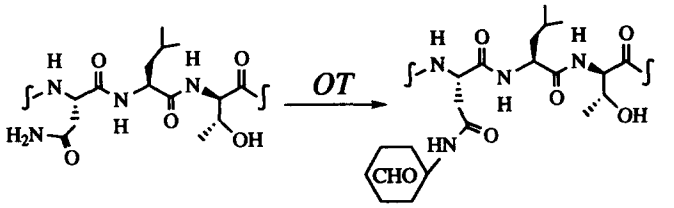
Asparagine-Linked Glycosylation: Specificity and Function of Oligosaccharyl Transferase

Bioorg. Med. Chem. **1995**, *3*, 1565

Barbara Imperiali* and Tamara L. Hendrickson
Department of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125

This review covers the recent studies on the composition and mechanism of action of Oligosaccharyl Transferase (OT) as well as the conformational consequences of N-linked protein glycosylation.

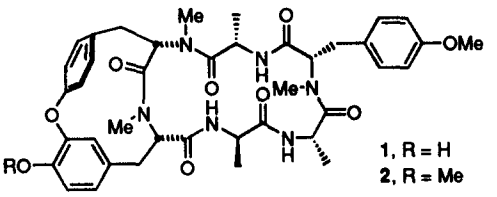


Key Analogs of the Tetrapeptide Subunit of RA-VII and Deoxybouvardin

Bioorg. Med. Chem. **1995**, *3*, 1579

Dale L. Boger,* Jiacheng Zhou, Brian Winter and Paul A. Kitos
Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, California, 92037, U.S.A. and Department of Biochemistry, University of Kansas, Lawrence, Kansas 66045, U.S.A.

Abstract—The synthesis and evaluation of two key analogs 3-4 of the potent antitumor antibiotics deoxybouvardin (1) and RA-VII (2) which contain fundamental modifications in the tetrapeptide subunit are described.

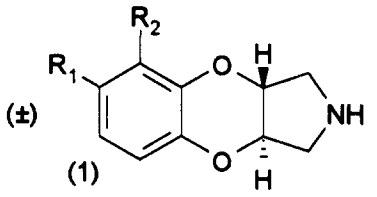


Synthesis of Benzodioxinopyrroles as Selective α_2-Adrenoceptor Antagonists

Bioorg. Med. Chem. **1995**, *3*, 1595

J. Kitchin,*[a] A. D. Borthwick,[a] A. C. Brodie,[b] P. C. Cherry,[a] A. J. Crame,[a] A. J. Pipe,[a] P. A. Procopiou,[a] M. A. Seaman,[a] and J. P. Turnbull[b]
[a]*Departments of Medicinal Chemistry and* [b]*Process Research, Glaxo-Wellcome, Medicines Research Centre, Gunnels Wood Road, Stevenage, Hertfordshire, SG1 2NY, United Kingdom.*

Tetrahydro–1*H*-benzodioxino[2,3-*c*]pyrroles (**1**) have been synthesized and found to be potent and selective α_2-adrenoceptor antagonists. A compound of particular interest is Fluparoxan (**1**; R_1 = H, R_2 = F).

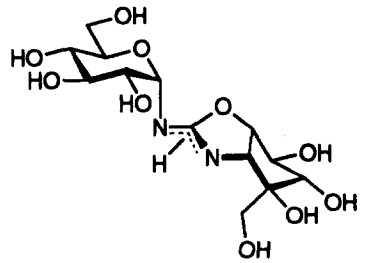


Further Chemical Modification of Trehalase Inhibitor Trehazolin: Structure and Inhibitory-Activity Relationship of the Inhibitor

Bioorg. Med. Chem. **1995**, *3*, 1605

C. Uchida, T. Yamagishi, H. Kitahashi, Y. Iwaisaki and S. Ogawa,
Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Kohoku-ku, Yokohama, 223 Japan

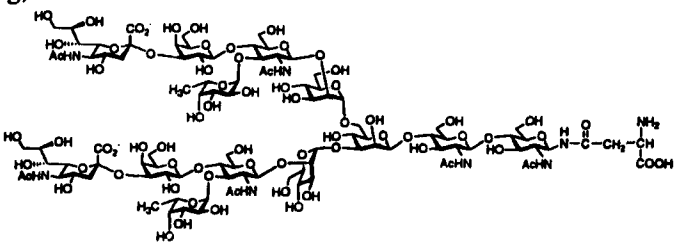
Eight trehazolin analogues were synthesized and assayed for trehalase inhibitor. The structure–activity relationship deduced here led to a finding of new lead compounds for development of glycohydrolase inhibitors.



Enzymatic Synthesis of a Sialyl Lewis X Dimer from Egg Yolk as an Inhibitor of E-Selectin

Bioorg. Med. Chem. **1995**, *3*, 1625

Chun-Hung Lin,[a] Makoto Shimazaki,[a] Chi-Huey Wong,[a]* Mamoru Koketsu,[b] Lekh Raj Juneja[b] and Mujo Kim[b]
[a]*Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, CA 92037, U.S.A.*
[b]*Central Research Laboratories, Taiyo Kagaku Co., Ltd, 1-3 Takaramachi, Yokkaichi, Mie 510, Japan*

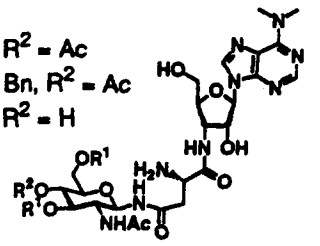


Synthesis of N-Acetylglucosaminyl Asparagine Substituted Puromycin Analogues

Bioorg. Med. Chem. **1995**, *3*, 1631

Peer Kirsch[a], Naoto Kusunose[a], Jun-ichi Aikawa[a], Takanori Kigawa[a], Shigeyuki Yokoyama[a,b] and Tomoya Ogawa[a,c,]*
[a]*The Institute of Physical and Chemical Research (RIKEN), Hirosawa 2-1, Wako-shi, Saitama 351-01, Japan*
[b]*Department of Cellular Biochemistry, Graduate School of Agriculture and Life Sciences, University of Tokyo, Yayoi 1-1-1, Bunkyo-ku, Tokyo 113, Japan*
[c]*Department of Biophysics and Biochemistry, Graduate School of Science, University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 113, Japan*

2a: $R^1 = R^2 = Ac$
2b: $R^1 = Bn$, $R^2 = Ac$
2c: $R^1 = R^2 = H$

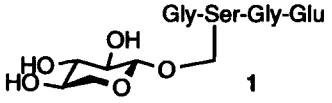


A Stereocontrolled Synthetic Approach to Glycopeptides Corresponding to the Carbohydrate-Protein Linkage Region of Cell-Surface Proteoglycans

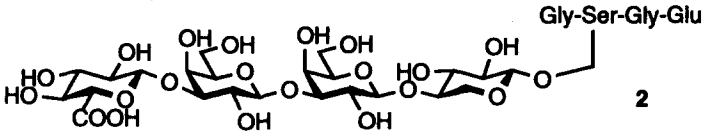
Bioorg. Med. Chem. **1995**, *3*, 1637

K.W. Neumann, J. Tamura, and T. Ogawa
The Institute of Physical and Chemical Research (RIKEN), Wako-shi, Saitama, Japan

The glycopeptides 1 and 2 which correspond to the carbohydrate-protein linkage region of cell-surface proteoglycans Thrombomodulin and Syndecan-1 were synthesized in a stereocontrolled manner.



1



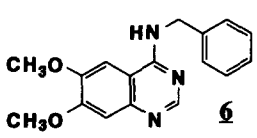
2

Enantioselective Inhibition of the Epidermal Growth Factor Receptor Tyrosine Kinase by 4-(α-Phenethylamino)quinazolines

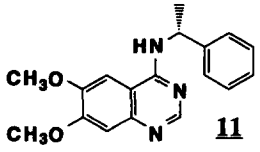
Bioorg. Med. Chem. **1995**, *3*, 1651

Alexander J. Bridges,* Donna R. Cody, Hairong Zhou, Amy McMichael and David W. Fry
Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, 2800 Plymouth Rd, Ann Arbor, MI 48105.

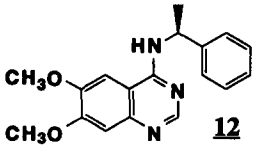
Compound **6** has a 10 nM IC_{50} for the EGFR TK. An [*R*]-methyl (**11**) potentiates the IC_{50} to 1.6 nM., whereas the [*S*]-enantiomer (**12**) is a 4 μM inhibitor. Similar results are seen for other quinazoline substituents, and a possible explanation for these very large potency differences is given.



6



11



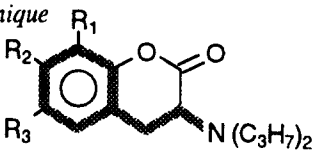
12

Bioorg. Med. Chem. **1995**, *3*, 1657

Syntheses and molecular structures of 3-N,N-di-*n*-propylamino-2-chromanones as new analogues of dopamine

M. Benoit-Guyod,[§] A. Namil,[§] E. Nicolle,[§] C. Coulombeau,[+] and G. Leclerc [§*]

[§]*Groupe de Pharmacochimie Moléculaire, Laboratoire de Chimie Organique, Université Joseph Fourier - Grenoble, UFR de Pharmacie, BP 138, 38240 Meylan Cedex, France*
[+]*LEDSS (Laboratoire d'Etudes Dynamiques et Structurales de la Sélectivité) Chimie bioorganique CNRS URA 332, Université Joseph Fourier - BP 53X 38041 Grenoble Cedex 2, France*

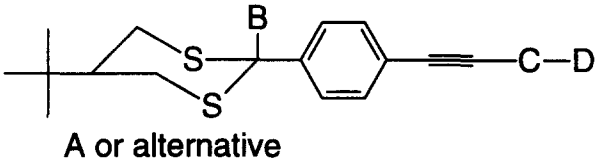


Seven chromanone derivatives (R_1, R_2, R_3 = OH or H) were synthesized in 6 or 7 steps and studied as rigid analogues of dopamine. Computer molecular modelling calculations were performed.

Bioorg. Med. Chem. **1995**, *3*, 1667

Affinity Probes for the GABA-Gated Chloride Channel: Selection of 5*e*-*tert*-Butyl-2*e*-[4-(substituted-ethynyl)phenyl]-1,3-dithianes and Optimization of Linker Moiety

Qing X. Li and John E. Casida*
Environmental Chemistry and Toxicology Laboratory, Dept. of ESPM, University of California, Berkeley, CA 94720-3112, U.S.A.

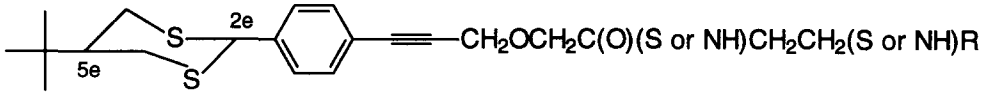


Structure–activity studies establish a preference for A = *tert*-butyldithiane, B = H, C = long, straight chain spacer and D = photoactivatable, biotin or other substituent

Bioorg. Med. Chem. **1995**, *3*, 1675

Affinity Probes for the GABA-Gated Chloride Channel: 5*e*-*tert*-Butyl-2*e*-[4-(substituted-ethynyl)phenyl]-1,3-dithianes with Photoactivatable, Fluorescent, Biotin, Agarose, and Protein Substituents

Qing X. Li and John E. Casida*
Environmental Chemistry and Toxicology Laboratory, Dept. of ESPM, University of California, Berkeley, CA 94720-3112, U.S.A.



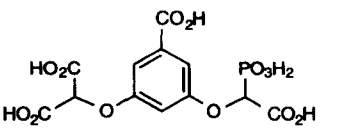
R is photoactivatable, fluorescent, biotin, agarose or protein substituent

Bioorg. Med. Chem. **1995**, *3*, 1685

New EPSP Synthase Inhibitors: Synthesis and Evaluation of an Aromatic Tetrahedral Intermediate Mimic Containing a 3-Malonate Ether as a 3-Phosphate Surrogate

Michael J. Miller,[a] Darryl G. Cleary,[a] Joel E. Ream,[a] Kristin R. Snyder,[a] and James A. Sikorski[b*]
[a]*Ceregen and* [b]*Monsanto Corporate Research, Units of Monsanto Company, 700 Chesterfield Parkway North, St. Louis, Missouri 63198, U.S.A.*

Aromatic analogues of the EPSP synthase reaction substrate, product, and tetrahedral intermediate were synthesized from 3,5-dihydroxybenzoic acid, containing a 3-malonate ether in place of the normal 3-phosphate group. These molecules more clearly define the scope and limitations of incorporating 3-malonate ethers as 3-phosphate replacements in this system. The potency of **5** suggests that a benzene ring is an effective substitute for the more complex shikimate ring in EPSP synthase inhibitors.



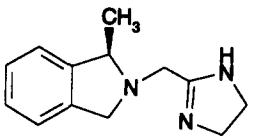
5, K_i (apparent) = 1.3 μM

Synthesis of a Selective Alpha-2A Adrenoceptor Antagonist, BRL 48962, and Its Characterization at Cloned Human Alpha-Adrenoceptors

Bioorg. Med. Chem. **1995**, *3*, 1693

Lee J. Beeley,[a*] John M. Berge,[a] Helen Chapman,[b] Paul Hieble,[c] John Kelly,[b] Diane P. Naselsky,[c] Caroline M. Rockell[a] and Paul W. Young[b]

[a]Department of Medicinal Chemistry, SmithKline Beecham Pharmaceuticals, Great Burgh, Yew Tree Bottom Road, Epsom, Surrey, KT18 5XQ, UK; [b]Department of Vascular Biology, SmithKline Beecham Pharmaceuticals, The Frythe, Welwyn, Herts., AL6 9AR, UK; and [c]Department of Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA., 19406, USA.



BRL 48962

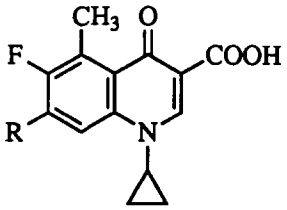
Abstract—The chiral synthesis of the potent and selective alpha-2A antagonist, BRL 48962, is described. Evaluation of BRL 48962 at cloned alpha-adrenoceptors indicates that this antagonist has a selectivity in the order of 30-fold for the alpha-2A subtype.

Synthesis and Biological properties of Substituted 1,4-dihydro-5-methyl-4-oxo-3-quinolinecarboxylic Acids

Bioorg. Med. Chem. **1995**, *3*, 1699

Hisashi Miyamoto, Hiroshi Yamashita, Hiraki Ueda, Hisashi Tamaoka, Kzunoli Ohmoli and Kazuyuki Nakagawa

Microbiological Research Institute, Otsuka Pharmaceutical Co., Ltd., Kagasuno 463-10, Kawauchi-cho, Tokushima 771-01 Japan



The synthesis and *in vitro* and *in vivo* antibacterial activity of 5-methylquinolone derivatives as described.