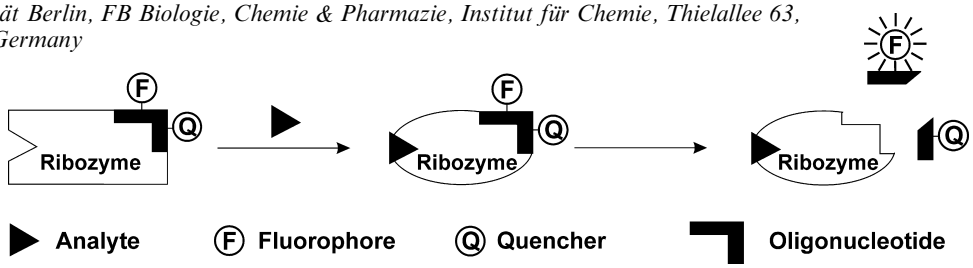
Detection of Small Organic Analytes by Fluorescing Molecular Switches

Bioorg. Med. Chem. 9 (2001) 2521

Christian Frauendorf and Andres Jäschke

Freie Universität Berlin, FB Biologie, Chemie & Pharmazie, Institut für Chemie, Thielallee 63, 14195 Berlin, Germany

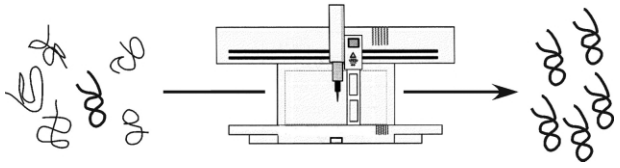


Automated Selection of Anti-Protein Aptamers

Bioorg. Med. Chem. 9 (2001) 2525

J. Colin Cox[a] and Andrew D. Ellington[b]

[a]*Institute for Cellular and Molecular Biology, University of Texas at Austin, Austin, TX 78712, USA*
[b]*Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, TX 78712, USA*

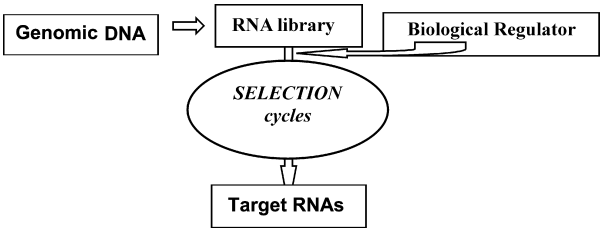


Selection of Genomic Target RNAs by Iterative Screening

Bioorg. Med. Chem. 9 (2001) 2533

Christine Brunel,[a,b] Bernard Ehresmann,[a] Chantal Ehresmann[a] and Michael McKeown[b]

[a]*UPR 9002 du CNRS, Institut de Biologie Cellulaire et Moléculaire, 15 rue Descartes, 67084 Strasbourg Cedex, France*
[b]*Molecular Biology and Virology Laboratory, Salk Institute, PO Box 85800, San Diego, CA 92186, USA*



In Vitro Selection of DNA Aptamers That Bind L-Tyrosinamide

Bioorg. Med. Chem. 9 (2001) 2543

Elena Vianini, Manlio Palumbo and Barbara Gatto*

Department of Pharmaceutical Sciences, University of Padova, via Marzolo 5, 35131 Padova, Italy

This communication describes the identification through the SELEX methodology of single stranded DNA molecules able to bind L-Tyrosinamide. Most of the selected aptamers share a common consensus sequence of 38 nucleotides with a K_d value for L-Tyrosinamide in the micromolar range.

```
pe35  --TGGAGCTTGGATT GATGTGGTGTGTGAG --TGC-GGTGCCC--
pe30  GCTGGAGCTTGGATT GATGTGGTGTGTGAG --TGC-GGTGCCC--
pe21  GCTGGAGCTTGGATT GATGTGGTGTGTCAG --TGC-GGAGCCC--
pe4   --TGGAGCCTGGATT GATGTGGTGTGTGAG --TGC-GGTGCCC--
pe27  --TGGAGCTTGGATT GATGTGGTGTGTGAG --TGA-GGTGCCC--
pe37  GCTGGAGCTTGGATT GATGTGGTGTGTGAG G-TGCCGGTGCCC--
pe36  --TGGAGCTTGGATT GATGTGGTGTGTGTG AGTGC-GGTGCCC--
pe45  --TGGAGCTTGGATT GATGTGGTGTGTGAC --TGC-GGTGCCC--
pe18  --TGGAGCTTGGATT GATGTGGTGTGTGAG --TGC-GGTGCCCCG
```

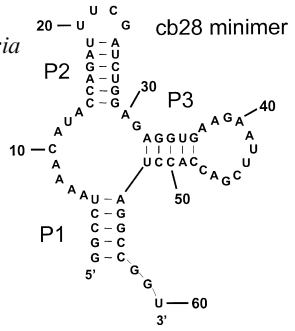
Bioorg. Med. Chem. 9 (2001) 2549

A Tetracycline-binding RNA Aptamer

Christian Berens, Alison Thain and Renée Schroeder

Institute of Microbiology and Genetics, Vienna Biocenter Dr. Bohrgasse 9/4, A-1030 Vienna, Austria

In vitro selection was employed to isolate small RNAs with high affinity to the antibiotic tetracycline.

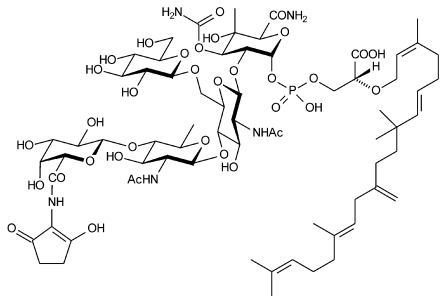


Bioorg. Med. Chem. 9 (2001) 2557

Aptamers That Bind to the Antibiotic Moenomycin A

Heike Schürer,[a] Katherina Stembera,[b] Dietmar Knoll,[b] Günter Mayer,[c] Michael Blind,[c] Hans-Heinrich Förster,[a] Michael Famulok,[c] Peter Welzel[b] and Ulrich Hahn[a]

[a]*Universität Leipzig, Institut für Biochemie, Talstr. 33, D-04103 Leipzig, Germany*
[b]*Universität Leipzig, Institut für Organische Chemie, Johannisallee 29, D-04103 Leipzig, Germany*
[c]*Rheinische Friedrich-Wilhelms-Universität Bonn, Kekulé-Institut für Organische Chemie und Biochemie, Gerhard-Domagk-Str. 1, D-53121 Bonn, Germany*

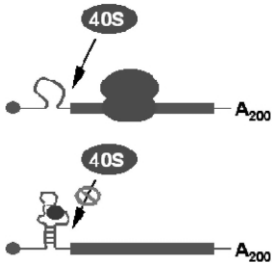


Bioorg. Med. Chem. 9 (2001) 2565

Inducible Regulation of the *S. cerevisiae* Cell Cycle Mediated by an RNA Aptamer–Ligand Complex

Dilara Grate and Charles Wilson

Department of Biology and Center for the Molecular Biology of RNA, University of California at Santa Cruz, Santa Cruz, CA 95064, USA



Bioorg. Med. Chem. 9 (2001) 2571

Uptake and Intracellular Transport of RNA Aptamers in African Trypanosomes Suggest Therapeutic "Piggy-Back" Approach

Matthias Homann and H. Ulrich Göringer

Department of Microbiology and Genetics, Darmstadt University of Technology, Schnittspahnstr. 10, 64287 Darmstadt, Germany

Living trypanosome cells were used as complex targets for the *in vitro* selection of RNA aptamers. One of these aptamers binds to a 42 kDa surface protein of *Trypanosoma brucei* and is rapidly endocytosed. Co-localisation experiments with transferrin suggest a receptor-mediated uptake and vesicular transport of the RNAs to the lysosome. Aptamer-coupled biotin molecules are effectively transported to the lysosome suggesting the use of RNA aptamers to target conjugated toxins to the lysosomal compartment of the parasite.

Bioorg. Med. Chem. 9 (2001) 2581

Selection of Deoxyribozyme Ligases That Catalyze the Formation of an Unnatural Internucleotide Linkage

Matthew Levy and Andrew D. Ellington

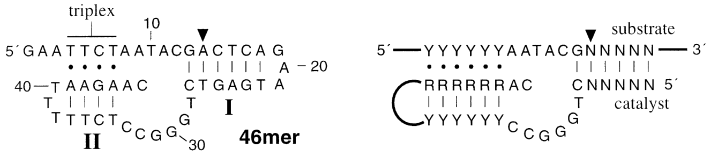
Department of Chemistry and Biochemistry, Institute for Cellular and Molecular Biology, University of Texas at Austin, Austin, TX 78712, USA

Bioorg. Med. Chem. 9 (2001) 2589

Characterization of a DNA-Cleaving Deoxyribozyme

Nir Carmi and Ronald R. Breaker

Department of Molecular, Cellular and Developmental Biology, Yale University, New Haven, CT 06520-8103, USA



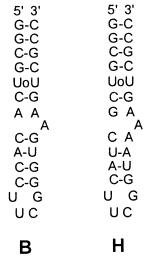
Bioorg. Med. Chem. 9 (2001) 2601

Aminoglycoside Binding to Human and Bacterial A-Site rRNA Decoding Region Constructs

Do Hyun Ryu and Robert R. Rando

Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, 45 Shattuck Street, Boston, MA 02115, USA

Quantitative aminoglycoside binding experiments for prokaryotic (**B**) and eukaryotic (**H**) A-site RNA constructs showed that there is little in the way of differential binding affinities of aminoglycosides for the two targets.

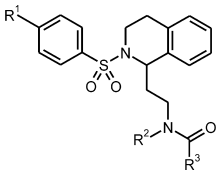


Bioorg. Med. Chem. 9 (2001) 2609

Parallel Synthesis and Biological Activity of a New Class of High Affinity and Selective δ-Opioid Ligand

D.R. Barn,[a] W.L. Caulfield,[a] J. Cottney,[a] K. McGurk,[b] J.R. Morphy,[a] Z. Rankovic[a] and B. Roberts[c]

[a]*Organon Laboratories Ltd, Newhouse, ML1 5SH, Scotland, UK*
[b]*N.V. Organon, Molenstraat 110, 5430 BH, Oss, The Netherlands*
[c]*AstraZeneca, Alderley Park, Macclesfield, Cheshire, SK10 4TG, UK*

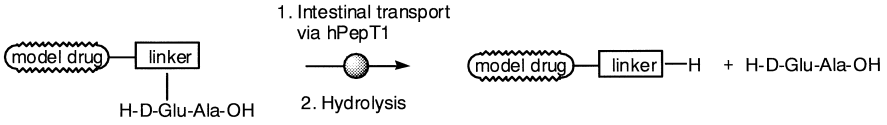


Bioorg. Med. Chem. 9 (2001) 2625

Application of Enzymatically Stable Dipeptides for Enhancement of Intestinal Permeability. Synthesis and In Vitro Evaluation of Dipeptide-Coupled Compounds

Gerda M. Friedrichsen,[a] Palle Jakobsen,[b] Mitchell Taub[c] and Mikael Begtrup[a]

[a]*Department of Medicinal Chemistry, The Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen, Denmark*
[b]*Medicinal Chemistry Research, Novo Nordisk A/S, Novo Nordisk Park, DK-2760 Maaloev, Denmark*
[c]*Department of Drug Metabolism, Novo Nordisk A/S, Novo Nordisk Park, DK-2760 Maaloev, Denmark*



Bioorg. Med. Chem. 9 (2001) 2633

The Role of Backbone Conformation in Deltorphin II Binding: A QSAR Study of New Analogues Modified in the 5-, 6-Positions of the Address Domain

Stephen E. Schullery,[a] David W. Rodgers,[a] Sakambari Tripathy,[a] Don Eranda Jayamaha,[a] Medha D. Sanvordekar,[a] Kutralanathan Renganathan,[a] Carol Mousigian[b] and Deborah L. Heyl[a]

[a]*Department of Chemistry, Eastern Michigan University, Ypsilanti, MI 48197, USA*
[b]*College of Pharmacy, The University of Michigan, Ann Arbor, MI 48109, USA*

The synthesis, opioid binding affinities, and a QSAR study of a series of deltorphin peptides modified in the Val^5 or Val^6 position are reported. A Langevin dynamics simulation approach was utilized to assess backbone conformational effects.

Tyr-D-Ala-Phe-Glu-X-Val-Gly-NH_2 and Tyr-D-Ala-Phe-Glu-Val-X-Gly-NH_2.

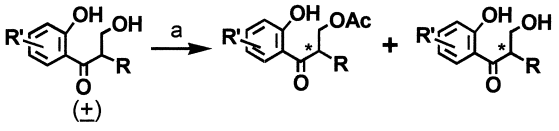
Bioorg. Med. Chem. 9 (2001) 2643

Lipase-Catalyzed Chemo- and Enantioselective Acetylation of 2-Alkyl/aryl-3-hydroxypropiophenones

Rajesh Kumar,[a] Abul Azim,[a] Vijayendra Kumar,[a] Sunil K. Sharma,[a] Ashok K. Prasad,[a] Oliver W. Howarth,[b] Carl E. Olsen,[c] Subhash C. Jain[a] and Virinder S. Parmar[a]

[a]*Department of Chemistry, University of Delhi, Delhi-110 007, India*
[b]*Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK*
[c]*Chemistry Department, Royal Veterinary and Agricultural University, DK-1871 Frederiksberg C, Copenhagen, Denmark*

The chemo- and enantioselective capabilities of porcine pancreatic lipase (PPL) in tetrahydrofuran, and *Candida rugosa* lipase (CRL) in diisopropyl ether have been investigated for the acetylation of racemic 2-alkyl/aryl-3-hydroxypropiophenones, which are important precursors in the synthesis of biologically active chromanones and isoflavanones.



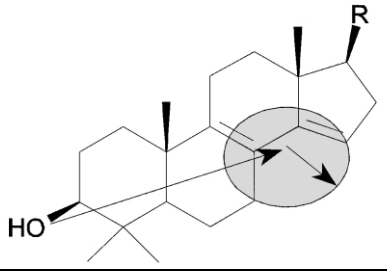
a) Vinyl acetate, PPL /CRL

Bioorg. Med. Chem. 9 (2001) 2653

Relation Between the Molecular Electrostatic Potential and Activity of Some FF-MAS Related Sterol Compounds

D.R. Boer,[a] H. Kooijman,[a] J. van der Louw,[b] M. Groen,[b] J. Kelder[c] and J. Kroon[a]

[a]*Department of Crystal & Structural Chemistry, Bijvoet Center for Biomolecular Research, Utrecht University, Utrecht, The Netherlands*
[b]*Department of Medicinal Chemistry, N.V. Organon, Oss, The Netherlands*
[c]*Department of Molecular Design and Informatics, N.V. Organon, Oss, The Netherlands*



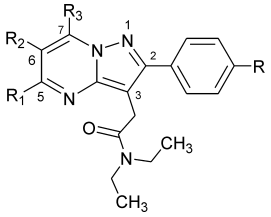
Bioorg. Med. Chem. 9 (2001) 2661

2-Arylpyrazolo[1,5-*a*]pyrimidin-3-yl Acetamides. New Potent and Selective Peripheral Benzodiazepine Receptor Ligands

Silvia Selleri,[a] Fabrizio Bruni,[a] Camilla Costagli,[a] Annarella Costanzo,[a] Gabriella Guerrini,[a] Giovanna Ciciani,[a] Barbara Costa[b] and Claudia Martini[b]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Firenze, Via G. Capponi 9, 50121 Firenze, Italy*
[b]*Dipartimento di Psichiatria, Neurobiologia, Farmacologia e Biotecnologie, Università di Pisa, Via Bonanno 6, 56126 Pisa, Italy*

Synthesis, SAR study and biological evaluation of a new series of pyrazolo[1,5-*a*]pyrimidine derivatives are reported.



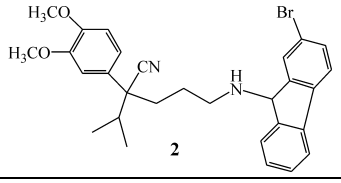
Bioorg. Med. Chem. 9 (2001) 2673

Structure–Activity Relationships and Optimisation of the Selective MDR Modulator 2-(3,4-Dimethoxyphenyl)-5-(9-fluorenylamino)-2-(methylethyl) Pentanenitrile and Its *N*-Methyl Derivative

Silvia Dei,[a] Elisabetta Teodori,[a] Arlette Garnier-Suillerot,[b] Fulvio Gualtieri,[a] Serena Scapecchi,[a] Roberta Budriesi[c] and Alberto Chiarini[c]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Firenze, Via Gino Capponi 9, 50121 Firenze, Italy*
[b]*Laboratoire de Physicochimie Biomoléculaire et Cellulaire, ESA CNRS 7033, Université Paris Nord,74 rue Marcel Cachin, 93017 Bobigny, France*
[c]*Dipartimento di Scienze Farmaceutiche, Università di Bologna, Via Belmeloro 6, 40126 Bologna, Italy*

Several ring-substituted derivatives of previously studied MDR inhibitors 2-(3,4-dimethoxyphenyl)-5-(9-fluorenylamino)-2-(methylethyl)pentanenitrile and 2-(3,4-dimethoxyphenyl)-5-[(9-fluorenyl)-*N*-methylamino)]-2-(methylethyl)pentanenitrile have been synthesised and studied with the aim of optimising activity and selectivity. The results show that MDR inhibition is scarcely sensitive to modulation of the electronic properties of the fluorene ring. Even if dramatic improvement was not obtained, one of the compounds (**2**) showed improved potency and selectivity with respect to the leads and appears to be a better candidate for drug development.

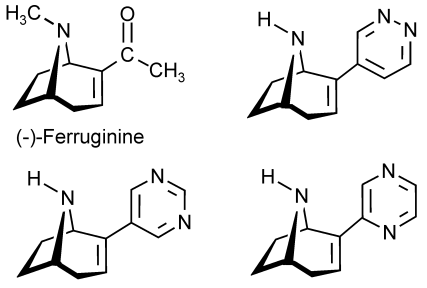


Bioorg. Med. Chem. 9 (2001) 2683

Synthesis and Evaluation of Diazine Containing Bioisosteres of (−)-Ferruginine as Ligands for Nicotinic Acetylcholine Receptors

Daniela Gündisch,[b] Klaus Harms,[c] Simone Schwarz,[a] Gunther Seitz,[a] Milton T. Stubbs[a] and Thomas Wegge[a]

[a]*Department of Pharmaceutical Chemistry, Philipps-University, Marbacher Weg 6, D-35032 Marburg, Germany*
[b]*Department of Pharmaceutical Chemistry, Rhein. Friedr.-Wilhelm-University, Kreuzbergweg 26, D-53115 Bonn, Germany*
[c]*Fachbereich Chemie, Philipps-University, Hans-Meerwein-Straße, D-35032 Marburg, Germany*

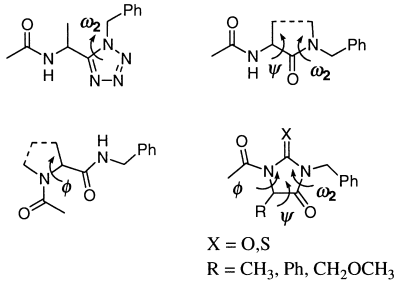


Bioorg. Med. Chem. 9 (2001) 2693

Functionalized Amino Acid Anticonvulsants: Synthesis and Pharmacological Evaluation of Conformationally Restricted Analogues

Arnaud LeTiran,[a] James P. Stables[b] and Harold Kohn[c]

[a]*Department of Chemistry, University of Houston, Houston, TX 77204-5641, USA*
[b]*Epilepsy Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Federal Building, Room 114, Bethesda, MD 20892-9020, USA*
[c]*Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-7360, USA*

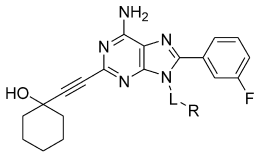


Bioorg. Med. Chem. 9 (2001) 2709

2-Alkynyl-8-aryladenines Possessing an Amide Moiety: Their Synthesis and Structure–Activity Relationships of Effects on Hepatic Glucose Production Induced Via Agonism of the A_{2B} Adenosine Receptor

Hitoshi Harada, Osamu Asano, Tsutomu Kawata, Takashi Inoue, Tatsuo Horizoe, Nobuyuki Yasuda, Kaya Nagata, Manabu Murakami, Junsaku Nagaoka, Seiichi Kobayashi, Isao Tanaka and Shinya Abe

Tsukuba Research Laboratories, Eisai Company, Ltd., 5-1-3 Tokodai, Tsukuba, Ibaraki 300-2635, Japan



L = alkylene, phenyl ring

R = amide, carbamate, sulfonamide

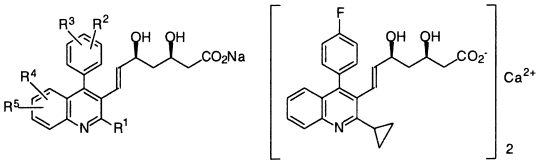
Bioorg. Med. Chem. 9 (2001) 2727

Synthesis and Biological Evaluations of Quinoline-based HMG-CoA Reductase Inhibitors

Mikio Suzuki,[a] Hiroshi Iwasaki,[b] Yoshihiro Fujikawa,[b] Masaki Kitahara,[c] Mitsuaki Sakashita[b] and Ryozo Sakoda[a]

[a]*Central Research Laboratories, Nissan Chemical Industries, Ltd., 722-1 Tsuboi-cho, Funabashi, Chiba 274-8507, Japan*
[b]*Pharmaceuticals Division, Nissan Chemical Industries, Ltd., 7-1, Kanda Nishiki-cho 3-chome, Chiyoda-ku, Tokyo 101-0054, Japan*
[c]*Biological Research Laboratories, Nissan Chemical Industries, Ltd., 1470 Shiraoka, Shiraoka-cho, Minamisaitama-gun, Saitama 349-0294, Japan*

A series of quinoline-based HMG-CoA reductase inhibitors were synthesized to evaluate which has a cyclopropyl side chain, showed the greatest potency.



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Bioorg. Med. Chem. 9 (2001) 2745

Design and Structure–Activity Relationship of Thrombin Inhibitors with an Azaphenylalanine Scaffold: Potency and Selectivity Enhancements Via P2 Optimization

A. Zega,[a] G. Mlinšek,[b] P. Šepic,[a] S. Golič Grdadolnik,[b] T. Šolmajer,[b,c] T.B. Tschopp,[d] B. Steiner,[d] D. Kikelj[a] and U. Urleb[a,c]

[a]*Faculty of Pharmacy, University of Ljubljana, Aškerčeva 7, 1000 Ljubljana, Slovenia*
[b]*National Institute of Chemistry, POB 3430, Hajdrihova 19, 1115 Ljubljana, Slovenia*
[c]*Lek, d.d., Pharmaceutical and Chemical Company, 1526 Ljubljana, Slovenia*
[d]*Pharma Division, Preclinical Research, F. Hoffmann La Roche Ltd, 4002 Basel, Switzerland*