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Letters

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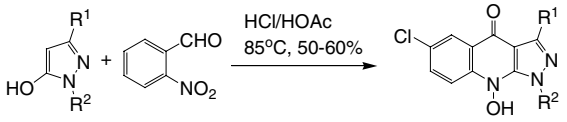
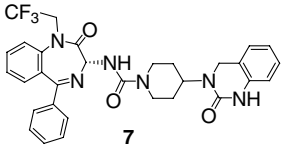
Contents

ARTICLES

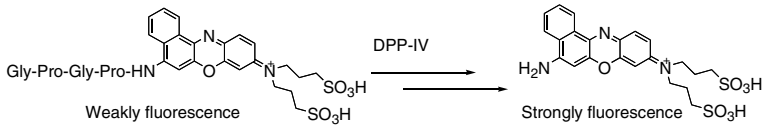


This paper describes a novel class of 1,9-dihydro-9-hydroxypyrazolo[3,4-*b*]quinolin-4-ones as c-Jun-N-terminal kinase (JNK) inhibitors. These compounds were synthesized via the condensation of 2-nitrobenzaldehydes and hydroxypyrazoles. The structure–activity relationships (SARs) and kinase selectivity profile of the inhibitors are also discussed. Compound **16** was identified as a potent JNK inhibitor with good cellular potency.

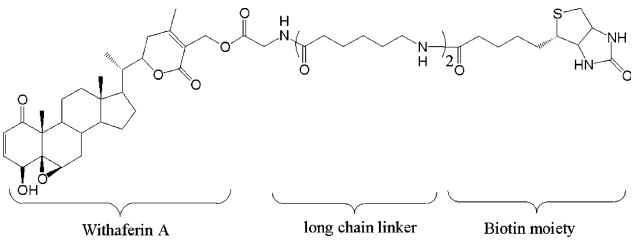


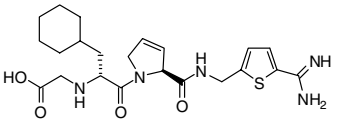
7

Structure activity studies led to the non-peptide CGRP antagonist, **7** (K_i = 44 nM, IC_{50} = 38 nM), which was orally bioavailable in rats. Benzodiazepinone **7** is a promising new lead in the development of orally bioavailable CGRP antagonists for the treatment of migraine.



A water-soluble far-red tetrapeptide substrate was developed to sense DPP-IV activity.

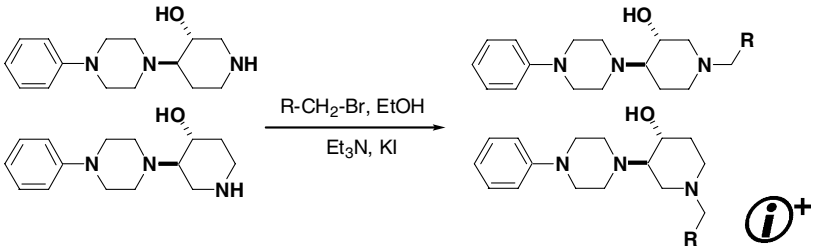


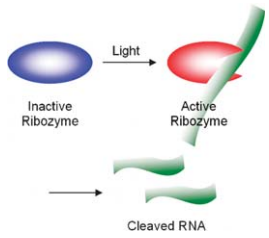


29 IC_{50} (thrombin) = 1.0 nM
F (dog) = 58 %

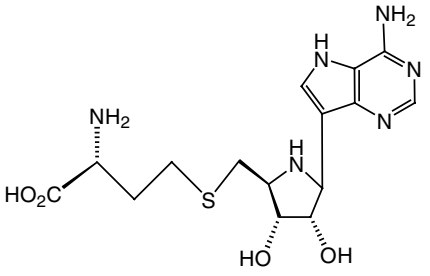
The convergent synthesis of highly potent thrombin inhibitors and their SAR with focus on the P2-position is described. The special 'dehydroproline' effect on the in vitro potency and in vivo activity is discussed for selected examples.

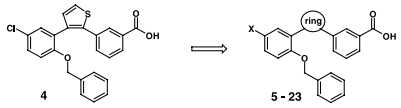
Aza-trozamicol derivatives substituted at the nitrogen of the piperidine ring with alkyl, alk-2-enyl or benzyl groups were synthesized. The N-substitution with *ortho* or *meta* bromobenzyl groups gave compounds with high affinity for human VAChT.





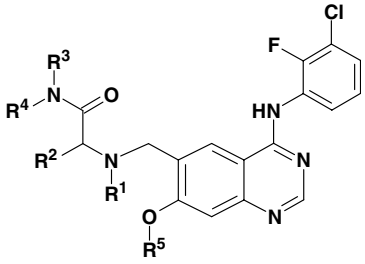
We report the light-activation of allosteric *cis* and *trans* acting ribozymes via decaging of a small organic molecule ligand. To achieve this effectively, we introduce an optimized N-caging group based on a nitrobenzyl core structure. This approach can potentially be employed toward a light-induced control of gene function.

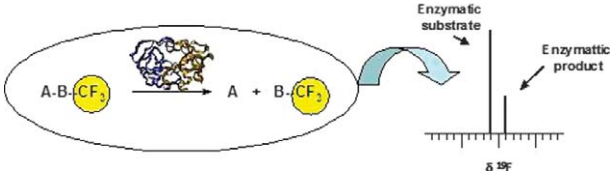


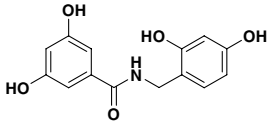


The synthesis and biological activity of a series of novel EP_1 receptor antagonists are described. In vitro and in vivo DMPK data are presented for selected compounds.

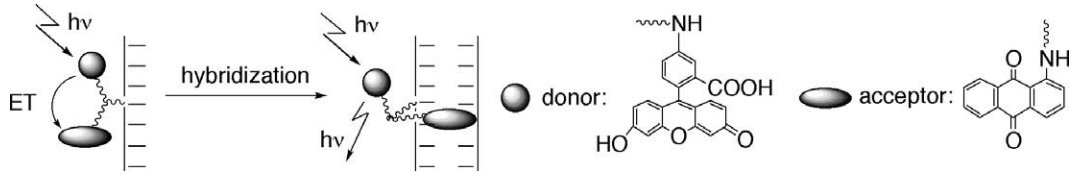
The discovery and SAR of a novel subseries of 4-anilinoquinazoline EGFR inhibitors substituted at the C-6 position with carbon-linked side chains are described.



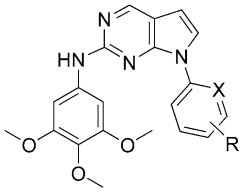




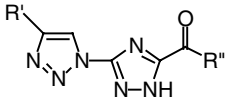
A series of potent inhibitors of tyrosinase and their structure–activity relationships are described. *N*-Benzylbenzamide derivatives (**1**–**21**) with hydroxyl(s) were synthesized and tested for their tyrosinase inhibitory activity. With this series, compound **15** provided a potent tyrosinase inhibition: it effectively inhibited the oxidation of L-DOPA catalyzed by mushroom tyrosinase with IC_{50} of 2.2 μM.



A set of 15mer linear oligoDNA probes bearing a modified nucleoside conjugated with a polyamine/fluorescein/anthraquinone reporting moiety exhibited marked fluorescence signal upon hybridization to the fully complementary stand.

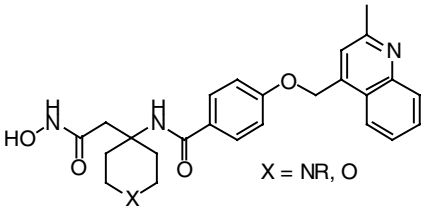


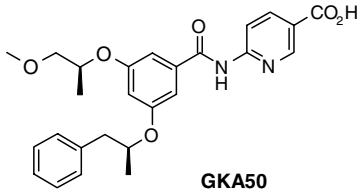
Potent focal adhesion kinase inhibitors

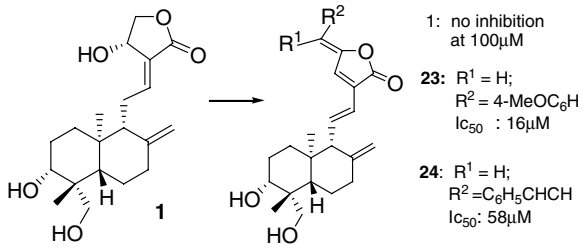


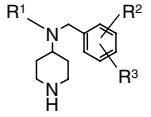
Bitriazolyl compounds have been discovered to show promising antiviral activity against tobacco mosaic virus and may constitute interesting leads for the development of new antiviral candidates.

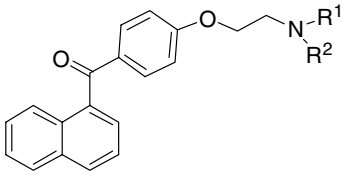
Several series of cyclic-β-aminohydroxamic acids have been synthesized and evaluated for activity against TNF-α-converting enzyme (TACE). The most promising compound exhibits a K_i of 0.35 nM in a pTACE assay and a whole blood activity of 150 nM.

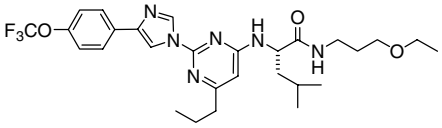


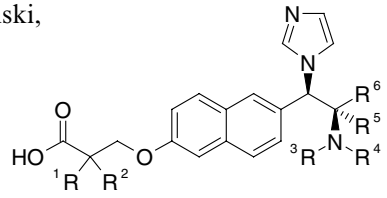


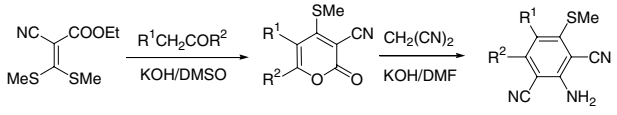


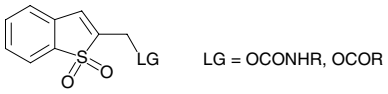


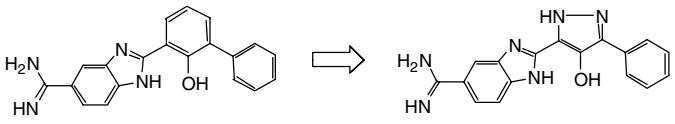








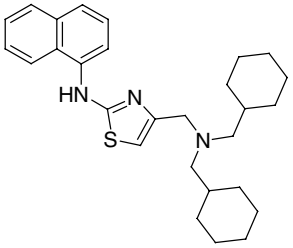


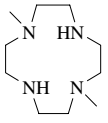


1 2

Replacement of central phenol in **1** with hydroxy pyrazole resulted in compound **2** which selectively inhibits factor IXa. It is also selective against trypsin-like serine proteases in the coagulation cascade.

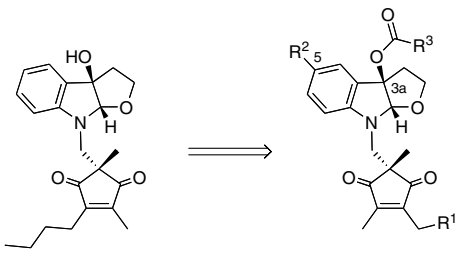
A series of 2-aminothiazole-derived antagonists of the CCR4 receptor has been synthesized and their affinity for the receptor evaluated using a [^{125}I]TARC (CCL17) displacement assay. Optimization of these compounds for potency and pharmacokinetic properties led to the discovery of potent, orally bioavailable antagonists.





DMC

The first metal free macrocyclic polyamine, 1,7-dimethyl-1,4,7,10-tetraazacyclododecane (DMC), was found to hydrolyze DNA under physiological conditions (37 °C, pH 7.2).



(+)-Madindoline A

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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