Bioorg. Med. Chem. Lett. 13 (2003) 2251

Synthesis of a Fluorescent Chemosensor Suitable for the Imaging of Zinc(II) in Live Cells

Nathaniel C. Lim,[a] Lili Yao,[b] Hedley C. Freake[b] and Christian Brückner[a,*]

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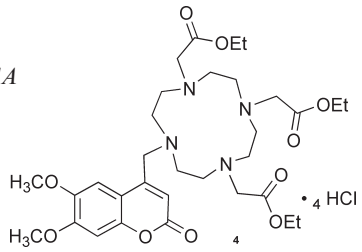
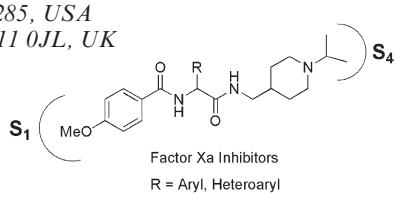


Bioorg. Med. Chem. Lett. 13 (2003) 2255

A Four Component Coupling Strategy for the Synthesis of D-Phenylglycinamide-derived Non-Covalent Factor Xa Inhibitors

Scott M. Sheehan,[a,*] John J. Masters,[a] Michael R. Wiley,[a] Stephen C. Young,[b] John W. Liebeschuetz,[b] Stuart D. Jones,[b] Christopher W. Murray,[b] Jeffrey B. Franciskovich,[a] David B. Engel,[a] Wayne W. Weber, II,[a] Jothirajah Marimuthu,[a] Jeffrey A. Kyle,[a] Jeffrey K. Smallwood,[a] Mark W. Farmen[a] and Gerald F. Smith[a]

[a]*Lilly Research Laboratories, A Division of Eli Lilly and Company, Indianapolis, IN 46285, USA*
[b]*Tularik Ltd., Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL, UK*



Bioorg. Med. Chem. Lett. 13 (2003) 2261

Novel, Potent and Selective Cyclin D1/CDK4 Inhibitors: Indolo[6,7-*a*]pyrrolo[3,4-*c*]carbazoles

Thomas A. Engler,[a,*] Kelly Furness,[a] Sushant Malhotra,[a] Concha Sanchez-Martinez,[b] Chuan Shih,[a] Walter Xie,[a] Guoxin Zhu,[a] Xun Zhou,[a] Scott Conner,[a] Margaret M. Faul,[c] Kevin A. Sullivan,[c] Stanley P. Kolis,[c] Harold B. Brooks,[a] Bharvin Patel,[a] Richard M. Schultz,[a] Tammy B. DeHahn,[a] Kashif Kirmani,[a] Charles D. Spencer,[a] Scott A. Watkins,[a] Eileen L. Considine,[a] Jack A. Dempsey,[a] Catherine A. Ogg,[a] Nancy B. Stamm,[a] Bryan D. Anderson,[a] Robert M. Campbell,[a] Vasu Vasudevan[a] and Michelle L. Lytle[a]

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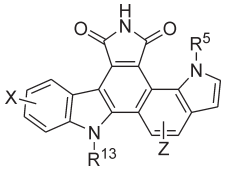


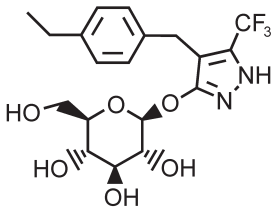
Bioorg. Med. Chem. Lett. 13 (2003) 2269

Pyrazole-*O*-Glucosides as Novel Na^+-Glucose Cotransporter (SGLT) Inhibitors

Koji Ohsumi,* Hiroyuki Matsueda, Toshihiro Hatanaka, Ryusuke Hirama, Takashi Umemura, Akiko Oonuki, Nozomu Ishida, Yoko Kageyama, Katsumi Maezono and Nobuo Kondo

Pharmaceutical Research Laboratories, Pharmaceutical Company, Ajinomoto Co., Inc. 1-1, Suzuki-cho, Kawasaki-ku, Kawasaki, 210-8681, Japan

A series of pyrazole-*O*-glucosides were synthesized and evaluated for their SGLT inhibitory activity.

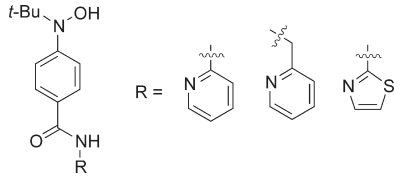


Bioorg. Med. Chem. Lett. 13 (2003) 2273

Design and Biological Evaluation of Novel Antioxidants Containing *N*-*t*-Butyl-*N*-hydroxylaminophenyl Moieties

Kyung-Mi Kim,[a] Kyung-Hwa Kim,[b] Tae-Cheon Kang,[c] Won-Yeon Kim,[d] Myung-ryul Lee,[a] Hyuk-Jun Jung,[b] In Koo Hwang,[c] Sung-Bo Ko,[b] Jae-Young Koh,[d] Moo Ho Won,[c] Eu-gene Oh[b,*] and Injae Shin[a,*]

[a]*Department of Chemistry, Yonsei University, Seoul 120-749, South Korea*
[b]*Department of Drug Discovery, Samsung Adv. Inst. Tech., Suwon 440-600, South Korea*
[c]*Department of Anatomy, Hallym University, Chunchon 200-702, South Korea*
[d]*Department of Neurology, University of Ulsan, Seoul 138-040, South Korea*



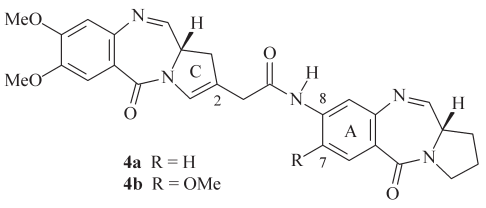
Bioorg. Med. Chem. Lett. 13 (2003) 2277

Synthesis of the First Examples of *A*-C8/*C*-C2 Amide-Linked Pyrrolo[2,1-*c*][1,4]benzodiazepine Dimers

Stephen J. Gregson, Philip W. Howard and David E. Thurston*

Cancer Research UK Gene Targeted Drug Design Research Group, The School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, UK

The first examples of novel *A*-**C8**/*C*-**C2** amide-linked pyrrolo[2,1-*c*][1,4]benzodiazepine dimers (**4a** and **4b**) are reported.



Bioorg. Med. Chem. Lett. 13 (2003) 2281

Semisynthetic Preparation of Amentoflavone: A Negative Modulator at $GABA_A$ Receptors

Jane R. Hanrahan,[a,*] Mary Chebib,[a] Neil L. M. Davucheron,[a] Belinda J. Hall[b] and Graham A. R. Johnston[b]

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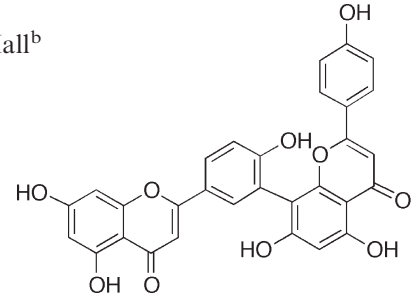
[b]*Department of Pharmacology, University of Sydney, Sydney, NSW 2006, Australia*

Amentoflavone was prepared semi-synthetically from biflavones isolated from *Ginkgo biloba* leaves and has been shown to be a negative modulator of GABA responses at functional $GABA_A$ $\alpha_1\beta_{2\gamma 2L}$ receptors expressed in *Xenopus laevis* oocytes. This action appears to be independent of the high affinity benzodiazepine modulatory sites on the $GABA_A$ receptor.



Bioorg. Med. Chem. Lett. 13 (2003) 2285

Xylo-Configured Oligonucleotides (XNA, Xylo Nucleic Acid): Synthesis of Conformationally Restricted Derivatives and Hybridization Towards DNA and RNA Complements

Nicolai E. Poopeiko,[a] Martin Juhl,[b] Birte Vester,[c] Mads D. Sørensen[b] and Jesper Wengel[a,*]

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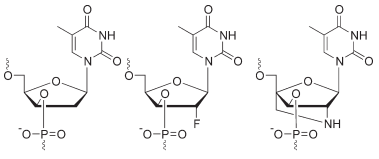
[c]*Nucleic Acid Center, Department of Biochemistry and Molecular Biology, University of Southern Denmark, Campusvej 55, DK-5230 Odense M, Denmark*



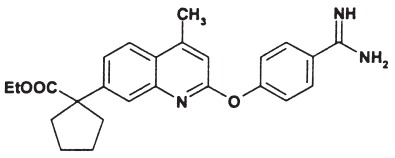
Bioorg. Med. Chem. Lett. 13 (2003) 2291

Heterocyclic Thrombin Inhibitors. Part 1: Design and Synthesis of Amidino-Phenoxy Quinoline Derivatives

Uwe J. Ries,[a,*] Henning W. M. Priepke,[a] Norbert H. Hauel,[a] Eric E. J. Haaksma,[a] Jean M. Stassen,[b] Wolfgang Wienen[b] and Herbert Nar[a]

[a]*Department of Chemical Research, Boehringer Ingelheim Pharma KG, Birkendorfer Straße 65, D-88397 Biberach/Riß, Germany*
[b]*Department of Biological Research, Boehringer Ingelheim Pharma KG, Birkendorfer Straße 65, D-88397 Biberach/Riß, Germany*

Amidino-phenoxy quinoline derivatives represent a new class of potent thrombin inhibitors with good selectivity and remarkably low molecular weight (MW: 335–391). X-ray analyses of thrombin-bound inhibitors revealed that enzyme inhibition is mainly based on hydrophobic interactions.



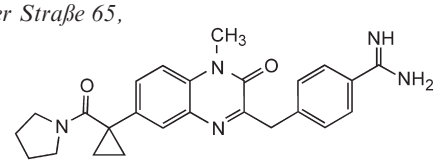
Bioorg. Med. Chem. Lett. 13 (2003) 2297

Heterocyclic Thrombin Inhibitors. Part 2: Quinoxalinone Derivatives as Novel, Potent Antithrombotic Agents

Uwe J. Ries,[a,*] Henning W. M. Priepke,[a] Norbert H. Hauel,[a] Sandra Handschuh,[a] Gerhard Mihm,[a] Jean M. Stassen,[b] Wolfgang Wienen[b] and Herbert Nar[a]

[a]*Department of Chemical Research, Boehringer Ingelheim Pharma KG, Birkendorfer Straße 65, D-88397 Biberach/Riß, Germany*
[b]*Department of Biological Research, Boehringer Ingelheim Pharma KG, Birkendorfer Straße 65, D-88397 Biberach/Riß, Germany*

Quinoxalinone derivatives as prototypes of dual thrombin and factor Xa inhibitors have been discovered. Nanomolar inhibition of both coagulation enzymes resulted in very potent antithrombotic activity in vitro.



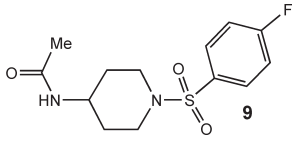
Bioorg. Med. Chem. Lett. 13 (2003) 2303

4-Aminopiperidine Derivatives as a New Class of Potent Cognition Enhancing Drugs

Dina Manetti,[a] Elisabetta Martini,[a] Carla Ghelardini,[b] Silvia Dei,[a] Nicoletta Galeotti,[b] Luca Guandalini,[a] Maria Novella Romanelli,[a] Serena Scapecchi,[a] Elisabetta Teodori,[a] Alessandro Bartolini[b] and Fulvio Gualtieri[a,*]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Firenze, Via G. Capponi 9, I-50121 Firenze, Italy*
[b]*Dipartimento di Farmacologia Preclinica e Clinica, Università di Firenze, Viale G. Pieraccini 6, I-50139 Firenze, Italy*

The synthesis and pharmacological evaluation of 4-aminopiperidine derivatives endowed with cognition enhancing activity is reported. One of the new compounds (**9**, active at 0.01 mg/kg ip in the mouse passive avoidance test) may represent a new lead for the development of cognition enhancers useful to treat the cognitive deficit produced by neurodegenerative pathologies like Alzheimer's disease.



9

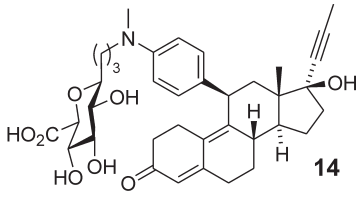
Bioorg. Med. Chem. Lett. 13 (2003) 2307

An Evaluation of a C-Glucuronide as a Liver Targeting Group: Conjugate of a Glucocorticoid Antagonist

Bryan K. Sorensen,[a,*] J. T. Link,[a] Thomas von Geldern,[a] Maurice Emery,[a] Jiahong Wang,[a] Bach Hickman,[a] Marlena Grynfarb,[b] Annika Goos-Nilsson[b] and Sherry Carroll[a]

[a]*Metabolic Disease Research, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064, USA*
[b]*Karo Bio AB Novum SE-141 57 Huddinge, Sweden*

The C-Glucuronide conjugate **14** was evaluated for its glucocorticoid receptor antagonist activity, metabolic stability, and ability to target the liver.



14

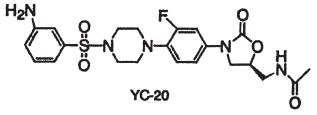
Bioorg. Med. Chem. Lett. 13 (2003) 2311

Synthesis and Antibacterial Activity of Oxazolidinone Containing Sulphonyl Group

Yingjie Cui,[a] Yushe Yang,[a,*] Kaixian Chen,[a] Ruyun Ji[a] and Shuhua Zhang[b]

[a]*Shanghai Institute of Materia Medica, Shanghai Institute for Biological Science, Chinese Academy of Sciences, Shanghai 200031, China*
[b]*Sichuan Industrial Institute of Antibiotics, Chengdu 610051, China*

The synthesis and SAR of a series of oxazolidinones with sulphonyl group are described resulting in identification of YC-20 as a potent inhibitor of Gram-positive bacteria.

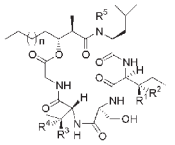


Bioorg. Med. Chem. Lett. 13 (2003) 2315

Synthesis and Antimicrobial Activity of Novel Globomycin Analogues

Toshihiro Kiho,[a] Mizuka Nakayama,[a] Kayo Yasuda,[b] Shunichi Miyakoshi,[b] Masatoshi Inukai[b] and Hiroshi Kogen[a,*]

[a]*Exploratory Chemistry Research Laboratories, Sankyo Co., Ltd., Tokyo 140–8710, Japan*
[b]*Lead Discovery Research Laboratories, Sankyo Co., Ltd., Tokyo 140–8710, Japan*



Compounds		n	R^1	R^2	R^3	R^4	R^5
globomycin	**1a**	3	Me	H	OH	H	Me
SF-1902 A_5	**1b**	5	Me	H	OH	H	Me
	1c	7	Me	H	OH	H	Me
	1d	3	H	Me	OH	H	Me
	1e	3	Me	H	H	OH	Me
	1f	3	H	Me	H	OH	Me
	1g	3	Me	H	H	H	Me
	1h	3	Me	H	OMe	H	Me
	1i	3	Me	H	OH	H	H

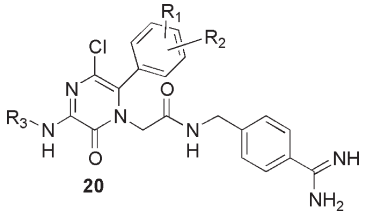
Bioorg. Med. Chem. Lett. 13 (2003) 2319

Structure-Based Drug Design of Pyrazinone Antithrombotics as Selective Inhibitors of the Tissue Factor VIIa Complex

Michael S. South,[a,*] Brenda L. Case,[a] Rhonda S. Wood,[a] Darin E. Jones,[a] Michael J. Hayes,[a] Thomas J. Girard,[b] Rhonda M. Lachance,[b] Nancy S. Nicholson,[c] Michael Clare,[d] Anna M. Stevens,[e] Roderick A. Stegeman,[e] William C. Stallings,[e] Ravi G. Kurumbail[e] and John J. Parlow[a]

[a]*Department of Medicinal and Combinatorial Chemistry, Pharmacia Corporation, 800 North Lindbergh Blvd., St. Louis, MO 63167, USA*
[b]*Department of Cardiovascular and Metabolic Disease, Pharmacia Corporation, 800 North Lindbergh Blvd., St. Louis, MO 63167, USA*
[c]*Department of Cardiovascular Pharmacology, Pharmacia Corporation, 4901 Searle Parkway, Skokie, IL 60077, USA*
[d]*Structure and Computational Chemistry, Pharmacia Corporation, 4901 Searle Parkway, Skokie, IL 60077, USA*
[e] *Structure and Computational Chemisty, Pharmacia Corporation, 700 Chesterfield Village Pkwy., St. Louis, MO 63198, USA*

Structure-based drug design coupled with polymer-assisted solution-phase library synthesis was utilized to develop a series of sub-nanomolar pyrazinone inhibitors **20** of the tissue factor/Factor VIIa complex.

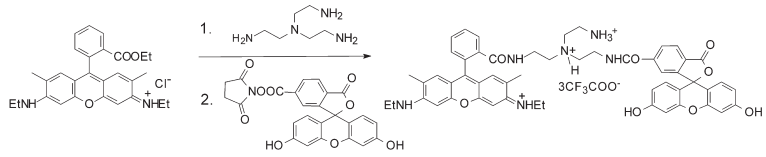


Bioorg. Med. Chem. Lett. 13 (2003) 2327

Synthesis of Probes with Broad pH Range Fluorescence

Maciej Adamczyk* and Jonathan Grote

Department of Chemistry (D9MD), Abbott Diagnostics Division, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-6016, USA



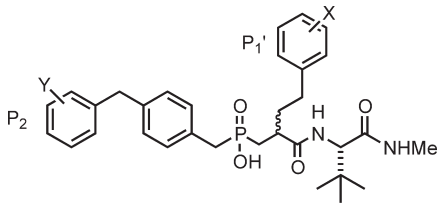
Bioorg. Med. Chem. Lett. 13 (2003) 2331

Phosphinic Acid-Based MMP-13 Inhibitors That Spare MMP-1 and MMP-3

Lawrence A. Reiter,* Peter G. Mitchell, Gary J. Martinelli, Lori L. Lopresti-Morrow, Sue A. Yocum and James D. Eskra

Pfizer Inc, Global Reseach & Development, Groton Laboratories, Eastern Point Rd., Groton, CT 06340, USA

Phosphinic acid-based inhibitors of MMP-13 have been investigated with the aim of identifying potent inhibitors with high selectivity versus MMP-1. Independent variation of the substituents on a P_1' phenethyl group and a P_2 benzyl group improved potencies in both cases around 3-fold over the unsubstituted parent (X,Y = H). Combining improved P_1' and P_2 groups into a single molecule gave an inhibitor (X = 4-Cl, Y = 2-OCH_3) with a 4.5 nM IC_{50} against MMP-13 and which is 270-fold selective over MMP-1.



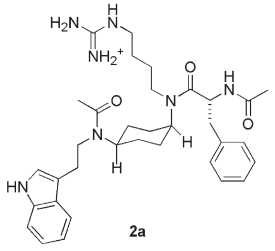
Bioorg. Med. Chem. Lett. 13 (2003) 2337

Design of a New Peptidomimetic Agonist for the Melanocortin Receptors Based on the Solution Structure of the Peptide Ligand, Ac-Nle-cyclo[Asp-Pro-DPhe-Arg-Trp-Lys]-NH_2

Christopher Fotsch,* Duncan M. Smith, Jeffrey A. Adams, Janet Cheetham, Michael Croghan, Elizabeth M. Doherty, Clarence Hale, Mark A. Jarosinski, Michael G. Kelly, Mark H. Norman, Nuria A. Tamayo, Ning Xi and James W. Baumgartner

Departments of Small Molecule Drug Discovery and Metabolic Disorders, Amgen Inc., One Amgen Center Drive, Thousand Oaks, CA 91320, USA

The solution structure of a potent melanocortin receptor agonist, Ac-Nle-cyclo[Asp-Pro-DPhe-Arg-Trp-Lys]-NH_2 (**1**) was calculated using distance restraints determined from ^1H NMR spectroscopy. Eight of the lowest energy conformations from this study were used to identify non-peptide cores that mimic the spatial arrangement of the critical tripeptide region, DPhe-Arg-Trp, found in **1**. From these studies, compound **2a**, containing the *cis*-cyclohexyl core, was identified as a functional agonist of the melanocortin-4 receptor (MC4R) with an IC_{50} and EC_{50} below 10 nM.



2a

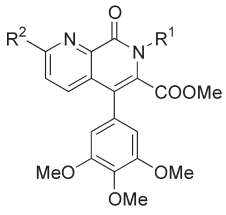
MC4R IC_{50} = 7.7 nM
MC4R EC_{50} = 4.0 nM

Bioorg. Med. Chem. Lett. 13 (2003) 2341

1,7- and 2,7-Naphthyridine Derivatives as Potent and Highly Specific PDE5 Inhibitors

Tatsuzo Ukita,[a,*] Yoshinori Nakamura,[a] Akira Kubo,[a] Yasuo Yamamoto,[a] Yasunori Moritani,[a] Kunio Saruta,[a] Takanori Higashijima,[a] Jun Kotera,[b] Kotomi Fujishige,[b] Michino Takagi,[b] Kohei Kikkawa[b] and Kenji Omori[b]

[a]*Discovery Research Laboratory, Tanabe Seiyaku Co., Ltd., 3-16-89, Kashima, Yodogawa, Osaka 532-8505, Japan*
[b]*Discovery Research Laboratory, Tanabe Seiyaku Co., Ltd., 2-2-50, Kawagishi, Toda, Saitama 335-8505, Japan*



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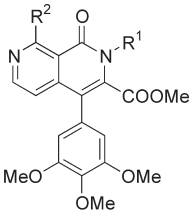

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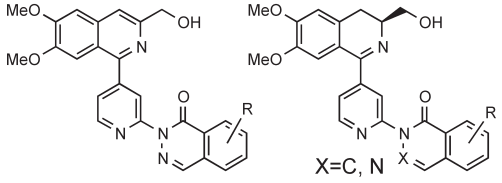
Bioorg. Med. Chem. Lett. 13 (2003) 2347

Synthesis and Biological Activities of 1-Pyridylisoquinoline and 1-Pyridyldihydroisoquinoline Derivatives as PDE4 Inhibitors

Tatsuzo Ukita,[a,*] Masakatsu Sugahara,[a] Yoshihiro Terakawa,[a] Tooru Kuroda,[a] Kazuteru Wada,[a] Aya Nakata,[b] Hideo Kikkawa,[b] Katsuo Ikezawa[b] and Kazuaki Naito[b]

[a]*Discovery Research Laboratory, Tanabe Seiyaku Co., Ltd., 3-16-89, Kashima, Yodogawa, Osaka 532-8505, Japan*
[b]*Discovery Research Laboratory, Tanabe Seiyaku Co., Ltd., 2-2-50, Kawagishi, Toda, Saitama 335-8505, Japan*

A novel series of 1-pyridylisoquinoline and 1-pyridyldihydroisoquinoline derivatives has been prepared. These compounds showed potent PDE4 inhibitory activities and a broad margin between the K_i value of the rolipram binding affinity and the IC_{50} value of PDE4 inhibition. They also exhibited potent inhibitory activities toward LPS-induced TNF-α production in mice.



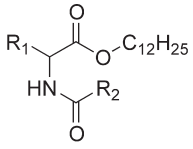
Bioorg. Med. Chem. Lett. 13 (2003) 2351

L-Serine and Glycine Based Ceramide Analogues as Transdermal Permeation Enhancers: Polar Head Size and Hydrogen Bonding

Kateřina Vávrová,[a,*] Alexandr Hrabálek,[a] Pavel Doležal,[b] Tomáš Holas[a] and Jarmila Zbytovská[b]

[a]*Department of Inorganic and Organic Chemistry, Faculty of Pharmacy, Charles University, Heyrovského 1203, 500 05 Hradec Králové, Czech Republic*
[b]*Department of Pharmaceutical Technology, Faculty of Pharmacy, Charles University, Heyrovského 1203, 500 05 Hradec Králové, Czech Republic*

The synthesis of a series of novel ceramide analogues and their enhancement activities in vitro are reported.



R_1=H; CH_2OH; R_2=$C_{11}H_{23}$; $(CH_2)_7CH{=}CH(CH_2)_7CH_3$; $CH(R_1)NHCOC_{11}H_{23}$; $CH{=}CHCOOC_{12}H_{25}$; $CH(OH)CH(OH)COOC_{12}H_{25}$

Bioorg. Med. Chem. Lett. 13 (2003) 2355

Improvement of Therapeutic Index of Phosphodiesterase Type IV Inhibitors as Anti-Asthmatics

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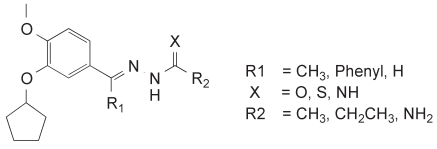
[a]*Pharmacology and Analytical Chemistry Research, 319 Hyundai I Valley, 223-12 Sandaewon-dong, Choongwon-gu, Sungnam-si, Kyonggi-do, 462-120, Republic of Korea*
[b]*Division of New Drug Discovery Project, Institute of Science & Technology, CJ Co., 522-1 Dokpyong-ri, Majang-myon, Ichon-si, Kyonggi-do, 467-810, Republic of Korea*
[c]*Department of Life Science, Division of Molecular and Life Science, Pohang University of Science & Technology, Pohang, Kyungbuk 790-784, Republic of Korea*
[d]*R & D Center, Leadgene Co., 319 Hyundai I Valley, 223-12 Sandaewon-dong, Choongwon-gu, Sungnam-si, Kyonggi-do, 462-120, Republic of Korea*



A new series of PDE4 inhibitors was developed. Significantly improved therapeutic index was observed from the analogue of H(R1), O(X), NH2(R2).

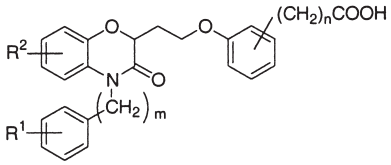
Bioorg. Med. Chem. Lett. 13 (2003) 2359

Benzoxazinones as PPARγ Agonists. Part 1: SAR of Three Aromatic Regions

Philip J. Rybczynski,* Roxanne E. Zeck, Donald W. Combs, Ignatius Turchi, Thomas P. Burris, Jun Z. Xu, Maria Yang and Keith T. Demarest

Johnson and Johnson Pharmaceutical Research and Development, LLC, Raritan, NJ 08869, USA

A set of benzoxazinones was synthesized as PPARγ agonists. The compounds were obtained in seven steps, and SAR was developed by variations to the core shown below. The compounds were tested as functional agonists in the induction of the aP2 gene in preadipocytes, and the most potent compound in the series has an EC_{50} = 0.51 μM.



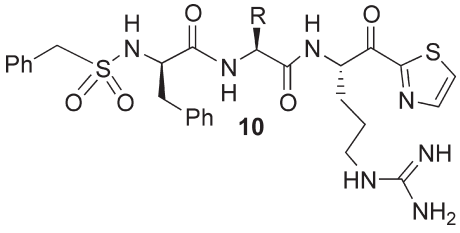
Bioorg. Med. Chem. Lett. 13 (2003) 2363

Polymer-Assisted Solution-Phase (PASP) Parallel Synthesis of an α-Ketothiazole Library as Tissue Factor VIIa Inhibitors

Michael S. South,[a,*] Thomas A. Dice,[a] Thomas J. Girard,[b] Rhonda M. Lachance,[b] Anna M. Stevens,[c] Roderick A. Stegeman,[c] William C. Stallings,[c] Ravi G. Kurumbail[c] and John J. Parlow[a]

[a]*Department of Medicinal and Combinatorial Chemistry, Pharmacia Corporation, 800 North Lindbergh Boulevard, St. Louis, MO 63167, USA*
[b]*Department of Cardiovascular and Metabolic Disease, Pharmacia Corporation, 800 North Lindbergh Boulevard, St. Louis, MO 63167, USA*
[c]*Structure and Computational Chemistry, Pharmacia Corporation, 700 Chesterfield Village Pkwy., St. Louis, MO 63198, USA*

A solution phase library synthesis of **10** is described. An X-ray crystal structure of the sub-micromolar inhibitors with the TF/VIIa enzyme explains the observed selectivity versus thrombin.



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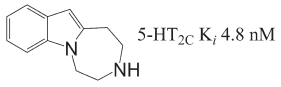
Bioorg. Med. Chem. Lett. 13 (2003) 2369

2,3,4,5-Tetrahydro- and 2,3,4,5,11,11a-Hexahydro-1H-[1,4]diazepino[1,7-*a*]indoles: New Templates for 5-HT$_{2C}$ Agonists

Michael D. Ennis,[a,*] Robert L. Hoffman,[a] Nabil B. Ghazal,[a] Rebecca M. Olson,[a] Christopher S. Knauer,[b] Chris L. Chio,[b] Deborah K. Hyslop,[b] Jeffery E. Campbell,[b] Lawrence W. Fitzgerald,[b] Nanette F. Nichols,[b] Kjell A. Svensson,[b] Robert B. McCall,[b] Christopher L. Haber,[c] Michelle L. Kagey[c] and and Dac M. Dinh[c]

[a]*Medicinal Chemistry III, Pharmacia Corporation, 301 Henrietta Street, Kalamazoo, MI 49009, USA*
[b]*CNS Diseases, Pharmacia Corporation, 301 Henrietta Street, Kalamazoo, MI 49009, USA*
[c]*Discovery Technologies, Pharmacia Corporation, 301 Henrietta Street, Kalamazoo, MI 49009, USA*



The SAR around a novel isoazepinoindole template is described.

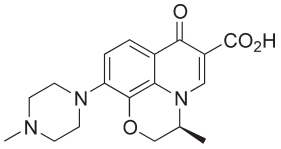
Bioorg. Med. Chem. Lett. 13 (2003) 2373

Synthesis and Biological Testing of Non-Fluorinated Analogues of Levofloxacin

Jeffrey L. Gray,* Ji-In K. Almstead, Corey P. Gallagher, X. Eric Hu, Nick K. Kim, Cynthia J. Taylor, Tracy L. Twinem, Cynthia D. Wallace and Benoit Ledoussal

Procter & Gamble Pharmaceuticals, 8700 Mason-Montgomery Rd, Mason, OH 45040, USA

The synthesis of a series of novel quinolone antibacterials including the non-fluorinated analogue of Levofloxacin (**1**) is reported.



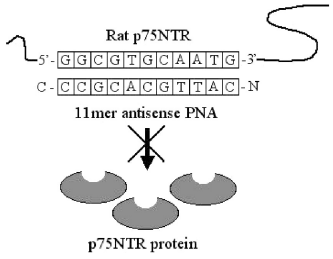
1

Bioorg. Med. Chem. Lett. 13 (2003) 2377

Design and Application of a Peptide Nucleic Acid Sequence Targeting the p75 Neurotrophin Receptor

Irwin K. Cheah,[a] Surindar S. Cheema,[b,*] Steven J. Langford,[a,*] Elizabeth C. Lopes,[b] Katherine J. Macfarlane,[a] Steven Petratos[b] and Bradley J. Turner[b]

[a]*School of Chemistry, Monash University, Victoria 3800, Australia*
[b]*Neurodegeneration Research Laboratory, Department of Anatomy & Cell Biology, Monash University, Victoria 3800, Australia*



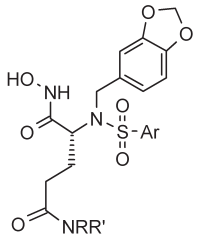
Bioorg. Med. Chem. Lett. 13 (2003) 2381

Novel Inhibitors of Procollagen *C*-Proteinase. Part 2: Glutamic Acid Hydroxamates

L. A. Robinson,[a] D. M. Wilson,[a] N. G. J. Delaet,[a] E. K. Bradley,[a] S. M. Dankwardt,[b] J. A. Campbell,[b] R. L. Martin,[b] H. E. Van Wart,[b] K. A. M. Walker[b] and R. W. Sullivan[a,*]

[a]*CombiChem Inc., 4570 Executive Drive, San Diego, CA 92121, USA*
[b]*Roche Bioscience, Inflammatory Diseases Unit, 3401 Hillview Ave, Palo Alto, CA 94304, USA*

The parallel synthesis and SAR studies of glutamic acid hydroxamates inhibitors of procollagen C-terminal proteinase is reported.



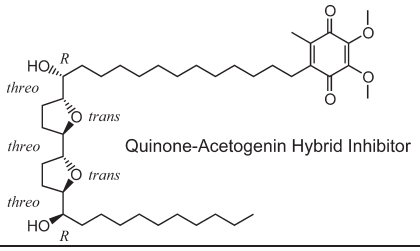
Bioorg. Med. Chem. Lett. 13 (2003) 2385

Synthesis and Inhibitory Activity of Ubiquinone–Acetogenin Hybrid Inhibitor with Bovine Mitochondrial Complex I

Hiromi Yabunaka, Masato Abe, Atsushi Kenmochi, Takeshi Hamada, Takaaki Nishioka and Hideto Miyoshi*

Division of Applied Life Sciences, Graduate School of Agriculture, Kyoto University, Sakyo-ku, Kyoto 606-8502, Japan

We synthesized a ubiquinone-acetogenin hybrid inhibitor that possesses a ubiquinnone ring in place of the α,β-unsaturated γ-lactone ring of natural acetogenins. Inhibitory action of this compound was examined with bovine heart mitochondrial complex I.

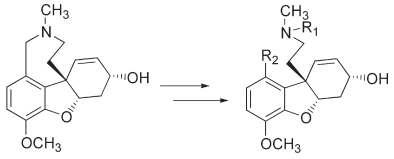


Bioorg. Med. Chem. Lett. 13 (2003) 2389

Synthesis and Structure–Activity Relationships of Open D-Ring Galanthamine Analogues

Denyse Herlem, Marie-Thérèse Martin, Claude Thal and Catherine Guillou*

Institut de Chimie des Substances Naturelles, C.N.R.S., 91198 Gif-sur-Yvette Cedex, France



(-)-galanthamine

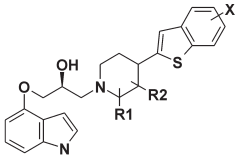
Bioorg. Med. Chem. Lett. 13 (2003) 2393

Advances Toward New Antidepressants Beyond SSRIs: 1-Aryloxy-3-piperidinylpropan-2-ols with Dual 5-HT_{1A} Receptor Antagonism/SSRI Activities. Part 2

Kumiko Takeuchi,* Todd J. Kohn, Nicholas A. Honigschmidt, Vincent P. Rocco, Patrick G. Spinazze, Daniel J. Koch, Steven T. Atkinson, Larry W. Hertel, David L. Nelson, D. Bradley Wainscott, Laura J. Ahmad, Janice Shaw, Penny G. Threlkeld and David T. Wong

Lilly Research Laboratories, A Division of Eli Lilly and Company, Indianapolis, IN 46285, USA

Potent 5-HT1A/SSRIs at low nanomolar and subnanomolar concentrations were identified in a series of 1-(1*H*-indol-4-yloxy)-3-(4-benzo[*b*]thiophen-2-ylpiperidinyl)propan-2-ols. Incorporation of an α-Me group in the piperidine ring with its specific stereochemistry enhanced binding affinity at the 5-HT reuptake site and in vitro 5-HT_{1A} antagonist functional activity.



Bioorg. Med. Chem. Lett. 13 (2003) 2399

Constrained Phytoestrogens and Analogues as ERβ Selective Ligands

Chris P. Miller,[a,]* Michael D. Collini[a] and Heather A. Harris[b]

[a]*Chemical Sciences, Wyeth Research, 500 Arcola Road, Collegeville, PA 19426, USA*
[b]*Women's Health Research Institute, Wyeth Research, 500 Arcola Road, Collegeville, PA 19426, USA*

A new series of ERβ selective ligands was prepared by constraining the pendant phenyl of the phytoestrogen Apigenin A through the intermediacy of an -oxa or -thia bridge atom. All of the prepared compounds demonstrated at least some selectivity for human ERβ (over ERα) with one compound having affinity selectivity of over 40-fold for ERβ.

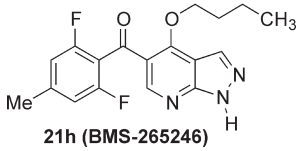
Bioorg. Med. Chem. Lett. 13 (2003) 2405

1*H*-Pyrazolo[3,4-*b*]pyridine Inhibitors of Cyclin-Dependent Kinases: Highly Potent 2,6-Difluorophenacyl Analogues

Raj N. Misra,* Hai-yun Xiao, David B. Rawlins, Weifang Shan, Kristen A. Kellar, Janet G. Mulheron, John S. Sack, John S. Tokarski, S. David Kimball and Kevin R. Webster

Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ 08543-4000, USA

Pyrazolopyridine **21h** (BMS-265246) has been identified as a potent, selective inhibitor of CDK1 ($IC_{50}=0.006$ μM) and CDK2 ($IC_{50}=0.009$ μM) in vitro which binds at the ATP site and shows cytotoxic activity in A2780 cells.



21h (BMS-265246)

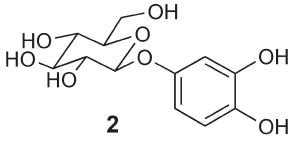
Bioorg. Med. Chem. Lett. 13 (2003) 2409

Identification of Oxidation Product of Arbutin in Mushroom Tyrosinase Assay System

Ken-ichi Nihei and Isao Kubo*

Department of Environmental Science, Policy and Management, University of California, Berkeley, CA 94720-3112, USA

In order to elucidate whitening mechanisms of arbutin (hydroquinone-*O*-β-D-glucopyranoside, **1**), its effects on mushroom tyrosinase were analyzed by spectrophotometric, polarographic, and HPLC experiments. It was found that as soon as catalytic amounts of L-DOPA become available as a cofactor, arbutin acts as a monophenol substrate. A significant enzymatic product was identified as 3,4-dihydroxyphenyl-*O*-β-D-glucopyranoside (**2**) by NMR and MS experiments.



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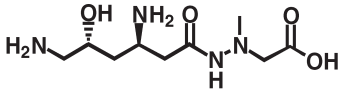
Bioorg. Med. Chem. Lett. 13 (2003) 2413

N- and C-Terminal Modifications of Negamycin

B. Raju,* Kathleen Mortell, Sampathkumar Anandan, Hardwin O'Dowd, Hongwu Gao, Marcela Gomez, Corinne Hackbarth, Charlotte Wu, Wen Wang, Zhengyu Yuan, Richard White, Joaquim Trias and Dinesh V. Patel

Versicor Inc., 34790 Ardentech Court, Fremont, CA 94555, USA

An orthogonally protected β-amino acid derivative was synthesized and used in synthesis of negamycin analogues. The N-terminal modifications have lead to the identification of active analogues, whereas the C-terminal modifications resulted in complete loss of antibacterial activity.



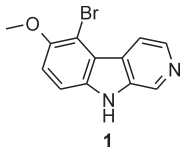
Bioorg. Med. Chem. Lett. 13 (2003) 2419

Novel IKK Inhibitors: β-Carbolines

Alfredo C. Castro, Luan C. Dang, François Soucy, Louis Grenier, Hormoz Mazdiyasni, Maria Hottelet, Lana Parent, Christine Pien, Vito Palombella and Julian Adams*

Millennium Pharmaceuticals Inc., 35 Landsdowne Street, Cambridge, MA 02139, USA

β-Carboline **1** was identified as a nonselective IκB kinase inhibitor. Optimization of this β-carboline natural product derivative resulted in a novel class of selective IKK inhibitors with IC50s in the nanomolar range and with biological activities in whole cells and *in vivo*.



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