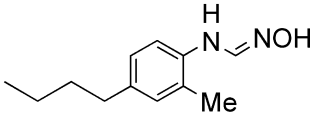
Bioorg. Med. Chem. Lett. 11 (2001) 2993

Discovery of a *N*′-Hydroxyphenylformamidine Derivative HET0016 as a Potent and Selective 20-HETE Synthase Inhibitor

Masakazu Sato, Takaaki Ishii,* Yuko Kobayashi-Matsunaga, Hideaki Amada, Kazuo Taniguchi, Noriyuki Miyata and Kazuya Kameo

Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., 1-403 Yoshino-cho, Saitama, Saitama 330-8530, Japan

A series of *N*′-hydroxyphenylformamidine derivatives were synthesized as potent and selective 20-HETE synthase inhibitors.



HET0016

Bioorg. Med. Chem. Lett. 11 (2001) 2997

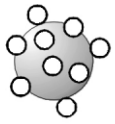
Cellular Solid-Phase Binding Assay and Mass Spectrometry for Screening of α4β7 Integrin Antagonists

Dirk Gottschling,[a] Jürgen Boer,[a] Anja Schuster,[b] Bernhard Holzmann[b] and Horst Kessler[a,*]

[a]*Institut für Organische Chemie und Biochemie, Technische Universität München, Lichtenbergstrasse 4, D-85747 Garching, Germany*

[b]*Institut für Medizinische Mikrobiologie, Immunologie und Hygiene, Technische Universität München, Trogerstrasse 4a, D-81675 München, Germany*

The development of a cellular solid-phase binding assay is reported.



Macrobead with adhered cells

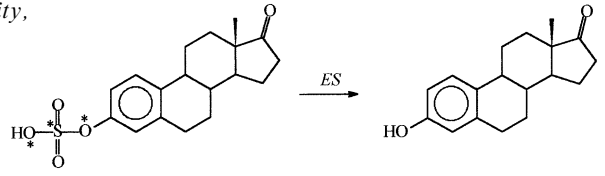
Bioorg. Med. Chem. Lett. 11 (2001) 3001

Determination and Use of a Transition State for the Enzyme Estrone Sulfatase (ES) from a Proposed Reaction Mechanism

Sabbir Ahmed,* Karen James, Caroline P. Owen, Chirag K. Patel and Mijal B. Patel

School of Chemical and Pharmaceutical Sciences, Kingston University, Penrhyn Road, Kingston upon Thames, Surrey KT1 2EE, UK

A potential transition state for the reaction catalysed by the enzyme estrone sulfatase (ES) has been derived.



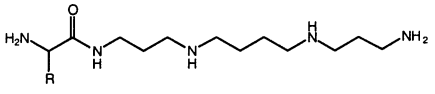
Bioorg. Med. Chem. Lett. 11 (2001) 3007

Novel Spermine–Amino Acid Conjugates and Basic Tripeptides Enhance Cleavage of the Hairpin Ribozyme at Low Magnesium Ion Concentration

Karen Stolze, Stephen C. Holmes, David J. Earnshaw, Mohinder Singh, Dmitry Stetsenko, Donna Williams and Michael J. Gait*

Medical Research Council, Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK

Synthesis of spermine–amino acid conjugates and tripeptides stimulate cleavage of the hairpin ribozyme at low magnesium ion concentration.



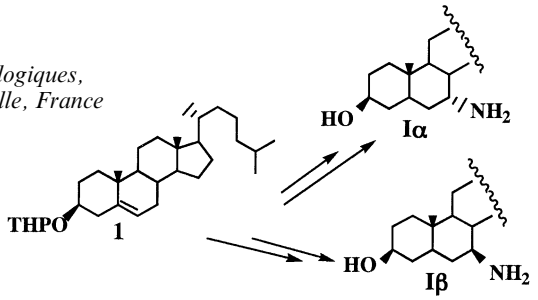
Bioorg. Med. Chem. Lett. 11 (2001) 3011

Stereoselective Synthesis of 7α- and 7β-Aminocholestanol as Potent Fungicidal Drugs

S. Fouace, L. El kihel,* M. Dherbomez and Y. Letourneux*

Laboratoire de Synthèse et Etude de Substances Naturelles à Activités Biologiques, Université de La Rochelle, Pôle Sciences et Technologies, 17042 La Rochelle, France

The synthesis and biological activity of these fungicidal drugs on resistant strains.

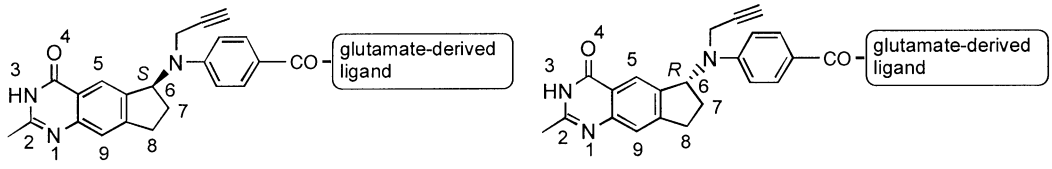


Bioorg. Med. Chem. Lett. 11 (2001) 3015

Cyclopenta[*g*]quinazoline-Based Antifolates: The Effect of the Chirality at the 6-Position on the Inhibition of Thymidylate Synthase (TS)

V. Bavetsias,* J. H. Marriott, D. S. Theti, J. C. Melin, S. C. Wilson and A. L. Jackman

CRC Centre for Cancer Therapeutics at The Institute of Cancer Research, Chemistry Department, CRC Laboratory, 15 Cotswold Road, Sutton, Surrey SM2 5NG, UK



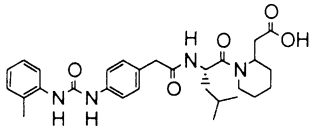
Bioorg. Med. Chem. Lett. 11 (2001) 3019

Discovery and Evaluation of Piperidinyl Carboxylic Acid Derivatives as Potent $\alpha_4\beta_1$ Integrin Antagonists

G. Müller,[a] M. Albers,[a] R. Fischer,[a] G. Heßler,[a] T. E. Lehmann,[a] H. Okigami,[b] M. Tajimi,[b] K. Bacon[b] and T. Rölle[a,*]

[a]*Bayer AG, Central Research, Building Q18, D-51368 Leverkusen, Germany*
[b]*Bayer Yakuhin Ltd., 6-5-1-3, Kunimi-dai, Kizu-cho, Soraku-gun, Kyoto 619-0216, Japan*

Piperidinyl carboxylic acid-based antagonists of the very late antigen 4 (VLA-4) are reported.



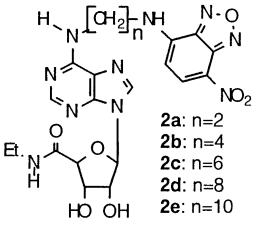
Bioorg. Med. Chem. Lett. 11 (2001) 3023

7-Nitrobenzofurazan (NBD)-Derivatives of 5′-*N*-Ethylcarboxamidoadenosine (NECA) as New Fluorescent Probes for Human A_3 Adenosine Receptors

Marco Macchia,[a,*] Francesca Salvetti,[b] Simone Bertini,[a] Valeria Di Bussolo,[c] Lisa Gattuso,[a] Marco Gesi,[d] Mahmoud Hamdan,[e] Karl-Norbert Klotz,[f] Teresina Laragione,[b] Antonio Lucacchini,[b] Filippo Minutolo,[a] Susanna Nencetti,[a] Chiara Papi,[a] Daniela Tuscano[b] and Claudia Martini[b]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Pisa, via Bonanno 6, 56126 Pisa, Italy*
[b]*Dipartimento di Psichiatria, Neurobiologia, Farmacologia e Biotecnologie, Università di Pisa, via Bonanno 6, 56126 Pisa, Italy*
[c]*Dipartimento di Chimica Bioorganica, Università di Pisa, via Bonanno 33, 56126 Pisa, Italy*
[d]*Dipartimento Morfologia Umana e Biologia Applicata, via Roma 55, 56126 Pisa, Italy*
[e]*GlaxoSmithKline Medicines Research Center, via Fleming 4, 37134 Verona, Italy*
[f]*Institut für Pharmakologie und Toxikologie, Universität, Würzburg, Germany*

Synthesis, binding and microscopy assays of new fluorescent probes (**2a**–**e**) for human A_3 adenosine receptors are reported.

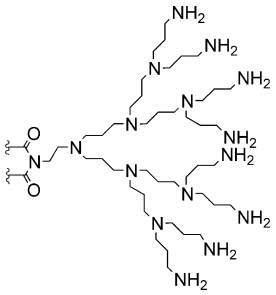


Bioorg. Med. Chem. Lett. 11 (2001) 3027

Synthesis of Antitumor Dendritic Imides

Miguel F. Braña,[a,*] Gema Domínguez,[a] Beatriz Sáez,[a] Cynthia Romerdahl,[b] Simmon Robinson[b] and Teresa Barlozzari[b]

[a]*Department of Organic and Pharmaceutical Chemistry, University San Pablo-CEU, Boadilla del Monte 28668, Madrid, Spain*
[b]*BASF Bioresearch Corporation, 100 Research Drive, 01605 Worcester, MA, USA*

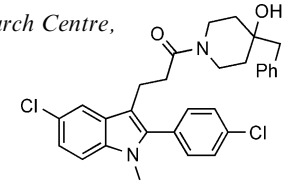


Bioorg. Med. Chem. Lett. 11 (2001) 3031

2-Aryl Indole NK_1 Antagonists: Optimisation of the Amide Substituent

Duncan Shaw,[a,*] Gary G. Chicchi,[c] Jason M. Elliott,[a] Marc Kurtz,[c] Denise Morrison,[a] Mark P. Ridgill,[a] Nicola Szeto,[a] Alan P. Watt,[a] Angela R. Williams[b] and Christopher J. Swain[a]

[a]*Department of Medicinal Chemistry, Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, Eastwick Road, Harlow, Essex CM20 2QR, UK*
[b]*Department of Pharmacology, Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, Eastwick Road, Harlow, Essex CM20 2QR, UK*
[c]*Department of Biochemistry, Merck Research Laboratories, 126 E. Lincoln Ave, Rahway, NJ 07065, USA*

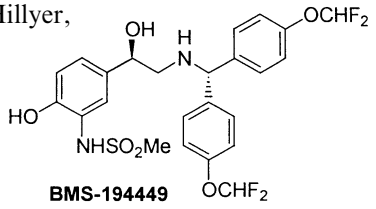


Bioorg. Med. Chem. Lett. 11 (2001) 3035

Beta 3 Agonists. Part 1: Evolution from Inception to BMS-194449

W. N. Washburn,* P. M. Sher, K. M. Poss, R. N. Girotra, P. J. McCann, A. V. Gavai, A. B. Mikkilineni, A. Mathur, P. Cheng, T. C. Dejneka, C. Q. Sun, T. C. Wang, T. W. Harper, A. D. Russell, D. A. Slusarchyk, S. Skwish, G. T. Allen, D. E. Hillyer, B. H. Frohlich, B. E. Abboa-Offei, M. Cap, T. L. Waldron, R. J. George, B. Tesfamariam, C. P. Ciosek, Jr., D. Ryono, D. A. Young, K. E. Dickinson, A. A. Seymour, C. M. Arbeeny and R. E. Gregg

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



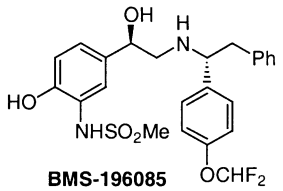
BMS-194449

Bioorg. Med. Chem. Lett. 11 (2001) 3041

BMS-196085: A Potent and Selective Full Agonist of the Human β_3 Adrenergic Receptor

A. V. Gavai,* P. M. Sher, A. B. Mikkilineni, K. M. Poss, P. J. McCann, R. N. Girotra, L. G. Fisher, G. Wu, M. S. Bednarz, A. Mathur, T. C. Wang, C. Q. Sun, D. A. Slusarchyk, S. Skwish, G. T. Allen, D. E. Hillyer, B. H. Frohlich, B. E. Abboa-Offei, M. Cap, T. L. Waldron, R. J. George, B. Tesfamariam, T. W. Harper, C. P. Ciosek, Jr., D. A. Young, K. E. Dickinson, A. A. Seymour, C. M. Arbeeny and W. N. Washburn

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



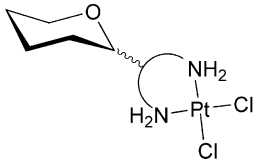
BMS-196085

Bioorg. Med. Chem. Lett. 11 (2001) 3045

Unprecedented Sugar-Dependent In Vivo Antitumor Activity of Carbohydrate-Pendant *cis*-Diamminedichloroplatinum(II) Complexes

Yuji Mikata,[a,*] Yoshie Shinohara,[b] Kazumi Yoneda,[c] Yuka Nakamura,[b] Izabela Brudziñska,[c] Tomoaki Tanase,[b] Takashi Kitayama,[d] Rie Takagi,[d] Tadashi Okamoto,[d] Isamu Kinoshita,[e] Matsumi Doe,[e] Chris Orvig[f] and Shigenobu Yano[c,*]

[a]*KYOUSEI Science Center, Nara Women's University, Nara 630-8506, Japan*
[b]*Department of Chemistry, Nara Women's University, Nara 630-8506, Japan*
[c]*Division of Material Science, Nara Women's University, Nara 630-8506, Japan*
[d]*Department of Agricultural Chemistry, Kinki University, Nara 631-8505, Japan*
[e]*Department of Chemistry, Faculty of Science, Osaka City University, Sumiyoshi-ku, Osaka 558-8585, Japan*
[f]*Medicinal Inorganic Chemistry Group, Department of Chemistry, University of British Columbia, Vancouver BC, Canada V6T 1Z1*



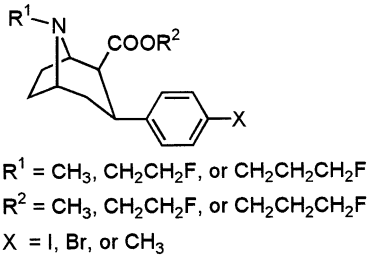
Bioorg. Med. Chem. Lett. 11 (2001) 3049

Synthesis and Biological Evaluation of a Series of Novel *N*- or *O*-Fluoroalkyl Derivatives of Tropane: Potential Positron Emission Tomography (PET) Imaging Agents for the Dopamine Transporter

Xiao-Hui Gu,[a,c] Rushi Zong,[a,c] Nora S. Kula,[b] Ross J. Baldessarini[b] and John L. Neumeyer[a,c,*]

[a]*Medicinal Chemistry Laboratory, Alcohol and Drug Abuse Research Center, Belmont, MA 02478-9106, USA*
[b]*Neuroscience Program, Mailman Research Center, McLean Hospital, Harvard Medical School, Belmont, MA 02478-9106, USA*
[c]*Natural Pharmacia International, Inc., 115 Mill Street, Belmont, MA 02478-9106, USA*

The synthesis and monoamine transporters binding affinities of a series of novel fluoroalkyl derivatives of tropane are described. Among these derivatives, the fluoropropyl ester (**19**) and the fluoroethyl ester (**20**) of β-CIT, the *N*-fluoropropyl derivative of β-CBT (**12**), and the fluoropropyl ester of β-CMT (**18**) displayed higher affinity and greater selectivity for the DAT than FP-CIT, which indicate that they are attractive candidates for development of ^{18}F-labeled PET imaging agents for the DAT.



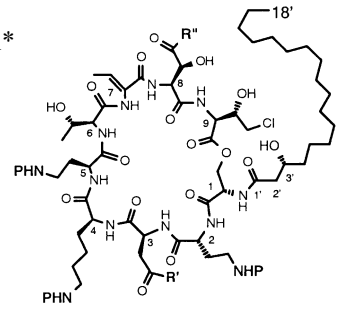
Bioorg. Med. Chem. Lett. 11 (2001) 3055

Synthesis and Evaluation of Novel Pseudomycin Side-Chain Analogues. Part 3

Xicheng Sun, Yan-Zhi Zhang, Doug Zeckner, William Current and Shu-Hui Chen*

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

The syntheses and evaluation of various core modified analogues and prodrugs of the C-18 side-chain bearing pseudomycin analogue **2** are described wherein R′,R″ = esters or amides; P = *N*-acyl prodrugs.



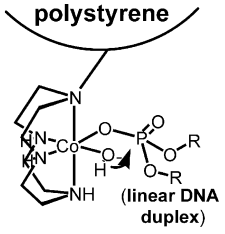
Bioorg. Med. Chem. Lett. 11 (2001) 3061

Hydrolysis of Linear DNA Duplex Catalyzed by Co(III) Complex of Cyclen Attached to Polystyrene

Chul-Seung Jeung,[a] Jung Bae Song,[b] Yong-Hyun Kim[b] and Junghun Suh[b,*]

[a]*School of Chemistry and Molecular Engineering and Center for Molecular Catalysis, Seoul National University, Seoul 151-747, Republic of Korea*
[b]*Artzyme Biotech Corporation, 403-1, Silim-2-Dong, Seoul 151-012, Republic of Korea*

The catalytic activity of CoCyc in hydrolysis of a linear DNA duplex is enhanced by >150 times on attachment to polystyrene derivatives, achieving half-lives as short as 30 min at 25 °C.



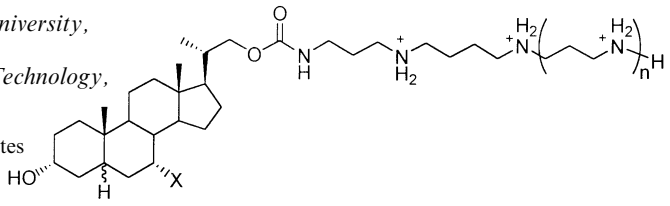
Bioorg. Med. Chem. Lett. 11 (2001) 3065

Synthesis and Antimicrobial Activity of New 3α-Hydroxy-23,24-bisnorcholane Polyamine Carbamates

Hong-Seok Kim,[a,*] Kyung-Chan Kwon,[a] Ki Soo Kim[a] and Cheol Hae Lee[b]

[a]*Department of Industrial Chemistry, Kyungpook National University, Taegu 702-701, South Korea*
[b]*Bioorganic Division, Korea Research Institute of Chemical Technology, Taejeon 305-600, South Korea*

3α Hydroxy-23,24-bisnorcholane spermidine and spermine carbamates **2**–**7** have been synthesized and their antimicrobial and hemolytic activities were evaluated. They exhibited excellent in vitro activities especially against methicillin-resistant *Staphylococcus aureus*.



2: 5β, X = H, n = 0; **3**: 5α, X = H, n = 0; **4**: 5α, X = OH, n = 0
5: 5α, X = F, n = 0; **6**: 5β, X = H, n = 1; **7**: 5α, X = H, n = 1.

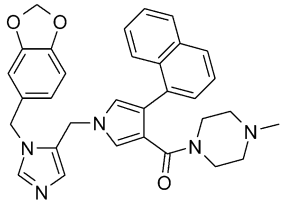
Bioorg. Med. Chem. Lett. 11 (2001) 3069

A Novel Class of Highly Potent, Selective, and Non-Peptidic Inhibitor of Ras Farnesyltransferase (FTase)

Hyunil Lee, Jinho Lee, Sangkyun Lee, Youseung Shin, Wonhee Jung, Jong-Hyun Kim, Kiwon Park, Kwihwa Kim, Heung Soo Cho, Seonggu Ro, Sunhwa Lee, ShinWu Jeong, Taesaeng Choi, Hyun-Ho Chung and Jong Sung Koh*

Life Science R&D, LGCI, Science Town, Taejon 305-380, Republic of Korea

Novel protein farnesyltransferase inhibitors containing pyrrole were designed and synthesized. Compound **2** showed a highyl potent anti-tumor activity in vitro (IC_{50} = 0.9 nM against H-Ras and 2.4 nM against K-Ras) and in vivo.



2

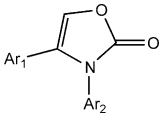
Bioorg. Med. Chem. Lett. 11 (2001) 3073

Combretoxazolones: Synthesis, Cytotoxicity and Antitumor Activity

Nguyen-Hai Nam,[a] Yong Kim,[a] Young-Jae You,[a] Dong-Ho Hong,[a] Hwan-Mook Kim[b] and Byung-Zun Ahn[a,*]

[a]*College of Pharmacy, Chungnam National University, Taejon 305-764, Republic of Korea*
[b]*Korea Research Institute of Bioscience and Biotechnology, Taejon 305-600, Republic of Korea*

Two series of combretoxazolones including 3,4-diaryloxazolones (**6**) and 4,5-diaryloxazolones (**7**) were synthesized and evaluated for cytotoxicity. Both series showed a strong cytotoxicity against a variety of tumor cell lines. One compound showed significant antitumor activity in BDF1/B16 model.



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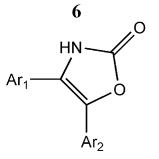


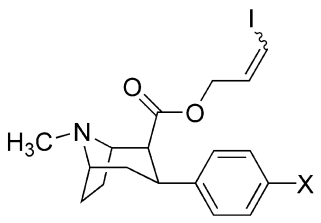
7

Bioorg. Med. Chem. Lett. 11 (2001) 3077

Synthesis and Binding Affinities of 2β-(3-Iodoallyloxycarbonyl)-3β-(4-substituted-aryl)tropane Analogues as Ligands for the Dopamine Transporter Studies

Kyoo-Hyun Chung,[a,*] Choong Hwan Lim,[a] Dong Reyoul Lee,[b] Changbae Jin[c] and Dae Yoon Chi[a,b,*]

[a]*Department of Chemistry, Inha University, 253 Yonghyundong, Namgu, Inchon, 402-751, Republic of Korea*
[b]*Future Chem. Co., 253 Yonghyundong, Namgu, Inchon, 402-751, Republic of Korea*
[c]*Bioanalysis & Biotransformation Research Center, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul, 130-650, Republic of Korea*

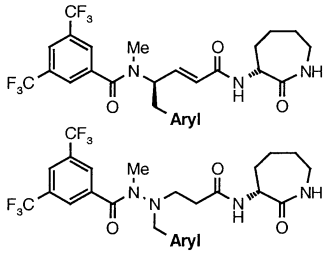


Bioorg. Med. Chem. Lett. 11 (2001) 3081

Dual Neurokinin NK_1/NK_2 Antagonists: *N*-[(*R*,*R*)-(*E*)-1-arylmethyl-3-(2-oxo-azepan-3-yl)carbamoyl]allyl-*N*-methyl-3,5-bis(trifluoromethyl)benzamides and 3-[*N*′-3,5-bis(trifluoromethyl)benzoyl-*N*-arylmethyl-*N*′-methylhydrazino]-*N*-[(*R*)-2-oxo-azepan-3-yl]propionamides

Marc Gerspacher,[a,*] Luigi La Vecchia,[a] Robert Mah,[a] Andreas von Sprecher,[a] Gary P. Anderson,[b] Natarajan Subramanian,[a] Kathleen Hauser,[a] Heinrich Bammerlin,[a] Sabine Kimmel,[a] Viviane Pawelzik,[a] Karin Ryffel[a] and Howard A. Ball[a]

[a]*Pharma Research, Novartis Pharma AG, CH-4002 Basel, Switzerland*
[b]*Department of Pharmacology, University of Melbourne, Parkville, 3052 VIC, Australia*



Bioorg. Med. Chem. Lett. 11 (2001) 3085

Identification of a Novel Family of Nucleosides That Specifically Inhibit HIV-1 Reverse Transcriptase

Cristina Chamorro,[a] Esther Lobatón,[a] María-Cruz Bonache,[a] Erik De Clercq,[b] Jan Balzarini,[b] Sonsoles Velázquez,[a] Ana San-Félix[a] and María-José Camarasa[a,*]

[a]*Instituto de Química Médica (C.S.I.C.), Juan de la Cierva 3, 28006-Madrid, Spain*
[b]*Rega Institute for Medical Research, K.U. Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium*

The synthesis and anti-HIV-1 evaluation of a novel family of HIV-1 specific nucleosides is reported.