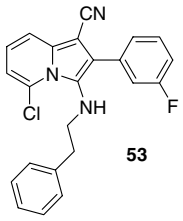


The novel bioactive 1-[bis(4-fluorophenyl)-methyl]piperazine derivatives were synthesized under mild conditions using different aryl/alkyl halides and heterocyclic alkyl halides with 1-[bis(4-fluorophenyl)-methyl]piperazine in the presence of powdered potassium carbonate in *N*,*N*-dimethylformamide. All the synthesized compounds were characterized by spectroscopic techniques, elemental analysis and were screened for their efficacy as AchE inhibitor. Some derivatives in this class showed good inhibition against AchE as compared to neostigmine as standard.



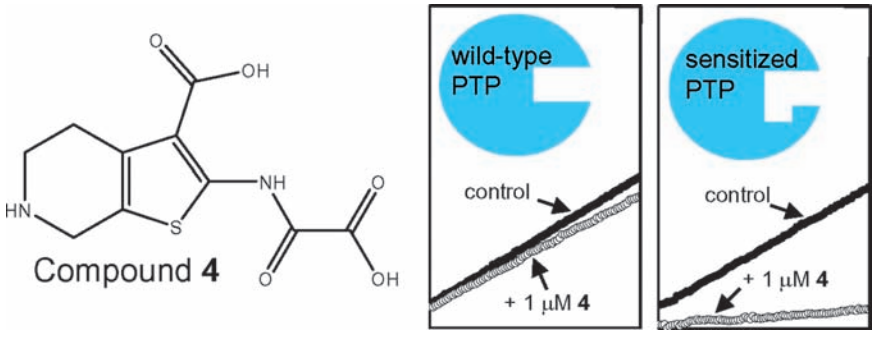
Synthesis and SAR of substituted pyrrolotriazine-4-one analogues as Eg5 inhibitors are described. Analogue **26** demonstrated in vivo efficacy in an iv P388 murine leukemia model.

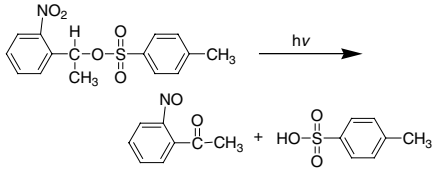




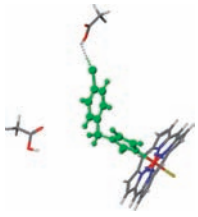
$IC_{50\ Elisa}$ = 2 μM
$IC_{50\ migration}$ = 8 μM

The synthesis of the compound **53** ($IC_{50\ ELISA}$ = 2 μM) and analogues is reported.

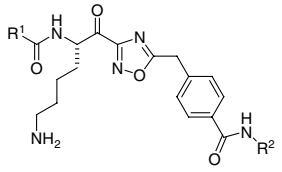




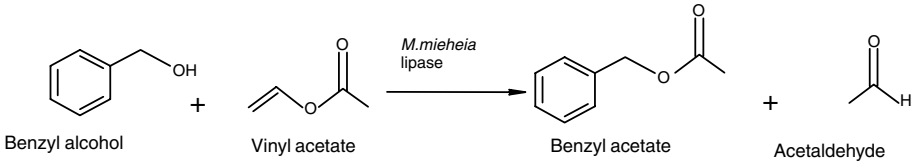
The synthesis and photodecomposition of 1-*o*-nitrophenylethyl derivatives amenable for the creation of photo-labile compounds are reported.



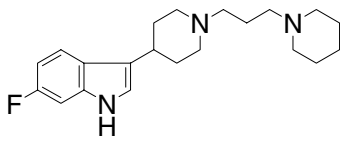
We report the synthesis and biochemical evaluation of a range of benzyl imidazole-based compounds which have been targeted against the two components of this enzyme, that is, 17α-hydroxylase (17α-OHase) and 17,20-lyase (lyase).



A series of novel α-keto-[1,2,4]-oxadiazoles has been synthesized as human tryptase inhibitors for evaluation as a new class of anti-asthmatic agent. The inhibitor design is focused on using a prime-side hydrophobic pocket and the S2 pocket of β-tryptase to achieve inhibition potency and selectivity over other serine proteases.

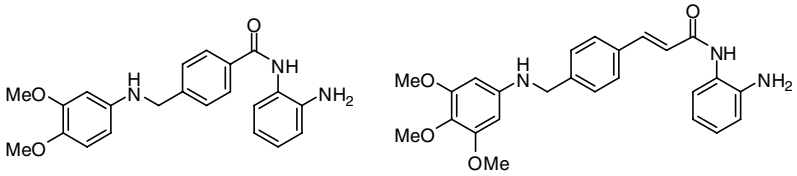


Commercially available immobilized *Mucor miehei* lipase, Lipozyme® RM IM, with benzyl alcohol and vinyl acetate in 1:6 molar ratio, in solvent-free medium, at pH 7 and at 45 °C gives 100% yield of benzyl acetate in 10 min.

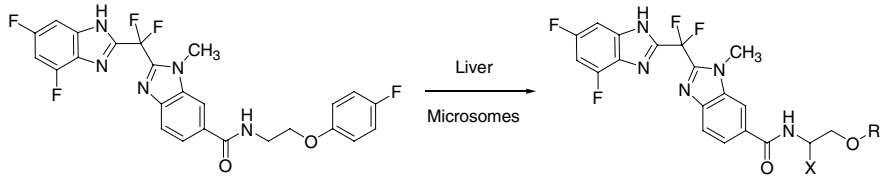


11 Ki = 0.63 nM

The synthesis of the potent and selective α_{1B} adrenoceptor antagonist **11** (K_i = 0.63 nM) is reported.



The synthesis and SAR studies of a structurally novel series of histone deacetylase (HDACs) inhibitors are described.



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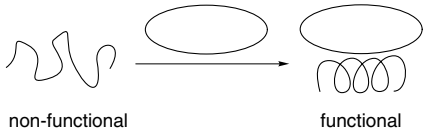
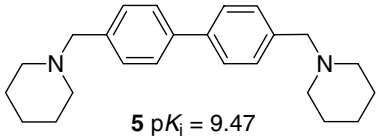
4, R = H, X = H
23, R = 4-FC$_6$H$_4$, X = OH

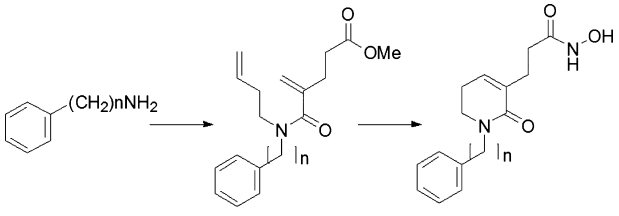


A peptide that functions only in the presence of a protein has been developed using reaction-based selection from peptide phage libraries.



5 pK_i = 9.47

A class of rigid dibasic H_3 antagonists is reported. Compound **5** with subnanomolar affinity for human H_3 receptor was identified.

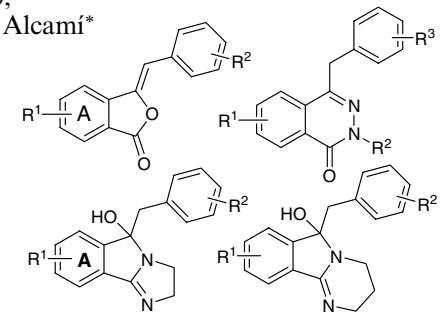


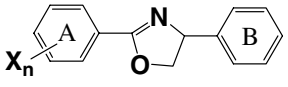
Synthesis and biological evaluation of novel δ-lactam-based hydroxamic acids as inhibitors of histone deacetylase (HDAC) is reported.

H-Phe-Gly-Gly-Phe-Thr-Gly-Ala-Arg-X^9-Ser-Ala-Arg-X^{13}-NH_2

$X^{9,13}$ = Lys (**1**); X^9 = Lys, X^{13} = Orn (**2**); X^9 = Orn, X^{13} = Lys (**3**); $X^{9,13}$ = Orn (**4**); $X^{9,13}$ = Dab (**5**); $X^{9,13}$ = Dap (**6**). The biological activities of the parent compound and its analogues were tested in vitro on electrically stimulated rat vas deferens.

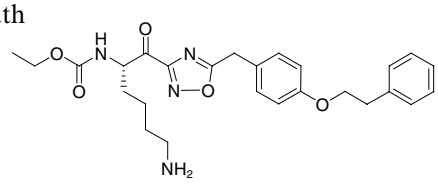
The inhibitory activity of several benzalphthalides, phthalazin-1-ones, imidazo-[2,1-*a*]isoindoles and pyrimido[2,1-*a*]isoindoles on NF-κB, Tat and HIV replication is evaluated.





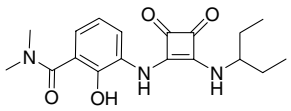
X_n = H, 2-F, 2-Cl, 2-Br, 2-I, 2-CH_3, 2-OCH_3, 2-SCH_3, 2-OC_6H_5, 2-NO_2, 2-CF_3, 3-Cl, 3-CH_3, 3-OCH_3, 3-Cl, 3-CH_3, 3-OCH_3, 2,3-Cl_2, 2,4-Cl_2, 2,5-Cl_2, 2,6-Cl_2, 2,6-F_2, 2-F-6-Cl, etc.

Log*P* (*P*, partition coefficient between 1-octanol and water) values of 2-(substituted phenyl)-1,3-oxazolines were experimentally measured and the QSAR analysis for the ovicidal activity of 2,4-diphenyl-1,3-oxazolines against the two-spotted spider mite *Tetranycus urticae* was executed.



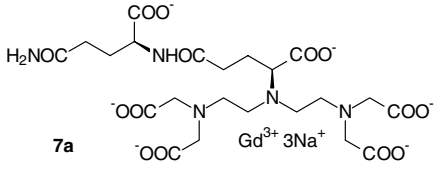
13 K_i (tryptase) = 0.0054 μM

The synthesis and structure–activity relationship of the potent and selective tryptase inhibitor **13** (K_i = 0.0054 μM) is reported.



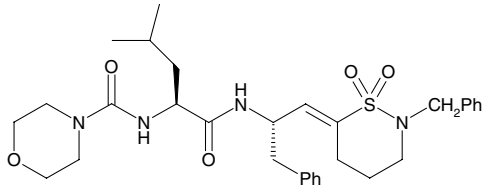
22 IC_{50} = 0.005 μM

A novel series of 3,4-diaminocyclobut-3-ene-1,2-diones was prepared with potent inhibitory activity of CXCR2 binding and IL-8-mediated chemotaxis.



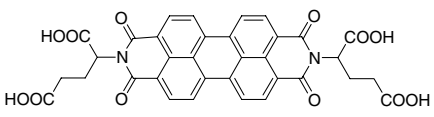
7a

With the aim of discovering an early diagnosis of cancer by magnetic resonance imaging (MRI), we synthesized and studied six DTPA and DOTA-like gadolinium complexes conjugated to agmatine, arginine, and glutamine (e.g., **7a**), able to target tumor cells by means of the glutamine transport system.

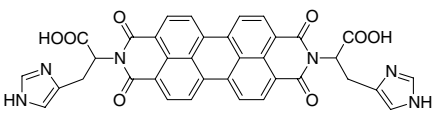


IC_{50} = 13.7 μM (falcipain-2) IC_{50} = 7.8 μM (*P. falciparum* W2)

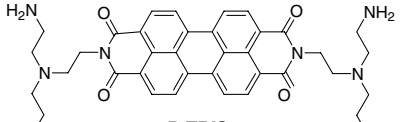
Vinyl sultams were prepared via the Wittig–Horner reaction and revealed to be active against recombinant falcipain-2 and *Plasmodium falciparum* W2.



P-GLU

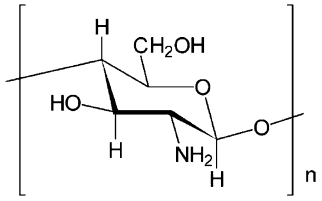


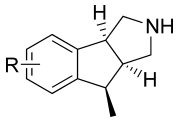
P-HIS



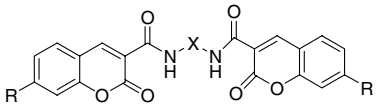
P-TRIS

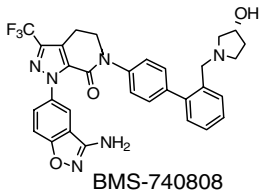
Three new perylene derivatives with branched ionizable side chains were investigated for their G-quadruplex binding specificities, in comparison with two well-studied G-quadruplex ligands: PIPER and $TmPyP_4$.





We describe the identification, SAR, and biological properties of a series of agonists to the 5-HT_{2C} receptor, a GPCR that has been implicated as an obesity target.





Efforts to further optimize the pyrazole factor Xa inhibitors by masking the aryl aniline P4 moiety resulted in a novel bicyclic tetrahydropyrazolo-pyridinone scaffold. Optimization of this series resulted in the identification of BMS-740808 (**6f**), a highly potent and selective orally bioavailable inhibitor of blood coagulation factor Xa.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

View of the crystal structure of the DB819-d(CGCGAATTCGCG)$_2$ complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 15). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, *14*, 33.]

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