

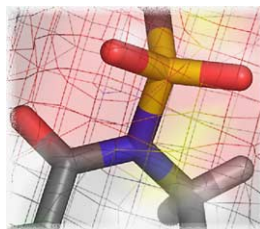
Contents

REVIEW

***N*-Acyl-*N*-alkyl-sulfonamide anchors derived from Kenner's safety-catch linker:
powerful tools in bioorganic and medicinal chemistry**

pp 585–599

Philipp Heidler and Andreas Link*



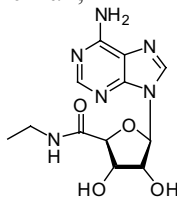
Kenner's safety-catch linker evolved over the years into a unique and versatile tool in various chemistry associated disciplines. An overview about linker construct variations, activation methods, applications and technical aspects is given.

ARTICLES

A radial distribution function approach to predict A_{2B} agonist effect of adenosine analogues

pp 601–608

Maykel Pérez González,* Carmen Terán, Yagamare Fall,
Marta Teijeira and Pedro Besada



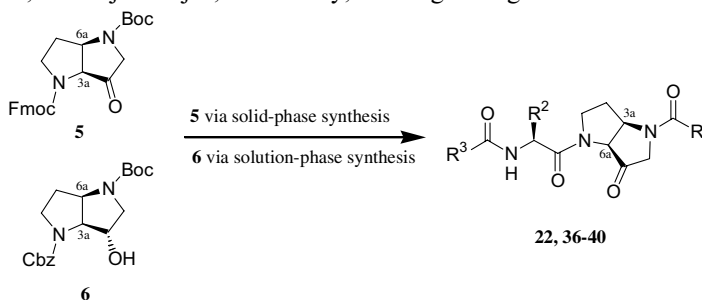
The RDF descriptors have been applied to the study of the A_{2B} agonist effect of adenosine analogues reported with this activity. A model able to describe more than 70% of the variance in the experimental activity was developed with the use of the mentioned approach. In contrast, none of the eleven different approaches was able to explain more than 47% of the variance in the mentioned property.

Synthesis and evaluation of *cis*-hexahydropyrrolo[3,2-*b*]pyrrol-3-one peptidomimetic inhibitors of CAC1 cysteinyl proteinases

pp 609–625

Martin Quibell,* Alex Benn, Nick Flinn, Tracy Monk, Manoj Ramjee, Peter Ray, Yikang Wang and John Watts

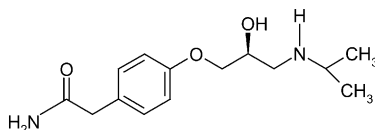
Fmoc-protected 5,5-bicyclic intermediates **5** and **6** were prepared through an intramolecular cyclisation of *anti*-epoxide **17**. Building block **5** was utilised in a solid phase synthesis and building block **6** in solution syntheses of potent peptidomimetic inhibitors of a range of CAC1 cysteinyl proteinases. Compound **22** was evaluated in vitro as a low nanomolar and selective inhibitor of human cathepsin K that exhibited sub-micromolar activity in a cell-based human osteoclast assay of bone resorption.



An efficient asymmetric synthesis of (*S*)-atenolol: using hydrolytic kinetic resolution

pp 627–630

D. Subhas Bose* and A. Venkat Narsaiah

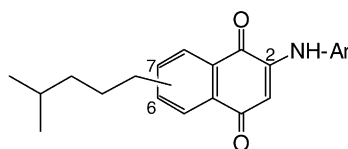


Enantioselective synthesis of (*S*)-atenolol has been described here. The chiral source used is the Jacobsen catalyst (*R,R*) (salen) Co(III)OAc complex for the resolution of terminal epoxide.

Synthesis and cytotoxicity of new aminoterpenylquinones

pp 631–644

José M. Miguel del Corral,* M^a Angeles Castro, Marina Gordaliza, M^a Luz Martín, Simone A. Gualberto, Ana M^a Gamito, Carmen Cuevas and Arturo San Feliciano



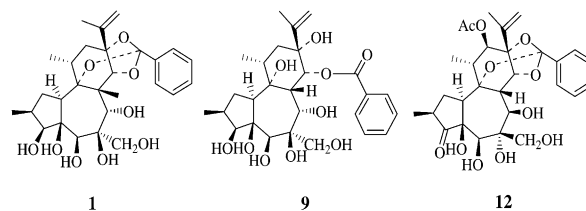
Several 6(7)-alkyl-2-(alkyl/arylamino)-1,4-naphthoquinones (NQ) have been prepared and evaluated as cytotoxics. Those with *p*-oxyarylamino substituents were the most potent compounds, showing GI₅₀ under μM level.

Novel diterpenoids with potent inhibitory activity against endothelium cell HMEC and cytotoxic activities from a well-known TCM plant *Daphne genkwa*

pp 645–655

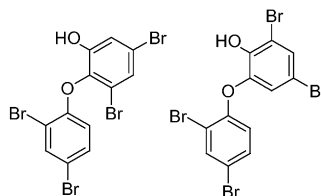
Zha-Jun Zhan, Cheng-Qi Fan, Jian Ding and Jian-Min Yue*

Twelve highly oxygenated novel daphnane-type diterpenoids genkwanines A–L (**1–12**), together with four known diterpenes (**13–16**), were isolated from the bud of *Daphne genkwa*, a well-known TCM. The inhibitory activity against endothelium cell HMEC proliferation and cytotoxic activities against two tumor cell lines were assessed for all the compounds **1–16**, and found to be significant and structure related.

**Polybrominated diphenyl ethers from a sponge of the *Dysidea* genus that inhibit Tie2 kinase**

pp 657–659

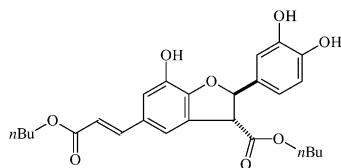
Ya-ming Xu, Randall K. Johnson and Sidney M. Hecht*



Antileishmanial activity, cytotoxicity and QSAR analysis of synthetic dihydrobenzofuran lignans and related benzofurans

pp 661–669

Sabine Van Miert, Stefaan Van Dyck, Thomas J. Schmidt, Reto Brun, Arnold Vlietinck, Guy Lemi re and Luc Pieters*

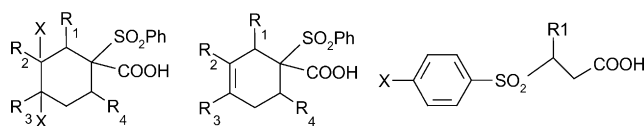


A synthetic dihydrobenzofuran lignan showed a high activity against chloroquine-resistant *Plasmodium falciparum* (strain K1) (IC_{50} 0.43 μ g/mL) and *Leishmania donovani* (axenic amastigotes) (IC_{50} 0.12 μ g/mL), which was confirmed in an infected macrophage assay (IC_{50} 0.19 μ g/mL).

**A structure–taste study of arylsulfonyl(cyclo)alkanecarboxylic acids**

pp 671–675

Violetta Lysiak, Aleksander Ratajczak, Agnieszka Mencil, Krystyna Jarzembek and Jaroslaw Polanski*



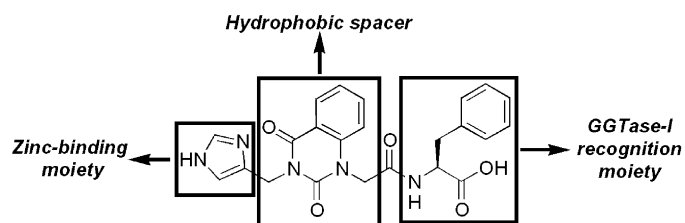
A structure–taste study of arylsulfonyl(cyclo)alkanecarboxylic acids is reported.

Design, synthesis, and evaluation of potent and selective benzoyleneurea-based inhibitors of protein geranylgeranyltransferase-I

pp 677–688

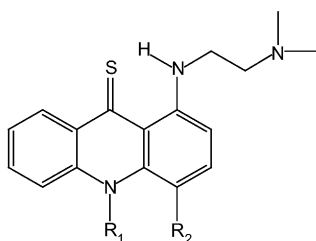
Dora Carrico, Michelle A. Blaskovich, Cynthia J. Bucher, Saïd M. Sebtı and Andrew D. Hamilton*

Using a benzoyleneurea scaffold as a mimetic for the central dipeptide (AA), CAAX peptidomimetic inhibitors that selectively block the activity of PGGTase-I over PFTase were synthesized. In this series, compound **6c** containing a L-phenylalanine moiety displayed the highest inhibition activity against PGGTase-I (IC_{50} = 170 nM). These PGGTase-I inhibitors represent novel and promising leads for the development of potent inhibitors of mammalian PGGTase-I as antitumor agents.

**Synthesis, biological evaluation, and molecular modeling of novel thioacridone derivatives related to the anticancer alkaloid acronycine**

pp 689–698

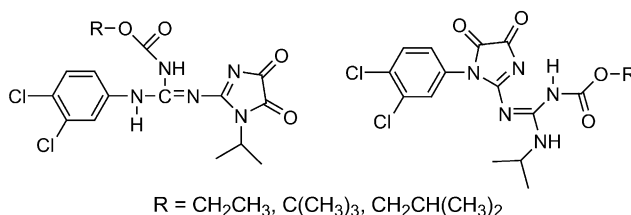
James P. Dheyongera, Werner J. Geldenhuys, Theodor G. Dekker and Cornelis J. Van der Schyf*



Structure identification and prophylactic antimalarial efficacy of 2-guanidinoimidazolidinedione derivatives

pp 699–704

Jian Guan,* Quan Zhang, Gettayacamin Montip, Jean M. Karle, Charles A. Ditusa, Wilbur K. Milhous, Donald R. Skillman and Ai J. Lin

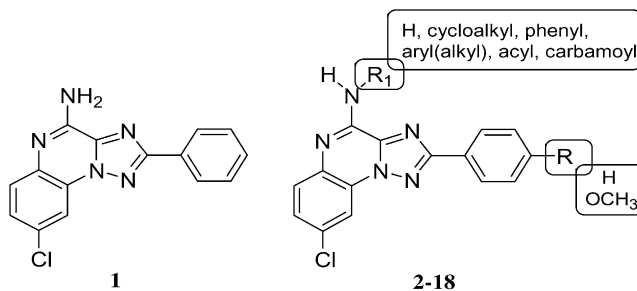


2-Aryl-8-chloro-1,2,4-triazolo[1,5-*a*]quinoxalin-4-amines as highly potent A₁ and A₃ adenosine receptor antagonists

pp 705–715

Daniela Catarzi,* Vittoria Colotta, Flavia Varano, Francesca Romana Calabri, Ombretta Lenzi, Guido Filacchioni, Letizia Trincavelli, Claudia Martini, Andrea Tralli, Christian Montopoli and Stefano Moro

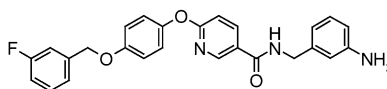
The synthesis and bA₁, bA_{2A}, and hA₃ adenosine receptor binding affinity of some 2-phenyl-1,2,4-triazolo[1,5-*a*]quinoxaline derivatives **2–18** bearing different substituents on either the 4-amino moiety (acyl or carbamoyl groups) or the 2-phenyl ring (4-OCH₃) of previously reported 8-chloro-2-phenyl-1,2,4-triazolo[1,5-*a*]quinoxalin-4-amine (**1**), are described. Structure–activity relationships have been explained analyzing the three-dimensional structure of the antagonist-A₃ receptor models obtained by molecular docking simulation.



Synthesis and structure–activity relationships of 6-{4-[(3-fluorobenzyl)oxy]phenoxy}-nicotinamide derivatives as a novel class of NCX inhibitors: a QSAR study

pp 717–724

Takahiro Kuramochi,* Akio Kakefuda, Ippei Sato, Issei Tsukamoto, Taku Taguchi and Shuichi Sakamoto

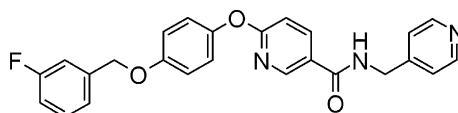


A series of 6-{4-[(3-fluorobenzyl)oxy]phenoxy}nicotinamide derivatives were prepared, and their inhibitory activities against the reverse and forward modes of the sodium–calcium exchanger were evaluated. The structure–activity relationships for these compounds are discussed, and the results of a QSAR study are presented.

Synthesis and structure–activity relationships of benzyloxyphenyl derivatives as a novel class of NCX inhibitors: effects on heart failure

pp 725–734

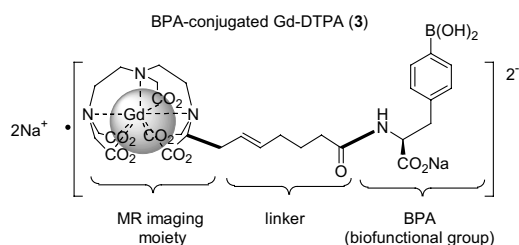
Takahiro Kuramochi,* Akio Kakefuda, Hiroyoshi Yamada, Takashi Ogiyama, Taku Taguchi and Shuichi Sakamoto



A series of benzyloxyphenyl derivatives were prepared, and their inhibitory activities against the reverse and forward modes of the sodium–calcium exchanger (NCX) were evaluated. The structure–activity relationships of these compounds are discussed. 6-{4-[(3-Fluorobenzyl)oxy]phenoxy}-*N*-(pyridin-4-ylmethyl)nicotinamide was further evaluated for its effects in a heart failure model.

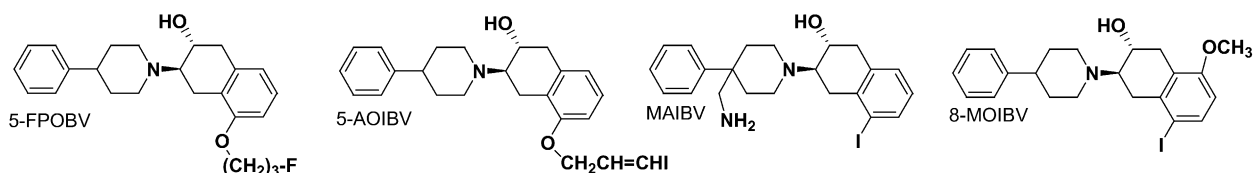
Synthesis and in vivo biodistribution of BPA–Gd–DTPA complex as a potential MRI contrast carrier for neutron capture therapy pp 735–743

Kazunori Takahashi, Hiroyuki Nakamura, Shozo Furumoto, Kazuyoshi Yamamoto, Hiroshi Fukuda,* Akira Matsumura and Yoshinori Yamamoto*



Synthesis and in vitro evaluation of new benzovesamicol analogues as potential imaging probes for the vesicular acetylcholine transporter pp 745–753

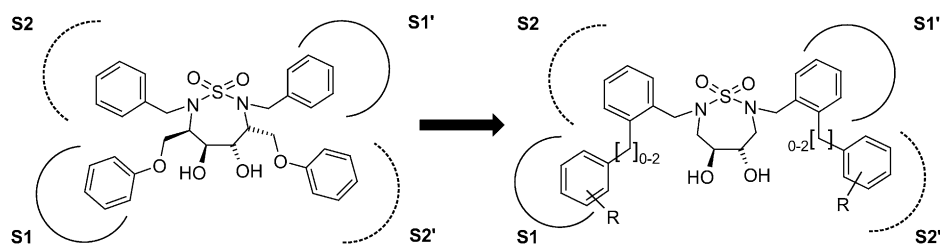
Yolanda Zea-Ponce, Sylvie Mavel,* Thaer Assaad, Shane E. Kruse, Stanley M. Parsons, Patrick Emond, Sylvie Chalon, Nicolas Giboureau, Michael Kassiou and Denis Guilloteau



Four sets of enantiomeric derivatives of benzovesamicol were synthesized and their binding affinities for the VACHT determined in vitro. The high affinity of the fluorinated (5-FPOBV) and the iodinated (5-AOIBV) derivatives make them potential PET or SPECT radiotracers.

Cyclic sulfamide HIV-1 protease inhibitors, with sidechains spanning from P2/P2' to P1/P1' pp 755–764

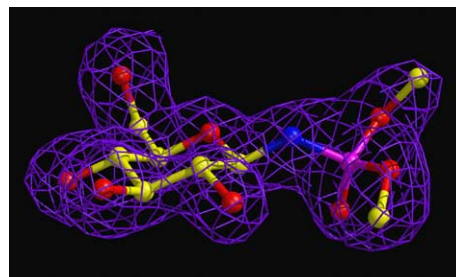
Anna Ax, Wesley Schaal, Lotta Vrang, Bertil Samuelsson, Anders Hallberg and Anders Karlén*



Binding of β-D-glucopyranosyl bismethoxyphosphoramidate to glycogen phosphorylase b: kinetic and crystallographic studies pp 765–772

Evangelia D. Chrysina, Magda N. Kosmopoulou, Rozina Kardakaris, Nicolas Bischler, Demetres D. Leonidas, Thanukrishnan Kannan, Duraikkannu Loganathan and Nikos G. Oikonomakos*

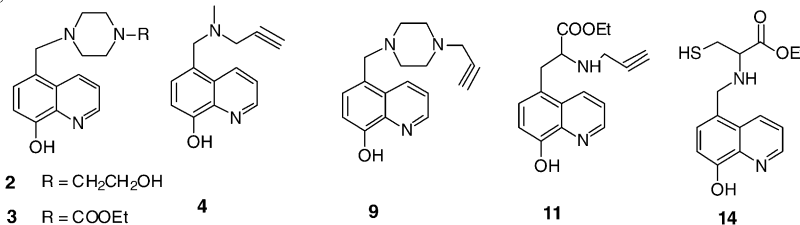
β-D-Glucopyranosyl bismethoxyphosphoramidate, a glucosyl phosphate analogue, was tested for inhibition of and binding to glycogen phosphorylase b. The structural basis of inhibition is presented by analysing the crystal structure of the enzyme in complex with the inhibitor at 1.83 Å resolution.



Design, synthesis, and evaluation of novel bifunctional iron-chelators as potential agents for neuroprotection in Alzheimer's, Parkinson's, and other neurodegenerative diseases

pp 773–783

Hailin Zheng, Lev M. Weiner, Orit Bar-Am, Silvina Epsztejn, Z. Ioav Cabantchik, Abraham Warshawsky, Moussa B. H. Youdim and Mati Fridkin*



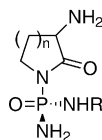
Several novel antioxidant iron chelators bearing 8-hydroxyxyquinoline moiety were synthesized, and their various properties related to neuroprotective action were investigated.



Synthesis and biological activity of sulphostin analogues, novel dipeptidyl peptidase IV inhibitors

pp 785–797

Masatoshi Abe,* Tetsuo Akiyama, Yōji Umezawa, Keiichi Yamamoto, Masashi Nagai, Hiroko Yamazaki, Yuh-ichiro Ichikawa and Yasuhiko Muraoka

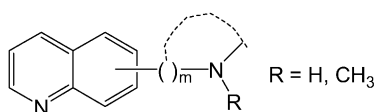


The required structure of sulphostin analogues for the dipeptidyl peptidase IV inhibitory activity. $n = 1-3$, R = H or SO₃H; Sulphostin: $n = 2$, R = SO₃H.

Design of novel nicotinic ligands through 3D database searching

pp 799–807

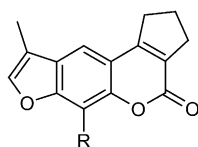
Luca Guandalini, Elisabetta Martini, Silvia Dei, Dina Manetti, Serena Scapecchi, Elisabetta Teodori, M. Novella Romanelli,* Katia Varani, Giovanni Greco, Loredana Spadola and Ettore Novellino



Design, synthesis and photobiological properties of 3,4-cyclopentenepsoralens

pp 809–817

Ornella Gia, Sebastiano Marciani Magno, Humberto Gonzalez-Diaz, Elias Quezada, Lourdes Santana, Eugenio Uriarte and Lisa Dalla Via*



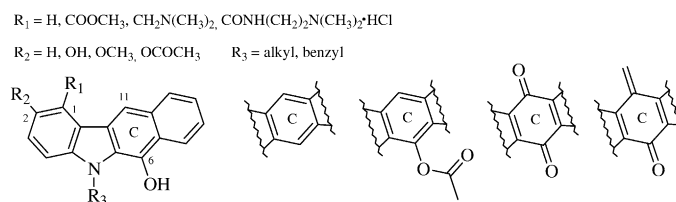
R = OCH₃, OH, O(CH₂)₃N(CH₃)₂

The QSAR directed synthesis of new cyclopentenepsoralens is reported. The derivative carrying the dimethylaminopropoxy side chain (5) exerted a noticeable photoantiproliferative activity, in agreement with the calculated posterior probability. The study of the photobiological properties evidenced the absence of skin phototoxicity and the ability to photoadd covalently to DNA.

Synthesis, antitumour activity and structure–activity relationships of 5*H*-benzo[*b*]carbazoles

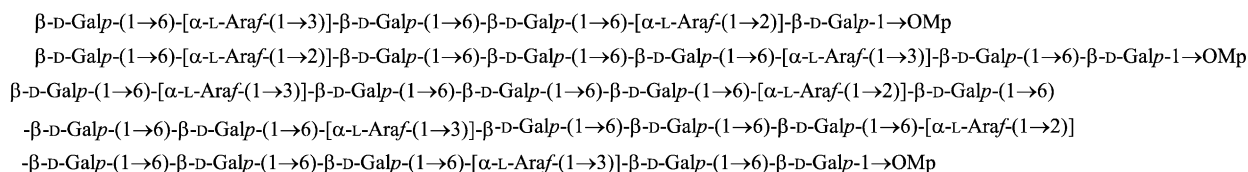
pp 819–837

Christian Asche,* Walter Frank, Antje Albert and Uwe Kucklaender

**Concise syntheses of arabinogalactans with β -(1 \rightarrow 6)-linked galactopyranose backbones and α -(1 \rightarrow 3)- and α -(1 \rightarrow 2)-linked arabinofuranose side chains**

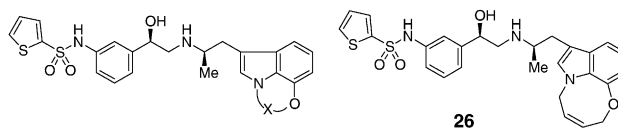
pp 839–853

Aixiao Li and Fanzuo Kong*

**Discovery of 1,7-cyclized indoles as a new class of potent and highly selective human β_3 -adrenergic receptor agonists with high cell permeability**

pp 855–868

Kazuhiro Mizuno,* Masaaki Sawa, Hiroshi Harada, Ikuko Taoka, Haruhisa Yamashita, Mayumi Oue, Hiroshi Tsujiuchi, Yukiyo Arai, Shinya Suzuki, Yasuji Furutani and Shiro Kato

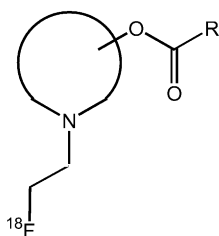


The synthesis and biological evaluation of a series of 1,7-cyclized indole-based human β_3 -adrenergic receptor (AR) agonists are described. SAR studies showed that the size of the 1,7-linker portion significantly affected subtype selectivity for the β_3 -AR. An unsaturated eight-membered ring analogue **26** exhibited potent agonistic activity and extremely high selectivity for human β_3 -AR.

Evaluation of ^{18}F -labeled acetylcholinesterase substrates as PET radiotracers

pp 869–875

Xia Shao, Robert A. Koeppe, Elizabeth R. Butch, Michael R. Kilbourn and Scott E. Snyder*

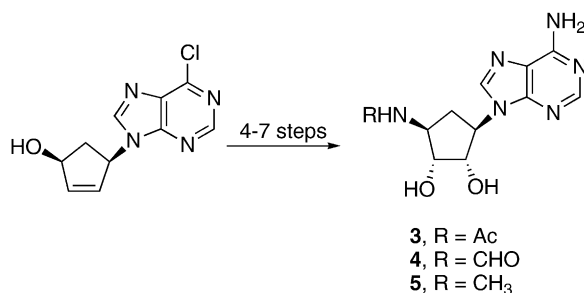


A series of ^{18}F -labeled PMP analogs was evaluated in vivo as AChE substrates for PET imaging.

Amino substituted derivatives of 5'-amino-5'-deoxy-5'-noraristeromycin

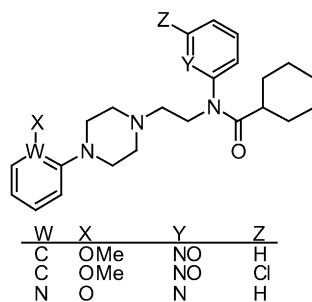
pp 877–882

Minmin Yang and Stewart W. Schneller*

**N-Oxide analogs of WAY-100635: new high affinity 5-HT_{1A} receptor antagonists**

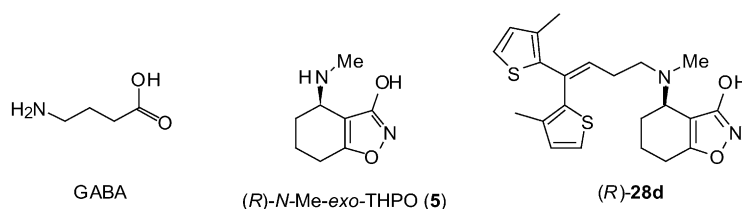
pp 883–893

Sandrine Marchais-Oberwinkler,* Bartek Nowicki, Victor W. Pike, Christer Halldin, Johan Sandell, Yuan-Hwa Chou, Balazs Gulyas, Lise T. Brennum, Lars Farde and Håkan V. Wikström

**Selective inhibitors of GABA uptake: synthesis and molecular pharmacology of 4-N-methylamino-4,5,6,7-tetrahydrobenzo[d]isoxazol-3-ol analogues**

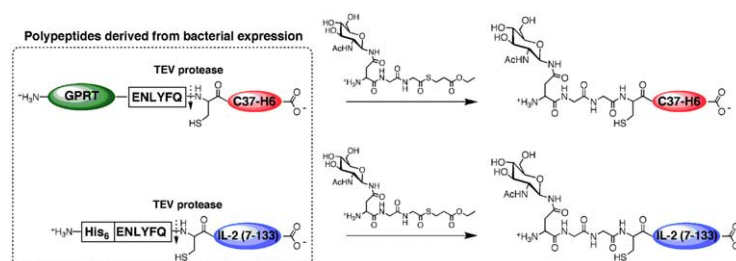
pp 895–908

Rasmus P. Clausen, Ejner K. Moltzen, Jens Perregaard, Sibylle M. Lenz, Connie Sanchez, Erik Falch, Bente Frølund, Tina Bolvig, Alan Sarup, Orla M. Larsson, Arne Schousboe and Povl Krosgaard-Larsen*

**A new strategy for glycoprotein synthesis: ligation of synthetic glycopeptides with truncated proteins expressed in *E. coli* as TEV protease cleavable fusion protein**

pp 909–915

Thomas J. Tolbert, Dirk Franke and Chi-Huey Wong*



OTHER CONTENTS**Bioorganic Medicinal Chemistry Reviews and Perspectives****pp 917–918****Contributors to this issue****p I****Instructions to contributors****pp III–VII**

*Corresponding author

Ⓜ⁺ Supplementary data available via ScienceDirect**COVER**

A safety pin ensures reliable connection as long as it is properly closed. Likewise *N*-acyl-sulfonamides can be used to link molecules, temporarily. Unlocking the safety-catch by controlled activation transforms the inert constructs into reactive species. These resulting *N*-acyl-*N*-alkyl-sulfonamide anchors depicted in the background possess attractive applicability in bioorganic and medicinal chemistry. [Heidler, P.; Link, A. *Bioorg. Med. Chem.* **2005**, *13*, 585–599].

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