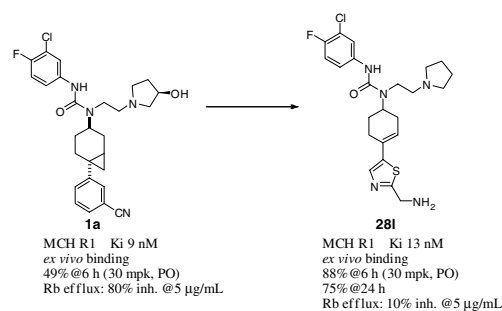


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SAR study of bicyclo[4.1.0]heptanes as melanin-concentrating hormone receptor R1 antagonists: Taming hERG

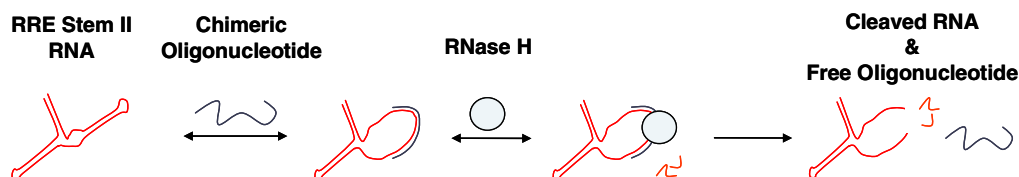
Jing Su,* Brian A. McKittrick, Haiqun Tang, Duane A. Burnett, John W. Clader, William J. Greenlee, Brian E. Hawes, Kim O'Neill, Brian Spar, Blair Weig, Timothy Kowalski, Steve Sorota, Cheng Li and Tongtong Liu



Chimeric RNase H-competent oligonucleotides directed to the HIV-1 Rev response element

Chrissy E. Prater, Anthony D. Saleh, Maggie P. Wear and Paul S. Miller*

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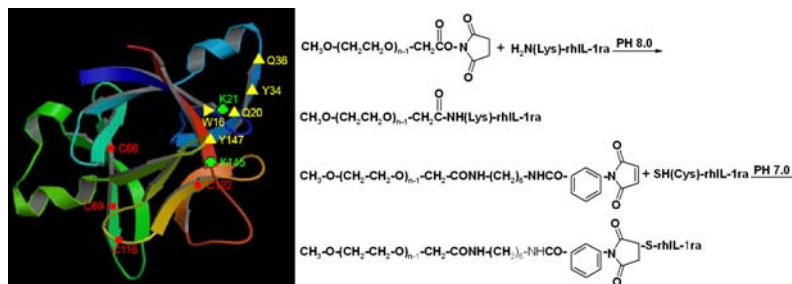


Investigation on PEGylation strategy of recombinant human interleukin-1 receptor antagonist

Pengzhan Yu, Chunyang Zheng, Jing Chen, Guifeng Zhang, Yongdong Liu, Xiaoyan Suo, Guicai Zhang and Zhiguo Su*

pp 5396–5405

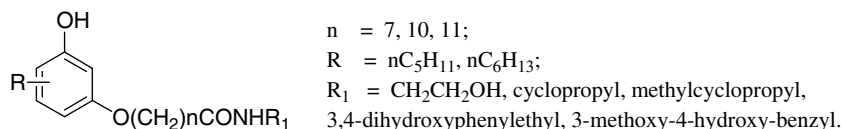
The PEGylated strategy of recombinant human interleukin-1 receptor antagonist was investigated, and we found that the random conjugation of polyethylene glycol to amino groups on the protein resulted in a severe loss of activity (9.8% of unmodified protein) and PEGylation at the thiol groups was desirable (40% of unmodified protein). The results suggested that the thiol-target PEGylation was more beneficial for IL-1ra.



Design, synthesis, binding, and molecular modeling studies of new potent ligands of cannabinoid receptors

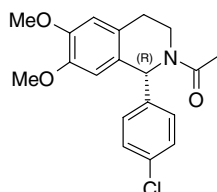
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Antonella Brizzi,* Maria Grazia Cascio, Vittorio Brizzi, Tiziana Bisogno, Maria Teresa Dinatolo, Adriano Martinelli, Tiziano Tuccinardi and Vincenzo Di Marzo


Synthesis, resolution, stereochemistry, and molecular modeling of (R)- and (S)-2-acetyl-1-(4'-chlorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline AMPAR antagonists

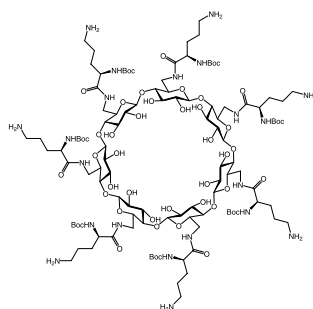
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Inhibition of *S. aureus* α -hemolysin and *B. anthracis* lethal toxin by β -cyclodextrin derivatives

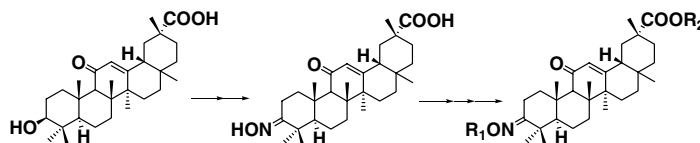
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Vladimir A. Karginov,* Ekaterina M. Nestorovich, Frank Schmidtman, Tanisha M. Robinson, Adiamseged Yohannes, Nour Eddine Fahmi, Sergey M. Bezrukov and Sidney M. Hecht


The synthesis of 18 β -glycyrrhetic acid derivatives which have increased antiproliferative and apoptotic effects in leukemia cells

pp 5432–5439

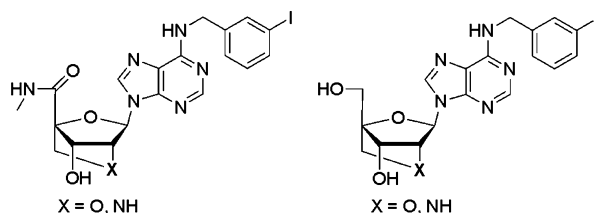
Dan Liu, Dandan Song, Gang Guo, Rui Wang, Jinling Lv, Yongkui Jing* and Linxiang Zhao*



Design, synthesis, and biological evaluation of LNA nucleosides as adenosine A₃ receptor ligands

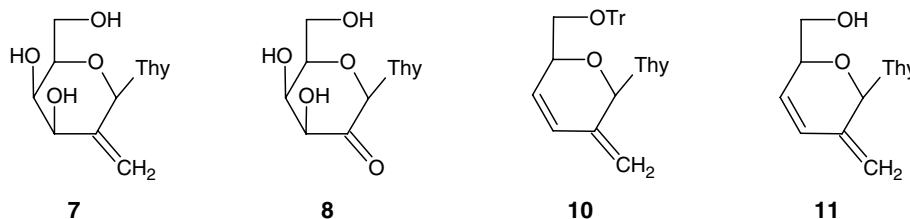
pp 5440–5447

Jacob Ravn,* Katrine Qvortrup, Christoph Rosenbohm and Troels Koch

Locked nucleic acid (LNA) analogs of the A₃AR agonist IB-MECA.**Exomethylene pyranonucleosides: Efficient synthesis and biological evaluation of 1-(2,3,4-trideoxy-2-methylene-β-D-glycero-hex-3-enopyranosyl)thymine**

pp 5448–5456

George Agelis, Niki Tzioumaki, Tanja Botić, Avreljia Cencič and Dimitri Komiotis*

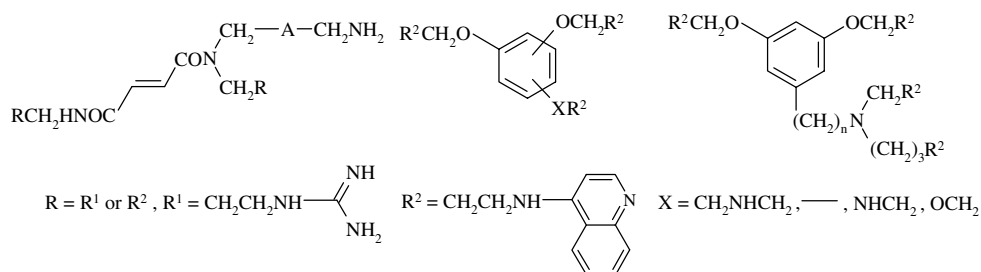


We report the synthesis of four novel pyranonucleosides. These novel synthesized molecules have a promising potential as anti-tumor and anti-rotavirus agents. Compounds **7** and **8** showed to be more efficient than currently used nucleoside analogue AZT, in rotavirus infections and in treatment of colon cancer.

Synthesis and pharmacological testing of polyaminoquinolines as blockers of the apamin-sensitive Ca²⁺-activated K⁺ channel (SK_{Ca})

pp 5457–5479

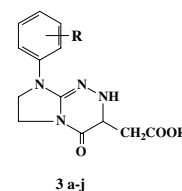
David I. Fletcher, C. Robin Ganellin,* Alessandro Piergentili, Philip M. Dunn and Donald H. Jenkinson

**Identification of antibacterial and antiviral activities of novel fused 1,2,4-triazine esters**

pp 5480–5486

Krzysztof Sztanke,* Kazimierz Pasternak, Barbara Rajtar, Małgorzata Sztanke, Magdalena Majek and Małgorzata Polz-Dacewicz

Biological activities of the designed novel fused 1,2,4-triazine esters (**3a**, **3d–j**) are reported. In particular, heterobicycles **3d** and **3e** revealed comparable antibacterial potencies in vitro to that of ampicillin. Compounds **3e**, **3g** and **3j** exhibited antiviral activities against the selected viruses' DNA (human adenovirus type 5-Ad-5) or/and RNA (human enterovirus Echo-9). Simultaneously, their cytotoxicities towards the normal HEK-293 and GMK cells were established. In particular, heterobicycle **3j**, non-toxic for GMK cells, was found to exhibit virucidal properties against Echo-9 virus justifying its further investigation as the potential antiviral agent.



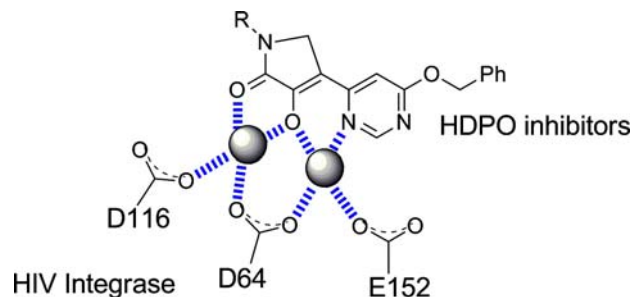
3	R	R'
a	H	CH ₃
b	4-CH ₃	CH ₃
c	2-OCH ₃	CH ₃
d	4-OCH ₃	CH ₃
e	3-Cl	CH ₃
f	4-Cl	CH ₃
g	4-CH ₃	C ₂ H ₅
h	4-OCH ₃	C ₂ H ₅
i	3-Cl	C ₂ H ₅
j	4-Cl	C ₂ H ₅

3-Hydroxy-1,5-dihydro-pyrrol-2-one derivatives as advanced inhibitors of HIV integrase

pp 5487–5492

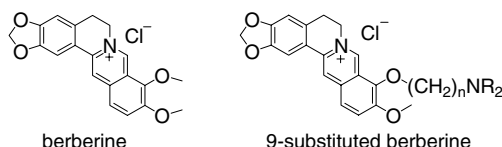
Takashi Kawasuji,* Masahiro Fuji, Tomokazu Yoshinaga, Akihiko Sato, Tamio Fujiwara and Ryuichi Kiyama

Designing of a new class of HIV integrase inhibitor using the two-metal binding model.

**9-Substituted berberine derivatives as G-quadruplex stabilizing ligands in telomeric DNA**

pp 5493–5501

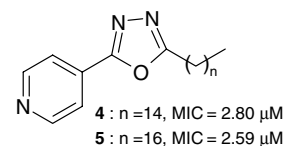
Wan-Jin Zhang, Tian-Miao Ou, Yu-Jing Lu, Ying-Yu Huang, Wei-Bin Wu, Zhi-Shu Huang,* Jin-Lin Zhou, Kwok-Yin Wong and Lian-Quan Gu*

**Synthesis and antimycobacterial activity of 4-(5-substituted-1,3,4-oxadiazol-2-yl)pyridines**

pp 5502–5508

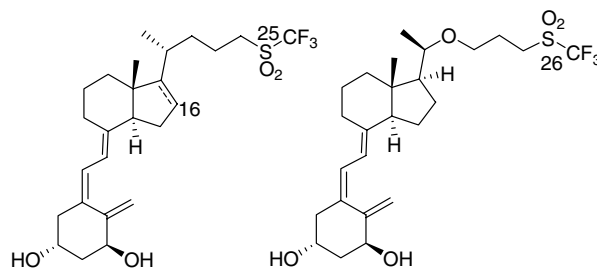
Gabriel Navarrete-Vázquez,* Gloria María Molina-Salinas, Zetel Vahi Duarte-Fajardo, Javier Vargas-Villarreal, Samuel Estrada-Soto, Francisco González-Salazar, Emanuel Hernández-Núñez and Salvador Said-Fernández

4-(5-Substituted-1,3,4-oxadiazol-2-yl)pyridine derivatives **1–12** were synthesized and evaluated for their in vitro antimycobacterial activity. Some compounds showed an interesting activity against strain of *Mycobacterium tuberculosis* H₃₇Rv and five clinical isolates (drug-sensitive and -resistant strains). Compound **4** was 10, 20, and 28 times more active than isoniazid, streptomycin, and ethambutol against multidrug-resistant strain CIBIN 112. Compound **5** showed the same behavior as compound **4**. Both structures bear a high lipophilic chain bonded to the 5-position of oxadiazole moiety.

**Antiproliferative, low-calcemic, fluorinated sulfone analogs of 1α,25-dihydroxyvitamin D₃: Chemical synthesis and biological evaluation**

pp 5509–5518

Aimee R. Usera, Patrick M. Dolan, Thomas W. Kensler and Gary H. Posner*

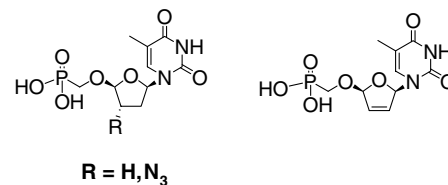


Synthesis, anti-HIV activity, and resistance profile of thymidine phosphonmethoxy nucleosides and their bis-isopropylloxymethylcarbonyl (bisPOC) prodrugs

pp 5519–5528

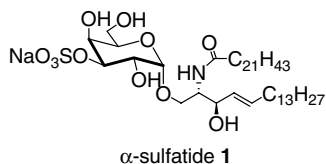
Richard L. Mackman,* Lijun Zhang, Vidya Prasad, Constantine G. Boojamra, Janet Douglas, Deborah Grant, Hon Hui, Choung U. Kim, Genevieve Laflamme, Jay Parrish, Antitsa D. Stoycheva, Swami Swaminathan, KeYu Wang and Tomas Cihlar

Phosphonmethoxy nucleoside analogs of the nucleoside reverse transcriptase inhibitors AZT, d4T, and ddT were synthesized. The anti-HIV activity against wild-type and several major nucleoside-resistant strains of HIV-1 was evaluated together with the inhibition of wild-type HIV reverse transcriptase (RT).

**Synthesis and evaluation of human T cell stimulating activity of an α -sulfatide analogue**

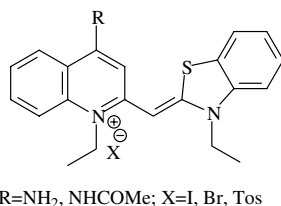
pp 5529–5536

Laura Franchini, Pamela Matto, Fiamma Ronchetti,* Luigi Panza, Lucia Barbieri, Valeria Costantino, Alfonso Mangoni, Marco Cavallari, Lucia Mori and Gennaro De Libero

**New amino and acetamido monomethine cyanine dyes for the detection of DNA in agarose gels**

pp 5537–5542

Reda M. El-Shishtawy, Cecília R. Santos, Isabel Gonçalves, Helena Marcelino and Paulo Almeida*

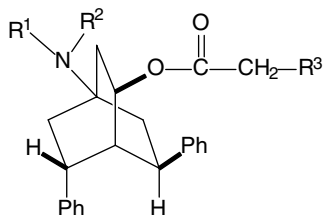


Five new monomethine cyanine dyes have been prepared and spectroscopically characterized. The acetamido dyes present to be promising tools for DNA analysis at low levels of concentration when UV light is required for visualization, overcoming the use of the mutagenic EtBr stain or radioactivity for detecting low levels of DNA.

Bicyclo[2.2.2]octyl esters of dialkylamino acids as antiprotozoals

pp 5543–5550

Christian Schlapper, Werner Seebacher, Marcel Kaiser, Reto Brun, Robert Saf and Robert Weis*



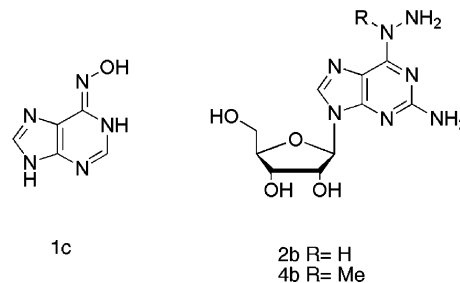
The newly prepared bicyclo[2.2.2]octyl esters are the so far most potent antimalarial and antitrypanosomal compounds of the bicyclo-octane series. The influence of the inserted dialkylamino groups on the antiprotozoal activity is remarkable. Furthermore, their selectivity indices have distinctly improved.

Anti-malarial activity of *N*⁶-modified purine analogues

pp 5551–5562

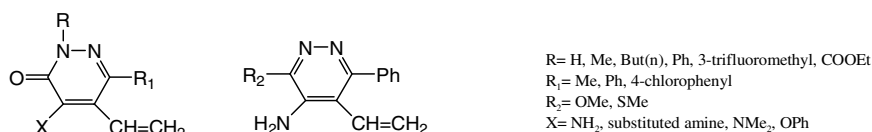
Kathleen Too, Daniel M. Brown, Emily Bongard, Vanessa Yardley, Livia Vivas and David Loakes*

Herein we report the synthesis, in vitro and in vivo biological evaluation for a series of purine analogues as anti-malarial agents. *N*⁶-hydroxyadenine (**1c**), 2-amino-*N*⁶-aminoadenosine (**2b**) and 2-amino-*N*⁶-amino-*N*⁶-methyladenosine (**4b**) displayed the most promising activity and were found to be non-toxic.

**4-Amino-5-vinyl-3(2*H*)-pyridazinones and analogues as potent antinociceptive agents: Synthesis, SARs, and preliminary studies on the mechanism of action**

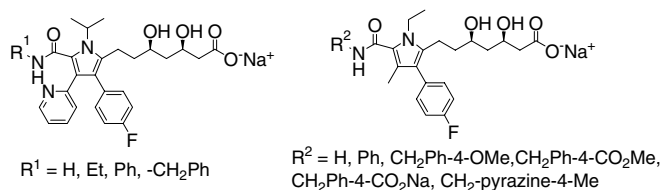
pp 5563–5575

Claudia Vergelli, Maria Paola Giovannoni,* Stefano Pieretti, Amalia Di Giannuario, Vittorio Dal Piaz, Pierfrancesco Biagini, Claudio Biancalani, Alessia Graziano and Nicoletta Cesari

**Discovery of pyrrole-based hepatoselective ligands as potent inhibitors of HMG-CoA reductase**

pp 5576–5589

Larry D. Bratton,* Bruce Auerbach, Chulho Choi, Lisa Dillon, Jeffrey C. Hanselman, Scott D. Larsen, Gina Lu, Karl Olsen, Jeffrey A. Pfefferkorn, Andrew Robertson, Catherine Sekerke, Bharat K. Trivedi and Paul C. Unangst

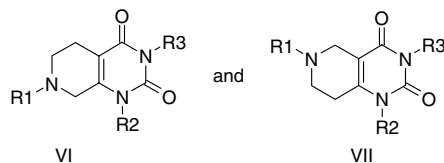


Novel substituted pyrroles containing lower alkyl groups and polar functionality were shown to be potent hepatoselective inhibitors of HMG-CoA reductase.

Selection, synthesis, and structure–activity relationship of tetrahydropyrido[4,3-*d*]pyrimidine-2,4-diones as human GnRH receptor antagonists

pp 5590–5603

Marion C. Lanier,* Miklos Feher, Neil J. Ashweek, Colin J. Loweth, Jaimie K. Rueter, Deborah H. Slee, John P. Williams, Yun-Fei Zhu, Susan K. Sullivan and Michael S. Brown

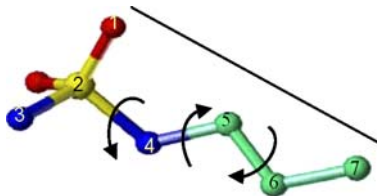


A series of tetrahydropyrido[4,3-*d*]pyrimidine-2,4-dione was selected in silico and evaluated as small molecules antagonists against the h-GnRH receptor. SAR is reported.

Design, synthesis, and anticonvulsant activity of some sulfamides

pp 5604–5614

L. Gavernet, I. A. Barrios, M. Sella Cravero and L. E. Bruno-Blanch*

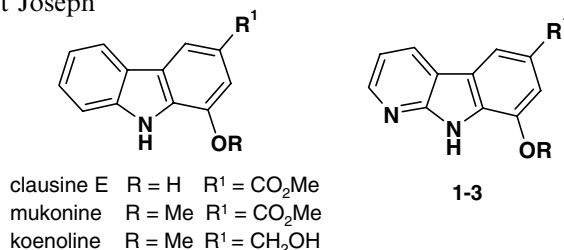


Anticonvulsant sulfamides were designed based on a proposed pharmacophore. They were synthesized and evaluated in preclinical phases. Some of the molecules show a promising anticonvulsant profile as selective anti-MES drugs.

Synthesis and antiproliferative activity of clausine E, mukonine, and koenoline bioisosteres

pp 5615–5619

François Liger, Florence Popowycz, Thierry Besson, Laurent Picot, Carlos M. Galmarini* and Benoît Joseph*

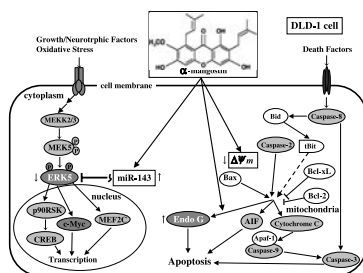


Antiproliferative activity of clausine E, mukonine, and koenoline bioisosteres 1–3 was evaluated against miscellaneous cancer cell lines and compared to those obtained with clausine E and mukonine.

Characterized mechanism of α -mangostin-induced cell death: Caspase-independent apoptosis with release of endonuclease-G from mitochondria and increased miR-143 expression in human colorectal cancer DLD-1 cells

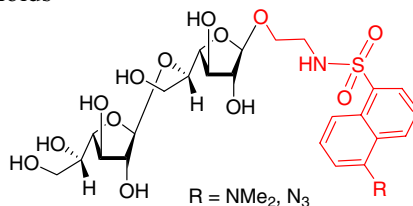
pp 5620–5628

Yoshihito Nakagawa, Munekazu Inuma, Tomoki Naoe, Yoshinori Nozawa and Yukihiro Akao*

**Disaccharide analogs as probes for glycosyltransferases in *Mycobacterium tuberculosis***

pp 5629–5650

Ashish K. Pathak, Vibha Pathak, Laine Seitz, Sudagar S. Gurcha, Gurdial S. Besra, James M. Riordan and Robert C. Reynolds*



The preparation and preliminary screening data are reported for several fluorescent or pro-fluorescent arabinofuranose and galactofuranose disaccharides as probes and substrates for new assays of arabinosyl- and galactosyltransferases of *Mycobacterium tuberculosis*.

OTHER CONTENTS**Summary of instructions to authors****p I**

*Corresponding author

①⁺ Supplementary data available via ScienceDirect**COVER**

Terfenadine (an antihistamine pulled from the market in 1997) bound to a model of an open form of the homo-tetrameric pore domain of hERG, produced using Schrödinger's "Induced Fit Docking" technology [Farid, R.; Day, T.; Friesner, R. A.; Pearlstein, R. A. *Bioorg. Med. Chem.* **2006**, *14*, 3160–3173].

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